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11 NEUROLOGICAL ASSESSMENT

11.1 INTRODUCTION

11.1.1 Background

The recent association of neurological symptoms with herbicide exposure has motivated much of the research toward the potential neurotoxicity of dioxin. Studies of industrial accidents, as discussed subsequently in this section, have demonstrated that the mixed sensorimotor neuropathy associated with extreme chlorophenol toxicity is reversible and that there is little scientific evidence to date for any chronic central or peripheral neurological disease in humans associated with low-level 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) exposure. Neurobehavioral endpoints in humans, the subject of intensive investigation in this and other studies of Vietnam veterans, are considered separately in Chapter 12, Psychological Assessment.

Much of the basic research in animal models has focused on neurobehavioral sequelae consequent to dichlorophenoxyacetic acid (2,4-D, a component of Agent Orange) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) rather than dioxin toxicity in laboratory animal experiments (1–4). In another series of studies, the neurobehavioral effects of exposure to an ester of 2,4-D were found to be rapidly reversible, and the authors proposed a cellular rather than biochemical basis for the tolerance that developed with repeated injections (5, 6).

Several studies have investigated the neurotoxic effects of dioxin in laboratory animals with inconsistent results. Rats given a high dose of dioxin (1,000 µg/kg) intraperitoneally demonstrated no apparent neurological deficits (7). The intracerebroventricular administration of dioxin proved far more toxic than the subcutaneous route in producing a wasting syndrome in rats, although specific neurological indices were not examined (8). In another study, the neuromuscular effects associated with acute lethal doses of dioxin in rats were primarily in muscle tissue rather than peripheral nerves (9).

Two experimental animal studies can be cited as more relevant to the question of dioxin-induced neurotoxicity in humans. In the first study (10), strengthened by the inclusion of electrophysiologic measurements, Wistar rats received a single intraperitoneal low dose of dioxin in one of four strengths. Electrophysiologic studies of the sciatic nerve after injection documented dose-dependent and statistically significant reductions in motor and sensory nerve conduction velocities relative to the controls. In a companion report, the same authors provide histopathologic correlations with electrophysiologic findings (11). Ten months after exposure, microscopic studies confirmed the histologic appearance of a severe peripheral neuropathy of the axonal and demyelinating type.

In humans, there is only circumstantial evidence linking 2,4-D exposure to neurotoxicity, and the arguments against a causal relation have been summarized in a review article (12). Toxic doses of 2,4-D, as much as 3,600 mg given intravenously in a single dose to a human and a cumulative dose of 16,312 mg administered over 5 weeks, induced transient neurological signs and symptoms but no long-term sequelae (13).

A host of neurological symptoms has been reported following dioxin exposure and has been grouped under the generic term of “neurasthenia.” Numerous studies have been published describing neurological sequelae in populations exposed to dioxin by occupation (14–21), environmental contamination (22–26)

and industrial accidents (27–33), and in association with service in Southeast Asia (SEA) during the Vietnam War (34–40).

The 1976 chemical explosion in Seveso, Italy, has provided a basis for numerous reports on the exposed population (27–30, 32, 33), and several of these reports have included clinical and laboratory indices in the examination protocols, most of which have focused on signs and symptoms of peripheral neuropathy as primary clinical endpoints. In one study, 152 subjects with chloracne, a marker for high-level dioxin exposure, were compared with controls. An abnormality was found in only 1 of 13 neurophysiologic indices, and none of the exposed subjects were found to have a peripheral neuropathy by World Health Organization criteria (30). Other investigators who included electromyographic studies in the examination protocols reached similar conclusions (27, 29, 32), as did those studying the populations exposed consequent to uncontrolled chemical reactions that occurred in Germany in 1953 (31) and in Nitro, West Virginia, in 1949 (17).

In contrast, one occupational study of 47 railroad workers examined 6 years after a chemical spill revealed evidence, through electrophysiologic measurements, for a peripheral neuropathy in 43 of these workers. High prevalences of dystonia (53%) and tremor (78%) were documented (14). These results have not been confirmed by any other studies, and the conclusions were limited by the lack of a control group and by exposure to other chemicals.

Point-source environmental exposure to dioxin has been the focus of numerous epidemiological studies, some of which have included neurological indices in their protocols (22–26). In 1971, waste byproducts contaminated with dioxin were mixed with oils and widely sprayed for dust control in residential areas in eastern Missouri. Soil concentrations in some areas reached 2,200 parts per billion, far exceeding the highest degree of ground contamination that occurred at Seveso. Comprehensive medical evaluations of exposed and unexposed cohorts included detailed neurological examinations and, in one report (24), quantitative studies of tactile, vibratory, and thermal sensory perception. The Missouri dioxin studies have been summarized in a review article (26) and, to date, none has found any clinical evidence for central or peripheral neurological disease associated with exposure to dioxin. In the only Missouri study to relate neurological endpoints to tissue levels of dioxin (23), no associations were found between the body burden of dioxin and abnormalities in deep tendon reflexes or pain and vibratory sensation.

An epidemiological study conducted by the National Institute of Occupational Safety and Health is one of few to relate serum dioxin levels to neurological indices (20). The prevalence of peripheral neuropathy was determined in 265 workers with a mean serum dioxin level of 220 parts per trillion (ppt) 15 years after exposure and in 244 referents with a level of 7 ppt. The diagnosis of peripheral neuropathy was established by symptoms and by data collected during physical examination, electrophysiologic studies, and quantitative sensory testing. Although the study could not rule out neurological symptoms associated with acute exposure, there was no evidence for a dose-response relation between dioxin levels and peripheral neuropathy.

Few studies of Vietnam veterans have incorporated neurological data into their protocols and, with the exception of the Air Force Health Study (AFHS), none has correlated neurological indices with tissue levels of dioxin. One large-scale study of American Legion veterans who served in Vietnam found an increased incidence of reported neurobehavioral disorders among veterans who reported exposure to herbicides (34).

The Vietnam Experience Study, conducted by the United States Centers for Disease Control and Prevention, compared the health status of 2,490 Vietnam veterans with 1,972 non-Vietnam veterans (35). The study protocol included comprehensive neurological examinations, nerve conduction velocity

studies, and neurophysiologic indices of vibratory, thermal, and auditory sensation. Aside from an increased prevalence of combat-related high frequency hearing loss in a pattern consistent with prior noise exposure, no neurological abnormalities were noted in association with service in Vietnam.

In the baseline examination of the AFHS (36), an increased prevalence of abnormal Babinski reflexes was noted in Ranch Hand personnel relative to Comparisons, a finding not confirmed at the 1985 (37), 1987 (38), or 1992 (39) follow-up examinations. In the 1987 examination, Ranch Hand participants were found to have more coordination abnormalities than Comparisons, but subsequent analyses found no correlation with serum dioxin levels. A few statistically significant associations were noted but not in a pattern consistent with a dose-response effect (40). In the AFHS 1992 examination, the prevalence of neurological disease was comparable in the Ranch Hand and Comparison groups, and there was no consistent evidence for a dose-response effect with either estimated initial dioxin levels or current dioxin levels (39). In the most recent report published by the Institute of Medicine (41), the committee concluded that there is “limited/suggestive” evidence of an association between exposure to certain herbicides used in Vietnam and the development of an acute or subacute transient peripheral neuropathy.

In summary, the animal research and human epidemiological studies cited above suggest that the peripheral nervous system is a target organ for acute dioxin toxicity. Longitudinal studies suggest that the neurological signs and symptoms attributable to heavy acute exposure resolve over time and are not associated with any long-term sequelae. Exposures equivalent to those likely to have been encountered by Vietnam veterans have not been associated with persistent neurological abnormalities.

11.1.2 Summary of Previous Analyses of the Air Force Health Study

11.1.2.1 1982 Baseline Study Summary Results

The 1982 AFHS neurological assessment consisted of questionnaire, physical examination, and electromyographic data obtained by examiners and technicians who were blind to the group identity of each participant. The physical examination required an average of 30 minutes to complete. Analyses were adjusted for reported alcohol usage, exposure to insecticides and industrial chemicals, and glucose intolerance (diabetes).

Results of the questionnaire disclosed no significant group differences in reported neurological diseases. The physical examination did not reveal any statistically significant group differences in the function of the 12 cranial nerves. Peripheral nerve function was assessed by the quality of four reflexes (patellar, Achilles, biceps, and Babinski); muscle strength or bulk; and reaction to the stimuli of pinprick, light touch, and vibration. Other than a statistically significant increase ($p=0.03$) in Ranch Hand Babinski reflexes, significant group differences were not detected.

Nerve conduction velocities were obtained on the ulnar nerve above and below the elbow and the peroneal nerve. The results for each segmental measurement were nearly identical in the Ranch Hand and Comparison groups. Conduction velocity showed highly significant inverse relations to both alcohol and diabetes in almost all of the anatomic measurements. No group associations or interactions were detected with the reported exposure to industrial and degreasing chemicals and insecticides.

No significant group differences were detected in four measures of central neurological function (tremor, finger-nose coordination, modified positive Romberg sign, or abnormal gait). Alcohol usage was significantly associated with the presence of tremor, and glucose intolerance was highly correlated to abnormal balance and the presence of tremor.

11.1.2.2 1985 Follow-up Study Summary Results

The 1985 AFHS neurological examination did not include the measurements of nerve conduction velocities, but otherwise repeated the baseline examination protocol. The questionnaire maintained a historical focus on neurasthenia through five questions for the 1982-1985 interval. With this similarity in examination and questionnaire, the dependent variables of the analyses were the same as those of the baseline study.

Interval questionnaire data (1982–1985) on neurological illness, verified by medical records, revealed no significant group differences. These data were added to verified baseline examination historical information to assess possible differences in the lifetime experience of neurological disease. Again, there was no significant difference between the Ranch Hand and Comparison groups.

The neurological examination evaluated neurological integrity in three broad areas: cranial nerve function, peripheral nerve status, and central nervous system (CNS) coordination. Assessment of the 12 cranial nerves was based on the measurement of 15 variables. Two summary indices were constructed. Neither the unadjusted nor the adjusted analyses disclosed any statistically significant group differences, although two variables (speech and tongue position) were of marginal significance, with Ranch Hands faring worse than Comparisons. One of the two cranial nerve summary indices was marginally significant, again with the Ranch Hands adversely affected. In contrast to the baseline examination, there was no significant group difference in Babinski reflex. The unadjusted and adjusted analyses of peripheral nerve function, as measured by eight variables (four reflexes, three sensory determinations, and muscle mass), did not reveal significant group differences. Coordination was evaluated by four measurements and a constructed summary variable. Hand tremor was found to be of marginal significance, with Ranch Hands faring slightly worse than Comparisons. The CNS summary index showed significant adverse effects for Ranch Hands.

In a longitudinal analysis of the Romberg sign and the Babinski reflex, only the Babinski reflex revealed a significant difference between the baseline examination and the 1985 follow-up examination, with the Ranch Hands shifting from significant adverse findings at the baseline examination to nonsignificant findings at the 1985 follow-up examination.

Overall, the 1985 follow-up examination findings were similar to the baseline examination findings; however, several distinct patterns were evident from the analyses:

- Substantially fewer abnormalities were detected at the 1985 follow-up examination than at the baseline examination for almost all of the variables.
- The decrease in abnormalities was similar in both groups.
- The adjusted analyses were uniformly similar to the unadjusted analyses.
- A significant result was found for the constructed CNS summary variable, and a marginally significant result was found for the constructed cranial nerve index excluding range of motion, both in the adverse direction.
- Although statistical significance at the pre-assigned significance level of 0.05 was not achieved for any of the measurement variables, the Ranch Hand group tended to have a greater percentage of abnormalities.

In conclusion, none of the 27 neurological variables demonstrated a significant group difference, although several showed an aggregation of abnormalities in the Ranch Hand group, which emphasized the need for continued surveillance. Historical reporting of neurological disease was similar in both

groups. The longitudinal analyses disclosed a reversal of significant increase in Babinski reflex abnormalities at the baseline examination to nonsignificant difference (RR=1.02) at the 1985 follow-up examination for the Ranch Hands.

11.1.2.3 1987 Follow-up Study Summary Results

The neurological health of the Ranch Hand group was not substantially different from the Comparison group. For the questionnaire variables related to neurological disease, Ranch Hands had significantly more hereditary and degenerative diseases, such as benign essential tremor. The statistical results of the group contrasts for 30 physical examination variables relating to cranial nerve function, peripheral nerve status, and CNS coordination processes generally were not significant. Unadjusted analyses disclosed marginally significantly more balance (Romberg sign) and coordination abnormalities for Ranch Hands than for Comparisons. Conversely, Ranch Hands had significantly fewer biceps reflex abnormalities than Comparisons. The longitudinal analyses for the cranial nerve index and the CNS index revealed no significant differences.

11.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Study Summary Results

Overall, the neurological assessment did not indicate that dioxin was associated with neurological disease, although some analyses revealed a significant association between dioxin levels and CNS index and coordination. The adjusted analyses for the historical questionnaire variables were not significant and few statistically significant results were noted for the physical examination variables. The group contrast from the 1987 follow-up examination found that Ranch Hands had significantly more hereditary and degenerative diseases (mostly benign essential tremor) than Comparisons, but the serum dioxin analyses provided no support for the hypothesis that dioxin levels were associated with an increased risk of these diseases. The adjusted categorized current dioxin analyses for coordination found that the relative risk was significantly greater than 1.0 for Ranch Hands in the high current dioxin category. This was consistent with the previous analysis of the 1987 follow-up data, where the Ranch Hand group had significantly more coordination abnormalities than the Comparison group (1.5 percent versus 0.6 percent). The serum dioxin analyses showed significant adverse associations with the CNS index, including a marginally significant association with initial dioxin in the longitudinal analyses.

11.1.2.5 1992 Follow-up Study Summary Results

Overall, the neurological assessment found the prevalence of neurological disease to be comparable between the Ranch Hand and Comparison groups, and showed no consistent evidence of a dose-response effect with either estimated initial dioxin levels or current dioxin levels. In the group contrasts stratified by occupation, Ranch Hand enlisted groundcrew had significantly more cranial nerve index abnormalities than Comparison enlisted groundcrew. The enlisted groundcrew was the military occupation category with the highest average levels of dioxin; however, analyses of serum dioxin levels did not exhibit a dose-response trend.

11.1.3 Parameters for the 1997 Neurological Assessment

11.1.3.1 Dependent Variables

The neurological assessment was based on extensive physical examination data on cranial nerve function, peripheral nerve status, and CNS coordination processes. This information was supplemented by verified histories of neurological diseases. Participants with a positive serological test for syphilis and

participants who tested positive for the human immunodeficiency virus (HIV) were excluded from the analysis of all dependent variables.

11.1.3.1.1 Medical Records Variables

The 1997 questionnaire captured data on the occurrence of neurological disorders. Positive responses were verified by a medical records review and combined with information from the baseline examination and the 1985, 1987, and 1992 follow-up examinations. The neurological diseases and disorders were classified into four categories of the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) manual: inflammatory diseases (ICD-9-CM codes 320.0–326), hereditary and degenerative diseases (ICD-9-CM codes 330.0–337.9), peripheral disorders (ICD-9-CM codes 350.1–359.9), and other neurological disorders (ICD-9-CM codes 340–349.9). The neurological inflammatory diseases found in this study consisted of meningitis caused by bacterial infection, meningitis of unknown cause, and encephalitis of unknown cause. The majority of other neurological disorders were unspecified encephalopathies, but conditions such as multiple sclerosis, other demyelinating diseases of the CNS, hemiplegia, other paralytic syndromes, epilepsy, migraine, catalepsy or narcolepsy, other conditions of the brain, and other unspecified disorders of the CNS were included. Each of the four disorders was coded as “yes” or “no.”

Participants with a verified pre-SEA history of the disorder were excluded from all analyses pertaining to that disorder.

11.1.3.1.2 Physical Examination Data

11.1.3.1.2.1 Cranial Nerve Function

The evaluation of cranial nerve function was based on the following 15 variables: smell, visual fields, light reaction, ocular movement, facial sensation, corneal reflex, jaw clench, smile, palpebral fissure, balance, gag reflex, speech, tongue position relative to midline, palate and uvula movement, and neck movement. All of these variables were scored as “normal” or “abnormal,” except for jaw clench and palate and uvula movement, which were scored as “symmetric” or “deviated.” For variables with left and right determinations, the two results were combined to produce a single normal or abnormal result, where normal indicated that both responses were normal, and abnormal indicated that at least one of the responses was abnormal. Abnormal speech conditions included aphasia, dysarthria, agnosia, and other speech abnormalities. Neck range of motion was coded as abnormal if there was a decreased range of motion forward or backward or to the left or right. Neck movement was evaluated by a shoulder shrug and by applying manual resistance to the cheeks to evaluate the strength of lateral rotation. No abnormal neck movements were found at the 1997 examination.

A cranial nerve index was created by combining responses for the 15 cranial nerve parameters. This index was classified as abnormal if at least one of the determinations was abnormal and was classified as normal if all of the cranial nerve parameters were normal.

11.1.3.1.2.2 Musculoskeletal and Vertebral Column Function

The examining neurologist asked each participant to move his head to the left and right, and to tilt his head forward and backward. This test assessed the musculoskeletal and vertebral column function. This neck range of motion variable was coded as abnormal if there was a decreased range of motion forward or backward or to the left or right.

11.1.3.1.2.3 *Peripheral Nerve Status*

Peripheral nerve status was assessed by light pinprick, light touch (cotton sticks), visual inspection of muscle mass (and palpation, if indicated), three deep tendon reflexes (patellar, Achilles, and biceps), and the Babinski reflex. In addition, four indices to assess bilateral symmetric distal sensory or sensorimotor polyneuropathy were analyzed. These indices were constructed based on testing of ankle and toe flexors, coordination, deep tendon reflexes, light touch, pinprick, vibration at the ankle, toe position, and a vibrotactile measurement of both great toes.

A vibrotactile measurement of both the left and right great toes was performed as part of a collaborative effort with the National Institute of Dental Research. A Vibratron II[®] device was used to measure vibrotactile threshold on both the left and right great toes. The Vibratron II[®] provided a noninvasive means of measuring the sensitivity to vibration of a participant's feet. Following instructions from the manufacturer, the Vibratron II[®] was calibrated prior to the start of the physical examinations and at the midpoint of the examination period. Participants whose great toes could be examined but who sensed no vibration were included in the analysis at a level equal to the highest recorded measurement (22.8 vibrational units [VU]) to represent an extreme loss of sensitivity to vibration. The Vibratron II[®] device recorded measurements in vibrational units. A transformation was used to convert the vibrational units to a standardized unit, such as microns of displacement, to facilitate comparison with other studies. The formula used in this study, as determined by the manufacturer, was

$$\text{Displacement (microns)} = 0.5 \cdot \text{VU}^2.$$

The instrument was calibrated prior to and once (at the midpoint) during the study period. The displacement measurements were transformed to the natural logarithm scale to enhance normal distribution assumptions for analysis. The left and right great toes were analyzed separately. For each great toe, the average (in log microns) of four of seven trials was determined. The four trials were those remaining after eliminating the results of the first of the seven trials and the high and low readings of the other six results following a method of limits protocol (42). The average was calculated for each participant who had four nonzero measurements, after eliminating the results of the first of the seven trials and the high and low readings of the other six results.

Pinprick and light touch were considered normal if the reaction was normal on both legs. A variable to judge muscle status was constructed using data on bulk; tone of upper and lower extremities; and the strength of distal wrist extensors, ankle and toe flexors, proximal deltoids, and hip flexors. Bulk was classified as either "normal" or "abnormal"; tone was classified as "abnormal" if there was either a decreased or increased response on either the left side, right side, or both sides. The strength of distal wrist extensors, ankle and toe flexors, proximal deltoids, and hip flexors was considered "abnormal" if either or both the left or right side was decreased. Composite muscle status was classified as "normal" if all of the components were normal on both the left and right sides and "abnormal" if at least one of the components was abnormal on either or both sides. The patellar, Achilles, and biceps reflexes were coded as "normal" if they were sluggish, active, or very active and were classified as "abnormal" if absent.

Three indices to assess polyneuropathy were based on a severity index. The endpoints discussed previously in this section assessed unilateral abnormalities, whereas these indices assessed bilateral abnormalities. These indices were considered abnormal only if both the left and right determinations were abnormal. These indices were based on the following seven conditions or sets of conditions:

- Both left and right ankle and toe flexors were abnormal (no=0, yes=1)

- The Romberg sign (equilibratory) was abnormal (no=0, yes=1)
- Both left and right Achilles reflexes were absent (no=0, yes=1)
- Reaction to a light touch was abnormal on both the left and right legs (no=0, yes=1)
- Reaction to a pinprick was abnormal on both the left and right legs (no=0, yes=1)
- Both left and right ankle vibrations were abnormal (no=0, yes=1)
- The position of both the left and right great toe was abnormal (no=0, yes=1).

A polyneuropathy severity index, which ranged from 0 to 7, was constructed as the sum of the above seven scores. The polyneuropathy severity index was classified as “mild” (index = 0, 1, or 2), “moderate” (index = 3 or 4), or “severe” (index = 5, 6, or 7). A second index, termed a polyneuropathy prevalence indicator, was coded as “abnormal” if the polyneuropathy severity index was at least 1 and “normal” if the polyneuropathy severity index was 0. A third index, termed a multiple polyneuropathy index, was coded as “abnormal” if the polyneuropathy severity index was at least 2 and “normal” if the polyneuropathy severity index was 0 or 1.

In addition, a confirmed polyneuropathy index was constructed as follows:

If at least two of the following three conditions hold,

- Both left and right Achilles reflexes were absent
- Reaction to a pinprick was abnormal on both the left and right legs
- Both left and right ankle vibrations were abnormal

and the minimum of the left and right toe averages (in log microns) was greater than 4.02, the confirmed polyneuropathy index was coded as “abnormal.” If the minimum vibrotactile measurement was less than or equal to 4.02, or no more than one of the above conditions was present, the confirmed polyneuropathy index was coded as “normal.” The value of 4.02 was determined by taking the minimum value of the left and right great toe average for each participant and using the 90th percentile of the minimum values for Comparisons.

Participants with peripheral edema in the lower extremities were excluded from the analyses of pinprick and light touch. The analysis of the Achilles reflex excluded participants with a transient or sustained clonus in this reflex. The analysis of the patellar reflex excluded participants with a transient or sustained clonus in this reflex. Participants with peripheral edema of the lower extremities and participants with transient clonus or sustained clonus results for the Achilles reflex were excluded from the analysis of polyneuropathy indices, because pinprick, light touch, and the Achilles reflex were a component of each of the polyneuropathy indices.

11.1.3.1.2.4 CNS Coordination Processes

The evaluation of CNS coordination processes was based on the analysis of the following variables: tremor, coordination, Romberg sign, gait, and a CNS index. For these variables, multiple determinations, which include left and right as well as upper and lower responses, were combined to form a single result. A result was classified as “normal” if all determinations were normal and “abnormal” if at least one determination was abnormal. Tremor was examined for the left and right upper and lower extremities. Abnormal tremors included resting, essential, intention, and “other tremors.” Coordination was a composite index defined as “normal” if the Romberg sign, finger-nose-finger and heel-knee-shin coordination processes, rapidly alternating movements of pronation and supination of hands, and rapid

patting were normal. The Romberg sign variable is equivalent to the “balance” variable analyzed as part of the cranial nerve function assessment. The gait variable was based on the examining physician’s assessment of the participant’s gait. An abnormal gait included conditions such as broad-based, small-stepped, ataxic, or other irregular gait patterns. A CNS index was constructed and was a composite variable based on tremor, coordination, and gait. This index was coded as “normal” if all three of the components were normal and abnormal otherwise.

11.1.3.2 Covariates

Age, race, military occupation, lifetime alcohol history, reported exposure to insecticides, reported exposure to industrial chemicals, reported exposure to degreasing chemicals, and diabetic class were covariates for all adjusted statistical analyses.

Age, race, and military occupation were determined from military records. Lifetime alcohol history was based on self-reported information from the 1997 questionnaire and combined with similar information gathered at the 1987 and 1992 follow-ups. The participants’ lifetime exposures through 1992 to insecticides, industrial chemicals, and degreasing chemicals were updated with information reported in the 1997 questionnaire.

Each participant was asked about his drinking patterns throughout his lifetime. When a participant’s drinking patterns changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant’s average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year.

In the 1997 questionnaire, a general screening question on diabetes was posed. Each participant was asked during the in-person health interview the following question: “Since the date of the last interview, has a doctor told you for the first time that you had diabetes?” All affirmative responses were verified by a medical records review and added to previously reported and verified information on diabetes from the 1982 baseline examination and the 1985, 1987, and 1992 follow-up examinations for each participant. Participants with a verified history of diabetes were combined with those participants with a 2-hour postprandial glucose level of 200 mg/dl or greater at the 1997 physical examination and classified as “diabetic” for the diabetic class covariate. Those participants without a verified history of diabetes and with a 2-hour postprandial glucose level of less than 200 mg/dl at the 1997 physical examination were classified as either “impaired” (140 mg/dl < 2-hour postprandial glucose < 200 mg/dl) or “normal” (2-hour postprandial glucose < 140 mg/dl).

Two additional covariates based on self-reported information were used for the confirmed polyneuropathy indicator dependent variable. The 1997 questionnaire asked each study participant whether he had worked for 30 days or more with lead, mercury, chromium, nickel, copper, cadmium, manganese, arsenic, selenium, or molybdenum. Responses were combined to form a composite exposure to heavy metals covariate. The participant also was asked in the 1997 questionnaire whether he had ever worked for 30 days or more with vibrating power equipment or tools. The response (yes or no) to this question also was used as a covariate in the assessment of the confirmed polyneuropathy indicator dependent variable.

11.1.4 Statistical Methods

Table 11-1 summarizes the statistical analyses performed for the neurological assessment. The first part of Table 11-1 lists the dependent variables analyzed, data source, data form, cutpoints, covariates, and statistical methods. The second part of this table provides a further description of covariates examined. A covariate was used in its continuous form whenever possible for adjusted analyses; if the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 11-1.

Table 11-1. Statistical Analysis for the Neurological Assessment

Dependent Variables

| Variable | Data Source | Data Form | Cutpoints | Covariates ^a | Exclusions ^b | Statistical Analysis and Methods |
|--------------------------------------|-------------|-----------|-----------------------|-------------------------|-------------------------|----------------------------------|
| Inflammatory Diseases | MR-V | D | Yes No | (1) | (a) | U:LR,CS A:LR |
| Hereditary and Degenerative Diseases | MR-V | D | Yes No | (1) | (a) | U:LR A:LR |
| Peripheral Disorders | MR-V | D | Yes No | (1) | (a) | U:LR A:LR |
| Other Neurological Disorders | MR-V | D | Yes No | (1) | (a) | U:LR A:LR |
| Smell | PE | D | Abnormal Normal | (1) | (b) | U:LR A:LR |
| Visual Fields | PE | D | Abnormal Normal | (1) | (b) | U:LR,CS A:LR |
| Light Reaction | PE | D | Abnormal Normal | (1) | (b) | U:LR,CS A:LR |
| Ocular Movement | PE | D | Abnormal Normal | (1) | (b) | U:LR A:LR |
| Facial Sensation | PE | D | Abnormal Normal | (1) | (b) | U:LR,CS A:LR |
| Corneal Reflex | PE | D | Abnormal Normal | -- | -- | Descriptive |
| Jaw Clench | PE | D | Deviated Symmetric | (1) | (b) | U:LR,CS A:LR |
| Smile | PE | D | Abnormal Normal | (1) | (b) | U:LR,CS A:LR |
| Palpebral Fissure | PE | D | Abnormal Normal | (1) | (b) | U:LR A:LR |
| Balance | PE | D | Abnormal Normal | (1) | (b) | U:LR,CS A:LR |
| Gag Reflex | PE | D | Abnormal Normal | -- | -- | Descriptive |
| Speech | PE | D | Abnormal Normal | (1) | (b) | U:LR,CS A:LR |
| Tongue Position Relative to Midline | PE | D | Deviated Symmetric | (1) | (b) | U:LR,CS A:LR |
| Palate and Uvula Movement | PE | D | Deviated Symmetric | (1) | (b) | U:LR,CS A:LR |

Table 11-1. Statistical Analysis for the Neurological Assessment (Continued)

| Variable | Data Source | Data Form | Cutpoints | Covariates ^a | Exclusions ^b | Statistical Analysis and Methods |
|------------------------------------|-------------|-----------|---------------------------------|-------------------------|-------------------------|----------------------------------|
| Cranial Nerve Index | PE | D | Abnormal Normal | (1) | (b) | U:LR A:LR L:LR |
| Neck Range of Motion | PE | D | Abnormal Normal | (1) | (b) | U:LR A:LR |
| Pinprick | PE | D | Abnormal Normal | (1) | (c) | U:LR A:LR |
| Light Touch | PE | D | Abnormal Normal | (1) | (c) | U:LR A:LR |
| Muscle Status | PE | D | Abnormal Normal | (1) | (b) | U:LR A:LR |
| Patellar Reflex | PE | D | Abnormal Normal | (1) | (d) | U:LR A:LR |
| Achilles Reflex | PE | D | Abnormal Normal | (1) | (e) | U:LR A:LR |
| Biceps Reflex | PE | D | Abnormal Normal | (1) | (b) | U:LR A:LR |
| Babinski Reflex | PE | D | Abnormal Normal | (1) | (b) | U:LR A:LR |
| Polyneuropathy Severity Index | PE | D | Severe Moderate None/Mild | (1) | (f) | U:PR A:PR |
| Polyneuropathy Prevalence Index | PE | D | Abnormal Normal | (1) | (f) | U:LR A:LR |
| Multiple Polyneuropathy Index | PE | D | Abnormal Normal | (1) | (f) | U:LR A:LR |
| Confirmed Polyneuropathy Indicator | PE | D | Abnormal Normal | (2) | (f) | U:LR,CS A:LR |
| Tremor | PE | D | Abnormal Normal | (1) | (b) | U:LR A:LR |
| Coordination | PE | D | Abnormal Normal | (1) | (b) | U:LR A:LR |
| Romberg Sign | PE | D | Abnormal Normal | (1) | (b) | U:LR,CS A:LR |
| Gait | PE | D | Abnormal Normal | (1) | (b) | U:LR A:LR |
| CNS Index | PE | D | Abnormal Normal | (1) | (b) | U:LR A:LR L:LR |

^aCovariates:

- (1) Age, race, military occupation, lifetime alcohol history, insecticide exposure, industrial chemical exposure, degreasing chemical exposure, diabetic class.
- (2) Age, race, military occupation, lifetime alcohol history, insecticide exposure, industrial chemical exposure, degreasing chemical exposure, diabetic class, composite exposure to heavy metals, worked with vibrating power equipment or tools.

