

TABLE 7-21. (Continued)

**Summary of Current Dioxin and Time Analyses for Malignancy
Variables Based on Minimal and Maximal Assumptions
(Ranch Hands Only)**

Variable	C*T	Minimal		Adjusted			
		≤ 18.6	> 18.6	C*T	≤ 18.6	> 18.6	
Skin Neoplasms							
<u>Behavior</u>							
All, Ear, Face, Head, and Neck	NS	ns*	ns	NS	ns	NS	
Malignant	NS	ns	ns	NS	ns	ns	
Benign (Non-Blacks only)	NS	ns	ns	NS	ns	NS	
Benign (Blacks Included)	NS	ns	ns	NS	ns	NS	
Uncertain Behavior or Unspecified Nature	--	--	--	--	--	--	
<u>Cell Type</u>							
Basal Cell Carcinoma							
All Sites Combined	NS	ns	ns	NS	ns	ns	
Ear, Face, Head, and Neck	ns	ns	-0.047	ns	ns	ns	
Trunk	ns	NS	NS	ns	NS	NS	
Upper Extremities	--	--	--	--	--	ns	
Lower Extremities	--	--	--	--	--	--	
Other Sites and NOS	--	--	NS	--	--	NS	
Sun Exposure-Related Malignant Skin Neoplasms							
All, Ear, Face, Head, and Neck	NS	ns	ns	NS	ns	ns	
Trunk	ns	ns	ns	ns	ns	ns	
Upper Extremities	--	--	--	--	--	ns	
Lower Extremities	--	--	--	--	--	--	
Other Sites and NOS	--	--	NS	--	--	NS	
<u>by Location/Site</u>							
Ear, Face, Head, and Neck							
Oral Cavity, Pharynx, and Larynx							

TABLE 7-21. (Continued)

**Summary of Current Dioxin and Time Analyses for Malignancy
Variables Based on Minimal and Maximal Assumptions
(Ranch Hands Only)**

Variable	C*T	Minimal		Adjusted		Maximal	
		≤ 18.6	> 18.6	C*T	≤ 18.6	> 18.6	
Melanoma							
All Sites Combined	--	--	--	--	--	--	--
Ear, Face, Head, and Neck	--	--	--	--	--	--	--
Trunk	--	--	--	--	--	--	--
Upper Extremities	--	--	--	--	--	--	--
Lower Extremities	--	--	--	--	--	--	--
Other Sites and NOS	--	--	--	--	--	--	--
Squamous Cell Carcinoma							
Basal Cell Carcinoma							
<u>by Occupation</u>							
Officer -							
Ear, Face, Head, and Neck vs. None	NS	ns	ns	NS	NS	NS	NS
Officer -							
Other Sites vs. None	--	--	--	NS	ns	ns	ns
Enlisted Flyer -							
Ear, Face, Head, and Neck vs. None	--	NS	--	--	ns	--	--
Enlisted Flyer -							
Other Sites vs. None	+0.017	NS	NS*	+0.027	NS	NS	NS*
Enlisted Groundcrew -							
Ear, Face, Head, and Neck vs. None	NS	ns*	ns	NS	ns*	ns	ns
Enlisted Groundcrew -							
Other Sites vs. None	NS	ns	ns	NS	ns	ns	ns

Note: *P-value given if $p < 0.05$.

**Capital "NS" denotes relative risk for sites category less than 1.00 or greater. A lowercase "ns" denotes relative risk for sites category or relative risk less than 1.00.

TABLE 7-21. (Continued)

**Summary of Current Dioxin and Time Analyses for Malignancy
Variables Based on Minimal and Maximal Assumptions
(Ranch Hands Only)**

Variable	C*T	Minimal		Adjusted		
		≤ 18.6	> 18.6	C*T	≤ 18.6	> 18.6
<u>Sun Exposure-Related Malignant Skin Neoplasm by Occupation</u>						
Officer -						
Ear, Face, Head, and Neck vs. None	NS	ns	ns	ns	NS	ns
Officer -	--	--	--	NS	ns	ns
Other Sites vs. None	--	NS	--	--	ns	--
Enlisted Flyer -						
Ear, Face, Head, and Neck vs. None	--	NS	--	ns	ns	--
Enlisted Flyer -						
Other Sites vs. None	+0.017	NS	NS*	+0.026	NS	NS*
Enlisted Groundcrew -						
Ear, Face, Head, and Neck vs. None	NS	ns*	ns	NS	ns	ns
Enlisted Groundcrew -						
Other Sites vs. None	NS	ns	ns	NS	ns	ns
<u>Basal Cell Carcinoma (Number)</u>						
One vs. None	NS	ns	ns	ns	ns	ns
Multiple vs. None	ns	ns	ns	NS	ns	ns
<u>Systemic Neoplasms</u>						
All	NS	NS	NS	ns	+0.036	NS*
Malignant	ns	ns	ns	ns	NS	ns
Benign	NS	NS	+0.026	NS	+0.030	+0.003
Uncertain Behavior or Unspecified Nature	--	--	--	--	--	--
<u>Malignant Systemic Neoplasms by Location/Site</u>						
Ear, Face, Head, and Neck	--	--	--	--	--	--
Oral Cavity, Pharynx, and Larynx	--	--	--	--	--	--

TABLE 7-21. (Continued)

**Summary of Current Dioxin and Time Analyses for Malignancy
Variables Based on Minimal and Maximal Assumptions
(Ranch Hands Only)**

Variable	C*T	Minimal		Adjusted			Maximal
		