Table 11-1. Statistical Analysis for the Neurological Assessment (Continued)

^bExclusions:

- (a) Participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with a verified pre-SEA history of the disorder.
- (b) Participants with positive serological tests for syphilis, participants who tested positive for HIV.
- (c) Participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with peripheral edema of the lower extremities.
- (d) Participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with transient or sustained clonus of the patellar reflex.
- (e) Participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with transient or sustained clonus of the Achilles reflex.
- (f) Participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with peripheral edema of the lower extremities, participants with transient or sustained clonus of the Achilles reflex.

Covariates

| Variable (units) | Data Source | Data Form | Cutpoints |
|--|-------------|-----------|---|
| Age (years) | MIL | D/C | Born ≥1942 Born <1942 |
| Race | MIL | D | Black Non-Black |
| Occupation | MIL | D | Officer Enlisted Flyer Enlisted Groundcrew |
| Lifetime Alcohol History (drink-years) | Q-SR | D/C | 0 >0–40 >40 |
| Insecticide Exposure | Q-SR | D | Yes No |
| Industrial Chemical Exposure | Q-SR | D | Yes No |
| Degreasing Chemical Exposure | Q-SR | D | Yes No |
| Diabetic Class | LAB/MR-V | D | <ul style="list-style-type: none"> • Diabetic: past history or ≥200 mg/dl 2-hr. postprandial glucose • Impaired: 140–<200 mg/dl 2-hr. postprandial glucose • Normal: <140 mg/dl 2-hr. postprandial glucose |
| Composite Exposure to Heavy Metals | Q-SR | D | Yes No |
| Worked With Vibrating Power Equipment or Tools | Q-SR | D | Yes No |

Abbreviations

Data Source: LAB: 1997 laboratory results
 MIL: Air Force military records
 MR-V: Medical records (verified)
 PE: 1997 physical examination
 Q-SR: Health questionnaire (self-reported)

Table 11-1. Statistical Analysis for the Neurological Assessment (Continued)

Data Form: D: Discrete analysis only
D/C: Appropriate form for analysis (either discrete or continuous)

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis
L: Longitudinal analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted)
LR: Logistic regression analysis
PR: Polytomous logistic regression analysis

Table 11-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants excluded because of medical conditions is given.

Table 11-2. Number of Participants Excluded or with Missing Data for the Neurological Assessment

| Variable | Variable Use | Group | | Dioxin (Ranch Hands Only) | | Categorized Dioxin | |
|--|--------------|------------|------------|---------------------------|------|--------------------|------------|
| | | Ranch Hand | Comparison | Initial | 1987 | Ranch Hand | Comparison |
| Smell | DEP | 4 | 2 | 2 | 4 | 4 | 2 |
| Visual Fields | DEP | 0 | 4 | 0 | 0 | 0 | 4 |
| Light Reaction | DEP | 5 | 2 | 1 | 5 | 5 | 2 |
| Facial Sensation | DEP | 1 | 1 | 0 | 1 | 1 | 1 |
| Corneal Reflex | DEP | 7 | 6 | 5 | 7 | 7 | 5 |
| Balance | DEP | 0 | 1 | 0 | 0 | 0 | 1 |
| Gag Reflex | DEP | 1 | 1 | 0 | 1 | 1 | 1 |
| Cranial Nerve Index | DEP | 16 | 4 | 7 | 16 | 16 | 4 |
| Muscle Status | DEP | 0 | 1 | 0 | 0 | 0 | 1 |
| Patellar Reflex | DEP | 1 | 2 | 1 | 1 | 1 | 1 |
| Achilles Reflex | DEP | 0 | 3 | 0 | 0 | 0 | 3 |
| Biceps Reflex | DEP | 0 | 1 | 0 | 0 | 0 | 1 |
| Babinski Reflex | DEP | 0 | 3 | 0 | 0 | 0 | 3 |
| Polyneuropathy Severity Index | DEP | 0 | 1 | 0 | 0 | 0 | 1 |
| Multiple Polyneuropathy Index | DEP | 1 | 0 | 1 | 1 | 1 | 0 |
| Confirmed Polyneuropathy Index | DEP | 14 | 10 | 7 | 13 | 13 | 9 |
| Coordination | DEP | 0 | 2 | 0 | 0 | 0 | 2 |
| Romberg Sign | DEP | 0 | 1 | 0 | 0 | 0 | 1 |
| CNS Index | DEP | 0 | 1 | 0 | 0 | 0 | 1 |
| Lifetime Alcohol History | COV | 6 | 2 | 3 | 6 | 6 | 1 |
| Diabetic Class | COV | 9 | 18 | 5 | 7 | 7 | 17 |
| Worked with Vibrating Power Equipment or Tools | COV | 1 | 2 | 1 | 1 | 1 | 2 |
| Composite Exposure to Heavy Metals | COV | 1 | 0 | 1 | 1 | 1 | 0 |
| Pre-SEA Inflammatory Diseases | EXC | 0 | 7 | 0 | 0 | 0 | 7 |

Table 11-2. Number of Participants Excluded or with Missing Data for the Neurological Assessment (Continued)

| Variable | Variable Use | Group | | Dioxin (Ranch Hands Only) | | Categorized Dioxin | |
|--|--------------|------------|------------|---------------------------|------|--------------------|------------|
| | | Ranch Hand | Comparison | Initial | 1987 | Ranch Hand | Comparison |
| Pre-SEA Peripheral Disorders | EXC | 3 | 2 | 0 | 3 | 3 | 2 |
| Pre-SEA Other Neurological Disorders | EXC | 4 | 5 | 1 | 4 | 4 | 5 |
| Positive Serological Test for Syphilis | EXC | 1 | 0 | 0 | 1 | 1 | 0 |
| HIV Positive | EXC | 3 | 2 | 3 | 3 | 3 | 2 |
| Peripheral Edema | EXC | 45 | 64 | 26 | 45 | 45 | 62 |
| Clonus – Patellar Reflex | EXC | 0 | 1 | 0 | 0 | 0 | 1 |
| Clonus – Achilles Reflex | EXC | 1 | 2 | 0 | 1 | 1 | 2 |

Note: DEP = Dependent variable.

COV = Covariate.

EXC = Exclusion.

870 Ranch Hands and 1,251 Comparisons.

482 Ranch Hands for initial dioxin; 863 Ranch Hands for 1987 dioxin.

863 Ranch Hands and 1,213 Comparisons for categorized dioxin.

11.1.4.1 Longitudinal Analysis

The neurological longitudinal analyses were based on the cranial nerve index, excluding neck range of motion and the CNS index. Substantially fewer neurological abnormalities have been found in the 1985, 1987, 1992, and 1997 examinations than at the 1982 baseline examination, as noted in previous AFHS reports. This observation suggested that different techniques for the examination of the neurological system were used in 1982 than in the subsequent examinations. To enhance the comparability of measurements between examinations, the longitudinal assessment contrasted differences between the 1985 and 1997 neurological examinations.

11.2 RESULTS

11.2.1 Dependent Variable-Covariate Associations

The associations between the dependent variables examined in the neurological assessment and the covariates used in the adjusted analysis were investigated; the results are presented in Appendix F, Table F-3. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. Participants were excluded from each of the analyses as given in Table 11-1. Statistically significant associations are discussed below.

Age and industrial chemical exposure each exhibited significant associations with a history of hereditary and degenerative diseases ($p=0.009$ and $p=0.022$, respectively). Hereditary and degenerative diseases were greater for older participants than for younger participants (10.4% vs. 7.0%) and higher for participants reporting exposure to industrial chemicals than for those not reporting exposure (10.0% vs. 7.0%).

Tests of covariate associations with a history of peripheral disorders were significant for age ($p<0.001$), insecticide exposure ($p=0.014$), and diabetic class ($p<0.001$). Peripheral disorders were higher among older participants than younger participants (24.6% vs. 14.9%). Peripheral disorders were greater for participants exposed to insecticides (21.8%) than for participants not exposed to insecticides (16.9%), and greatest for diabetics (33.4%).

Several covariates were associated significantly with a history of other neurological disorders. Significant associations were found with age ($p<0.001$), race ($p<0.001$), occupation ($p<0.001$), industrial chemical exposure ($p<0.001$), degreasing chemical exposure ($p<0.001$), and diabetic class ($p<0.001$). Older participants had a greater history of other neurological disorders (22.0%) than did younger participants (13.4%). Blacks exhibited a greater history of other neurological disorders (33.1%) than did non-Blacks (17.3%). Other neurological disorders were highest for enlisted flyers (27.0%), followed by enlisted groundcrew (24.1%), and then by officers (8.1%). Participants reporting exposure to industrial chemicals and degreasing chemicals had more neurological disorders than participants who did not report exposure. Diabetics had the greatest history of other neurological disorders (23.9%).

Covariate association tests for the light reaction variable were significant for race ($p=0.046$). Blacks exhibited more light reaction abnormalities (2.3%) than did non-Blacks (0.5%).

Covariate association tests for smile, palpebral fissure, and balance were each significant for diabetic class ($p=0.030$, $p=0.007$, and $p=0.036$, respectively). For each variable, the most abnormalities were among diabetics, followed by those classified as normal, and then by those in the impaired diabetic category.

The neck range of motion variable was associated significantly with age ($p<0.001$), occupation ($p=0.006$), and diabetic class ($p=0.022$). A restricted range of motion was greater for older participants (22.0%) than for younger participants (9.9%). Enlisted flyers had the greatest prevalence of an abnormal neck range of motion (20.7%), followed by officers (18.1%), then enlisted groundcrew (14.0%). Diabetics displayed the highest prevalence of neck range of motion abnormalities (21.6%), followed by nondiabetics (15.6%), then by participants in the impaired diabetic category (15.4%).

Tests of covariate association for the cranial nerve index variable were significant for age ($p=0.004$) and diabetic class ($p=0.014$). An abnormal index was found in 7.5 percent of older participants and 4.4 percent of younger participants. More abnormalities were found as the level of diabetic impairment increased.

Covariate association tests were similar for the pinprick and light touch dependent variables. Each were associated significantly with age ($p=0.006$ and $p=0.022$, respectively), occupation ($p=0.006$ and $p=0.036$, respectively), and diabetic class ($p<0.001$ for both). Both variables displayed higher abnormalities among older participants, enlisted flyers, and diabetics.

The patellar reflex variable was associated significantly with age ($p<0.001$), race ($p=0.030$), and diabetic class ($p<0.001$). The higher abnormality prevalences were among older participants (4.0%, compared to 1.3% for younger participants), Blacks (6.3%, compared to 2.6% for non-Blacks), and diabetics (7.3%, compared to 2.6% for participants in the impaired category and 1.8% for nondiabetics).

Tests of covariate association for the Achilles reflex variable showed significant results for age ($p<0.001$), lifetime alcohol history ($p=0.027$), and diabetic class ($p<0.001$). Older participants had a higher prevalence of Achilles reflex abnormalities than did younger participants (22.8% vs. 9.3%). The

heaviest drinkers (in terms of drink-years) had an abnormal Achilles reflex most often (20.2%), followed by nondrinkers (18.6%), and moderate drinkers (15.4%). Achilles reflex abnormalities increased as the level of diabetic impairment increased (nondiabetic: 13.4%; impaired: 16.2%; diabetic: 31.9%).

An abnormal biceps reflex was associated significantly with diabetic class ($p=0.007$), where the prevalence of biceps reflex abnormalities increased as the level of diabetic impairment increased.

Tests of covariate association for the polyneuropathy severity index were significant for age ($p=0.002$), race ($p=0.005$), and diabetic class ($p<0.001$). Older participants displayed a greater percentage of moderate and severe index scores (2.6% and 0.4%, respectively) than younger participants (0.7% and 0.1%, respectively). Non-Blacks displayed the higher moderate index score (1.8%), while Blacks displayed the higher severe index score (1.6%). Diabetics exhibited the highest percentage of both the moderate and severe index scores (5.9% and 0.9%, respectively), followed by nondiabetics (0.9% and 0.1%, respectively). Participants in the impaired diabetic category displayed the smallest percentage of moderate and severe index scores (0.4% and 0.0%, respectively).

Covariate tests of association for the polyneuropathy prevalence index revealed significant associations with age, occupation, lifetime alcohol history, and diabetic class ($p<0.001$ for each). The percentage of abnormal polyneuropathy prevalence index results increased with age, lifetime alcohol history, and level of diabetic impairment. Enlisted flyers had the highest percentage of abnormal polyneuropathy prevalence index results (20.8%), followed by officers (16.5%), then enlisted groundcrew (12.5%).

The multiple polyneuropathy index variable was significantly associated with age ($p<0.001$), occupation ($p=0.006$), and diabetic class ($p<0.001$). The percentage of abnormal multiple polyneuropathy index findings increased with age. Enlisted flyers had the highest percentage of abnormalities (6.7%), followed by officers (4.2%), and enlisted groundcrew (2.7%). Diabetic participants had the highest prevalence of abnormal results (12.7%), followed by nondiabetics (2.4%), and participants in the impaired diabetic class (1.2%).

Age and diabetic classes were associated significantly with the confirmed polyneuropathy indicator variable ($p=0.007$ and $p<0.001$, respectively). Older participants had a higher percentage of abnormal findings than did younger participants (1.5% vs. 0.2%). Diabetic participants had the highest prevalence of confirmed polyneuropathy results (2.9%), followed by nondiabetics (0.6%), then participants in the impaired diabetic class (0.0%).

Insecticide exposure and industrial chemical exposure both were significantly associated with tremor ($p=0.003$ and $p=0.004$, respectively). Participants reporting exposure to insecticides had a higher percentage of tremors than participants who did not report exposure (8.2% vs. 4.5%). Similarly, participants reporting exposure to industrial chemicals had a higher prevalence of tremors than those who did not report exposure (8.4% vs. 5.0%).

Tests of covariate association for coordination revealed diabetic class to be significant ($p=0.013$). Abnormality rates increased as the level of diabetic impairment increased.

Diabetic class was significantly associated with Romberg sign ($p=0.036$). Diabetic participants had the highest percentage of abnormal Romberg sign results (1.7%), followed by nondiabetics (0.5%), and participants in the impaired diabetic class (0.4%).

Age and diabetic classes were associated significantly with gait ($p < 0.001$ for each). Older participants had a higher percentage of an abnormal gait than did younger participants (6.8% vs. 2.8%). The prevalence of a gait abnormality increased with diabetic impairment.

Tests of covariate association for the CNS index revealed significant associations with age ($p < 0.001$), insecticide exposure ($p < 0.001$), and industrial chemical exposure ($p = 0.021$). The percentage of participants with an abnormal index increased with age. Participants reporting exposure to insecticides had a higher percentage of abnormal CNS index results than did participants who did not report exposure (13.7% vs. 8.2%). Similarly, participants reporting exposure to industrial chemicals had a higher prevalence of abnormal results than those who did not report exposure (13.4% vs. 9.9%).

11.2.2 Exposure Analysis

The following section presents results of the statistical analysis of the dependent variables shown in Table 11-1. Dependent variables were derived from a medical records review and verification and a neurological examination to assess the cranial nerve function, peripheral nerve status, and CNS coordination processes.

Four models were examined for each dependent variable given in Table 11-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for relevant covariates. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as “yes” for Ranch Hands and “no” for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports, the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, and officers.

Model 2 explored the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. If a participant did not have a 1987 dioxin level, the 1992 level was used to estimate the initial dioxin level. If a participant did not have a 1987 or a 1992 dioxin level, the 1997 level was used to estimate the initial dioxin level. A statistical adjustment for the percentage of body fat at the time of the participant’s blood measurement of dioxin was included in this model to account for body-fat-related differences in elimination rate (43).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories are referred to as “low Ranch Hand” and “high Ranch Hand.” Two additional categories, Ranch Hands with 1987 serum dioxin levels at or below 10 ppt and Comparisons with 1987 serum dioxin levels at or below 10 ppt, were formed and included in the model. Ranch Hands with 1987 serum dioxin levels at or below 10 ppt are referred to as the “background Ranch Hand” category. Dioxin levels in 1992 were used if the 1987 level was not available, and dioxin levels in 1997 were used if the 1987 and 1992 levels were not available. These four categories—Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the three Ranch Hand categories and the dependent variable in the Comparison category was examined. A fourth contrast, exploring the relation of the dependent variable in the combined low and high Ranch Hand categories relative to Comparisons, also was conducted. This combination is referred to in the tables as the “low plus high Ranch Hand”

category. As in Model 2, a statistical adjustment for the percentage of body fat at the time of the participant's blood measurement of dioxin was included in this model.

Model 4 examined the relation between the dependent variable and 1987 lipid-adjusted dioxin levels in all Ranch Hands with a dioxin measurement. If a participant did not have a 1987 dioxin measurement, the 1992 measurement was used to determine the dioxin level. If a participant did not have a 1987 or a 1992 dioxin measurement, the 1997 measurement was used to determine the dioxin level.

11.2.2.1 Medical Records Variables

11.2.2.1.1 Inflammatory Diseases

A significant difference in the history of inflammatory diseases between Ranch Hands and Comparisons was revealed in both the unadjusted and adjusted analyses (Table 11-3(a,b): Est. RR=10.11, p=0.006; and Adj. RR=13.50, p=0.002, respectively). Seven Ranch Hands (0.8%) and one Comparison (0.1%) have had an inflammatory disease. Of the seven Ranch Hands with inflammatory diseases, three had meningitis caused by bacterial infections, three had meningitis of unknown cause, and one had encephalitis of unknown cause. The single Comparison with an inflammatory disease had encephalitis of unknown cause. All other Model 1 contrasts, as well as the Model 2 results, were nonsignificant (Table 11-3(a-d): p>0.11 for each Model 1 and Model 2 analysis).

Table 11-3. Analysis of Inflammatory Diseases

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|---------------------------|--|--------------------|
| Occupational Category | Group | n | Number (%) Yes | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>866</i> | <i>7 (0.8)</i> | <i>10.11 (1.24,82.35)</i> | <i>0.006</i> |
| | <i>Comparison</i> | <i>1,242</i> | <i>1 (0.1)</i> | | |
| Officer | Ranch Hand | 340 | 2 (0.6) | -- | 0.327 ^a |
| | Comparison | 490 | 0 (0.0) | | |
| Enlisted Flyer | Ranch Hand | 151 | 2 (1.3) | -- | 0.391 ^a |
| | Comparison | 185 | 0 (0.0) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 3 (0.8) | 4.56 (0.47,44.05) | 0.189 |
| | Comparison | 567 | 1 (0.2) | | |

^a P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a history of an inflammatory disease.

--: Results not presented because of the sparse number of participants with an inflammatory disease.

Table 11-3. Analysis of Inflammatory Diseases (Continued)

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>13.50 (1.61,113.13)</i> | <i>0.002</i> |
| Officer | -- | -- |
| Enlisted Flyer | -- | -- |
| Enlisted Groundcrew | 6.38 (0.64,63.30) | 0.114 |

--: Results not presented because of the sparse number of participants with an inflammatory disease.

Note: Results are not adjusted for race and diabetic class because of the sparse number of participants with an inflammatory disease.

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|----------|---------------------------|--|----------------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (Initial Dioxin)^a | |
| Initial Dioxin | n | Number (%) Yes | Estimated Relative Risk (95% C.I.)^b | p-Value |
| Low | 160 | 2 (1.3) | 1.03 (0.48,2.18) | 0.943 |
| Medium | 162 | 1 (0.6) | | |
| High | 157 | 1 (0.6) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 476 | 0.98 (0.45,2.17) | 0.964 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of participants with an inflammatory disease.

Table 11-3. Analysis of Inflammatory Diseases (Continued)

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|---------------------------|---|----------------|
| Dioxin Category | n | Number (%) Yes | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,204 | 1 (0.1) | | |
| Background RH | 380 | 3 (0.8) | 8.82 (0.91,85.93) | 0.061 |
| Low RH | 239 | 2 (0.8) | 10.31 (0.93,114.27) | 0.057 |
| High RH | 240 | 2 (0.8) | 10.86 (0.97,121.25) | 0.053 |
| Low plus High RH | 479 | 4 (0.8) | 10.58 (1.18,95.25) | 0.035 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,203 | | |
| Background RH | 377 | 13.28 (1.31,135.01) | 0.029 |
| Low RH | 238 | 13.85 (1.20,160.07) | 0.035 |
| High RH | 238 | 12.43 (1.03,149.42) | 0.047 |
| Low plus High RH | 476 | 13.12 (1.39,123.67) | 0.024 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race and diabetic class because of the sparse number of participants with an inflammatory disease.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|---------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Yes | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 2 (0.7) | 0.97 (0.58,1.63) | 0.920 |
| Medium | 287 | 3 (1.1) | | |
| High | 285 | 2 (0.7) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-3. Analysis of Inflammatory Diseases (Continued)

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|--|---|---------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 853 | 0.90 (0.52,1.57) | 0.716 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race and diabetic class because of the sparse number of participants with an inflammatory disease.

The Model 3 unadjusted analysis of history of inflammatory diseases revealed marginally significant differences for each contrast involving Ranch Hands in the background, low, and high dioxin categories (Table 11-3(e): Est. RR=8.82, p=0.061; Est. RR=10.31, p=0.057; and Est. RR=10.86, p=0.053, respectively). The remaining unadjusted contrast combining Ranch Hands in the low plus high dioxin category revealed significant differences between Ranch Hands and Comparisons (Table 11-3(e): Est. RR=10.58, p=0.035). Each Model 3 contrast was significant in the adjusted analysis, and each also displayed more Ranch Hands than Comparisons with inflammatory diseases (Table 10-3(f): Adj. RR=13.28, p=0.029; Adj. RR=13.85, p=0.035; Adj. RR=12.43, p=0.047; and Adj. RR=13.12, p=0.024).

Both the unadjusted and adjusted Model 4 analyses of inflammatory diseases were nonsignificant (Table 11-3(g,h): p>0.71 for each Model 4 analysis).

11.2.2.1.2 Hereditary and Degenerative Diseases

All results from Models 1 through 4 for hereditary and degenerative diseases were nonsignificant (Table 11-4(a–h): p≥0.38 for each analysis).

Table 11-4. Analysis of Hereditary and Degenerative Diseases

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|-------------------|----------------------------------|--------------|
| Occupational Category | Group | n | Number (%) Yes | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>866</i> | <i>80 (9.2)</i> | <i>1.08 (0.79,1.46)</i> | <i>0.639</i> |
| | <i>Comparison</i> | <i>1,249</i> | <i>108 (8.7)</i> | | |
| Officer | Ranch Hand | 340 | 30 (8.8) | 1.19 (0.72,1.97) | 0.492 |
| | Comparison | 493 | 37 (7.5) | | |
| Enlisted Flyer | Ranch Hand | 151 | 19 (12.6) | 1.27 (0.65,2.50) | 0.484 |
| | Comparison | 187 | 19 (10.2) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 31 (8.3) | 0.90 (0.56,1.43) | 0.643 |
| | Comparison | 569 | 52 (9.1) | | |

Table 11-4. Analysis of Hereditary and Degenerative Diseases (Continued)

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.07 (0.78,1.46)</i> | <i>0.688</i> |
| Officer | 1.13 (0.68,1.89) | 0.635 |
| Enlisted Flyer | 1.31 (0.66,2.62) | 0.444 |
| Enlisted Groundcrew | 0.92 (0.57,1.48) | 0.737 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|----------|---------------------------|--|----------------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (Initial Dioxin)^a | |
| Initial Dioxin | n | Number (%) Yes | Estimated Relative Risk (95% C.I.)^b | p-Value |
| Low | 160 | 17 (10.6) | 1.01 (0.79,1.28) | 0.952 |
| Medium | 162 | 12 (7.4) | | |
| High | 157 | 14 (8.9) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 471 | 1.02 (0.76,1.36) | 0.909 |

^a Relative risk for a twofold increase in initial dioxin.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|---------------------------|---|----------------|
| Dioxin Category | n | Number (%) Yes | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,211 | 107 (8.8) | | |
| Background RH | 380 | 37 (9.7) | 1.08 (0.73,1.61) | 0.697 |
| Low RH | 239 | 21 (8.8) | 1.00 (0.61,1.63) | 0.999 |
| High RH | 240 | 22 (9.2) | 1.07 (0.66,1.73) | 0.792 |
| Low plus High RH | 479 | 43 (9.0) | 1.03 (0.71,1.50) | 0.864 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-4. Analysis of Hereditary and Degenerative Diseases (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,193 | | |
| Background RH | 375 | 1.16 (0.77,1.76) | 0.474 |
| Low RH | 235 | 0.92 (0.56,1.52) | 0.736 |
| High RH | 236 | 1.01 (0.61,1.67) | 0.979 |
| Low plus High RH | 471 | 0.96 (0.65,1.41) | 0.841 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | |
|--|----------|---------------------------|---|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) |
| 1987 Dioxin | n | Number (%) Yes | Estimated Relative Risk (95% C.I.)^a |
| Low | 287 | 27 (9.4) | 0.96 (0.82,1.12) |
| Medium | 287 | 30 (10.5) | |
| High | 285 | 23 (8.1) | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|---|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 846 | 0.92 (0.77,1.11) | 0.380 |

^a Relative risk for a twofold increase in 1987 dioxin.

11.2.2.1.3 Peripheral Disorders

Results from the Model 1 analysis of history of peripheral disorders displayed no significant differences between Ranch Hands and Comparisons (Table 11-5(a,b): $p > 0.11$ for each unadjusted and adjusted contrast). The unadjusted and adjusted results from the Model 2 analysis also did not display a significant relation between peripheral disorders and initial dioxin (Table 11-5(c,d): $p \geq 0.40$ for the unadjusted and adjusted Model 2 analysis).

Table 11-5. Analysis of Peripheral Disorders

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|-------------------|----------------------------------|--------------|
| Occupational Category | Group | n | Number (%) Yes | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 863 | 188 (21.8) | <i>1.16 (0.94,1.44)</i> | <i>0.169</i> |
| | <i>Comparison</i> | 1,247 | 241 (19.3) | | |
| Officer | Ranch Hand | 339 | 78 (23.0) | 1.32 (0.94,1.85) | 0.113 |
| | Comparison | 492 | 91 (18.5) | | |
| Enlisted Flyer | Ranch Hand | 150 | 36 (24.0) | 1.02 (0.62,1.69) | 0.941 |
| | Comparison | 186 | 44 (23.7) | | |
| Enlisted Groundcrew | Ranch Hand | 374 | 74 (19.8) | 1.08 (0.77,1.50) | 0.658 |
| | Comparison | 569 | 106 (18.6) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--------------------------------------|--------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.12 (0.89,1.40)</i> | <i>0.341</i> |
| Officer | 1.25 (0.88,1.78) | 0.215 |
| Enlisted Flyer | 0.91 (0.54,1.54) | 0.733 |
| Enlisted Groundcrew | 1.09 (0.77,1.54) | 0.622 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|-------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Yes | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 160 | 40 (25.0) | 1.01 (0.86,1.18) | 0.915 |
| Medium | 162 | 42 (25.9) | | |
| High | 157 | 38 (24.2) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|---|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 471 | 1.09 (0.90,1.32) | 0.400 |

^a Relative risk for a twofold increase in initial dioxin.

Table 11-5. Analysis of Peripheral Disorders (Continued)

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|-------------------|--|---------|
| Dioxin Category | n | Number (%) Yes | Est. Relative Risk (95% C.I.) ^{ab} | p-Value |
| Comparison | 1,209 | 233 (19.3) | | |
| Background RH | 377 | 65 (17.2) | 0.91 (0.67,1.23) | 0.531 |
| Low RH | 239 | 61 (25.5) | 1.42 (1.03,1.97) | 0.033 |
| High RH | 240 | 59 (24.6) | 1.32 (0.95,1.83) | 0.097 |
| Low plus High RH | 479 | 120 (25.1) | 1.37 (1.07,1.76) | 0.014 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|-------|---|---------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| Comparison | 1,191 | | |
| Background RH | 372 | 0.88 (0.64,1.21) | 0.437 |
| Low RH | 235 | 1.25 (0.89,1.76) | 0.190 |
| High RH | 236 | 1.33 (0.94,1.90) | 0.111 |
| Low plus High RH | 471 | 1.29 (0.99,1.69) | 0.059 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|-----|-------------------|---|---------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Yes | Estimated Relative Risk (95% C.I.) ^a | p-Value |
| Low | 285 | 44 (15.4) | 1.15 (1.04,1.29) | 0.010 |
| Medium | 286 | 71 (24.8) | | |
| High | 285 | 70 (24.6) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-5. Analysis of Peripheral Disorders (Continued)

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|--|---|---------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 843 | 1.20 (1.04,1.38) | 0.011 |

^a Relative risk for a twofold increase in 1987 dioxin.

The Model 3 unadjusted analysis indicated a significantly greater percentage of Ranch Hands in the low dioxin category than Comparisons with a peripheral disorder (Table 11-5(e): Est. RR=1.42, p=0.033). The result was nonsignificant after adjustment for covariates (Table 11-5(f): p=0.190). The unadjusted analysis also revealed a marginally significant increase for the Ranch Hands in the high dioxin category (Table 11-5(e): Est. RR=1.32, p=0.097). This result was nonsignificant in the adjusted analysis (Table 11-5(f): p=0.111). The contrast of Ranch Hands in the low plus high dioxin category with Comparisons displayed a significant difference in the percentage of participants with a peripheral disorder (Table 11-5(e): Est. RR=1.37, p=0.014), indicating a greater occurrence of peripheral disorders among Ranch Hands than Comparisons. The result was marginally significant after adjustment for covariates (Table 11-5(f): Adj. RR=1.29, p=0.059).

The Model 4 unadjusted and adjusted analyses each displayed a significant association between peripheral disorders and 1987 dioxin levels (Table 11-5(g): Est. RR=1.15, p=0.010; and Adj. RR=1.20, p=0.011, respectively). The occurrence of peripheral disorders increased as 1987 dioxin increased.

11.2.2.1.4 Other Neurological Disorders

A marginally significant increase in a history of other neurological disorders was found in Ranch Hands relative to Comparisons in the Model 1 analyses, both unadjusted and adjusted (Table 11-6(a,b): Est. RR=1.23, p=0.070; and Adj. RR=1.25, p=0.078). When differences were examined within each occupation, the results were nonsignificant in both the unadjusted and adjusted analyses (Table 11-6(a,b): p>0.13 for each contrast). Each Model 2 analysis also was nonsignificant (Table 11-6(c,d): p>0.48 for both analyses).

Table 11-6. Analysis of Other Neurological Disorders

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|-------------------|----------------------------------|---------|
| Occupational Category | Group | n | Number (%) Yes | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 862 | 173 (20.1) | 1.23 (0.98,1.54) | 0.070 |
| | <i>Comparison</i> | 1,244 | 211 (17.0) | | |
| Officer | Ranch Hand | 338 | 29 (8.6) | 1.12 (0.68,1.86) | 0.656 |
| | Comparison | 492 | 38 (7.7) | | |
| Enlisted Flyer | Ranch Hand | 151 | 46 (30.5) | 1.37 (0.85,2.22) | 0.198 |
| | Comparison | 186 | 45 (24.2) | | |
| Enlisted Groundcrew | Ranch Hand | 373 | 98 (26.3) | 1.22 (0.90,1.65) | 0.200 |
| | Comparison | 566 | 128 (22.6) | | |

Table 11-6. Analysis of Other Neurological Disorders (Continued)

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.25 (0.98,1.59)</i> | <i>0.078</i> |
| Officer | 1.09 (0.65,1.84) | 0.734 |
| Enlisted Flyer | 1.33 (0.79,2.21) | 0.283 |
| Enlisted Groundcrew | 1.28 (0.92,1.78) | 0.136 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|----------|---------------------------|--|----------------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (Initial Dioxin)^a | |
| Initial Dioxin | n | Number (%) Yes | Estimated Relative Risk (95% C.I.)^b | p-Value |
| Low | 160 | 34 (21.3) | 1.06 (0.90,1.24) | 0.483 |
| Medium | 161 | 41 (25.5) | | |
| High | 157 | 38 (24.2) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | | |
|--|--|--|----------------|
| Analysis Results for Log₂ (Initial Dioxin) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 470 | 0.99 (0.81,1.20) | | 0.922 |

^a Relative risk for a twofold increase in initial dioxin.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|---------------------------|---|----------------|
| Dioxin Category | n | Number (%) Yes | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,206 | 204 (16.9) | | |
| Background RH | 377 | 59 (15.7) | 0.88 (0.64,1.21) | 0.442 |
| Low RH | 239 | 55 (23.0) | 1.48 (1.06,2.07) | 0.023 |
| High RH | 239 | 58 (24.3) | 1.62 (1.16,2.26) | 0.005 |
| Low plus High RH | 478 | 113 (23.6) | 1.55 (1.19,2.01) | 0.001 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-6. Analysis of Other Neurological Disorders (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,188 | | |
| Background RH | 372 | 1.21 (0.85,1.73) | 0.281 |
| Low RH | 235 | 1.31 (0.90,1.89) | 0.161 |
| High RH | 235 | 1.23 (0.85,1.77) | 0.271 |
| Low plus High RH | 470 | 1.27 (0.95,1.69) | 0.106 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|---------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Yes | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 285 | 45 (15.8) | 1.13 (1.01,1.26) | 0.038 |
| Medium | 286 | 54 (18.9) | | |
| High | 284 | 73 (25.7) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 842 | 0.97 (0.84,1.11) | | 0.625 |

^a Relative risk for a twofold increase in 1987 dioxin.

The Model 3 unadjusted analysis displayed significant differences between Ranch Hands in each of the low, high, and low plus high dioxin categories and Comparisons (Table 11-6(e): Est. RR=1.48, p=0.023; Est. RR=1.62, p=0.005; and Est. RR=1.55, p=0.001, respectively). Each result became nonsignificant after adjustment for covariates (Table 11-6(f): p>0.10 for each adjusted result). The Model 3 contrast of Ranch Hands in the background dioxin category with Comparisons was nonsignificant in both the unadjusted and adjusted analysis (Table 11-6(g,h): p>0.28 for the unadjusted and adjusted analyses).

A significant positive association between other neurological disorders and the 1987 dioxin levels was found in the Model 4 unadjusted analysis (Table 11-6(g): Est. RR=1.13, p=0.038). After adjustment for covariates, the association became nonsignificant (Table 11-6(h): p=0.625).

11.2.2.2 Physical Examination Variables – Cranial Nerve Function

11.2.2.2.1 Smell

A marginally significant difference was found between Ranch Hand and Comparison enlisted flyers from the Model 1 unadjusted analysis of an abnormal sense of smell (Table 11-7(a): Est. RR=7.70, p=0.060). After adjustment for covariates, the result was nonsignificant (Table 11-7(b): p=0.148). All other Model 1 contrasts, as well as all other results from Models 2 through 4, were nonsignificant (Table 11-7(a–h): p>0.12 for each remaining analysis).

Table 11-7. Analysis of Smell

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|---------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 862 | 20 (2.3) | 1.54 (0.81,2.89) | 0.186 |
| | <i>Comparison</i> | 1,247 | 19 (1.5) | | |
| Officer | Ranch Hand | 337 | 5 (1.5) | 0.73 (0.25,2.14) | 0.562 |
| | Comparison | 492 | 10 (2.0) | | |
| Enlisted Flyer | Ranch Hand | 151 | 6 (4.0) | 7.70 (0.92,64.65) | 0.060 |
| | Comparison | 187 | 1 (0.5) | | |
| Enlisted Groundcrew | Ranch Hand | 374 | 9 (2.4) | 1.73 (0.66,4.51) | 0.266 |
| | Comparison | 568 | 8 (1.4) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|---------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | 1.20 (0.60,2.36) | 0.609 |
| Officer | 0.53 (0.16,1.71) | 0.286 |
| Enlisted Flyer | 5.12 (0.56,46.70) | 0.148 |
| Enlisted Groundcrew | 1.57 (0.58,4.27) | 0.376 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 159 | 5 (3.1) | 0.94 (0.58,1.51) | 0.782 |
| Medium | 162 | 2 (1.2) | | |
| High | 156 | 4 (2.6) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-7. Analysis of Smell (Continued)

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|----------------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 469 | 0.83 (0.46,1.50) | 0.534 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with an abnormal sense of smell.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,209 | 18 (1.5) | | |
| Background RH | 378 | 8 (2.1) | 1.42 (0.61,3.31) | 0.420 |
| Low RH | 238 | 7 (2.9) | 2.01 (0.83,4.86) | 0.122 |
| High RH | 239 | 4 (1.7) | 1.14 (0.38,3.40) | 0.821 |
| Low plus High RH | 477 | 11 (2.3) | 1.51 (0.69,3.29) | 0.300 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,191 | | |
| Background RH | 373 | 1.04 (0.40,2.73) | 0.929 |
| Low RH | 234 | 1.57 (0.61,4.06) | 0.353 |
| High RH | 235 | 0.82 (0.23,2.92) | 0.758 |
| Low plus High RH | 469 | 1.13 (0.48,2.68) | 0.777 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-7. Analysis of Smell (Continued)

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|----------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 285 | 7 (2.5) | 0.89 (0.65,1.23) | 0.481 |
| Medium | 286 | 6 (2.1) | | |
| High | 284 | 6 (2.1) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 842 | 0.83 (0.56,1.22) | | 0.333 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race because of the sparse number of Ranch Hands with an abnormal sense of smell.

11.2.2.2.2 Visual Fields

All results from the analysis of visual fields from Models 1, 3, and 4 were nonsignificant (Table 11-8(a,b,e-h): $p > 0.38$ for each analysis). A significant positive association between visual fields and initial dioxin was found in both the unadjusted and adjusted Model 2 analyses (Table 11-8(c,d): Est. RR=3.93, $p=0.040$; and Adj. RR=4.37, $p=0.049$, respectively). One Ranch Hand in the high initial dioxin category had abnormal visual fields.

Table 11-8. Analysis of Visual Fields

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|--------------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 866 | 2 (0.2) | 0.57 (0.11,2.97) | 0.493 |
| | <i>Comparison</i> | 1,245 | 5 (0.4) | | |
| Officer | Ranch Hand | 340 | 0 (0.0) | -- | 0.999 ^a |
| | Comparison | 492 | 1 (0.2) | | |
| Enlisted Flyer | Ranch Hand | 151 | 1 (0.7) | 0.61 (0.06,6.83) | 0.691 |
| | Comparison | 186 | 2 (1.1) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 1 (0.3) | 0.76 (0.07,8.36) | 0.819 |
| | Comparison | 567 | 2 (0.4) | | |

^a P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal visual fields.

--: Results not presented because of the sparse number of participants with abnormal visual fields.

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|---------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | 0.49 (0.09,2.64) | 0.387 |
| Officer | -- | -- |
| Enlisted Flyer | 0.48 (0.04,5.78) | 0.566 |
| Enlisted Groundcrew | 0.70 (0.06,8.00) | 0.778 |

--: Results not presented because of the sparse number of participants with abnormal visual fields.

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 160 | 0 (0.0) | 3.93 (0.93,16.64) | 0.040 |
| Medium | 162 | 0 (0.0) | | |
| High | 157 | 1 (0.6) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-8. Analysis of Visual Fields (Continued)

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|---|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 476 | 4.37 (0.84,22.64) | 0.049 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with abnormal visual fields.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|------------------------|--|--------------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) ^{ab} | p-Value |
| Comparison | 1,207 | 5 (0.4) | | |
| Background RH | 380 | 1 (0.3) | 0.70 (0.08,6.09) | 0.746 |
| Low RH | 239 | 0 (0.0) | -- | 0.694 ^c |
| High RH | 240 | 1 (0.4) | 0.92 (0.11,8.03) | 0.940 |
| Low plus High RH | 479 | 1 (0.2) | -- | 0.853 ^c |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

^c P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal visual fields.

--: Results not presented because of the sparse number of participants with abnormal visual fields.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|-------|---|---------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| Comparison | 1,189 | | |
| Background RH | 375 | 0.86 (0.10,7.83) | 0.897 |
| Low RH | 235 | -- | -- |
| High RH | 236 | 0.57 (0.06,5.52) | 0.629 |
| Low plus High RH | 471 | -- | -- |

^a Relative risk and confidence interval relative to Comparisons.

--: Results not presented because of the sparse number of participants with abnormal visual fields.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-8. Analysis of Visual Fields (Continued)

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|----------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 1 (0.4) | 1.43 (0.62,3.31) | 0.421 |
| Medium | 287 | 0 (0.0) | | |
| High | 285 | 1 (0.4) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 853 | 1.40 (0.58,3.38) | | 0.456 |

^a Relative risk for a twofold increase in 1987 dioxin

Note: Results are not adjusted for race, occupation, insecticide exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with abnormal visual fields.

11.2.2.2.3 Light Reaction

More Comparisons than Ranch Hands had an abnormal light reaction, and the unadjusted and adjusted Model 1 analyses combining all occupations were significant (Table 11-9(a,b): Est. RR=0.12, p=0.007 for the unadjusted analysis; and Adj. RR=0.13, p=0.010 for the adjusted analysis). Results were nonsignificant when examined separately for each occupation in both the unadjusted and adjusted analyses (Table 11-9(a,b): p>0.17 for each remaining Model 1 contrast).

Table 11-9. Analysis of Light Reaction

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|--------------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 861 | 1 (0.1) | 0.12 (0.02,0.92) | 0.007 |
| | <i>Comparison</i> | 1,247 | 12 (1.0) | | |
| Officer | Ranch Hand | 336 | 0 (0.0) | -- | 0.399 ^a |
| | Comparison | 493 | 3 (0.6) | | |
| Enlisted Flyer | Ranch Hand | 151 | 1 (0.7) | 0.31 (0.03,2.76) | 0.291 |
| | Comparison | 187 | 4 (2.1) | | |
| Enlisted Groundcrew | Ranch Hand | 374 | 0 (0.0) | -- | 0.173 ^a |
| | Comparison | 567 | 5 (0.9) | | |

^a P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal light reaction.

--: Results not presented because of the sparse number of participants with an abnormal light reaction.

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|---------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | 0.13 (0.02,0.98) | 0.010 |
| Officer | -- | -- |
| Enlisted Flyer | 0.36 (0.04,3.38) | 0.371 |
| Enlisted Groundcrew | -- | -- |

--: Results not presented because of the sparse number of participants with an abnormal light reaction.

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | | |
|---|-----|---------------------|--|--|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) | | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) | | p-Value |
| Low | 160 | 0 (0.0) | -- | | -- |
| Medium | 162 | 0 (0.0) | | | |
| High | 156 | 0 (0.0) | | | |

--: Results not presented because of the sparse number of participants with an abnormal light reaction.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|-----------------------------------|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) | p-Value |
| -- | -- | -- |

--: Results not presented because of the sparse number of participants with an abnormal light reaction.

Table 11-9. Analysis of Light Reaction (Continued)

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|--------------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,209 | 11 (0.9) | | |
| Background RH | 376 | 1 (0.3) | 0.30 (0.04,2.35) | 0.252 |
| Low RH | 239 | 0 (0.0) | -- | 0.283 ^c |
| High RH | 239 | 0 (0.0) | -- | 0.283 ^c |
| Low plus High RH | 478 | 0 (0.0) | -- | 0.079 ^c |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

^c P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal light reaction.

--: Results not presented because of the sparse number of participants with an abnormal light reaction.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,191 | | |
| Background RH | 371 | 0.38 (0.05,3.03) | 0.359 |
| Low RH | 235 | -- | -- |
| High RH | 235 | -- | -- |
| Low plus High RH | 470 | -- | -- |

^a Relative risk and confidence interval relative to Comparisons.

--: Results not presented because of the sparse number of participants with an abnormal light reaction.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 284 | 0 (0.0) | 0.77 (0.18,3.29) | 0.715 |
| Medium | 286 | 1 (0.4) | | |
| High | 284 | 0 (0.0) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-9. Analysis of Light Reaction (Continued)

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 848 | 0.75 (0.18,3.12) | 0.681 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of participants with an abnormal light reaction.

The Model 2 analysis of light reaction was not possible because of the absence of any Ranch Hands with an abnormal light reaction and an initial dioxin estimate.

The unadjusted Model 3 analysis displayed a marginally significant difference between Ranch Hands in the low plus high dioxin category and Comparisons (Table 11-9(e): $p=0.079$). The percentage of participants with an abnormal light reaction was 0.0 percent for Ranch Hands in the low plus high category and 0.9 percent for Comparisons. All other Model 3 contrasts examined, as well as the Model 4 analysis results, were nonsignificant (Table 11-9(e-h): $p>0.25$ for each remaining Model 3 contrast and Model 4 analysis).

11.2.2.2.4 Ocular Movement

All results from the analyses of ocular movement from Models 1 through 4 were nonsignificant (Table 11-10(a-h): $p>0.15$ for each analysis).

Table 11-10. Analysis of Ocular Movement

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|--------------------------------|--|----------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>866</i> | <i>14 (1.6)</i> | <i>1.19 (0.58,2.43)</i> | <i>0.632</i> |
| | <i>Comparison</i> | <i>1,249</i> | <i>17 (1.4)</i> | | |
| Officer | Ranch Hand | 340 | 2 (0.6) | 0.58 (0.11,2.99) | 0.513 |
| | Comparison | 493 | 5 (1.0) | | |
| Enlisted Flyer | Ranch Hand | 151 | 3 (2.0) | 1.87 (0.31,11.37) | 0.494 |
| | Comparison | 187 | 2 (1.1) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 9 (2.4) | 1.37 (0.55,3.42) | 0.493 |
| | Comparison | 569 | 10 (1.8) | | |

Table 11-10. Analysis of Ocular Movement (Continued)

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.17 (0.56,2.42)</i> | <i>0.675</i> |
| Officer | 0.56 (0.11,2.90) | 0.485 |
| Enlisted Flyer | 1.76 (0.29,10.81) | 0.543 |
| Enlisted Groundcrew | 1.37 (0.54,3.45) | 0.508 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|----------|--------------------------------|--|----------------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (Initial Dioxin)^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^b | p-Value |
| Low | 160 | 4 (2.5) | 0.77 (0.44,1.32) | 0.315 |
| Medium | 162 | 4 (2.5) | | |
| High | 157 | 2 (1.3) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | | |
|--|--|--|----------------|
| Analysis Results for Log₂ (Initial Dioxin) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 471 | 0.74 (0.40,1.36) | | 0.318 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race and insecticide exposure because of the sparse number of participants with an abnormal ocular movement.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,211 | 14 (1.2) | | |
| Background RH | 380 | 4 (1.1) | 0.93 (0.30,2.85) | 0.896 |
| Low RH | 239 | 5 (2.1) | 1.82 (0.65,5.10) | 0.256 |
| High RH | 240 | 5 (2.1) | 1.79 (0.63,5.04) | 0.271 |
| Low plus High RH | 479 | 10 (2.1) | 1.80 (0.79,4.10) | 0.159 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-10. Analysis of Ocular Movement (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,193 | | |
| Background RH | 375 | 1.18 (0.37,3.73) | 0.781 |
| Low RH | 235 | 1.76 (0.61,5.07) | 0.291 |
| High RH | 236 | 1.32 (0.45,3.83) | 0.614 |
| Low plus High RH | 471 | 1.52 (0.65,3.55) | 0.328 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 3 (1.1) | 1.09 (0.77,1.54) | 0.643 |
| Medium | 287 | 5 (1.7) | | |
| High | 285 | 6 (2.1) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 846 | 0.91 (0.63,1.32) | | 0.614 |

^a Relative risk for a twofold increase in 1987 dioxin.

11.2.2.2.5 Facial Sensation

All analyses of facial sensation in Models 1 through 4 were nonsignificant (Table 11-11(a–h): p>0.45 for each analysis).

Table 11-11. Analysis of Facial Sensation

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|--------------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 865 | 2 (0.2) | <i>1.44 (0.20,10.27)</i> | <i>0.714</i> |
| | <i>Comparison</i> | 1,248 | 2 (0.2) | | |
| Officer | Ranch Hand | 339 | 1 (0.3) | 1.46 (0.09,23.35) | 0.791 |
| | Comparison | 493 | 1 (0.2) | | |
| Enlisted Flyer | Ranch Hand | 151 | 0 (0.0) | -- | 0.999 ^a |
| | Comparison | 187 | 1 (0.5) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 1 (0.3) | -- | 0.834 ^a |
| | Comparison | 568 | 0 (0.0) | | |

^aP-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal facial sensation.

--: Results not presented because of the sparse number of participants with an abnormal facial sensation.

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|--------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.38 (0.19,9.87)</i> | <i>0.750</i> |
| Officer | 1.45 (0.09,23.48) | 0.792 |
| Enlisted Flyer | -- | -- |
| Enlisted Groundcrew | -- | -- |

--: Results not presented because of the sparse number of participants with an abnormal facial sensation.

Note: Results are not adjusted for race, insecticide exposure, and diabetic class because of the sparse number of participants with an abnormal facial sensation.

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | | |
|---|-----|---------------------|---|--|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | | p-Value |
| Low | 160 | 1 (0.6) | 0.45 (0.04,5.19) | | 0.455 |
| Medium | 162 | 0 (0.0) | | | |
| High | 157 | 0 (0.0) | | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-11. Analysis of Facial Sensation (Continued)

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|----------------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 476 | 0.55 (0.06,5.38) | 0.553 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal facial sensation.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|--------------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,210 | 2 (0.2) | | |
| Background RH | 379 | 1 (0.3) | 1.77 (0.16,19.96) | 0.646 |
| Low RH | 239 | 1 (0.4) | 2.46 (0.22,27.39) | 0.463 |
| High RH | 240 | 0 (0.0) | -- | 0.999 ^c |
| Low plus High RH | 479 | 1 (0.2) | -- | 0.999 ^c |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

^c P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal facial sensation.

--: Results not presented because of the sparse number of participants with an abnormal facial sensation.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-11. Analysis of Facial Sensation (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,209 | | |
| Background RH | 376 | 1.70 (0.14,19.96) | 0.672 |
| Low RH | 238 | 2.04 (0.18,23.31) | 0.564 |
| High RH | 238 | -- | -- |
| Low plus High RH | 476 | -- | -- |

^a Relative risk and confidence interval relative to Comparisons.

--: Results not presented because of the sparse number of participants with an abnormal facial sensation.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for race, insecticide exposure, and diabetic class because of the sparse number of participants with an abnormal facial sensation.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | |
|--|----------|--------------------------------|---|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a |
| Low | 286 | 1 (0.4) | 0.75 (0.27,2.11) |
| Medium | 287 | 1 (0.4) | |
| High | 285 | 0 (0.0) | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 852 | 0.79 (0.23,2.66) | | 0.694 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal facial sensation.

11.2.2.2.6 Corneal Reflex

Statistical analysis of corneal reflex was not performed because of the absence of abnormalities among Ranch Hands. A corneal reflex abnormality was noted in one Black enlisted groundcrew Comparison.

11.2.2.2.7 *Jaw Clench*

Each result obtained from the analyses of jaw clench conducted from Models 1 through 4 was nonsignificant (Table 11-12(a-h): $p > 0.32$ for each analysis).

Table 11-12. Analysis of Jaw Clench

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|--------------------------------|--|--------------------------|
| Occupational Category | Group | n | Number (%) Deviated | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>866</i> | <i>2 (0.2)</i> | -- | <i>0.327^a</i> |
| | <i>Comparison</i> | <i>1,249</i> | <i>0 (0.0)</i> | | |
| Officer | Ranch Hand | 340 | 2 (0.6) | -- | 0.325 ^a |
| | Comparison | 493 | 0 (0.0) | | |
| Enlisted Flyer | Ranch Hand | 151 | 0 (0.0) | -- | -- |
| | Comparison | 187 | 0 (0.0) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 0 (0.0) | -- | -- |
| | Comparison | 569 | 0 (0.0) | | |

^a P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated jaw clench.

--: Results not presented because of the sparse number of participants with a deviated jaw clench.

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | -- | -- |
| Officer | -- | -- |
| Enlisted Flyer | -- | -- |
| Enlisted Groundcrew | -- | -- |

--: Results not presented because of the sparse number of participants with a deviated jaw clench.

Table 11-12. Analysis of Jaw Clench (Continued)

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|----------|----------------------------|--|----------------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (Initial Dioxin)^a | |
| Initial Dioxin | n | Number (%) Deviated | Estimated Relative Risk (95% C.I.)^b | p-Value |
| Low | 160 | 0 (0.0) | 0.59 (0.09,3.87) | 0.539 |
| Medium | 162 | 1 (0.6) | | |
| High | 157 | 0 (0.0) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 476 | 0.59 (0.08,4.24) | 0.562 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with a deviated jaw clench.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|----------------------------|--------------------------------------|--------------------|
| Dioxin Category | n | Number (%) Deviated | Est. Relative Risk (95% C.I.) | p-Value |
| Comparison | 1,211 | 0 (0.0) | | |
| Background RH | 380 | 1 (0.3) | -- | 0.540 ^a |
| Low RH | 239 | 1 (0.4) | -- | 0.366 ^a |
| High RH | 240 | 0 (0.0) | -- | -- |
| Low plus High RH | 479 | 1 (0.2) | -- | 0.631 ^a |

^a P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated jaw clench.

--: Results not presented because of the sparse number of participants with a deviated jaw clench.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-12. Analysis of Jaw Clench (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.) | p-Value |
| Comparison | -- | | |
| Background RH | -- | -- | -- |
| Low RH | -- | -- | -- |
| High RH | -- | -- | -- |
| Low plus High RH | -- | -- | -- |

--: Results not presented because of the sparse number of participants with a deviated jaw clench.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin \leq 10 ppt.

Background (Ranch Hand): 1987 Dioxin \leq 10 ppt.

Low (Ranch Hand): 1987 Dioxin $>$ 10 ppt, 10 ppt $<$ Initial Dioxin \leq 94 ppt.

High (Ranch Hand): 1987 Dioxin $>$ 10 ppt, Initial Dioxin $>$ 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | |
|--|----------|--------------------------------|---|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) |
| 1987 Dioxin | n | Number (%) Deviated | Estimated Relative Risk (95% C.I.)^a |
| Low | 287 | 0 (0.0) | 0.92 (0.35,2.44) |
| Medium | 287 | 2 (0.7) | 0.864 |
| High | 285 | 0 (0.0) | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = \leq 7.9 ppt; Medium = $>$ 7.9–19.6 ppt; High = $>$ 19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 853 | 1.02 (0.34,3.08) | | 0.969 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, and diabetic class because of the sparse number of Ranch Hands with a deviated jaw clench.

11.2.2.2.8 Smile

Each result obtained from the analyses of smile conducted from Models 1 through 4 was nonsignificant (Table 11-13(a–h): $p \geq 0.11$ for each analysis).

Table 11-13. Analysis of Smile

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|--------------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 866 | 7 (0.8) | 2.54 (0.74,8.69) | 0.129 |
| | <i>Comparison</i> | 1,249 | 4 (0.3) | | |
| Officer | Ranch Hand | 340 | 1 (0.3) | 0.72 (0.07,8.02) | 0.793 |
| | Comparison | 493 | 2 (0.4) | | |
| Enlisted Flyer | Ranch Hand | 151 | 1 (0.7) | -- | 0.915 ^a |
| | Comparison | 187 | 0 (0.0) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 5 (1.3) | 3.83 (0.74,19.85) | 0.110 |
| | Comparison | 569 | 2 (0.4) | | |

^aP-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal smile.

--: Results not presented because of the sparse number of participants with an abnormal smile.

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|---------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | 2.45 (0.71,8.50) | 0.149 |
| Officer | 0.71 (0.06,7.91) | 0.777 |
| Enlisted Flyer | -- | -- |
| Enlisted Groundcrew | 3.62 (0.69,19.00) | 0.128 |

--: Results not presented because of the sparse number of participants with an abnormal smile.

Note: Results are not adjusted for diabetic class because of the sparse number of participants with an abnormal smile.

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | | |
|---|-----|---------------------|---|--|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | | p-Value |
| Low | 160 | 1 (0.6) | 1.38 (0.70,2.70) | | 0.372 |
| Medium | 162 | 1 (0.6) | | | |
| High | 157 | 2 (1.3) | | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-13. Analysis of Smile (Continued)

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | | |
|---|---|--|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | | p-Value |
| 476 | 1.50 (0.75,3.02) | | 0.274 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal smile.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|------------------------|--|---------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) ^{ab} | p-Value |
| Comparison | 1,211 | 4 (0.3) | | |
| Background RH | 380 | 3 (0.8) | 2.61 (0.57,11.87) | 0.214 |
| Low RH | 239 | 2 (0.8) | 2.49 (0.45,13.68) | 0.295 |
| High RH | 240 | 2 (0.8) | 2.35 (0.42,13.05) | 0.328 |
| Low plus High RH | 479 | 4 (0.8) | 2.42 (0.60,9.77) | 0.215 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|-------|---|---------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| Comparison | 1,210 | | |
| Background RH | 377 | 3.14 (0.65,15.08) | 0.152 |
| Low RH | 238 | 2.38 (0.42,13.43) | 0.326 |
| High RH | 238 | 1.80 (0.30,10.67) | 0.517 |
| Low plus High RH | 476 | 2.07 (0.50,8.57) | 0.315 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for diabetic class because of the sparse number of Ranch Hands with an abnormal smile.

Table 11-13. Analysis of Smile (Continued)

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|-----|---------------------|---|---------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^a | p-Value |
| Low | 287 | 2 (0.7) | 1.16 (0.72,1.88) | 0.541 |
| Medium | 287 | 2 (0.7) | | |
| High | 285 | 3 (1.1) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|--|--|---------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 853 | 0.99 (0.59,1.65) | 0.972 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for diabetic class because of the sparse number of Ranch Hands with an abnormal smile.

11.2.2.2.9 Palpebral Fissure

All results from the analyses of palpebral fissure from Models 1 through 4 were nonsignificant (Table 11-14(a–h): p>0.32 for each analysis).

Table 11-14. Analysis of Palpebral Fissure

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|---------------------|-------------------------------|--------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>866</i> | <i>7 (0.8)</i> | <i>0.84 (0.33,2.14)</i> | <i>0.713</i> |
| | <i>Comparison</i> | <i>1,249</i> | <i>12 (1.0)</i> | | |
| Officer | Ranch Hand | 340 | 2 (0.6) | 0.58 (0.11,2.99) | 0.513 |
| | Comparison | 493 | 5 (1.0) | | |
| Enlisted Flyer | Ranch Hand | 151 | 1 (0.7) | 1.24 (0.08,19.99) | 0.879 |
| | Comparison | 187 | 1 (0.5) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 4 (1.1) | 1.01 (0.28,3.61) | 0.986 |
| | Comparison | 569 | 6 (1.1) | | |

Table 11-14. Analysis of Palpebral Fissure (Continued)

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>0.71 (0.26,1.94)</i> | <i>0.502</i> |
| Officer | 0.63 (0.12,3.31) | 0.582 |
| Enlisted Flyer | 0.87 (0.05,14.32) | 0.921 |
| Enlisted Groundcrew | 0.90 (0.25,3.27) | 0.876 |

Note: Results are not adjusted for diabetic class because of the sparse number of participants with an abnormal palpebral fissure. Results for analyses stratified by occupation also are not adjusted for lifetime alcohol history because of the sparse number of participants with an abnormal palpebral fissure.

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|----------|----------------------------|--|----------------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (Initial Dioxin)^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^b | p-Value |
| Low | 160 | 2 (1.3) | 1.15 (0.50,2.64) | 0.750 |
| Medium | 162 | 0 (0.0) | | |
| High | 157 | 1 (0.6) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 476 | 1.25 (0.54,2.93) | 0.613 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal palpebral fissure.

Table 11-14. Analysis of Palpebral Fissure (Continued)

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,211 | 12 (1.0) | | |
| Background RH | 380 | 4 (1.1) | 1.20 (0.38,3.78) | 0.759 |
| Low RH | 239 | 2 (0.8) | 0.81 (0.18,3.66) | 0.785 |
| High RH | 240 | 1 (0.4) | 0.37 (0.05,2.91) | 0.347 |
| Low plus High RH | 479 | 3 (0.6) | 0.55 (0.14,2.10) | 0.381 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | | |
|---|----------|--|-------------|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| Comparison | 1,210 | | | |
| Background RH | 377 | 0.96 | (0.26,3.60) | 0.955 |
| Low RH | 238 | 0.79 | (0.17,3.64) | 0.761 |
| High RH | 238 | 0.35 | (0.04,2.84) | 0.324 |
| Low plus High RH | 476 | 0.52 | (0.13,2.05) | 0.352 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for diabetic class because of the sparse number of participants with an abnormal palpebral fissure.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | |
| | | | | p-Value |
| Low | 287 | 2 (0.7) | 1.05 (0.64,1.73) | 0.840 |
| Medium | 287 | 4 (1.4) | | |
| High | 285 | 1 (0.4) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-14. Analysis of Palpebral Fissure (Continued)

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 853 | 1.17 (0.65,2.12) | 0.598 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, and diabetic class because of the sparse number of participants with an abnormal palpebral fissure.

11.2.2.2.10 Balance

All results from the analyses of balance from Models 1 through 4 were nonsignificant (Table 11-15(a–h): p>0.12 for each analysis).

Table 11-15. Analysis of Balance

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|--------------------------------|--|--------------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>866</i> | <i>7 (0.8)</i> | <i>1.44 (0.50,4.13)</i> | <i>0.494</i> |
| | <i>Comparison</i> | <i>1,248</i> | <i>7 (0.6)</i> | | |
| Officer | Ranch Hand | 340 | 5 (1.5) | 3.66 (0.71,19.00) | 0.122 |
| | Comparison | 493 | 2 (0.4) | | |
| Enlisted Flyer | Ranch Hand | 151 | 0 (0.0) | -- | 0.999 ^a |
| | Comparison | 186 | 1 (0.5) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 2 (0.5) | 0.76 (0.14,4.16) | 0.749 |
| | Comparison | 569 | 4 (0.7) | | |

^a P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal balance.

--: Results not presented because of the sparse number of participants with abnormal balance.

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.38 (0.47,4.03)</i> | <i>0.553</i> |
| Officer | 3.37 (0.64,17.73) | 0.151 |
| Enlisted Flyer | -- | -- |
| Enlisted Groundcrew | 0.73 (0.13,4.07) | 0.719 |

--: Results not presented because of the sparse number of participants with abnormal balance.

Table 11-15. Analysis of Balance (Continued)

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 160 | 0 (0.0) | 1.27 (0.48,3.35) | 0.638 |
| Medium | 162 | 1 (0.6) | | |
| High | 157 | 1 (0.6) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 476 | 1.65 (0.61,4.45) | 0.350 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, and diabetic class because of the sparse number of Ranch Hands with abnormal balance.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|---------------------|---|---------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) ^{ab} | p-Value |
| Comparison | 1,210 | 7 (0.6) | | |
| Background RH | 380 | 5 (1.3) | 2.52 (0.78,8.10) | 0.121 |
| Low RH | 239 | 1 (0.4) | 0.70 (0.09,5.74) | 0.741 |
| High RH | 240 | 1 (0.4) | 0.66 (0.08,5.43) | 0.699 |
| Low plus High RH | 479 | 2 (0.4) | 0.68 (0.14,3.31) | 0.633 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-15. Analysis of Balance (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,192 | | |
| Background RH | 375 | 2.54 (0.74,8.72) | 0.138 |
| Low RH | 235 | 0.63 (0.08,5.24) | 0.667 |
| High RH | 236 | 0.63 (0.07,5.49) | 0.672 |
| Low plus High RH | 471 | 0.63 (0.13,3.11) | 0.567 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 3 (1.1) | 0.88 (0.52,1.50) | 0.642 |
| Medium | 287 | 2 (0.7) | | |
| High | 285 | 2 (0.7) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 846 | 0.95 (0.52,1.73) | | 0.860 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race and occupation because of the sparse number of participants with abnormal balance.

11.2.2.2.11 Gag Reflex

Because of the absence of gag reflex abnormalities among Ranch Hands, statistical analysis was not performed. One gag reflex abnormality was present for a non-Black enlisted flyer Comparison.

11.2.2.2.12 *Speech*

The Model 2 adjusted analysis of speech revealed a marginally significant inverse association between initial dioxin and speech (Table 11-16(d): Adj. RR=0.19, p=0.078). All other analysis results from Models 1 through 4 were nonsignificant (Table 11-16(a–c,e–h): p>0.14 for each remaining analysis).

Table 11-16. Analysis of Speech

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|--------------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 866 | 4 (0.5) | 0.57 (0.18,1.84) | 0.334 |
| | <i>Comparison</i> | 1,249 | 10 (0.8) | | |
| Officer | Ranch Hand | 340 | 1 (0.3) | 0.72 (0.07,8.02) | 0.793 |
| | Comparison | 493 | 2 (0.4) | | |
| Enlisted Flyer | Ranch Hand | 151 | 0 (0.0) | -- | 0.999 ^a |
| | Comparison | 187 | 1 (0.5) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 3 (0.8) | 0.65 (0.17,2.52) | 0.531 |
| | Comparison | 569 | 7 (1.2) | | |

^a P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal speech.

--: Results not presented because of the sparse number of participants with abnormal speech.

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|---------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | 0.60 (0.18,1.97) | 0.388 |
| Officer | 0.76 (0.07,8.59) | 0.828 |
| Enlisted Flyer | -- | -- |
| Enlisted Groundcrew | 0.66 (0.16,2.63) | 0.551 |

--: Results not presented because of the sparse number of participants with abnormal speech.

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 160 | 2 (1.3) | 0.29 (0.03,2.42) | 0.143 |
| Medium | 162 | 0 (0.0) | | |
| High | 157 | 0 (0.0) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-16. Analysis of Speech (Continued)

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|---|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 476 | 0.19 (0.02,2.32) | 0.078 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation and diabetic class because of the sparse number of Ranch Hands with abnormal speech.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|------------------------|--|--------------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) ^{ab} | p-Value |
| Comparison | 1,211 | 9 (0.7) | | |
| Background RH | 380 | 2 (0.5) | 0.81 (0.17,3.83) | 0.793 |
| Low RH | 239 | 2 (0.8) | 1.07 (0.23,5.02) | 0.929 |
| High RH | 240 | 0 (0.0) | -- | 0.374 ^c |
| Low plus High RH | 479 | 2 (0.4) | -- | 0.678 ^c |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

^c P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal speech.

--: Results not presented because of the sparse number of participants with abnormal speech.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|-------|---|---------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| Comparison | 1,193 | | |
| Background RH | 375 | 1.09 (0.22,5.46) | 0.919 |
| Low RH | 235 | 1.38 (0.28,6.71) | 0.688 |
| High RH | 236 | -- | -- |
| Low plus High RH | 471 | -- | -- |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-16. Analysis of Speech (Continued)

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|-----|---------------------|---|---------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^a | p-Value |
| Low | 287 | 2 (0.7) | 0.77 (0.37,1.59) | 0.462 |
| Medium | 287 | 2 (0.7) | | |
| High | 285 | 0 (0.0) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|--|--|--|---------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | | p-Value |
| 853 | 0.73 (0.36,1.47) | | 0.370 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation and diabetic class because of the sparse number of Ranch Hands with abnormal speech.

11.2.2.2.13 Tongue Position Relative to Midline

Each result obtained from the Model 1 through 4 analyses of tongue position relative to midline was nonsignificant (Table 11-17(a–h): p>0.32 for each analysis).

Table 11-17. Analysis of Tongue Position Relative to Midline

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|---------------------|-------------------------------|--------------------------|
| Occupational Category | Group | n | Number (%) Deviated | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>866</i> | <i>2 (0.2)</i> | -- | <i>0.327^a</i> |
| | <i>Comparison</i> | <i>1,249</i> | <i>0 (0.0)</i> | | |
| Officer | Ranch Hand | 340 | 2 (0.6) | -- | 0.325 ^a |
| | Comparison | 493 | 0 (0.0) | | |
| Enlisted Flyer | Ranch Hand | 151 | 0 (0.0) | -- | -- |
| | Comparison | 187 | 0 (0.0) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 0 (0.0) | -- | -- |
| | Comparison | 569 | 0 (0.0) | | |

^aP-value determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated tongue position relative to midline.

--: Results not presented because of the sparse number of participants with a deviated tongue position relative to midline.

Table 11-17. Analysis of Tongue Position Relative to Midline (Continued)

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | -- | -- |
| Officer | -- | -- |
| Enlisted Flyer | -- | -- |
| Enlisted Groundcrew | -- | -- |

--: Results not presented because of the sparse number of participants with a deviated tongue position relative to midline.

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|----------|--------------------------------|--|----------------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (Initial Dioxin)^a | |
| Initial Dioxin | n | Number (%) Deviated | Estimated Relative Risk (95% C.I.)^b | p-Value |
| Low | 160 | 0 (0.0) | 0.59 (0.09,3.87) | 0.539 |
| Medium | 162 | 1 (0.6) | | |
| High | 157 | 0 (0.0) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 476 | 0.59 (0.08,4.24) | 0.562 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with a deviated tongue position relative to midline.

Table 11-17. Analysis of Tongue Position Relative to Midline (Continued)

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|------------------------|--|--------------------|
| Dioxin Category | n | Number (%) Deviated | Est. Relative Risk (95% C.I.) ^{ab} | p-Value |
| Comparison | 1,211 | 0 (0.0) | | |
| Background RH | 380 | 1 (0.3) | -- | 0.540 ^c |
| Low RH | 239 | 1 (0.4) | -- | 0.366 ^c |
| High RH | 240 | 0 (0.0) | -- | -- |
| Low plus High RH | 479 | 1 (0.2) | -- | 0.631 ^c |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

^c P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated tongue position relative to midline.

--: Results not presented because of the sparse number of participants with a deviated tongue position relative to midline.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----|--------------------------------------|---------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.) | p-Value |
| Comparison | -- | | |
| Background RH | -- | -- | -- |
| Low RH | -- | -- | -- |
| High RH | -- | -- | -- |
| Low plus High RH | -- | -- | -- |

--: Results not presented because of the sparse number of participants with a deviated tongue position relative to midline.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|-----|------------------------|---|---------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Deviated | Estimated Relative Risk (95% C.I.) ^a | p-Value |
| Low | 287 | 0 (0.0) | 0.92 (0.35,2.44) | 0.864 |
| Medium | 287 | 2 (0.7) | | |
| High | 285 | 0 (0.0) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-17. Analysis of Tongue Position Relative to Midline (Continued)

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 853 | 1.02 (0.34,3.08) | 0.969 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, and diabetic class because of the sparse number of Ranch Hands with a deviated tongue position relative to midline.

11.2.2.2.14 Palate and Uvula Movement

Each result obtained from the Model 1 through 4 analyses of the palate and uvula movement was nonsignificant (Table 11-18(a–h): p>0.36 for each analysis).

Table 11-18. Analysis of Palate and Uvula Movement

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|--------------------------------|--|--------------------------|
| Occupational Category | Group | n | Number (%) Deviated | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>866</i> | <i>1 (0.1)</i> | -- | <i>0.854^a</i> |
| | <i>Comparison</i> | <i>1,249</i> | <i>0 (0.0)</i> | | |
| Officer | Ranch Hand | 340 | 1 (0.3) | -- | 0.852 ^a |
| | Comparison | 493 | 0 (0.0) | | |
| Enlisted Flyer | Ranch Hand | 151 | 0 (0.0) | -- | -- |
| | Comparison | 187 | 0 (0.0) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 0 (0.0) | -- | -- |
| | Comparison | 569 | 0 (0.0) | | |

^a P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated palate and uvula movement.

--: Results not presented because of the sparse number of participants with a deviated palate and uvula movement.

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | -- | -- |
| Officer | -- | -- |
| Enlisted Flyer | -- | -- |
| Enlisted Groundcrew | -- | -- |

--: Results not presented because of the sparse number of participants with a deviated palate and uvula movement.

Table 11-18. Analysis of Palate and Uvula Movement (Continued)

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Deviated | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 160 | 0 (0.0) | 0.59 (0.09,3.87) | 0.539 |
| Medium | 162 | 1 (0.6) | | |
| High | 157 | 0 (0.0) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 476 | 0.59 (0.08,4.24) | 0.562 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with a deviated palate and uvula movement.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|---------------------|-------------------------------|--------------------|
| Dioxin Category | n | Number (%) Deviated | Est. Relative Risk (95% C.I.) | p-Value |
| Comparison | 1,211 | 0 (0.0) | | |
| Background RH | 380 | 0 (0.0) | -- | -- |
| Low RH | 239 | 1 (0.4) | -- | 0.366 ^a |
| High RH | 240 | 0 (0.0) | -- | -- |
| Low plus High RH | 479 | 1 (0.2) | -- | 0.631 ^a |

^a P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated palate and uvula movement.

--: Results not presented because of the sparse number of participants with a deviated palate and uvula movement.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-18. Analysis of Palate and Uvula Movement (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.) | p-Value |
| Comparison | -- | | |
| Background RH | -- | -- | -- |
| Low RH | -- | -- | -- |
| High RH | -- | -- | -- |
| Low plus High RH | -- | -- | -- |

--: Results not presented because of the sparse number of participants with a deviated palate and uvula movement.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin \leq 10 ppt.

Background (Ranch Hand): 1987 Dioxin \leq 10 ppt.

Low (Ranch Hand): 1987 Dioxin $>$ 10 ppt, 10 ppt $<$ Initial Dioxin \leq 94 ppt.

High (Ranch Hand): 1987 Dioxin $>$ 10 ppt, Initial Dioxin $>$ 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Deviated | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 0 (0.0) | 1.13 (0.31,4.05) | 0.857 |
| Medium | 287 | 1 (0.4) | | |
| High | 285 | 0 (0.0) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = \leq 7.9 ppt; Medium = $>$ 7.9–19.6 ppt; High = $>$ 19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 853 | 1.19 (0.32,4.46) | | 0.800 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with a deviated palate and uvula movement.

11.2.2.2.15 Cranial Nerve Index

All results from the analyses of cranial nerve index from Models 1 through 4 were nonsignificant (Table 11-19(a–h): $p \geq 0.11$ for each analysis).

Table 11-19. Analysis of Cranial Nerve Index

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|--------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 850 | 56 (6.6) | <i>1.15 (0.80,1.65)</i> | <i>0.452</i> |
| | <i>Comparison</i> | 1,245 | 72 (5.8) | | |
| Officer | Ranch Hand | 329 | 17 (5.2) | 0.98 (0.52,1.83) | 0.941 |
| | Comparison | 492 | 26 (5.3) | | |
| Enlisted Flyer | Ranch Hand | 151 | 13 (8.6) | 1.66 (0.71,3.89) | 0.246 |
| | Comparison | 186 | 10 (5.4) | | |
| Enlisted Groundcrew | Ranch Hand | 370 | 26 (7.0) | 1.11 (0.66,1.88) | 0.683 |
| | Comparison | 567 | 36 (6.4) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|--------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.01 (0.69,1.48)</i> | <i>0.940</i> |
| Officer | 0.88 (0.46,1.68) | 0.694 |
| Enlisted Flyer | 1.23 (0.49,3.08) | 0.656 |
| Enlisted Groundcrew | 1.05 (0.61,1.80) | 0.856 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 157 | 13 (8.3) | 0.86 (0.63,1.17) | 0.331 |
| Medium | 162 | 9 (5.6) | | |
| High | 153 | 8 (5.2) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 464 | 0.75 (0.53,1.08) | 0.110 |

^a Relative risk for a twofold increase in initial dioxin.

Table 11-19. Analysis of Cranial Nerve Index (Continued)

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,207 | 68 (5.6) | | |
| Background RH | 371 | 25 (6.7) | 1.27 (0.79,2.05) | 0.329 |
| Low RH | 236 | 19 (8.1) | 1.45 (0.86,2.47) | 0.166 |
| High RH | 236 | 11 (4.7) | 0.78 (0.41,1.51) | 0.469 |
| Low plus High RH | 472 | 30 (6.4) | 1.07 (0.68,1.69) | 0.776 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,189 | | |
| Background RH | 366 | 1.20 (0.72,2.02) | 0.484 |
| Low RH | 232 | 1.29 (0.74,2.24) | 0.369 |
| High RH | 232 | 0.60 (0.30,1.22) | 0.158 |
| Low plus High RH | 464 | 0.88 (0.54,1.43) | 0.604 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 280 | 18 (6.4) | 0.93 (0.77,1.13) | 0.462 |
| Medium | 282 | 21 (7.5) | | |
| High | 281 | 16 (5.7) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-19. Analysis of Cranial Nerve Index (Continued)

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 830 | 0.88 (0.71,1.10) | 0.254 |

^a Relative risk for a twofold increase in 1987 dioxin.

11.2.2.3 Physical Examination Variables – Musculoskeletal and Vertebral Column Function

11.2.2.3.1 Neck Range of Motion

From the Model 1 unadjusted and adjusted analyses of neck range of motion, differences between Ranch Hands and Comparisons were significant across all occupations and within enlisted flyers (Table 11-20(a,b): Est. RR=1.33, p=0.016, Adj. RR=1.35, p=0.015, respectively, for all occupations combined; Est. RR=2.03, p=0.009; Adj. RR=1.97, p=0.016, respectively, for enlisted flyers). Both contrasts showed more Ranch Hands than Comparisons with a restricted neck range of motion. All other Model 1 contrasts were nonsignificant (Table 11-20(a,b): p>0.12 for each remaining contrast).

Table 11-20. Analysis of Neck Range of Motion

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|----------|--------------------------------|--|----------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 866 | 165 (19.1) | 1.33 (1.06,1.67) | 0.016 |
| | <i>Comparison</i> | 1,249 | 188 (15.1) | | |
| Officer | Ranch Hand | 340 | 70 (20.6) | 1.32 (0.92,1.88) | 0.126 |
| | Comparison | 493 | 81 (16.4) | | |
| Enlisted Flyer | Ranch Hand | 151 | 41 (27.2) | 2.03 (1.19,3.46) | 0.009 |
| | Comparison | 187 | 29 (15.5) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 54 (14.4) | 1.06 (0.73,1.54) | 0.764 |
| | Comparison | 569 | 78 (13.7) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | 1.35 (1.06,1.72) | 0.015 |
| Officer | 1.31 (0.90,1.89) | 0.153 |
| Enlisted Flyer | 1.97 (1.13,3.42) | 0.016 |
| Enlisted Groundcrew | 1.16 (0.78,1.71) | 0.466 |

Table 11-20. Analysis of Neck Range of Motion (Continued)

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|----------|----------------------------|--|----------------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (Initial Dioxin)^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^b | p-Value |
| Low | 160 | 38 (23.8) | 0.85 (0.72,1.02) | 0.069 |
| Medium | 162 | 39 (24.1) | | |
| High | 157 | 26 (16.6) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 471 | 0.91 (0.74,1.13) | 0.411 |

^a Relative risk for a twofold increase in initial dioxin.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|----------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,211 | 180 (14.9) | | |
| Background RH | 380 | 60 (15.8) | 1.16 (0.84,1.60) | 0.366 |
| Low RH | 239 | 56 (23.4) | 1.73 (1.23,2.43) | 0.002 |
| High RH | 240 | 47 (19.6) | 1.31 (0.91,1.87) | 0.142 |
| Low plus High RH | 479 | 103 (21.5) | 1.50 (1.15,1.97) | 0.003 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-20. Analysis of Neck Range of Motion (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,193 | | |
| Background RH | 375 | 1.12 (0.80,1.57) | 0.523 |
| Low RH | 235 | 1.60 (1.12,2.29) | 0.010 |
| High RH | 236 | 1.55 (1.05,2.29) | 0.028 |
| Low plus High RH | 471 | 1.57 (1.18,2.11) | 0.002 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin \leq 10 ppt.

Background (Ranch Hand): 1987 Dioxin \leq 10 ppt.

Low (Ranch Hand): 1987 Dioxin $>$ 10 ppt, 10 ppt $<$ Initial Dioxin \leq 94 ppt.

High (Ranch Hand): 1987 Dioxin $>$ 10 ppt, Initial Dioxin $>$ 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | |
|--|----------|--------------------------------|---|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a |
| Low | 287 | 48 (16.7) | 1.03 (0.92,1.15) |
| Medium | 287 | 60 (20.9) | |
| High | 285 | 55 (19.3) | 0.632 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = \leq 7.9 ppt; Medium = $>$ 7.9–19.6 ppt; High = $>$ 19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 846 | 1.09 (0.94,1.26) | | 0.267 |

^a Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis displayed a marginally significant inverse association between neck range of motion and initial dioxin (Table 11-20(c): Est. RR=0.85, p=0.069). After adjustment for covariates, the association was nonsignificant (Table 11-20(d): p=0.411).

Both the unadjusted and adjusted Model 3 analyses of neck range of motion displayed a significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 11-20(e,f): Est. RR=1.73, p=0.002 and Adj. RR=1.60, p=0.010) and between Ranch Hands in the low plus high dioxin category and Comparisons (Table 11-20(e,f): Est. RR=1.50, p=0.003 and Adj. RR=1.57, p=0.002). In addition, the adjusted contrast between Ranch Hands in the high category and Comparisons was significant (Table 11-20(f): Adj. RR=1.55, p=0.028). All significant contrasts showed more Ranch

Hands than Comparisons with neck range of motion abnormalities. Other Model 3 contrasts, as well as the Model 4 analyses of neck range of motion, were nonsignificant (Table 11-20(e-h): $p > 0.14$ for each remaining analysis).

11.2.2.4 Physical Examination Variables – Peripheral Nerve Status

11.2.2.4.1 Pinprick

A marginally significant difference between Ranch Hands in the high dioxin category and Comparisons was found in the Model 3 unadjusted analysis of pinprick, showing more Ranch Hands than Comparisons with a pinprick abnormality (Table 11-21(e): Est. RR=1.64, $p=0.062$). After adjustment for covariates, the difference was nonsignificant (Table 11-21(f): $p=0.126$). All other analysis results from Models 1 through 4 for pinprick were nonsignificant (Table 11-21(a-h): $p \geq 0.11$ for each remaining analysis).

Table 11-21. Analysis of Pinprick

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|--------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 822 | 57 (6.9) | <i>1.24 (0.86,1.79)</i> | <i>0.244</i> |
| | <i>Comparison</i> | 1,185 | 67 (5.7) | | |
| Officer | Ranch Hand | 322 | 20 (6.2) | 1.35 (0.72,2.51) | 0.350 |
| | Comparison | 469 | 22 (4.7) | | |
| Enlisted Flyer | Ranch Hand | 145 | 19 (13.1) | 1.81 (0.87,3.75) | 0.110 |
| | Comparison | 182 | 14 (7.7) | | |
| Enlisted Groundcrew | Ranch Hand | 355 | 18 (5.1) | 0.87 (0.48,1.57) | 0.638 |
| | Comparison | 534 | 31 (5.8) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|--------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.19 (0.81,1.76)</i> | <i>0.368</i> |
| Officer | 1.28 (0.67,2.43) | 0.451 |
| Enlisted Flyer | 1.81 (0.84,3.89) | 0.131 |
| Enlisted Groundcrew | 0.85 (0.45,1.60) | 0.618 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 152 | 11 (7.2) | 1.10 (0.86,1.41) | 0.460 |
| Medium | 151 | 13 (8.6) | | |
| High | 150 | 12 (8.0) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-21. Analysis of Pinprick (Continued)

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|---|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 445 | 1.29 (0.92,1.81) | 0.134 |

^a Relative risk for a twofold increase in initial dioxin.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|------------------------|--|---------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) ^{ab} | p-Value |
| Comparison | 1,149 | 63 (5.5) | | |
| Background RH | 362 | 19 (5.3) | 1.03 (0.61,1.76) | 0.900 |
| Low RH | 226 | 15 (6.6) | 1.20 (0.67,2.15) | 0.542 |
| High RH | 227 | 21 (9.3) | 1.64 (0.98,2.76) | 0.062 |
| Low plus High RH | 453 | 36 (8.0) | 1.40 (0.91,2.16) | 0.123 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|-------|---|---------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| Comparison | 1,132 | | |
| Background RH | 357 | 1.11 (0.63,1.95) | 0.716 |
| Low RH | 222 | 0.95 (0.51,1.77) | 0.868 |
| High RH | 223 | 1.55 (0.88,2.73) | 0.126 |
| Low plus High RH | 445 | 1.21 (0.77,1.93) | 0.410 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-21. Analysis of Pinprick (Continued)

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|-----|---------------------|---|---------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^a | p-Value |
| Low | 272 | 15 (5.5) | 1.15 (0.96,1.37) | 0.137 |
| Medium | 275 | 16 (5.8) | | |
| High | 268 | 24 (9.0) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|--|--|--|---------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | | p-Value |
| 802 | 1.12 (0.88,1.42) | | 0.345 |

^a Relative risk for a twofold increase in 1987 dioxin.

11.2.2.4.2 Light Touch

All results from the analyses of light touch from Models 1 through 4 were nonsignificant (Table 11-22(a–h): p>0.16 for each analysis).

Table 11-22. Analysis of Light Touch

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|---------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 822 | 38 (4.6) | 1.23 (0.79,1.91) | 0.363 |
| | <i>Comparison</i> | 1,185 | 45 (3.8) | | |
| Officer | Ranch Hand | 322 | 15 (4.7) | 1.71 (0.80,3.65) | 0.163 |
| | Comparison | 469 | 13 (2.8) | | |
| Enlisted Flyer | Ranch Hand | 145 | 12 (8.3) | 1.55 (0.65,3.70) | 0.322 |
| | Comparison | 182 | 10 (5.5) | | |
| Enlisted Groundcrew | Ranch Hand | 355 | 11 (3.1) | 0.74 (0.36,1.55) | 0.432 |
| | Comparison | 534 | 22 (4.1) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|---------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | 1.13 (0.71,1.81) | 0.597 |
| Officer | 1.67 (0.77,3.61) | 0.193 |
| Enlisted Flyer | 1.40 (0.56,3.50) | 0.470 |
| Enlisted Groundcrew | 0.67 (0.31,1.47) | 0.321 |

Table 11-22. Analysis of Light Touch (Continued)

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 152 | 9 (5.9) | 0.92 (0.66,1.28) | 0.616 |
| Medium | 151 | 7 (4.6) | | |
| High | 150 | 7 (4.7) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 445 | 1.01 (0.65,1.59) | 0.956 |

^a Relative risk for a twofold increase in initial dioxin.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|---------------------|---|---------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) ^{ab} | p-Value |
| Comparison | 1,149 | 43 (3.7) | | |
| Background RH | 362 | 13 (3.6) | 1.01 (0.54,1.92) | 0.965 |
| Low RH | 226 | 12 (5.3) | 1.42 (0.74,2.74) | 0.295 |
| High RH | 227 | 11 (4.9) | 1.25 (0.63,2.46) | 0.528 |
| Low plus High RH | 453 | 23 (5.1) | 1.33 (0.79,2.24) | 0.283 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-22. Analysis of Light Touch (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,132 | | |
| Background RH | 357 | 1.07 (0.54,2.10) | 0.852 |
| Low RH | 222 | 1.12 (0.55,2.27) | 0.751 |
| High RH | 223 | 1.09 (0.53,2.26) | 0.808 |
| Low plus High RH | 445 | 1.11 (0.64,1.93) | 0.718 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 272 | 11 (4.0) | 1.02 (0.81,1.28) | 0.865 |
| Medium | 275 | 12 (4.4) | | |
| High | 268 | 13 (4.9) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 802 | 1.01 (0.75,1.36) | | 0.940 |

^a Relative risk for a twofold increase in 1987 dioxin.

11.2.2.4.3 Muscle Status

Both the unadjusted and adjusted Model 1 analyses of muscle status displayed a marginally significant difference between Ranch Hands and Comparisons (Table 11-23(a,b): Est. RR=1.54, p=0.064 and Adj. RR=1.50, p=0.094). The contrast of Ranch Hand and Comparison enlisted groundcrew revealed a marginally significant result in the unadjusted analysis and a significant result in the adjusted analysis (Table 11-23(a,b): Est. RR=2.06, p=0.062 and Adj. RR=2.24, p=0.046). Both contrasts showed more Ranch Hands than Comparisons with a muscle status abnormality. All other Model 1 contrasts, as well as the Model 2 analysis of muscle status, were nonsignificant (Table 11-23(a–d): p>0.23 for each remaining Model 1 contrast and each Model 2 analysis).

Table 11-23. Analysis of Muscle Status

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|--------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 866 | 39 (4.5) | <i>1.54 (0.98,2.44)</i> | <i>0.064</i> |
| | <i>Comparison</i> | 1,248 | 37 (3.0) | | |
| Officer | Ranch Hand | 340 | 13 (3.8) | 1.05 (0.51,2.17) | 0.897 |
| | Comparison | 493 | 18 (3.7) | | |
| Enlisted Flyer | Ranch Hand | 151 | 10 (6.6) | 1.82 (0.68,4.91) | 0.235 |
| | Comparison | 187 | 7 (3.7) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 16 (4.3) | 2.06 (0.97,4.42) | 0.062 |
| | Comparison | 568 | 12 (2.1) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|--------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.50 (0.93,2.40)</i> | <i>0.094</i> |
| Officer | 0.98 (0.47,2.05) | 0.960 |
| Enlisted Flyer | 1.72 (0.63,4.70) | 0.289 |
| Enlisted Groundcrew | 2.24 (1.01,4.93) | 0.046 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 160 | 10 (6.3) | 0.87 (0.62,1.23) | 0.418 |
| Medium | 162 | 9 (5.6) | | |
| High | 157 | 5 (3.2) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 471 | 0.95 (0.64,1.41) | 0.792 |

^a Relative risk for a twofold increase in initial dioxin.

Table 11-23. Analysis of Muscle Status (Continued)

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,210 | 35 (2.9) | | |
| Background RH | 380 | 14 (3.7) | 1.23 (0.65,2.31) | 0.530 |
| Low RH | 239 | 14 (5.9) | 2.11 (1.12,3.99) | 0.021 |
| High RH | 240 | 10 (4.2) | 1.52 (0.74,3.12) | 0.254 |
| Low plus High RH | 479 | 24 (5.0) | 1.79 (1.05,3.06) | 0.033 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | | |
|---|----------|--|-------------|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| Comparison | 1,192 | | | |
| Background RH | 375 | 1.22 | (0.63,2.35) | 0.550 |
| Low RH | 235 | 1.90 | (0.98,3.66) | 0.056 |
| High RH | 236 | 1.58 | (0.73,3.39) | 0.242 |
| Low plus High RH | 471 | 1.73 | (0.99,3.04) | 0.056 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 10 (3.5) | 1.02 (0.82,1.27) | 0.863 |
| Medium | 287 | 15 (5.2) | | |
| High | 285 | 13 (4.6) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-23. Analysis of Muscle Status (Continued)

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 846 | 0.98 (0.76,1.27) | 0.897 |

^a Relative risk for a twofold increase in 1987 dioxin.

The Model 3 unadjusted analysis revealed significantly more Ranch Hands in the low dioxin category with an abnormal muscle status than Comparisons (Table 11-23(e): Est. RR=2.11, p=0.021). Significantly more Ranch Hands in the low plus high dioxin category than Comparisons also had an abnormal muscle status (Table 11-23(e): Est. RR=1.79, p=0.033). Both contrasts were marginally significant in the adjusted analysis (Table 11-23(f): Adj. RR=1.90, p=0.056 for the low dioxin category contrast; and Adj. RR=1.73, p=0.056 for the low plus high dioxin category contrast). All other Model 3 contrasts, as well as the Model 4 analysis results, were nonsignificant (Table 11-23(e-h): p>0.24 for each remaining analysis).

11.2.2.4.4 Patellar Reflex

The Model 1 analysis of the patellar reflex revealed a marginally significant difference between Ranch Hands and Comparison enlisted flyers in both the unadjusted and adjusted analyses (Table 11-24(a,b): Est. RR=0.17, p=0.100 and Adj. RR=0.16, p=0.089). The prevalence of a patellar reflex abnormality was higher among Comparisons than Ranch Hands. All other Model 1 contrasts were nonsignificant (Table 11-24(a,b): p>0.40 for each remaining Model 1 contrast).

Table 11-24. Analysis of Patellar Reflex

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|----------|----------------------------|--------------------------------------|----------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 865 | 24 (2.8) | <i>0.99 (0.58,1.67)</i> | <i>0.962</i> |
| | <i>Comparison</i> | 1,246 | 35 (2.8) | | |
| Officer | Ranch Hand | 340 | 12 (3.5) | 1.09 (0.51,2.34) | 0.823 |
| | Comparison | 493 | 16 (3.3) | | |
| Enlisted Flyer | Ranch Hand | 151 | 1 (0.7) | 0.17 (0.02,1.40) | 0.100 |
| | Comparison | 186 | 7 (3.8) | | |
| Enlisted Groundcrew | Ranch Hand | 374 | 11 (2.9) | 1.40 (0.61,3.21) | 0.425 |
| | Comparison | 567 | 12 (2.1) | | |

Table 11-24. Analysis of Patellar Reflex (Continued)

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>0.97 (0.56,1.67)</i> | <i>0.910</i> |
| Officer | 1.05 (0.48,2.29) | 0.901 |
| Enlisted Flyer | 0.16 (0.02,1.32) | 0.089 |
| Enlisted Groundcrew | 1.43 (0.61,3.34) | 0.408 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|----------|--------------------------------|--|----------------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (Initial Dioxin)^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^b | p-Value |
| Low | 159 | 5 (3.1) | 1.18 (0.82,1.71) | 0.374 |
| Medium | 162 | 3 (1.9) | | |
| High | 157 | 7 (4.5) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 470 | 1.81 (1.10,2.99) | 0.019 |

^a Relative risk for a twofold increase in initial dioxin.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,209 | 33 (2.7) | | |
| Background RH | 380 | 9 (2.4) | 0.91 (0.43,1.93) | 0.812 |
| Low RH | 238 | 7 (2.9) | 1.06 (0.46,2.44) | 0.882 |
| High RH | 240 | 8 (3.3) | 1.17 (0.53,2.58) | 0.693 |
| Low plus High RH | 478 | 15 (3.1) | 1.12 (0.60,2.08) | 0.727 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-24. Analysis of Patellar Reflex (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,191 | | |
| Background RH | 375 | 0.88 (0.40,1.91) | 0.742 |
| Low RH | 234 | 0.86 (0.37,2.02) | 0.737 |
| High RH | 236 | 1.39 (0.60,3.26) | 0.446 |
| Low plus High RH | 470 | 1.10 (0.57,2.10) | 0.778 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 8 (2.8) | 1.08 (0.83,1.42) | 0.568 |
| Medium | 286 | 7 (2.5) | | |
| High | 285 | 9 (3.2) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 845 | 1.15 (0.80,1.64) | | 0.447 |

^a Relative risk for a twofold increase in 1987 dioxin.

The unadjusted Model 2 analysis of patellar reflex was nonsignificant (Table 11-24(c): p=0.374). After adjustment for covariates, a significant positive association between patellar reflex and initial dioxin was revealed (Table 11-24(d): Adj. RR=1.81, p=0.019). As initial dioxin increased in Ranch Hands, the prevalence of an abnormal patellar reflex increased.

All results from the analyses of patellar reflex from Models 3 and 4 were nonsignificant (Table 11-24(e–h): p>0.44 for each Model 3 and 4 analysis).

11.2.2.4.5 Achilles Reflex

The Model 2 adjusted analysis revealed a marginally significant association between an abnormal Achilles reflex and initial dioxin (Table 11-25 (d): Adj. RR=1.22, p=0.075). The marginally significant result indicates that Achilles reflex abnormalities increased in Ranch Hands as the initial dioxin levels increased. All other analysis results for Achilles reflex from Models 1 through 4 were nonsignificant (Table 11-25(a-h): p>0.15 for each analysis).

Table 11-25. Analysis of Achilles Reflex

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|---------------------|-------------------------------|--------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>865</i> | <i>153 (17.7)</i> | <i>1.10 (0.88,1.39)</i> | <i>0.410</i> |
| | <i>Comparison</i> | <i>1,244</i> | <i>203 (16.3)</i> | | |
| Officer | Ranch Hand | 340 | 67 (19.7) | 1.22 (0.86,1.75) | 0.267 |
| | Comparison | 491 | 82 (16.7) | | |
| Enlisted Flyer | Ranch Hand | 151 | 30 (19.9) | 1.00 (0.58,1.71) | 0.995 |
| | Comparison | 186 | 37 (19.9) | | |
| Enlisted Groundcrew | Ranch Hand | 374 | 56 (15.0) | 1.01 (0.70,1.46) | 0.947 |
| | Comparison | 567 | 84 (14.8) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|--------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.07 (0.84,1.37)</i> | <i>0.594</i> |
| Officer | 1.17 (0.80,1.70) | 0.413 |
| Enlisted Flyer | 0.91 (0.51,1.60) | 0.737 |
| Enlisted Groundcrew | 1.05 (0.71,1.55) | 0.815 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 160 | 29 (18.1) | 1.04 (0.87,1.23) | 0.688 |
| Medium | 162 | 31 (19.1) | | |
| High | 157 | 33 (21.0) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-25. Analysis of Achilles Reflex (Continued)

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|---|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 471 | 1.22 (0.98,1.51) | 0.075 |

^a Relative risk for a twofold increase in initial dioxin.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|------------------------|--|---------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) ^{ab} | p-Value |
| Comparison | 1,206 | 197 (16.3) | | |
| Background RH | 379 | 57 (15.0) | 0.99 (0.72,1.37) | 0.963 |
| Low RH | 239 | 46 (19.3) | 1.20 (0.84,1.71) | 0.325 |
| High RH | 240 | 47 (19.6) | 1.16 (0.81,1.65) | 0.425 |
| Low plus High RH | 479 | 93 (19.4) | 1.18 (0.89,1.55) | 0.247 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | | |
|---|-------|---|---------|--|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.) ^a | p-Value | |
| Comparison | 1,188 | | | |
| Background RH | 374 | 0.96 (0.68,1.35) | 0.811 | |
| Low RH | 235 | 0.97 (0.66,1.42) | 0.880 | |
| High RH | 236 | 1.32 (0.89,1.95) | 0.168 | |
| Low plus High RH | 471 | 1.13 (0.84,1.52) | 0.416 | |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-25. Analysis of Achilles Reflex (Continued)

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|-----|---------------------|---|---------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^a | p-Value |
| Low | 286 | 44 (15.4) | 1.07 (0.95,1.21) | 0.250 |
| Medium | 287 | 49 (17.1) | | |
| High | 285 | 57 (20.0) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|--|--|---------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 845 | 1.12 (0.96,1.31) | 0.157 |

^a Relative risk for a twofold increase in 1987 dioxin.

11.2.2.4.6 Biceps Reflex

A significant increase of Ranch Hands in the low dioxin category relative to Comparisons was found from the unadjusted Model 3 analysis of the biceps reflex (Table 11-26(e): Est. RR=2.88, p=0.029). The result was marginally significant in the adjusted analysis (Table 11-26(f): Adj. RR=2.52, p=0.064). All other Model 3 contrasts, as well as all other analysis results from Models 1, 2, and 4, were nonsignificant (Table 11-26(a–h): p≥0.12 for all remaining analyses).

Table 11-26. Analysis of Biceps Reflex

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|---------------------|-------------------------------|--------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>866</i> | <i>12 (1.4)</i> | <i>1.45 (0.65,3.24)</i> | <i>0.369</i> |
| | <i>Comparison</i> | <i>1,248</i> | <i>12 (1.0)</i> | | |
| Officer | Ranch Hand | 340 | 5 (1.5) | 1.21 (0.37,4.00) | 0.753 |
| | Comparison | 493 | 6 (1.2) | | |
| Enlisted Flyer | Ranch Hand | 151 | 2 (1.3) | 1.24 (0.17,8.92) | 0.830 |
| | Comparison | 187 | 2 (1.1) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 5 (1.3) | 1.91 (0.51,7.14) | 0.339 |
| | Comparison | 568 | 4 (0.7) | | |

Table 11-26. Analysis of Biceps Reflex (Continued)

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.31 (0.57,3.05)</i> | <i>0.527</i> |
| Officer | 1.13 (0.33,3.80) | 0.848 |
| Enlisted Flyer | 1.34 (0.18,9.89) | 0.776 |
| Enlisted Groundcrew | 1.61 (0.39,6.58) | 0.509 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|----------|--------------------------------|--|----------------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (Initial Dioxin)^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^b | p-Value |
| Low | 160 | 3 (1.9) | 0.72 (0.41,1.24) | 0.203 |
| Medium | 162 | 6 (3.7) | | |
| High | 157 | 1 (0.6) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 471 | 0.87 (0.44,1.70) | 0.675 |

^a Relative risk for a twofold increase in initial dioxin.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,210 | 12 (1.0) | | |
| Background RH | 380 | 2 (0.5) | 0.61 (0.14,2.77) | 0.524 |
| Low RH | 239 | 7 (2.9) | 2.88 (1.12,7.44) | 0.029 |
| High RH | 240 | 3 (1.3) | 1.10 (0.30,3.96) | 0.887 |
| Low plus High RH | 479 | 10 (2.1) | 1.78 (0.73,4.35) | 0.209 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-26. Analysis of Biceps Reflex (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,192 | | |
| Background RH | 375 | 0.27 (0.03,2.13) | 0.213 |
| Low RH | 235 | 2.52 (0.95,6.70) | 0.064 |
| High RH | 236 | 1.37 (0.35,5.29) | 0.651 |
| Low plus High RH | 471 | 1.85 (0.73,4.69) | 0.193 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 0 (0.0) | 1.16 (0.80,1.68) | 0.437 |
| Medium | 287 | 8 (2.8) | | |
| High | 285 | 4 (1.4) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 846 | 1.52 (0.89,2.61) | | 0.120 |

^a Relative risk for a twofold increase in 1987 dioxin.

11.2.2.4.7 Babinski Reflex

All analysis results from Models 1 through 3 for Babinski reflex were nonsignificant (Table 11-27(a–f): $p > 0.23$ for each analysis). The result from the unadjusted Model 4 analysis of Babinski reflex was marginally significant and inverse in direction (Table 11-27(g): Est. RR=0.58, $p=0.056$). After adjustment for covariates, the association between Babinski reflex and the 1987 dioxin levels was nonsignificant (Table 11-27(h): $p=0.223$).

Table 11-27. Analysis of Babinski Reflex

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|---------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 866 | 8 (0.9) | 0.88 (0.36,2.14) | 0.785 |
| | <i>Comparison</i> | 1,246 | 13 (1.0) | | |
| Officer | Ranch Hand | 340 | 3 (0.9) | 2.18 (0.36,13.12) | 0.394 |
| | Comparison | 492 | 2 (0.4) | | |
| Enlisted Flyer | Ranch Hand | 151 | 1 (0.7) | 0.40 (0.04,3.93) | 0.435 |
| | Comparison | 185 | 3 (1.6) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 4 (1.1) | 0.76 (0.23,2.53) | 0.650 |
| | Comparison | 569 | 8 (1.4) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|---------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | 0.81 (0.31,2.10) | 0.666 |
| Officer | 2.16 (0.35,13.17) | 0.403 |
| Enlisted Flyer | 0.36 (0.04,3.59) | 0.385 |
| Enlisted Groundcrew | 0.64 (0.16,2.51) | 0.526 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 160 | 1 (0.6) | 0.89 (0.28,2.86) | 0.848 |
| Medium | 162 | 0 (0.0) | | |
| High | 157 | 1 (0.6) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 476 | 1.08 (0.34,3.42) | 0.896 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, industrial chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal Babinski reflex.

Table 11-27. Analysis of Babinski Reflex (Continued)

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,208 | 11 (0.9) | | |
| Background RH | 380 | 5 (1.3) | 1.48 (0.50,4.33) | 0.477 |
| Low RH | 239 | 1 (0.4) | 0.46 (0.06,3.55) | 0.452 |
| High RH | 240 | 1 (0.4) | 0.45 (0.06,3.50) | 0.444 |
| Low plus High RH | 479 | 2 (0.4) | 0.45 (0.10,2.05) | 0.303 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | | |
|---|----------|--|-------------|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| Comparison | 1,190 | | | |
| Background RH | 375 | 1.53 | (0.45,5.14) | 0.496 |
| Low RH | 235 | 0.38 | (0.05,3.05) | 0.364 |
| High RH | 236 | 0.41 | (0.05,3.33) | 0.405 |
| Low plus High RH | 471 | 0.40 | (0.08,1.85) | 0.239 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 5 (1.7) | 0.58 (0.32,1.03) | 0.056 |
| Medium | 287 | 1 (0.4) | | |
| High | 285 | 1 (0.4) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-27. Analysis of Babinski Reflex (Continued)

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|---|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 853 | 0.65 (0.33,1.29) | 0.223 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for diabetic class because of the sparse number of Ranch Hands with an abnormal Babinski reflex.

11.2.2.4.8 Polyneuropathy Severity Index

The results from the Model 1 unadjusted analysis of the polyneuropathy severity index revealed a significant difference between Ranch Hands and Comparisons in the percentage of participants with a moderate polyneuropathy severity index (Table 11-28(a): Est. RR=2.37, p=0.015). A marginally significant difference between Ranch Hand and Comparison enlisted flyers in the percentage of participants with a moderate polyneuropathy severity index also was observed (Table 11-28(a): Est. RR=4.54, p=0.062). Results were consistent in the adjusted analysis for both contrasts (Table 11-28(b): Adj. RR=2.32, p=0.020 for all occupations combined; Adj.RR=4.13, p=0.083 for enlisted flyers). All other Model 1 contrasts performed were nonsignificant (Table 11-28(a,b): p>0.11 for each remaining Model 1 contrast).

The Model 2 adjusted analysis revealed a significant positive association between a moderate polyneuropathy severity index and initial dioxin (Table 11-28(d): Adj. RR=1.52, p=0.042). All other Model 2 results were nonsignificant (Table 11-28(c,d): p>0.16 for the remaining Model 2 analyses results).

The Model 3 unadjusted analysis of the polyneuropathy severity index displayed several significant associations between categorized dioxin and a moderate polyneuropathy severity index. The contrasts of Ranch Hands in the low, high, and low plus high dioxin categories versus Comparisons each were significant and displayed more Ranch Hands than Comparisons with a moderate polyneuropathy severity index (Table 11-28(e): Est. RR=2.76, p=0.032; Est. RR=2.64, p=0.042; and Est. RR=2.70, p=0.011, respectively). The results remained significant in the adjusted analysis for the contrast of Comparisons with Ranch Hands in the high and the low plus high dioxin categories, and was marginally significant for the contrast of Ranch Hands in the low dioxin category with Comparisons (Table 11-28(f): Adj. RR=3.06, p=0.024; Adj. RR=2.68, p=0.014; and Adj. RR=2.35, p=0.079, respectively). The background Ranch Hand contrast was nonsignificant in both the unadjusted and adjusted analyses (Table 10-28(e): p>0.61 for each contrast).

Table 11-28. Analysis of Polyneuropathy Severity Index

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | | | | | |
|--|-------------------|--------------|---------------------|-----------------|----------------|--------------------------------------|----------------|--------------------------------------|----------------|
| Occupational Category | Group | n | Number (%) | | | Moderate vs. None/Mild | | Severe vs. None/Mild | |
| | | | None/Mild | Moderate | Severe | Est. Relative Risk (95% C.I.) | p-Value | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>821</i> | <i>796 (97.0)</i> | <i>21 (2.6)</i> | <i>4 (0.5)</i> | <i>2.37 (1.18,4.76)</i> | <i>0.015</i> | <i>5.87 (0.65,52.61)</i> | <i>0.114</i> |
| | <i>Comparison</i> | <i>1,182</i> | <i>1,168 (98.8)</i> | <i>13 (1.1)</i> | <i>1 (0.1)</i> | | | | |
| Officer | Ranch Hand | 322 | 312 (96.9) | 7 (2.2) | 3 (0.9) | 1.73 (0.58,5.19) | 0.330 | -- | 0.130 |
| | Comparison | 468 | 462 (98.7) | 6 (1.3) | 0 (0.0) | | | | |
| Enlisted Flyer | Ranch Hand | 145 | 138 (95.2) | 7 (4.8) | 0 (0.0) | 4.54 (0.93,22.20) | 0.062 | -- | -- |
| | Comparison | 181 | 179 (98.9) | 2 (1.1) | 0 (0.0) | | | | |
| Enlisted Groundcrew | Ranch Hand | 354 | 346 (97.7) | 7 (2.0) | 1 (0.3) | 2.13 (0.67,6.77) | 0.199 | 1.52 (0.09,24.45) | 0.766 |
| | Comparison | 533 | 527 (98.9) | 5 (0.9) | 1 (0.2) | | | | |

^a P-value determined using a chi-square test with continuity correction because of the sparse number of participants with a severe polyneuropathy severity index.

--: Results not presented because of the sparse number of participants with a severe polyneuropathy severity index.

Table 11-28. Analysis of Polyneuropathy Severity Index (Continued)

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | | | |
|--|--------------------------------------|----------------|--------------------------------------|----------------|
| Occupational Category | Moderate vs. None/Mild | | Severe vs. None/Mild | |
| | Adj. Relative Risk (95% C.I.) | p-Value | Adj. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | 2.32 (1.14,4.73) | 0.020 | 5.44 (0.59,50.52) | 0.136 |
| Officer | 1.72 (0.57,5.24) | 0.338 | -- | -- |
| Enlisted Flyer | 4.13 (0.83,20.52) | 0.083 | -- | -- |
| Enlisted Groundcrew | 2.16 (0.67,7.01) | 0.200 | 1.64 (0.09,29.24) | 0.738 |

--: Results not presented because of the sparse number of participants with a severe polyneuropathy severity index.

Note: Results are not adjusted for diabetic class because of the sparse number of participants with a moderate or severe polyneuropathy severity index. Results for all occupations combined also are not adjusted for occupation because of the sparse number of participants with a moderate or severe polyneuropathy severity index.

Table 11-28. Analysis of Polyneuropathy Severity Index (Continued)

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | | | | | |
|---|-----|------------|----------|---------|---|---------|--|---------|
| Initial Dioxin Category Summary Statistics | | | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | | | |
| | | Number (%) | | | Moderate vs. None/Mild | | Severe vs. None/Mild | |
| Initial Dioxin Category | n | None/Mild | Moderate | Severe | Est. Relative Risk (95% C.I.) ^b | p-Value | Est. Relative Risk (95% C.I.) ^b | p-Value |
| Low | 152 | 146 (96.1) | 4 (2.6) | 2 (1.3) | 1.29 (0.90,1.87) | 0.168 | 0.68 (0.23,1.98) | 0.476 |
| Medium | 151 | 147 (97.4) | 4 (2.7) | 0 (0.0) | | | | |
| High | 150 | 143 (95.3) | 6 (4.0) | 1 (0.7) | | | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | | | |
|---|--|---------|--|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | | | |
| Moderate vs. None/Mild | | | Severe vs. None/Mild | |
| n | Adj. Relative Risk (95% C.I.) ^a | p-Value | Adj. Relative Risk (95% C.I.) ^a | p-Value |
| 450 | 1.52 (1.02,2.28) | 0.042 | 0.87 (0.24,3.20) | 0.832 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation and diabetic class because of the sparse number of Ranch Hands with a moderate or severe polyneuropathy severity index.

Table 11-28. Analysis of Polyneuropathy Severity Index (Continued)

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | | | | | |
|---|----------|-------------------|-----------------|---------------|---|----------------|---|----------------|
| Dioxin Category | n | Number (%) | | | Moderate vs. None/Mild | | Severe vs. None/Mild | |
| | | None/Mild | Moderate | Severe | Est. Relative Risk (95% C.I.)^{ab} | p-Value | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,146 | 1,132 (98.8) | 13 (1.1) | 1 (0.1) | | | | |
| Background RH | 361 | 355 (98.3) | 5 (1.4) | 1 (0.3) | 1.30 (0.46,3.71) | 0.619 | 3.03 (0.19,49.25) | 0.435 |
| Low RH | 226 | 217 (96.0) | 7 (3.1) | 2 (0.9) | 2.76 (1.09,7.02) | 0.032 | 10.54 (0.95,116.83) | 0.055 |
| High RH | 227 | 219 (96.5) | 7 (3.1) | 1 (0.4) | 2.64 (1.03,6.73) | 0.042 | 5.41 (0.33,87.73) | 0.235 |
| Low plus High RH | 453 | 436 (96.3) | 14 (3.1) | 3 (0.7) | 2.70 (1.26,5.81) | 0.011 | 7.54 (0.75,75.71) | 0.086 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-28. Analysis of Polyneuropathy Severity Index (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | | | |
|---|----------|--|----------------|--|----------------|
| Dioxin Category | n | Moderate vs. None/Mild | | Severe vs. None/Mild | |
| | | Adj. Relative Risk (95% C.I.)^a | p-Value | Adj. Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,145 | | | | |
| Background RH | 358 | 1.29 (0.45,3.70) | 0.641 | 2.59 (0.15,43.89) | 0.511 |
| Low RH | 225 | 2.35 (0.90,6.09) | 0.079 | 7.43 (0.62,89.56) | 0.114 |
| High RH | 225 | 3.06 (1.16,8.11) | 0.024 | 9.83 (0.52,186.07) | 0.128 |
| Low plus High RH | 450 | 2.68 (1.22,5.90) | 0.014 | 8.55 (0.77,94.34) | 0.080 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for occupation and diabetic class because of the sparse number of participants with a moderate or severe polyneuropathy severity index.

Table 11-28. Analysis of Polyneuropathy Severity Index (Continued)

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | | | | | |
|--|-----|------------|----------|---------|---|---------|--|---------|
| 1987 Dioxin Category Summary Statistics | | | | | Analysis Results for Log ₂ (1987 Dioxin + 1) | | | |
| 1987 Dioxin Category | n | Number (%) | | | Moderate vs. None/Mild | | Severe vs. None/Mild | |
| | | None/Mild | Moderate | Severe | Est. Relative Risk (95% C.I.) ^a | p-Value | Est. Relative Risk (95% C.I.) ^a | p-Value |
| Low | 271 | 267 (98.5) | 4 (1.5) | 0 (0.0) | 1.38 (1.04,1.84) | 0.024 | 1.13 (0.59,2.15) | 0.717 |
| Medium | 275 | 266 (96.7) | 6 (2.2) | 3 (1.1) | | | | |
| High | 268 | 258 (96.3) | 9 (3.4) | 1 (0.4) | | | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | | |
|--|--|---------|--|---------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | | | |
| n | Moderate vs. None/Mild | | Severe vs. None/Mild | |
| | Adj. Relative Risk (95% C.I.) ^a | p-Value | Adj. Relative Risk (95% C.I.) ^a | p-Value |
| 808 | 1.51 (1.09,2.09) | 0.013 | 1.48 (0.62,3.50) | 0.376 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for occupation and diabetic class because of the sparse number of Ranch Hands with a moderate or severe polyneuropathy severity index.

The Model 3 unadjusted analysis of participants with a severe polyneuropathy severity index showed a marginally significant difference between Ranch Hands in the low dioxin category and Comparisons, and between Ranch Hands in the low plus high dioxin category and Comparisons (Table 11-28(e): Est. RR=10.54, p=0.055 and Est. RR=7.54, p=0.086, respectively). The contrast of Ranch Hands in the low plus high dioxin category remained marginally significant in the adjusted analysis (Table 11-28(f): Adj. RR=8.55, p=0.080). All other Model 3 contrasts of participants with a severe polyneuropathy severity index were nonsignificant (Table 11-28(e,f): p>0.11 for each remaining contrast).

The results from the Model 4 analysis of the polyneuropathy severity index were significant in both the unadjusted and adjusted analyses, showing a positive association between the percentage of Ranch Hands with a moderate polyneuropathy severity index and 1987 dioxin (Table 11-28(g,h): Est. RR=1.38, p=0.024 for the unadjusted analysis; and Adj. RR=1.51, p=0.013 for the adjusted analysis). The association between 1987 dioxin and a severe polyneuropathy severity index was nonsignificant (Table 11-28(g,h): p>0.37 for both the unadjusted and adjusted analyses).

11.2.2.4.9 Polyneuropathy Prevalence Index

All analysis results contrasting Ranch Hands and Comparisons on the polyneuropathy prevalence index in Models 1 and 3 were nonsignificant (Table 11-29(a,b,e,f): p>0.20 for each Model 1 and 3 contrast).

Table 11-29. Analysis of Polyneuropathy Prevalence Index

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|----------|----------------------------|--------------------------------------|----------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 821 | 130 (15.8) | 1.06 (0.83,1.35) | 0.668 |
| | <i>Comparison</i> | 1,183 | 179 (15.1) | | |
| Officer | Ranch Hand | 322 | 55 (17.1) | 1.08 (0.74,1.58) | 0.694 |
| | Comparison | 468 | 75 (16.0) | | |
| Enlisted Flyer | Ranch Hand | 145 | 29 (20.0) | 0.92 (0.53,1.57) | 0.752 |
| | Comparison | 182 | 39 (21.4) | | |
| Enlisted Groundcrew | Ranch Hand | 354 | 46 (13.0) | 1.08 (0.72,1.61) | 0.725 |
| | Comparison | 533 | 65 (12.2) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | 0.99 (0.76,1.28) | 0.923 |
| Officer | 1.02 (0.68,1.51) | 0.941 |
| Enlisted Flyer | 0.86 (0.48,1.52) | 0.601 |
| Enlisted Groundcrew | 1.03 (0.67,1.59) | 0.877 |

Table 11-29. Analysis of Polyneuropathy Prevalence Index (Continued)

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 152 | 23 (15.1) | 1.09 (0.91,1.31) | 0.344 |
| Medium | 151 | 28 (18.5) | | |
| High | 150 | 29 (19.3) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 445 | 1.30 (1.03,1.65) | 0.029 |

^a Relative risk for a twofold increase in initial dioxin.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|---------------------|---|---------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) ^{ab} | p-Value |
| Comparison | 1,147 | 175 (15.3) | | |
| Background RH | 361 | 47 (13.0) | 0.89 (0.63,1.27) | 0.530 |
| Low RH | 226 | 38 (16.8) | 1.10 (0.75,1.62) | 0.618 |
| High RH | 227 | 42 (18.5) | 1.18 (0.81,1.72) | 0.376 |
| Low plus High RH | 453 | 80 (17.7) | 1.14 (0.85,1.53) | 0.370 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-29. Analysis of Polyneuropathy Prevalence Index (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,130 | | |
| Background RH | 356 | 0.83 (0.57,1.20) | 0.315 |
| Low RH | 222 | 0.86 (0.57,1.30) | 0.484 |
| High RH | 223 | 1.31 (0.86,1.98) | 0.206 |
| Low plus High RH | 445 | 1.06 (0.77,1.46) | 0.708 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 271 | 39 (14.4) | 1.09 (0.96,1.24) | 0.198 |
| Medium | 275 | 38 (13.8) | | |
| High | 268 | 50 (18.7) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 801 | 1.16 (0.98,1.37) | | 0.080 |

^a Relative risk for a twofold increase in 1987 dioxin.

The Model 2 unadjusted analysis of the polyneuropathy prevalence index was nonsignificant (Table 11-29(c): p=0.344). After adjustment for covariates, the association between the polyneuropathy prevalence index and initial dioxin was positive and significant (Table 11-29(d): Adj. RR=1.30, p=0.029). Similarly, the Model 4 unadjusted analysis was nonsignificant (Table 11-29(g): p=0.198, but the association between the polyneuropathy prevalence index and 1987 dioxin was marginally significant in the adjusted analysis (Table 11-29(h): Adj. RR=1.16, p=0.080).

11.2.2.4.10 Multiple Polyneuropathy Index

The difference in the multiple polyneuropathy index between Ranch Hands and Comparisons was significant and showed more Ranch Hands than Comparisons with an abnormal multiple polyneuropathy

index (Table 11-30(a): Est. RR=1.58, p=0.046). After adjustment for covariates, the difference became marginally significant (Table 11-30(b): Adj. RR=1.51, p=0.092). All other Model 1 contrasts were nonsignificant (Table 11-30(a,b): p>0.15 for all remaining Model 1 contrasts).

Table 11-30. Analysis of Multiple Polyneuropathy Index

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|---------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 821 | 41 (5.0) | 1.58 (1.01,2.49) | 0.046 |
| | <i>Comparison</i> | 1,183 | 38 (3.2) | | |
| Officer | Ranch Hand | 322 | 16 (5.0) | 1.39 (0.69,2.79) | 0.358 |
| | Comparison | 468 | 17 (3.6) | | |
| Enlisted Flyer | Ranch Hand | 145 | 13 (9.0) | 1.89 (0.79,4.56) | 0.155 |
| | Comparison | 182 | 9 (5.0) | | |
| Enlisted Groundcrew | Ranch Hand | 354 | 12 (3.4) | 1.52 (0.68,3.43) | 0.309 |
| | Comparison | 533 | 12 (2.3) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|---------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | 1.51 (0.94,2.45) | 0.092 |
| Officer | 1.44 (0.69,2.98) | 0.330 |
| Enlisted Flyer | 1.77 (0.69,4.56) | 0.234 |
| Enlisted Groundcrew | 1.43 (0.60,3.39) | 0.421 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 152 | 6 (4.0) | 1.30 (0.98,1.73) | 0.076 |
| Medium | 151 | 8 (5.3) | | |
| High | 150 | 11 (7.3) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-30. Analysis of Multiple Polyneuropathy Index (Continued)

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|---|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 445 | 1.85 (1.20,2.87) | 0.004 |

^a Relative risk for a twofold increase in initial dioxin.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|------------------------|--|---------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) ^{ab} | p-Value |
| Comparison | 1,147 | 36 (3.1) | | |
| Background RH | 361 | 14 (3.9) | 1.29 (0.68,2.43) | 0.432 |
| Low RH | 226 | 10 (4.4) | 1.42 (0.69,2.90) | 0.340 |
| High RH | 227 | 15 (6.6) | 2.12 (1.14,3.95) | 0.018 |
| Low plus High RH | 453 | 25 (5.5) | 1.73 (1.02,2.94) | 0.042 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|-------|---|---------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| Comparison | 1,130 | | |
| Background RH | 356 | 1.37 (0.69,2.72) | 0.366 |
| Low RH | 222 | 0.96 (0.44,2.10) | 0.914 |
| High RH | 223 | 2.38 (1.18,4.82) | 0.016 |
| Low plus High RH | 445 | 1.51 (0.84,2.71) | 0.165 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-30. Analysis of Multiple Polyneuropathy Index (Continued)

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|-----|---------------------|---|---------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^a | p-Value |
| Low | 271 | 11 (4.1) | 1.19 (0.96,1.46) | 0.110 |
| Medium | 275 | 10 (3.6) | | |
| High | 268 | 18 (6.7) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|--|--|--|---------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | | p-Value |
| 801 | 1.29 (0.95,1.76) | | 0.101 |

^a Relative risk for a twofold increase in 1987 dioxin.

The Model 2 unadjusted analysis displayed a marginally significant positive association between the multiple polyneuropathy index and initial dioxin (Table 11-30(c): Est. RR=1.30, p=0.076). After adjustment for covariates, the association became significant (Table 11-30(d): Adj. RR=1.85, p=0.004).

A significant difference between Ranch Hands in the high dioxin category and Comparisons was found from the Model 3 unadjusted and adjusted analyses of the multiple polyneuropathy index (Table 11-30(e,f): Est. RR=2.12, p=0.018 and Adj. RR=2.38, p=0.016, respectively). The difference was also significant for the unadjusted contrast of Ranch Hands in the low plus high dioxin category with Comparisons (Table 11-30(e): Est. RR=1.73, p=0.042). This contrast was nonsignificant in the adjusted analysis (Table 11-30(f): p=0.165). The other Model 3 contrasts were nonsignificant in both the unadjusted and adjusted analyses as were the results from the analyses of Model 4 (Table 11-30(e–h): p>0.10 for each remaining Model 3 contrast and Model 4 analyses).

11.2.2.4.11 Confirmed Polyneuropathy Indicator

Differences between Ranch Hands and Comparisons were marginally significant for several contrasts from the Model 1 unadjusted analysis of the confirmed polyneuropathy indicator. For all contrasts, Ranch Hands showed a higher percentage of participants with an abnormal confirmed polyneuropathy indicator than did Comparisons. The difference was marginally significant when examined across all occupations (Table 11-31(a): Est. RR=2.30, p=0.082), for enlisted flyers (Table 11-31(a): p=0.079), and for enlisted groundcrew (Table 11-31(a): Est. RR=7.62, p=0.064). After adjustment for covariates, the results were marginally significant for the analysis across all occupations and for enlisted groundcrew (Table 11-31(b): Adj. RR=2.35, p=0.082; and Adj. RR=8.59, p=0.054, respectively). The analysis of the confirmed polyneuropathy indicator was nonsignificant for officers for both the unadjusted and adjusted analyses (Table 11-31(a,b): p=0.381 and p=0.414, respectively).

Table 11-31. Analysis of Confirmed Polyneuropathy Indicator

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|---------------------|-------------------------------|--------------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>811</i> | <i>11 (1.4)</i> | <i>2.30 (0.89,5.95)</i> | <i>0.082</i> |
| | <i>Comparison</i> | <i>1,176</i> | <i>7 (0.6)</i> | | |
| Officer | Ranch Hand | 318 | 2 (0.6) | 0.49 (0.10,2.43) | 0.381 |
| | Comparison | 468 | 6 (1.3) | | |
| Enlisted Flyer | Ranch Hand | 142 | 4 (2.8) | -- | 0.079 ^a |
| | Comparison | 180 | 0 (0.0) | | |
| Enlisted Groundcrew | Ranch Hand | 351 | 5 (1.4) | 7.62 (0.89,65.47) | 0.064 |
| | Comparison | 528 | 1 (0.2) | | |

^a P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal confirmed polyneuropathy indicator.

--: Results not presented because of the sparse number of participants with an abnormal confirmed polyneuropathy indicator.

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|--------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>2.35 (0.88,6.22)</i> | <i>0.082</i> |
| Officer | 0.51 (0.10,2.59) | 0.414 |
| Enlisted Flyer | -- | -- |
| Enlisted Groundcrew | 8.59 (0.97,76.27) | 0.054 |

--: Results not presented because of the sparse number of participants with an abnormal confirmed polyneuropathy indicator.

Note: Results are not adjusted for diabetic class because of the sparse number of participants with an abnormal confirmed polyneuropathy indicator.

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 150 | 2 (1.3) | 1.63 (1.05,2.53) | 0.033 |
| Medium | 150 | 2 (1.3) | | |
| High | 147 | 5 (3.4) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-31. Analysis of Confirmed Polyneuropathy Indicator (Continued)

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log ₂ (Initial Dioxin) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 444 | 1.98 (1.19,3.29) | | 0.008 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation, industrial chemicals exposure, degreasing chemicals exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal confirmed polyneuropathy indicator.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,141 | 7 (0.6) | | |
| Background RH | 358 | 2 (0.6) | 1.06 (0.22,5.16) | 0.944 |
| Low RH | 224 | 3 (1.3) | 2.08 (0.53,8.17) | 0.293 |
| High RH | 223 | 6 (2.7) | 3.89 (1.28,11.86) | 0.017 |
| Low plus High RH | 447 | 9 (2.0) | 2.85 (1.02,7.97) | 0.047 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | | |
|---|----------|--|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| Comparison | 1,138 | | | |
| Background RH | 355 | 0.99 (0.20,4.97) | | 0.988 |
| Low RH | 223 | 1.56 (0.38,6.40) | | 0.536 |
| High RH | 221 | 6.04 (1.63,22.42) | | 0.007 |
| Low plus High RH | 444 | 3.06 (1.02,9.23) | | 0.047 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Results are not adjusted for diabetic class because of the sparse number of participants with an abnormal confirmed polyneuropathy indicator.

Table 11-31. Analysis of Confirmed Polyneuropathy Indicator (Continued)

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | |
|--|----------|----------------------------|---|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a |
| Low | 270 | 1 (0.4) | 1.80 (1.26,2.58) |
| Medium | 271 | 3 (1.1) | |
| High | 264 | 7 (2.7) | 0.002 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 799 | 2.21 (1.24,3.96) | | 0.003 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for diabetic class because of the sparse number of Ranch Hands with an abnormal confirmed polyneuropathy indicator.

Both the unadjusted and adjusted analyses from Model 2 displayed a significant positive association between the confirmed polyneuropathy indicator and initial dioxin (Table 11-31(c,d): Est. RR=1.63, p=0.033, and Adj. RR=1.98, p=0.008).

In the unadjusted Model 3 analysis, significant results were found for the contrast of Ranch Hands in the high dioxin category and Ranch Hands in the low plus high dioxin category with Comparisons. The prevalence of an abnormal confirmed polyneuropathy indicator for Ranch Hands in the high dioxin category was significantly greater than for Comparisons (Table 11-31(e,f): Est. RR=3.89, p=0.017 and Adj. RR=6.04, p=0.007). The contrast of Ranch Hands from the low plus high dioxin category with Comparisons also was significant in both unadjusted and adjusted analyses (Table 11-31(e,f): Est. RR=2.85, p=0.047 and Adj. RR=3.06, p=0.047). All other Model 3 contrasts were nonsignificant (Table 11-31(e,f): p>0.29 for each remaining Model 3 contrast).

Both the unadjusted and adjusted analyses of Model 4 displayed a significant positive association between the confirmed polyneuropathy indicator and the 1987 dioxin levels (Table 11-31(g,h): Est. RR=1.80, p=0.002 and Adj. RR=2.21, p=0.003). As 1987 dioxin increased, the prevalence of an abnormal confirmed polyneuropathy indicator increased.

11.2.2.5 Physical Examination Variables – CNS Coordination Processes

11.2.2.5.1 Tremor

All results from the analyses of tremor from Models 1 through 4 were nonsignificant (Table 11-32(a–h): p>0.19 for each analysis).

Table 11-32. Analysis of Tremor

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|---------------------|-------------------------------|--------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>866</i> | <i>60 (6.9)</i> | <i>0.95 (0.68,1.33)</i> | <i>0.753</i> |
| | <i>Comparison</i> | <i>1,249</i> | <i>91 (7.3)</i> | | |
| Officer | Ranch Hand | 340 | 22 (6.5) | 1.11 (0.62,1.96) | 0.728 |
| | Comparison | 493 | 29 (5.9) | | |
| Enlisted Flyer | Ranch Hand | 151 | 15 (9.9) | 1.26 (0.60,2.68) | 0.540 |
| | Comparison | 187 | 15 (8.0) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 23 (6.1) | 0.73 (0.43,1.22) | 0.224 |
| | Comparison | 569 | 47 (8.3) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|--------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>0.90 (0.64,1.28)</i> | <i>0.564</i> |
| Officer | 1.06 (0.59,1.89) | 0.850 |
| Enlisted Flyer | 1.14 (0.53,2.44) | 0.734 |
| Enlisted Groundcrew | 0.72 (0.42,1.21) | 0.212 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 160 | 11 (6.9) | 1.02 (0.77,1.36) | 0.869 |
| Medium | 162 | 10 (6.2) | | |
| High | 157 | 9 (5.7) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 471 | 1.02 (0.73,1.44) | 0.893 |

^a Relative risk for a twofold increase in initial dioxin.

Table 11-32. Analysis of Tremor (Continued)

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,211 | 90 (7.4) | | |
| Background RH | 380 | 30 (7.9) | 1.05 (0.68,1.62) | 0.821 |
| Low RH | 239 | 14 (5.9) | 0.78 (0.43,1.39) | 0.396 |
| High RH | 240 | 16 (6.7) | 0.90 (0.52,1.57) | 0.713 |
| Low plus High RH | 479 | 30 (6.3) | 0.84 (0.55,1.29) | 0.417 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | | |
|---|----------|--|-------------|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| Comparison | 1,193 | | | |
| Background RH | 375 | 1.11 | (0.71,1.74) | 0.659 |
| Low RH | 235 | 0.71 | (0.39,1.28) | 0.248 |
| High RH | 236 | 0.79 | (0.44,1.40) | 0.420 |
| Low plus High RH | 471 | 0.75 | (0.48,1.16) | 0.194 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 23 (8.0) | 0.94 (0.79,1.13) | 0.527 |
| Medium | 287 | 21 (7.3) | | |
| High | 285 | 16 (5.6) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-32. Analysis of Tremor (Continued)

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|--|---|---------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 846 | 0.93 (0.75,1.14) | 0.478 |

^a Relative risk for a twofold increase in 1987 dioxin.

11.2.2.5.2 Coordination

All results from the analyses of coordination from Models 1 through 4 were nonsignificant (Table 11-33(a-h): p>0.11 for each analysis).

Table 11-33. Analysis of Coordination

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|------------------------|----------------------------------|---------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 866 | 19 (2.2) | 0.88 (0.49,1.57) | 0.663 |
| | <i>Comparison</i> | 1,247 | 31 (2.5) | | |
| Officer | Ranch Hand | 340 | 10 (2.9) | 1.84 (0.72,4.70) | 0.205 |
| | Comparison | 493 | 8 (1.6) | | |
| Enlisted Flyer | Ranch Hand | 151 | 1 (0.7) | 0.30 (0.03,2.74) | 0.288 |
| | Comparison | 186 | 4 (2.2) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 8 (2.1) | 0.63 (0.27,1.45) | 0.279 |
| | Comparison | 568 | 19 (3.4) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | | |
|--|--------------------------------------|--|---------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | | p-Value |
| <i>All</i> | 0.86 (0.48,1.56) | | 0.622 |
| Officer | 1.65 (0.64,4.26) | | 0.302 |
| Enlisted Flyer | 0.28 (0.03,2.58) | | 0.263 |
| Enlisted Groundcrew | 0.64 (0.27,1.50) | | 0.305 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | | |
|---|-----|------------------------|---|--|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | | p-Value |
| Low | 160 | 2 (1.3) | 0.90 (0.49,1.65) | | 0.735 |
| Medium | 162 | 4 (2.5) | | | |
| High | 157 | 1 (0.6) | | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Table 11-33. Analysis of Coordination (Continued)

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|----------------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 471 | 1.18 (0.62,2.24) | 0.632 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for occupation because of the sparse number of participants with abnormal coordination.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,209 | 30 (2.5) | | |
| Background RH | 380 | 12 (3.2) | 1.33 (0.67,2.65) | 0.412 |
| Low RH | 239 | 4 (1.7) | 0.66 (0.23,1.90) | 0.443 |
| High RH | 240 | 3 (1.3) | 0.48 (0.15,1.59) | 0.231 |
| Low plus High RH | 479 | 7 (1.5) | 0.56 (0.24,1.30) | 0.181 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,191 | | |
| Background RH | 375 | 1.46 (0.71,3.01) | 0.298 |
| Low RH | 235 | 0.61 (0.21,1.79) | 0.371 |
| High RH | 236 | 0.42 (0.12,1.42) | 0.161 |
| Low plus High RH | 471 | 0.51 (0.22,1.19) | 0.117 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-33. Analysis of Coordination (Continued)

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | | |
|--|-----|---------------------|---|--|---------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (1987 Dioxin + 1) | | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^a | | p-Value |
| Low | 287 | 8 (2.8) | 0.81 (0.58,1.13) | | 0.211 |
| Medium | 287 | 7 (2.4) | | | |
| High | 285 | 4 (1.4) | | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|--|--|--|---------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | | p-Value |
| 846 | 0.83 (0.57,1.21) | | 0.330 |

^a Relative risk for a twofold increase in 1987 dioxin.

11.2.2.5.3 Romberg Sign

All results from the analyses of Romberg sign from Models 1 through 4 were nonsignificant (Table 11-34(a–h): p>0.12 for each analysis).

Table 11-34. Analysis of Romberg Sign

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|---------------------|-------------------------------|--------------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>866</i> | <i>7 (0.8)</i> | <i>1.44 (0.50,4.13)</i> | <i>0.494</i> |
| | <i>Comparison</i> | <i>1,248</i> | <i>7 (0.6)</i> | | |
| Officer | Ranch Hand | 340 | 5 (1.5) | 3.66 (0.71,19.00) | 0.122 |
| | Comparison | 493 | 2 (0.4) | | |
| Enlisted Flyer | Ranch Hand | 151 | 0 (0.0) | -- | 0.999 ^a |
| | Comparison | 186 | 1 (0.5) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 2 (0.5) | 0.76 (0.14,4.16) | 0.749 |
| | Comparison | 569 | 4 (0.7) | | |

^a P-value determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal Romberg sign.

--: Results not presented because of the sparse number of participants with an abnormal Romberg sign.

Table 11-34. Analysis of Romberg Sign (Continued)

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.38 (0.47,4.03)</i> | <i>0.553</i> |
| Officer | 3.37 (0.64,17.73) | 0.151 |
| Enlisted Flyer | -- | -- |
| Enlisted Groundcrew | 0.73 (0.13,4.07) | 0.719 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|----------|--------------------------------|--|----------------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (Initial Dioxin)^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^b | p-Value |
| Low | 160 | 0 (0.0) | 1.27 (0.48,3.35) | 0.638 |
| Medium | 162 | 1 (0.6) | | |
| High | 157 | 1 (0.6) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | | |
|--|--|--|----------------|
| Analysis Results for Log₂ (Initial Dioxin) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 476 | 1.65 (0.61,4.45) | | 0.350 |

^a Relative risk for a twofold increase in initial dioxin.

Note: Results are not adjusted for race, occupation, insecticide exposure, and diabetic class because of the sparse number of participants with an abnormal Romberg sign.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,210 | 7 (0.6) | | |
| Background RH | 380 | 5 (1.3) | 2.52 (0.78,8.10) | 0.121 |
| Low RH | 239 | 1 (0.4) | 0.70 (0.09,5.74) | 0.741 |
| High RH | 240 | 1 (0.4) | 0.66 (0.08,5.43) | 0.699 |
| Low plus High RH | 479 | 2 (0.4) | 0.68 (0.14,3.31) | 0.633 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-34. Analysis of Romberg Sign (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,192 | | |
| Background RH | 375 | 2.54 (0.74,8.72) | 0.138 |
| Low RH | 235 | 0.63 (0.08,5.24) | 0.667 |
| High RH | 236 | 0.63 (0.07,5.49) | 0.672 |
| Low plus High RH | 471 | 0.63 (0.13,3.11) | 0.567 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|----------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 3 (1.1) | 0.88 (0.52,1.50) | 0.642 |
| Medium | 287 | 2 (0.7) | | |
| High | 285 | 2 (0.7) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 846 | 0.95 (0.52,1.73) | | 0.860 |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Results are not adjusted for race and occupation because of the sparse number of participants with an abnormal Romberg sign.

11.2.2.5.4 Gait

The adjusted Model 1 analysis of gait displayed a marginally significant increase in the prevalence of an abnormal gait for Ranch Hand enlisted groundcrew relative to Comparison enlisted groundcrew (Table 11-35(b): Adj. RR=1.79, p=0.090). All other results from the analysis of gait for Models 1 through 4 were nonsignificant (Table 11-35(a–h): p>0.11 for all remaining analyses).

Table 11-35. Analysis of Gait

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|-------|---------------------|-------------------------------|--------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | 866 | 50 (5.8) | <i>1.28 (0.87,1.89)</i> | <i>0.214</i> |
| | <i>Comparison</i> | 1,249 | 57 (4.6) | | |
| Officer | Ranch Hand | 340 | 19 (5.6) | 1.06 (0.58,1.95) | 0.844 |
| | Comparison | 493 | 26 (5.3) | | |
| Enlisted Flyer | Ranch Hand | 151 | 11 (7.3) | 1.26 (0.53,2.98) | 0.604 |
| | Comparison | 187 | 11 (5.9) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 20 (5.3) | 1.55 (0.82,2.92) | 0.178 |
| | Comparison | 569 | 20 (3.5) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|-----------------------------------|--------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>1.26 (0.83,1.89)</i> | <i>0.275</i> |
| Officer | 1.01 (0.54,1.89) | 0.972 |
| Enlisted Flyer | 1.05 (0.43,2.59) | 0.911 |
| Enlisted Groundcrew | 1.79 (0.91,3.49) | 0.090 |

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 160 | 8 (5.0) | 1.00 (0.74,1.35) | 0.998 |
| Medium | 162 | 11 (6.8) | | |
| High | 157 | 7 (4.5) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 471 | 1.12 (0.79,1.60) | 0.530 |

^a Relative risk for a twofold increase in initial dioxin.

Table 11-35. Analysis of Gait (Continued)

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|----------|--------------------------------|---|----------------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.)^{ab} | p-Value |
| Comparison | 1,211 | 55 (4.5) | | |
| Background RH | 380 | 23 (6.1) | 1.50 (0.91,2.49) | 0.115 |
| Low RH | 239 | 11 (4.6) | 0.98 (0.51,1.91) | 0.963 |
| High RH | 240 | 15 (6.3) | 1.28 (0.71,2.32) | 0.414 |
| Low plus High RH | 479 | 26 (5.4) | 1.12 (0.69,1.83) | 0.640 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | | |
|---|----------|--|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| Comparison | 1,193 | | | |
| Background RH | 375 | 1.52 (0.90,2.59) | | 0.121 |
| Low RH | 235 | 0.77 (0.38,1.57) | | 0.479 |
| High RH | 236 | 1.44 (0.76,2.74) | | 0.262 |
| Low plus High RH | 471 | 1.06 (0.63,1.78) | | 0.832 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|--------------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 17 (5.9) | 1.00 (0.83,1.22) | 0.966 |
| Medium | 287 | 15 (5.2) | | |
| High | 285 | 17 (6.0) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

Table 11-35. Analysis of Gait (Continued)

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | |
|--|--|----------------|
| Analysis Results for Log ₂ (1987 Dioxin + 1) | | |
| n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| 846 | 0.99 (0.78,1.25) | 0.905 |

^a Relative risk for a twofold increase in 1987 dioxin.

11.2.2.5.5 CNS Index

All results from the analyses of the CNS index from Models 1 through 4 were nonsignificant (Table 11-36(a-h): p>0.10 for each analysis).

Table 11-36. Analysis of CNS Index

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED | | | | | |
|--|-------------------|--------------|--------------------------------|--|----------------|
| Occupational Category | Group | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>Ranch Hand</i> | <i>866</i> | <i>107 (12.4)</i> | <i>1.05 (0.80,1.37)</i> | <i>0.731</i> |
| | <i>Comparison</i> | <i>1,248</i> | <i>148 (11.9)</i> | | |
| Officer | Ranch Hand | 340 | 39 (11.5) | 1.08 (0.69,1.67) | 0.745 |
| | Comparison | 493 | 53 (10.8) | | |
| Enlisted Flyer | Ranch Hand | 151 | 24 (15.9) | 1.07 (0.59,1.94) | 0.816 |
| | Comparison | 187 | 28 (15.0) | | |
| Enlisted Groundcrew | Ranch Hand | 375 | 44 (11.7) | 0.99 (0.66,1.49) | 0.977 |
| | Comparison | 568 | 67 (11.8) | | |

| (b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED | | |
|--|--|----------------|
| Occupational Category | Adjusted Relative Risk (95% C.I.) | p-Value |
| <i>All</i> | <i>0.99 (0.75,1.31)</i> | <i>0.957</i> |
| Officer | 1.01 (0.64,1.58) | 0.975 |
| Enlisted Flyer | 0.92 (0.50,1.70) | 0.799 |
| Enlisted Groundcrew | 1.01 (0.67,1.54) | 0.950 |

Table 11-36. Analysis of CNS Index (Continued)

| (c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED | | | | |
|---|-----|---------------------|---|---------|
| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
| Initial Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.) ^b | p-Value |
| Low | 160 | 18 (11.3) | 1.00 (0.81,1.24) | 0.976 |
| Medium | 162 | 21 (13.0) | | |
| High | 157 | 15 (9.6) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

| (d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED | | |
|---|--|---------|
| Analysis Results for Log ₂ (Initial Dioxin) | | |
| n | Adjusted Relative Risk (95% C.I.) ^a | p-Value |
| 471 | 1.03 (0.80,1.33) | 0.840 |

^a Relative risk for a twofold increase in initial dioxin.

| (e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED | | | | |
|---|-------|---------------------|---|---------|
| Dioxin Category | n | Number (%) Abnormal | Est. Relative Risk (95% C.I.) ^{ab} | p-Value |
| Comparison | 1,210 | 146 (12.1) | | |
| Background RH | 380 | 52 (13.7) | 1.18 (0.84,1.66) | 0.339 |
| Low RH | 239 | 24 (10.0) | 0.81 (0.51,1.28) | 0.363 |
| High RH | 240 | 30 (12.5) | 1.02 (0.67,1.56) | 0.923 |
| Low plus High RH | 479 | 54 (11.3) | 0.91 (0.65,1.27) | 0.576 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

Table 11-36. Analysis of CNS Index (Continued)

| (f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED | | | |
|---|----------|--|----------------|
| Dioxin Category | n | Adjusted Relative Risk (95% C.I.)^a | p-Value |
| Comparison | 1,192 | | |
| Background RH | 375 | 1.24 (0.86,1.77) | 0.249 |
| Low RH | 235 | 0.67 (0.42,1.09) | 0.105 |
| High RH | 236 | 0.94 (0.60,1.47) | 0.789 |
| Low plus High RH | 471 | 0.80 (0.56,1.13) | 0.205 |

^a Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin > 10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin > 10 ppt, Initial Dioxin > 94 ppt.

| (g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED | | | | |
|--|----------|----------------------------|---|----------------|
| 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (1987 Dioxin + 1) | |
| 1987 Dioxin | n | Number (%) Abnormal | Estimated Relative Risk (95% C.I.)^a | p-Value |
| Low | 287 | 39 (13.6) | 0.97 (0.84,1.12) | 0.672 |
| Medium | 287 | 35 (12.2) | | |
| High | 285 | 32 (11.2) | | |

^a Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.9 ppt; Medium = >7.9–19.6 ppt; High = >19.6 ppt.

| (h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED | | | |
|---|--|--|----------------|
| Analysis Results for Log₂ (1987 Dioxin + 1) | | | |
| n | Adjusted Relative Risk (95% C.I.)^a | | p-Value |
| 846 | 0.94 (0.80,1.10) | | 0.443 |

^a Relative risk for a twofold increase in 1987 dioxin.

11.2.3 Longitudinal Analysis

Longitudinal analyses were conducted on two indices—the cranial nerve function index and the CNS index—to examine whether changes across time differed with respect to group membership (Model 1), initial dioxin (Model 2), and categorized dioxin (Model 3). Model 4 was not examined in longitudinal analyses because 1987 dioxin, the measure of exposure in these models, changes over time and is not available for all participants for 1985 or 1997. For both indices, the longitudinal analyses investigated the differences between the 1985 follow-up examination and the 1997 follow-up examination, because Scripps Clinic conducted both of the neurological examinations. A different clinic performed the

neurological examinations for the 1982 baseline study, and the prevalence of abnormalities was much higher for the neurological parameters in 1982, suggesting a different method of examination.

The longitudinal analyses for all of these variables investigated the difference between the 1985 examination and the 1997 examination. These analyses were used to investigate the temporal effects of dioxin during the 12-year period between 1985 and 1997. Participants considered abnormal in 1985 were not included in the analyses because they were already abnormal before this period. Consequently, only participants considered normal at the 1985 examination (i.e., a normal index) were considered to be at risk when the effects of dioxin over this period of time were explored. The rate of abnormalities under this restriction approximates an incidence rate between 1985 and 1997. That is, an incidence rate is a measure of the rate at which people without a condition develop the condition during a specified period of time (44). Summary statistics are provided for reference purposes for the 1987 and 1992 examinations. All three models were adjusted for age; Models 2 and 3 also were adjusted for the percentage of body fat at the time of the blood measurement of dioxin.

11.2.3.1 Physical Examination Variables

11.2.3.1.1 Cranial Nerve Index

The longitudinal analysis of the cranial nerve index was based on participants with a normal index in 1985. All results from the Model 1 analysis indicate no significant difference between Ranch Hands and Comparisons (Table 11-37(a): $p > 0.61$ for each contrast).

Table 11-37. Longitudinal Analysis of Cranial Nerve Index

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS | | | | | |
|---|-------------------|--|---------------------|---------------------|---------------------|
| Occupational Category | Group | Number (%) Abnormal/(n) Examination | | | |
| | | 1985 | 1987 | 1992 | 1997 |
| <i>All</i> | <i>Ranch Hand</i> | 30 (3.7) (802) | 35 (4.5) (777) | 39 (5.0) (777) | 55 (6.9) (802) |
| | <i>Comparison</i> | 21 (2.0) (1,048) | 43 (4.2) (1,018) | 31 (3.1) (1,014) | 59 (5.6) (1,048) |
| Officer | Ranch Hand | 8 (2.6) (308) | 11 (3.6) (302) | 13 (4.3) (301) | 17 (5.5) (308) |
| | Comparison | 7 (1.7) (414) | 11 (2.7) (403) | 16 (4.0) (404) | 23 (5.6) (414) |
| Enlisted Flyer | Ranch Hand | 5 (3.4) (146) | 7 (4.9) (143) | 5 (3.5) (142) | 13 (8.9) (146) |
| | Comparison | 1 (0.6) (156) | 7 (4.7) (150) | 3 (2.0) (154) | 8 (5.1) (156) |
| Enlisted Groundcrew | Ranch Hand | 17 (4.9) (348) | 17 (5.1) (332) | 21 (6.3) (334) | 25 (7.2) (348) |
| | Comparison | 13 (2.7) (478) | 25 (5.4) (465) | 12 (2.6) (456) | 28 (5.9) (478) |

Table 11-37. Longitudinal Analysis of Cranial Nerve Index (Continued)

| Occupational Category | Group | Normal in 1985 | | Adj. Relative Risk (95% C.I.) ^a | p-Value ^a |
|-----------------------|------------------------------|----------------|-----------------------------|--|----------------------|
| | | n in 1997 | Number (%) Abnormal in 1997 | | |
| <i>All</i> | <i>Ranch Hand Comparison</i> | 772 1,027 | 41 (5.3) 52 (5.1) | 1.05 (0.69,1.59) | 0.836 |
| Officer | Ranch Hand Comparison | 300 407 | 16 (5.3) 18 (4.4) | 1.20 (0.60,2.39) | 0.613 |
| Enlisted Flyer | Ranch Hand Comparison | 141 155 | 9 (6.4) 8 (5.2) | 1.23 (0.46,3.28) | 0.684 |
| Enlisted Groundcrew | Ranch Hand Comparison | 331 465 | 16 (4.8) 26 (5.6) | 0.89 (0.47,1.68) | 0.710 |

^a Relative risk, confidence interval, and p-values are in reference to a contrast of 1985 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985, 1992, and 1997 examinations. Statistical analyses are based only on participants with a normal cranial nerve index in 1985 (see Chapter 7, Statistical Methods).

| (b) MODEL 2: RANCH HANDS – INITIAL DIOXIN | | | | |
|--|-------------------------------------|-------------------|------------------|-------------------|
| Initial Dioxin | Number (%) Abnormal/(n) Examination | | | |
| | 1985 | 1987 | 1992 | 1997 |
| Low | 3 (2.0) (148) | 6 (4.1) (147) | 9 (6.3) (142) | 13 (8.8) (148) |
| Medium | 5 (3.1) (159) | 10 (6.5) (154) | 4 (2.6) (155) | 9 (5.7) (159) |
| High | 5 (3.4) (146) | 5 (3.6) (140) | 9 (6.4) (141) | 7 (4.8) (146) |

| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log ₂ (Initial Dioxin) ^a | |
|--|----------------|-----------------------------|---|---------|
| Initial Dioxin | Normal in 1985 | | Adj. Relative Risk (95% C.I.) ^b | p-Value |
| | n in 1997 | Number (%) Abnormal in 1997 | | |
| Low | 145 | 12 (8.3) | 0.66 (0.42,1.03) | 0.049 |
| Medium | 154 | 5 (3.3) | | |
| High | 141 | 4 (2.8) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985, 1992, and 1997 examinations. Statistical analyses are based only on participants with a normal cranial nerve index in 1985 (see Chapter 7, Statistical Methods).

Table 11-37. Longitudinal Analysis of Cranial Nerve Index (Continued)

| (c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY | | | | |
|--|--|-------------------|-------------------|---------------------|
| Dioxin Category | Number (%) Abnormal/(n) Examination | | | |
| | 1985 | 1987 | 1992 | 1997 |
| Comparison | 20 (2.0) (1,019) | 43 (4.3) (991) | 30 (3.0) (987) | 56 (5.5) (1,019) |
| Background RH | 17 (5.0) (343) | 14 (4.2) (330) | 17 (5.1) (333) | 25 (7.3) (343) |
| Low RH | 7 (3.1) (224) | 13 (5.9) (220) | 12 (5.6) (215) | 19 (8.5) (224) |
| High RH | 6 (2.6) (229) | 8 (3.6) (221) | 10 (4.5) (223) | 10 (4.4) (229) |
| Low plus High RH | 13 (2.9) (453) | 21 (4.8) (441) | 22 (5.0) (438) | 29 (6.4) (453) |

| Dioxin Category | Normal in 1985 | | Adj. Relative Risk (95% C.I.)^{ab} | p-Value^b |
|------------------------|-----------------------|--|---|----------------------------|
| | n in 1997 | Number (%) Abnormal in 1997 | | |
| Comparison | 999 | 50 (5.0) | | |
| Background RH | 326 | 19 (5.8) | 1.21 (0.70,2.10) | 0.496 |
| Low RH | 217 | 15 (6.9) | 1.29 (0.71,2.35) | 0.410 |
| High RH | 223 | 6 (2.7) | 0.54 (0.23,1.29) | 0.167 |
| Low plus High RH | 440 | 21 (4.8) | 0.83 (0.47,1.47) | 0.522 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin ≤ 10 ppt.

Background (Ranch Hand): 1987 Dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 Dioxin >10 ppt, 10 ppt < Initial Dioxin ≤ 94 ppt.

High (Ranch Hand): 1987 Dioxin >10 ppt, Initial Dioxin > 94 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985, 1992, and 1997 examinations. Statistical analyses are based only on participants with a normal cranial nerve index in 1985 (see Chapter 7, Statistical Methods).

The Model 2 longitudinal analysis revealed an inverse significant relation between initial dioxin and the cranial nerve index (Table 11-37(b): Adj. RR=0.66, p=0.049). As initial dioxin increased, the prevalence of an abnormal cranial nerve index decreased.

All results from the Model 3 longitudinal analysis of cranial nerve index were nonsignificant (Table 11-37(c): p>0.16 for each Model 3 contrast).

11.2.3.1.2 CNS Index

Based on participants with a normal CNS index in 1985, all results from the longitudinal analysis of the CNS index for Models 1 through 3 were nonsignificant (Table 11-38(a-c): $p > 0.20$ for each analysis).

Table 11-38. Longitudinal Analysis of CNS Index

| (a) MODEL 1: RANCH HANDS VS. COMPARISONS | | | | | |
|---|-------------------|-------------------------------------|---------------------|---------------------|-----------------------|
| Occupational Category | Group | Number (%) Abnormal/(n) Examination | | | |
| | | 1985 | 1987 | 1992 | 1997 |
| <i>All</i> | <i>Ranch Hand</i> | 29 (3.5) (826) | 44 (5.5) (805) | 39 (4.9) (804) | 105 (12.7) (826) |
| | <i>Comparison</i> | 27 (2.6) (1,060) | 45 (4.4) (1,034) | 50 (4.8) (1,033) | 128 (12.1) (1,060) |
| Officer | Ranch Hand | 7 (2.2) (322) | 10 (3.2) (316) | 15 (4.8) (316) | 38 (11.8) (322) |
| | Comparison | 5 (1.2) (420) | 17 (4.2) (410) | 24 (5.8) (413) | 47 (11.2) (420) |
| Enlisted Flyer | Ranch Hand | 7 (4.8) (146) | 6 (4.2) (143) | 8 (5.6) (144) | 24 (16.4) (146) |
| | Comparison | 7 (4.4) (159) | 5 (3.2) (155) | 2 (1.3) (157) | 21 (13.2) (159) |
| Enlisted Groundcrew | Ranch Hand | 15 (4.2) (358) | 28 (8.1) (346) | 16 (4.7) (344) | 43 (12.0) (358) |
| | Comparison | 15 (3.1) (481) | 23 (4.9) (469) | 24 (5.2) (463) | 60 (12.5) (481) |

| Occupational Category | Group | Normal in 1985 | | Adj. Relative Risk (95% C.I.) ^a | p-Value ^a |
|-----------------------|-------------------|----------------|--------------------------------|---|----------------------|
| | | n in 1997 | Number (%) Abnormal in 1997 | | |
| <i>All</i> | <i>Ranch Hand</i> | 797 | 90 (11.3) | 1.05 (0.78,1.42) | 0.725 |
| | <i>Comparison</i> | 1,033 | 111 (10.8) | | |
| Officer | Ranch Hand | 315 | 34 (10.8) | 0.99 (0.61,1.59) | 0.955 |
| | Comparison | 415 | 45 (10.8) | | |
| Enlisted Flyer | Ranch Hand | 139 | 21 (15.1) | 1.59 (0.78,3.24) | 0.201 |
| | Comparison | 152 | 15 (9.9) | | |
| Enlisted Groundcrew | Ranch Hand | 343 | 35 (10.2) | 0.95 (0.60,1.51) | 0.835 |
| | Comparison | 466 | 51 (10.9) | | |

^a Relative risk, confidence interval, and p-values are in reference to a contrast of 1982 and 1997 results; results adjusted for age in 1997.

Note: Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985, 1992, and 1997 examinations. Statistical analyses are based only on participants with a normal CNS index in 1985 (see Chapter 7, Statistical Methods).

Table 11-38. Longitudinal Analysis of CNS Index (Continued)

| (b) MODEL 2: RANCH HANDS – INITIAL DIOXIN | | | | |
|--|--|-------------------|------------------|--------------------|
| Initial Dioxin | Number (%) Abnormal/(n) Examination | | | |
| | 1985 | 1987 | 1992 | 1997 |
| Low | 7 (4.6) (153) | 4 (2.6) (153) | 6 (4.1) (148) | 18 (11.8) (153) |
| Medium | 4 (2.5) (159) | 8 (5.1) (156) | 8 (5.2) (155) | 21 (13.2) (159) |
| High | 4 (2.7) (151) | 10 (6.8) (147) | 4 (2.7) (147) | 15 (9.9) (151) |

| Initial Dioxin Category Summary Statistics | | | Analysis Results for Log₂ (Initial Dioxin)^a | |
|---|-----------------------|--|--|----------------|
| Initial Dioxin | Normal in 1985 | | Adj. Relative Risk (95% C.I.)^b | p-Value |
| | n in 1997 | Number (%) Abnormal in 1997 | | |
| Low | 146 | 15 (10.3) | 1.13 (0.89,1.42) | 0.319 |
| Medium | 155 | 20 (12.9) | | |
| High | 147 | 14 (9.5) | | |

^a Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

^b Relative risk for a twofold increase in initial dioxin.

Note: Low = 27–63 ppt; Medium = >63–152 ppt; High = >152 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985, 1992, and 1997 examinations. Statistical analyses are based only on participants with a normal CNS index in 1985 (see Chapter 7, Statistical Methods).

| (c) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY | | | | |
|--|--|---------------------|---------------------|-----------------------|
| Dioxin Category | Number (%) Abnormal/(n) Examination | | | |
| | 1985 | 1987 | 1992 | 1997 |
| Comparison | 26 (2.5) (1,031) | 44 (4.4) (1,007) | 49 (4.9) (1,006) | 126 (12.2) (1,031) |
| Background RH | 14 (3.9) (357) | 21 (6.1) (343) | 20 (5.8) (348) | 50 (14.0) (357) |
| Low RH | 7 (3.1) (229) | 6 (2.6) (227) | 9 (4.1) (221) | 24 (10.5) (229) |
| High RH | 8 (3.4) (234) | 16 (7.0) (229) | 9 (3.9) (229) | 30 (12.8) (234) |
| Low plus High RH | 15 (3.2) (463) | 22 (4.8) (456) | 18 (4.0) (450) | 54 (11.7) (463) |

Table 11-38. Longitudinal Analysis of CNS Index (Continued)

| Dioxin Category | Normal in 1985 | | Adj. Relative Risk (95% C.I.) ^{ab} | p-Value ^b |
|------------------|----------------|--------------------------------|--|----------------------|
| | n in 1997 | Number (%) Abnormal in 1997 | | |
| Comparison | 1,005 | 110 (11.0) | | |
| Background RH | 343 | 40 (11.7) | 1.07 (0.72,1.58) | 0.749 |
| Low RH | 222 | 21 (9.5) | 0.76 (0.46,1.25) | 0.279 |
| High RH | 226 | 28 (12.4) | 1.31 (0.83,2.06) | 0.244 |
| Low plus High RH | 448 | 49 (10.9) | 1.00 (0.69,1.44) | 0.999 |

^a Relative risk and confidence interval relative to Comparisons.

^b Adjusted for percent body fat at the time of the blood measurement of dioxin and age in 1997.

Note: RH = Ranch Hand.

Comparison: 1987 Dioxin \leq 10 ppt.

Background (Ranch Hand): 1987 Dioxin \leq 10 ppt.

Low (Ranch Hand): 1987 Dioxin $>$ 10 ppt, 10 ppt $<$ Initial Dioxin \leq 94 ppt.

High (Ranch Hand): 1987 Dioxin $>$ 10 ppt, Initial Dioxin $>$ 94 ppt.

Summary statistics for 1987 are provided for reference purposes for participants who attended the 1985, 1987, and 1997 examinations. Summary statistics for 1992 are provided for reference purposes for participants who attended the 1985, 1992, and 1997 examinations. Statistical analyses are based only on participants with a normal CNS index in 1985 (see Chapter 7, Statistical Methods).

11.3 DISCUSSION

The data analyzed in the neurological assessment can be relied upon to detect the presence, if not the cause, of neurological disease, including disorders of the peripheral nervous system. CNS, cranial, and peripheral nerve variables examined can provide specific clues to the anatomical site of neurological lesions and clarify the need for additional diagnostic studies. Pertinent to the current study, the neurological examination is highly sensitive in detecting the presence of peripheral neuropathy, a suspected clinical condition related to herbicide exposure.

In clinical practice, it is convenient to divide the neurological assessment into examinations of the peripheral and cranial nerves. The motor and sensory peripheral nerve variables and the cranial nerve variables examined provide highly specific clues to the anatomic site of neurological lesions and clarify which additional diagnostic studies would be most helpful in establishing a diagnosis. As indices of CNS function, tremor and coordination are less specific and more subject to individual variation in the absence of underlying neurological disease. Tremor, for example, may occur as a benign familial trait, may be reflective of alcohol withdrawal, or may be a marker of extra-pyramidal motor system disease as in Parkinson's syndrome. The Romberg sign may signal a lesion in the cerebellum but is more often indicative of impaired position sense in the lower extremities or of inner ear disease. Finally, the mental status examination is of obvious importance in the CNS assessment and, as in previous AFHS examinations, extensive psychometric studies were conducted and are reported in Chapter 12, Psychology Assessment.

Analysis of inflammatory diseases confirmed by a medical records review found a significant excess among Ranch Hands (n=7 or 0.8%) relative to Comparisons (n=1 or 0.1%). Of the seven Ranch Hands with inflammatory diseases, three (42.9%) had meningitis caused by bacterial infections. The single Comparison with an inflammatory disease had encephalitis of unknown cause, suggesting that this

finding is unrelated to herbicide or dioxin exposure. Consistent with the 1987 and 1992 examinations, Ranch Hands with low and high levels of categorized dioxin were more likely than Comparisons to develop other neurological disorders, although the associations were not significant after adjustment for covariates. Similar results were noted with respect to 1987 serum dioxin levels. Although the prevalence of peripheral neurological disorders established by a medical records review was similar in Ranch Hands and Comparisons (21.8% and 19.3%, respectively), there was evidence for an association with dioxin levels in two of the models. Ranch Hands in the low plus high dioxin category were at significantly greater risk than Comparisons (25.1% versus 19.3%, respectively), a contrast that remained marginally significant after adjustment for covariates. Further, in both the unadjusted and adjusted analyses, a significant positive association was noted between the occurrence of peripheral disorders and 1987 dioxin levels.

With one exception, no significant associations were noted in the analyses of any of the directly measured physical examination variables. Ranch Hands were significantly more likely than Comparisons to develop restricted range of motion at the neck, a common occurrence in any aging population and one that is usually related to osteoarthritis of the cervical spine rather than any primary neurological cause. Across occupational strata, the contrast was significant only in the enlisted flyer category. Ranch Hands with low and high levels of categorized dioxin were at significantly greater risk for the development of restricted neck range of motion.

Only one of the analyses of peripheral motor and sensory nerve function yielded significant group differences. By inspection and palpation, Ranch Hands were more likely than Comparisons to have abnormalities of muscle mass (4.5% versus 3.0%, respectively) particularly in the enlisted groundcrew occupational category (4.3% versus 2.1%), even after adjustment for covariates. In none of the individual analyses was there any significant associations with 1987 serum dioxin levels, nor were any group differences detected in the analyses of CNS coordination variables.

Significant group differences were found in three of the four composite polyneuropathy indices described earlier in this chapter. Ranch Hands were significantly more likely than Comparisons to have abnormalities in the confirmed polyneuropathy index (1.4% versus 0.6%), the polyneuropathy severity index of moderate degree (2.6% versus 1.1%), and the multiple polyneuropathy index (5.0% versus 3.2%). In each case, Ranch Hands in the high dioxin category were at a significantly greater risk for abnormal scores than Comparisons; the prevalence of abnormalities increased as initial dioxin increased.

Longitudinal analyses conducted during 12 years of observation yielded no significant differences between the Ranch Hand and Comparison cohorts, nor was there any evidence for dose responses with respect to either initial or 1987 dioxin levels.

Dependent variable-covariate analyses confirmed associations with age and diabetes that are well established. Diabetes was by far the strongest covariate and significantly associated with neurological disease historically, on physical examination, and as assessed by all of the composite indices. Associations with alcohol were sporadic and less prominent than during previous AFHS examinations.

In summary, in contrast to previous examinations, the history of neurological disease now appears significantly greater in Ranch Hands than Comparisons historically (diseases of inflammatory origin and peripheral disorders), on physical examination (restriction of range of motion), and as reflected in several of the composite indices described above. Further, the associations of neck range of motion with categorized dioxin and a history of peripheral disorders with 1987 dioxin provide evidence of an

association of neurological disease with prior exposure to dioxin. The results of the analysis of the polyneuropathy indices also provide support of an association between dioxin and neurological disease.

11.4 SUMMARY

Four neurological disorders, which were verified by a medical records review, and extensive physical examination data on cranial nerve function, peripheral nerve status, and CNS coordination processes were analyzed in the neurological assessment. Each endpoint was examined for a significant association, both unadjusted and adjusted for covariates, with group (Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4). Summaries of the Model 1 through 4 analyses are tabled and discussed below, with emphasis on significant findings from the adjusted analysis.

11.4.1 Model 1: Group Analysis

The prevalence of inflammatory diseases, a restricted neck range of motion, and a moderate polyneuropathy severity index was significantly greater for Ranch Hands than for Comparisons when combining all occupations. Significantly more Comparisons than Ranch Hands had an abnormal light reaction. Other neurological disorders, the multiple polyneuropathy index, the confirmed polyneuropathy index, and muscle status showed a marginally significant increase in all Ranch Hands relative to Comparisons. No significant differences were observed between Ranch Hand and Comparison officers. The neck range of motion and moderate polyneuropathy severity index results were significant or marginally significant in the contrast of Ranch Hand and Comparison enlisted flyers. The confirmed polyneuropathy indicator and muscle status results were significant or marginally significant in the enlisted groundcrew. Table 11-39 displays the Model 1 results of all unadjusted and adjusted analyses.

Table 11-39. Summary of Group Analysis (Model 1) for Neurology Variables (Ranch Hands vs. Comparisons)

| Variable | UNADJUSTED | | | |
|--------------------------------------|------------|---------|----------------|---------------------|
| | All | Officer | Enlisted Flyer | Enlisted Groundcrew |
| Medical Records | | | | |
| Inflammatory Diseases | +0.006 | NS | NS | NS |
| Hereditary and Degenerative Diseases | NS | NS | NS | ns |
| Peripheral Disorders | NS | NS | NS | NS |
| Other Neurological Disorders | NS* | NS | NS | NS |
| Physical Examination | | | | |
| Smell | NS | ns | NS* | NS |
| Visual Fields | ns | ns | ns | ns |
| Light Reaction | -0.007 | ns | ns | ns |
| Ocular Movement | NS | ns | NS | NS |
| Facial Sensation | NS | NS | ns | NS |
| Jaw Clench | NS | NS | -- | -- |
| Smile | NS | ns | NS | NS |
| Palpebral Fissure | ns | ns | NS | NS |
| Balance | NS | NS | ns | ns |
| Speech | ns | ns | ns | ns |
| Tongue Position Relative to Midline | NS | NS | -- | -- |
| Palate and Uvula Movement | NS | NS | -- | -- |

Table 11-39. Summary of Group Analysis (Model 1) for Neurology Variables (Ranch Hands vs. Comparisons) (Continued)

| Variable | UNADJUSTED | | | |
|------------------------------------|------------|---------|----------------|---------------------|
| | All | Officer | Enlisted Flyer | Enlisted Groundcrew |
| Cranial Nerve Index | NS | ns | NS | NS |
| Neck Range of Motion | +0.016 | NS | +0.009 | NS |
| Pinprick | NS | NS | NS | ns |
| Light Touch | NS | NS | NS | ns |
| Muscle Status | NS* | NS | NS | NS* |
| Patellar Reflex | ns | NS | ns* | NS |
| Achilles Reflex | NS | NS | NS | NS |
| Biceps Reflex | NS | NS | NS | NS |
| Babinski Reflex | ns | NS | ns | ns |
| Polyneuropathy Severity Index | | | | |
| Moderate vs. None/Mild | +0.015 | NS | NS* | NS |
| Severe vs. None/Mild | NS | NS | -- | NS |
| Polyneuropathy Prevalence Index | NS | NS | ns | NS |
| Multiple Polyneuropathy Index | +0.046 | NS | NS | NS |
| Confirmed Polyneuropathy Indicator | NS* | ns | NS* | NS* |
| Tremor | ns | NS | NS | ns |
| Coordination | ns | NS | ns | ns |
| Romberg Sign | NS | NS | ns | ns |
| Gait | NS | NS | NS | NS |
| CNS Index | NS | NS | NS | ns |

Note: NS or ns: Not significant ($p > 0.10$).

NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).

+: Relative risk ≥ 1.00 .

-: Relative risk < 1.00 .

--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if $p \leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00.

| Variable | ADJUSTED | | | |
|--------------------------------------|----------|---------|----------------|---------------------|
| | All | Officer | Enlisted Flyer | Enlisted Groundcrew |
| Medical Records | | | | |
| Inflammatory Diseases | +0.002 | -- | -- | NS |
| Hereditary and Degenerative Diseases | NS | NS | NS | ns |
| Peripheral Disorders | NS | NS | ns | NS |
| Other Neurological Disorders | NS* | NS | NS | NS |
| Physical Examination | | | | |
| Smell | NS | ns | NS | NS |
| Visual Fields | ns | -- | ns | ns |
| Light Reaction | -0.010 | -- | ns | -- |
| Ocular Movement | NS | ns | NS | NS |
| Facial Sensation | NS | NS | -- | -- |
| Jaw Clench | -- | -- | -- | -- |
| Smile | NS | ns | -- | NS |
| Palpebral Fissure | ns | ns | ns | ns |

Table 11-39. Summary of Group Analysis (Model 1) for Neurology Variables (Ranch Hands vs. Comparisons) (Continued)

| Variable | ADJUSTED | | | |
|-------------------------------------|----------|---------|----------------|---------------------|
| | All | Officer | Enlisted Flyer | Enlisted Groundcrew |
| Balance | NS | NS | -- | ns |
| Speech | ns | ns | -- | ns |
| Tongue Position Relative to Midline | -- | -- | -- | -- |
| Palate and Uvula Movement | -- | -- | -- | -- |
| Cranial Nerve Index | NS | ns | NS | NS |
| Neck Range of Motion | +0.015 | NS | +0.016 | NS |
| Pinprick | NS | NS | NS | ns |
| Light Touch | NS | NS | NS | ns |
| Muscle Status | NS* | ns | NS | +0.046 |
| Patellar Reflex | ns | NS | ns* | NS |
| Achilles Reflex | NS | NS | ns | NS |
| Biceps Reflex | NS | NS | NS | NS |
| Babinski Reflex | ns | NS | ns | ns |
| Polyneuropathy Severity Index | | | | |
| Moderate vs. None/Mild | +0.020 | NS | NS* | NS |
| Severe vs. None/Mild | NS | -- | -- | NS |
| Polyneuropathy Prevalence Index | ns | NS | ns | NS |
| Multiple Polyneuropathy Index | NS* | NS | NS | NS |
| Confirmed Polyneuropathy Indicator | NS* | ns | -- | NS* |
| Tremor | ns | NS | NS | ns |
| Coordination | ns | NS | ns | ns |
| Romberg Sign | NS | NS | -- | ns |
| Gait | NS | NS | NS | NS* |
| CNS Index | ns | NS | ns | NS |

Note: NS or ns: Not significant ($p > 0.10$).

NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).

+: Relative risk ≥ 1.00 .

-: Relative risk < 1.00 .

--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if $p \leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00.

11.4.2 Model 2: Initial Dioxin Analysis

Table 11-40 summarizes the results from the Model 2 analyses. Several positive and significant associations between the neurological variables and initial dioxin were found in adjusted analyses. In assessing the cranial nerve function, abnormal visual fields increased as initial dioxin increased. The assessment of measures of peripheral nerve status showed a significant or marginally significant positive association between initial dioxin and the patellar and Achilles reflexes. An association between all four polyneuropathy indices and dioxin was observed. The moderate classification of the polyneuropathy severity index, the polyneuropathy prevalence index, the multiple polyneuropathy index, and the confirmed polyneuropathy indicator were all significant and positively associated with initial dioxin.

Table 11-40. Summary of Initial Dioxin Analysis (Model 2) for Neurology Variables (Ranch Hands Only)

| Variable | Unadjusted | Adjusted |
|--------------------------------------|------------|----------|
| Medical Records | | |
| Inflammatory Diseases | NS | ns |
| Hereditary and Degenerative Diseases | NS | NS |
| Peripheral Disorders | NS | NS |
| Other Neurological Disorders | NS | ns |
| Physical Examination | | |
| Smell | ns | ns |
| Visual Fields | +0.040 | +0.049 |
| Light Reaction | -- | -- |
| Ocular Movement | ns | ns |
| Facial Sensation | ns | ns |
| Jaw Clench | ns | ns |
| Smile | NS | NS |
| Palpebral Fissure | NS | NS |
| Balance | NS | NS |
| Speech | ns | ns* |
| Tongue Position Relative to Midline | ns | ns |
| Palate and Uvula Movement | ns | ns |
| Cranial Nerve Index | ns | ns |
| Neck Range of Motion | ns* | ns |
| Pinprick | NS | NS |
| Light Touch | ns | NS |
| Muscle Status | ns | ns |
| Patellar Reflex | NS | +0.019 |
| Achilles Reflex | NS | NS* |
| Biceps Reflex | ns | ns |
| Babinski Reflex | ns | NS |
| Polyneuropathy Severity Index | | |
| Moderate vs. None/Mild | NS | +0.042 |
| Severe vs. None/Mild | ns | ns |
| Polyneuropathy Prevalence Index | | |
| Multiple Polyneuropathy Index | NS* | +0.004 |
| Confirmed Polyneuropathy Indicator | +0.033 | +0.008 |
| Tremor | NS | NS |
| Coordination | ns | NS |
| Romberg Sign | NS | NS |
| Gait | NS | NS |
| CNS Index | NS | NS |

Note: NS or ns: Not significant ($p > 0.10$).

NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).

+: Relative risk ≥ 1.00 .

--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if $p \leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00.

11.4.3 Model 3: Categorized Dioxin Analysis

Results from the Model 3 analyses of the neurology variables are presented in Table 11-41. Each significant or marginally significant result from the Model 3 adjusted analyses displayed more Ranch Hands than Comparisons with a neurological abnormality. The adjusted analysis of inflammatory diseases displayed significant results for all levels of categorized dioxin. Results for peripheral disorders showed a marginally significant increased prevalence in the low plus high Ranch Hand dioxin category after adjustment for covariates. Neck range of motion was significantly greater for Ranch Hands in the low, high, and low plus high dioxin categories than for Comparisons. An increased prevalence of an abnormal muscle status was observed in the low and low plus high Ranch Hand dioxin categories. A marginally significant increase in an abnormal biceps reflex also was found for Ranch Hands in the low dioxin category. The polyneuropathy severity index showed an increase in the moderate classification of severity for Ranch Hands in the low, high, and low plus high dioxin categories. An increase in the severe classification of the polyneuropathy index was found for Ranch Hands in the low plus high dioxin category. Significant results also were found for Ranch Hands in the high dioxin category for the multiple polyneuropathy index and the confirmed polyneuropathy indicator. The prevalence of an abnormal confirmed polyneuropathy indicator was significantly greater for the low plus high Ranch Hand dioxin category than for Comparisons.

Table 11-41. Summary of Categorized Dioxin Analysis (Model 3) for Neurology Variables (Ranch Hands vs. Comparisons)

| Variable | UNADJUSTED | | | |
|--------------------------------------|--|---------------------------------|----------------------------------|---|
| | Background Ranch Hands vs. Comparisons | Low Ranch Hands vs. Comparisons | High Ranch Hands vs. Comparisons | Low plus High Ranch Hands vs. Comparisons |
| Medical Records | | | | |
| Inflammatory Diseases | NS* | NS* | NS* | +0.035 |
| Hereditary and Degenerative Diseases | NS | NS | NS | NS |
| Peripheral Disorders | ns | +0.033 | NS* | +0.014 |
| Other Neurological Disorders | ns | +0.023 | +0.005 | +0.001 |
| Physical Examination | | | | |
| Smell | NS | NS | NS | NS |
| Visual Fields | ns | ns | ns | ns |
| Light Reaction | ns | ns | ns | ns* |
| Ocular Movement | ns | NS | NS | NS |
| Facial Sensation | NS | NS | ns | NS |
| Jaw Clench | NS | NS | -- | NS |
| Smile | NS | NS | NS | NS |
| Palpebral Fissure | NS | ns | ns | ns |
| Balance | NS | ns | ns | ns |
| Speech | ns | NS | ns | ns |
| Tongue Position Relative to Midline | NS | NS | -- | NS |
| Palate and Uvula Movement | -- | NS | -- | NS |
| Cranial Nerve Index | NS | NS | ns | NS |
| Neck Range of Motion | NS | +0.002 | NS | +0.003 |
| Pinprick | NS | NS | NS* | NS |
| Light Touch | NS | NS | NS | NS |
| Muscle Status | NS | +0.021 | NS | +0.033 |
| Patellar Reflex | ns | NS | NS | NS |
| Achilles Reflex | ns | NS | NS | NS |
| Biceps Reflex | ns | +0.029 | NS | NS |

Table 11-41. Summary of Categorized Dioxin Analysis (Model 3) for Neurology Variables (Ranch Hands vs. Comparisons) (Continued)

| Variable | UNADJUSTED | | | |
|------------------------------------|--|---------------------------------|----------------------------------|---|
| | Background Ranch Hands vs. Comparisons | Low Ranch Hands vs. Comparisons | High Ranch Hands vs. Comparisons | Low plus High Ranch Hands vs. Comparisons |
| Babinski Reflex | NS | ns | ns | ns |
| Polyneuropathy Severity Index | | | | |
| Moderate vs. None/Mild | NS | +0.032 | +0.042 | +0.011 |
| Severe vs. None/Mild | NS | NS* | NS | NS* |
| Polyneuropathy Prevalence Index | ns | NS | NS | NS |
| Multiple Polyneuropathy Index | NS | NS | +0.018 | +0.042 |
| Confirmed Polyneuropathy Indicator | NS | NS | +0.017 | +0.047 |
| Tremor | NS | ns | ns | ns |
| Coordination | NS | ns | ns | ns |
| Romberg Sign | NS | ns | ns | ns |
| Gait | NS | ns | NS | NS |
| CNS Index | NS | ns | NS | ns |

Note: NS or ns: Not significant ($p > 0.10$).

NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).

+: Relative risk ≥ 1.00 .

--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if $p \leq 0.05$.

A capital “NS” denotes a relative risk of 1.00 or greater. A lowercase “ns” denotes a relative risk less than 1.00.

| Variable | ADJUSTED | | | |
|--------------------------------------|--|---------------------------------|----------------------------------|---|
| | Background Ranch Hands vs. Comparisons | Low Ranch Hands vs. Comparisons | High Ranch Hands vs. Comparisons | Low plus High Ranch Hands vs. Comparisons |
| Medical Records | | | | |
| Inflammatory Diseases | +0.029 | +0.035 | +0.047 | +0.024 |
| Hereditary and Degenerative Diseases | NS | ns | NS | ns |
| Peripheral Disorders | ns | NS | NS | NS* |
| Other Neurological Disorders | NS | NS | NS | NS |
| Physical Examination | | | | |
| Smell | NS | NS | ns | NS |
| Visual Fields | ns | -- | ns | -- |
| Light Reaction | ns | -- | -- | -- |
| Ocular Movement | NS | NS | NS | NS |
| Facial Sensation | NS | NS | -- | -- |
| Jaw Clench | -- | -- | -- | -- |
| Smile | NS | NS | NS | NS |
| Palpebral Fissure | ns | ns | ns | ns |
| Balance | NS | ns | ns | ns |
| Speech | NS | NS | -- | -- |
| Tongue Position Relative to Midline | -- | -- | -- | -- |
| Palate and Uvula Movement | -- | -- | -- | -- |

Table 11-41. Summary of Categorized Dioxin Analysis (Model 3) for Neurology Variables (Ranch Hands vs. Comparisons) (Continued)

| Variable | ADJUSTED | | | |
|------------------------------------|--|---------------------------------|----------------------------------|---|
| | Background Ranch Hands vs. Comparisons | Low Ranch Hands vs. Comparisons | High Ranch Hands vs. Comparisons | Low plus High Ranch Hands vs. Comparisons |
| Cranial Nerve Index | NS | NS | ns | ns |
| Neck Range of Motion | NS | +0.010 | +0.028 | +0.002 |
| Pinprick | NS | ns | NS | NS |
| Light Touch | NS | NS | NS | NS |
| Muscle Status | NS | NS* | NS | NS* |
| Patellar Reflex | ns | ns | NS | NS |
| Achilles Reflex | ns | ns | NS | NS |
| Biceps Reflex | ns | NS* | NS | NS |
| Babinski Reflex | NS | ns | ns | ns |
| Polyneuropathy Severity Index | | | | |
| Moderate vs. None/Mild | NS | NS* | +0.024 | +0.014 |
| Severe vs. None/Mild | NS | NS | NS | NS* |
| Polyneuropathy Prevalence Index | ns | ns | NS | NS |
| Multiple Polyneuropathy Index | NS | ns | +0.016 | NS |
| Confirmed Polyneuropathy Indicator | ns | NS | +0.007 | +0.047 |
| Tremor | NS | ns | ns | ns |
| Coordination | NS | ns | ns | ns |
| Romberg Sign | NS | ns | ns | ns |
| Gait | NS | ns | NS | NS |
| CNS Index | NS | ns | ns | ns |

Note: NS or ns: Not significant ($p > 0.10$).

NS*: Marginally significant ($0.05 < p \leq 0.10$).

+: Relative risk ≥ 1.00 .

--: Analysis not performed because of the sparse number of participants with an abnormality.

P-value given if $p \leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00.

11.4.4 Model 4: 1987 Dioxin Analysis

Significant positive associations were found between 1987 dioxin and peripheral disorders, the moderate classification of the polyneuropathy severity index, and the confirmed polyneuropathy indicator. A marginally significant positive association between the polyneuropathy prevalence index and 1987 dioxin was found. Complete Model 4 analysis results are presented in Table 11-42.

Table 11-42. Summary of 1987 Dioxin Analysis (Model 4) for Neurology Variables (Ranch Hands Only)

| Variable | Unadjusted | Adjusted |
|--------------------------------------|------------|----------|
| Medical Records | | |
| Inflammatory Diseases | ns | ns |
| Hereditary and Degenerative Diseases | ns | ns |
| Peripheral Disorders | +0.010 | +0.011 |
| Other Neurological Disorders | +0.038 | ns |
| Physical Examination | | |
| Smell | ns | ns |
| Visual Fields | NS | NS |
| Light Reaction | ns | ns |
| Ocular Movement | NS | ns |
| Facial Sensation | ns | ns |
| Jaw Clench | ns | NS |
| Smile | NS | ns |
| Palpebral Fissure | NS | NS |
| Balance | ns | ns |
| Speech | ns | ns |
| Tongue Position Relative to Midline | ns | NS |
| Palate and Uvula Movement | NS | NS |
| Cranial Nerve Index | ns | ns |
| Neck Range of Motion | NS | NS |
| Pinprick | NS | NS |
| Light Touch | NS | NS |
| Muscle Status | NS | ns |
| Patellar Reflex | NS | NS |
| Achilles Reflex | NS | NS |
| Biceps Reflex | NS | NS |
| Babinski Reflex | ns* | ns |
| Polyneuropathy Severity Index | | |
| Moderate vs. None/Mild | +0.024 | +0.013 |
| Severe vs. None/Mild | NS | NS |
| Polyneuropathy Prevalence Index | NS | NS* |
| Multiple Polyneuropathy Index | NS | NS |
| Confirmed Polyneuropathy Indicator | +0.002 | +0.003 |
| Tremor | ns | ns |
| Coordination | ns | ns |
| Romberg Sign | ns | ns |
| Gait | NS | ns |
| CNS Index | ns | ns |

Table 11-42. Summary of 1987 Dioxin Analysis (Model 4) for Neurology Variables (Ranch Hands Only) (Continued)

Note: NS or ns: Not significant ($p > 0.10$).

NS* or ns*: Marginally significant ($0.05 < p \leq 0.10$).

+: Relative risk ≥ 1.00 .

P-value given if $p \leq 0.05$.

A capital "NS" denotes a relative risk of 1.00 or greater. A lowercase "ns" denotes a relative risk less than 1.00.

11.5 CONCLUSION

Four neurological disorders and extensive physical examination data on cranial nerve function, peripheral nerve status, and CNS coordination processes were analyzed in the neurological assessment. Inflammatory diseases verified by a medical records review found a significant excess among Ranch Hands ($n=7$) relative to Comparisons ($n=1$); however, three of the seven Ranch Hand diseases were caused by bacterial infections, suggesting that this finding is unrelated to herbicide or dioxin exposure. Peripheral disorders, as verified by a medical records review, increased in Ranch Hands as levels of 1987 dioxin increased. Neck range of motion abnormalities were increased in Ranch Hands relative to Comparisons in terms of both a group designation and categorized dioxin levels. The increase in abnormalities for Ranch Hands relative to Comparisons was noted in enlisted flyers. An increase in the risk of an abnormal muscle status was observed in Ranch Hand enlisted groundcrew. A significant association between initial dioxin and both visual field and patellar reflex abnormalities was observed. Indices of polyneuropathy showed an increase in the prevalence of abnormality in Ranch Hands relative to Comparisons and a positive association with initial and 1987 dioxin levels. The clinical importance of the increased risk of polyneuropathy is uncertain due to the small number of affected veterans.

In summary, although a common etiology in these findings is not apparent, a statistically significant increase in neurological disease appears in Ranch Hands historically, on physical examination, and as reflected in several of the composite polyneuropathy indices. Further, the associations of neck range of motion abnormalities with categorized dioxin and a history of peripheral disorders with 1987 dioxin provide evidence of an association of neurological disease with elevated dioxin levels. The results of the analysis of the polyneuropathy indices also provide support of an association between elevated dioxin levels and neurological disease; however, the clinical importance of this finding is uncertain.

REFERENCES

1. Mohammad, F. K., and V. E. V. St. Omer. 1986. Behavioral and developmental effects in rats following in utero exposure to 2,4-D/2,4,5-T mixture. *Neurobehavioral Toxicology and Teratology* 8:551-60.
2. Mohammad, F. K., and V. E. V. St. Omer. 1988. Behavioral and neurochemical alterations in rats prenatally exposed to 2,4-dichlorophenoxyacetate (2,4-D) and 2,4,5-trichlorophenoxyacetate (2,4,5-T) mixture. *Teratology* 37:515.
3. St. Omer, V. E. V., and F. K. Mohammad. 1987. Ontogeny of swimming behavior and brain catecholamine turnover in rats prenatally exposed to a mixture of 2,4-D and 2,4,5-T. *Neuropharmacology* 26:1351-8.
4. Kim, C. S., R. F. Keizer, and J. B. Pritchard. 1988. 2,4-dichlorophenoxyacetic acid intoxication increases its accumulation within the brain. *Brain Research* 440:216-26.
5. Schulze, G. E., and J. A. Dougherty. 1988. Neurobehavioral toxicity of 2,4-D-n-butyl ester (2,4-D ester): Tolerance and lack of cross-tolerance. *Neurotoxicology and Teratology* 10:75-9.
6. Schulze, G. E., and J. A. Dougherty. 1988. Neurobehavioral toxicity and tolerance to the herbicide 2,4-dichlorophenoxyacetic acid-n-butyl ester (2,4-D ester). *Fundamental and Applied Toxicology* 10:413-24.
7. Sirkka, U., R. Pohjanvirta, S. A. Nieminen, J. Tuomisto, and P. Ylitalo. 1992. Acute neurobehavioral effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in Han/Wistar rats. *Pharmacology and Toxicology* 71:284-8.
8. Pohjanvirta, R., L. Tuomisto, and J. Tuomisto. 1989. The central nervous system may be involved in TCDD toxicity. *Toxicology* 58:167-74.
9. Silbergeld, E. K., and S. R. Max. 1986. Neuromuscular targets for the action of 2,3,7,8-TCDD. Abstract of a paper presented at the 6th International Symposium on Chlorinated Dioxins and Related Compounds, September 16-19, Fukuoka, Japan.
10. Grahmann, F., D. Claus, H. Grehl, and B. Neundorfer. 1993. Electrophysiologic evidence for a toxic polyneuropathy in rats after exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Journal of the Neurological Sciences* 115(1):71-5.
11. Grehl, H., F. Grahmann, D. Claus, and B. Neundorfer. 1993. Histologic evidence for a toxic polyneuropathy due to exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in rats. *Acta Neurologica Scandinavica* 88:354-7.
12. Mattsson, J. L., and D. L. Eisenbrandt. 1990. The improbable association between the herbicide 2,4-D and polyneuropathy. *Biomedical and Environmental Sciences* 3:43-51.
13. Seabury, J. H. 1963. Toxicity of 2,4-dichlorophenoxyacetic acid. *Archives of Environmental Health* 7:202-9.
14. Klawans, H. L. 1987. Dystonia and tremor following exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Movement Disorders* 2:255-61.
15. Oliver, R. M. 1975. Toxic effects of 2,3,7,8-tetrachlorodibenzo-1,4-dioxin in laboratory workers. *British Journal of Industrial Medicine* 32:49-53.

16. Singer, R., M. Moses, J. Valciukas, R. Lilis, and I. J. Selikoff. 1982. Nerve conduction velocity studies of workers employed in the manufacture of phenoxy herbicides. *Environmental Research* 29:297-311.
17. Moses, M., R. Lilis, K. D. Crow, J. Thornton, A. Fischbein, H. A. Anderson, and I. J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *American Journal of Industrial Medicine* 5:161-82.
18. Suskind, R. R., and V. S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *Journal of the American Medical Association* 251:2372-80.
19. Pazderova-Vejlupkova, J., M. Nemcova, J. Pickova, L. Jirasek, and E. Lukas. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Archives of Environmental Health* 36:5-11.
20. Sweeney, M. H., M. A. Fingerhut, J. C. Arezzo, R. W. Hornung, and L. B. Connally. 1993. Peripheral neuropathy after occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *American Journal of Industrial Medicine* 23:845-58.
21. Cheng, W. N., P. J. Coenraads, Z. H. Hao, and G. F. Liu. 1993. A health survey of workers in the pentachlorophenol section of a chemical manufacturing plant. *American Journal of Industrial Medicine* 24:81-92.
22. Webb, K. B., R. G. Evans, P. A. Stehr, and S. M. Ayres. 1987. Pilot study on health effects of environmental 2,3,7,8-TCDD in Missouri. *American Journal of Industrial Medicine* 11:685-91.
23. Webb, K. B., R. G. Evans, A. P. Knutsen, S. T. Roodman, D. W. Roberts, W. F. Schramm, B. B. Gibson, J. S. Andrews Jr., L. L. Needham, and D. G. Patterson. 1989. Medical evaluation of subjects with known body levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 28:183-93.
24. Hoffman, R. E., P. A. Stehr-Green, K. B. Webb, R. G. Evans, A. P. Knutsen, W. F. Schramm, B. B. Gibson, and K. K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of the American Medical Association* 225:2031-8.
25. Stehr, P. A., G. Stein, H. Falk, E. Sampson, S. J. Smith, K. Steinberg, K. Webb, S. Ayres, W. F. Schramm, H. D. Donnell, and W. B. Gedney. 1986. A pilot epidemiologic study of possible health effects associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin contaminations in Missouri. *Archives of Environmental Health* 41:16-22.
26. Stehr-Green, P. A., J. S. Andrews Jr., R. E. Hoffman, K. B. Webb, and W. F. Schramm. 1988. An overview of the Missouri dioxin studies. *Archives of Environmental Health* 43:174-7.
27. Filippini, G., B. Bordo, P. Crenna, N. Massetto, M. Musicco, and R. Boeri. 1981. Relationship between clinical and electrophysiological findings and indicators of heavy exposure to 2,3,7,8-tetrachlorodibenzo-dioxin. *Scandinavian Journal of Work, Environment and Health* 7:257-62.
28. Bertazzi, P. A. 1991. Long-term effects of chemical disasters. Lessons and results from Seveso. *Science of the Total Environment* 196(1-2):5-20.
29. Boeri, R., B. Bordo, P. Crenna, G. Filippini, M. Massetto, and A. Zecchini. 1978. Preliminary results of a neurological investigation of the population exposed to TCDD in the Seveso region. *Rivista di Patologia Nervosa e Mentale* 99:111-28.

30. Barbieri, S., C. Pirovano, G. Scarlato, P. Tarchini, A. Zappa, and M. Maranzana. 1988. Long-term effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on the peripheral nervous system. Clinical and neurophysiological controlled study on subjects with chloracne from the Seveso area. *Neuroepidemiology* 7:29-37.
31. Zober, A., M. G. Ott, and P. Messerer. 1994. Morbidity followup study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.
32. Assennato, G., D. Cervino, E. A. Emmett, G. Longo, and F. Merlo. 1989. Followup of subjects who developed chloracne following TCDD exposure at Seveso. *American Journal of Industrial Medicine* 16:119-25.
33. Morcarelli, P., A. Marocchi, P. Brambilla, P. Gerthoux, C. Beretta, L. Colombo, M. Bertona, C. Sarto, P. Tramacere, A. Mondonico, C. Crespi, S. Signorini, and R. Brivio. 1992. Human data derived from the Seveso accident, relevance for human risk assessment. *Toxic Substances Journal* 12(2-4):151-73.
34. Stellman, S. D., J. M. Stellman, and J. F. Sommer Jr. 1988. Health and reproductive outcomes among American Legionnaires in relation to combat and herbicide exposure in Vietnam. *Environmental Research* 47:150-74.
35. United States Centers for Disease Control. 1988. Health status of Vietnam veterans. II. Physical health. *Journal of the American Medical Association* 259:2708-14.
36. Lathrop, G. D., W. H. Wolfe, R. A. Albanese, and P. M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline Morbidity Study Results. NTIS: AD A-138-340. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.
37. Lathrop, G. D., S. G. Machado, T. G. Karrison, W. D. Grubbs, W. F. Thomas, W. H. Wolfe, J. E. Michalek, J. C. Miner, and M. R. Peterson. 1987. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188262. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.
38. Thomas, W. F., W. D. Grubbs, T. G. Karrison, M. B. Lustik, R. H. Roegner, D. E. Williams, W. H. Wolfe, J. E. Michalek, J. C. Miner, and R. W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: I. 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. United States Air Force School of Aerospace Medicine, Human Systems Division (AFSC), Brooks Air Force Base, Texas.
39. Grubbs, W. D., W. H. Wolfe, J. E. Michalek, D. E. Williams, M. B. Lustik, A. S. Brockman, S. C. Henderson, F. R. Burnett, R. G. Land, D. J. Osborne, V. K. Rocconi, M. E. Schreiber, J. C. Miner, G. L. Henriksen, and J. A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 Followup Examination Results. NTIS: AD A 304 306, 304 308-316. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

40. Roegner, R. H., W. D. Grubbs, M. B. Lustik, A. S. Brockman, S. C. Henderson, D. E. Williams, W. H. Wolfe, J. E. Michalek, and J. C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides. Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. United States Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.
41. Institute of Medicine. 1999. *Veterans and Agent Orange: Update 1998*. National Academy Press: Washington, DC.
42. Gerr, F., D. Hershman, and R. Letz. 1990. Vibrotactile threshold measurement for detecting neurotoxicity: reliability and determination of age- and height-standardized normative values. *Archives of Environmental Health* 45:148-54.
43. Michalek, J. E., J. L. Pirkle, S. P. Caudill, R. C. Tripathi, D. G. Patterson Jr., and L. L. Needham. 1996. Pharmacokinetics of TCDD in Veterans of Operation Ranch Hand: 10-year Followup. *Journal of Toxicology and Environmental Health* 47:209-20.
44. Mausner, J. S., and A. K. Bahn. 1974. *Epidemiology – An Introductory Text*. Philadelphia: W. B. Saunders Company.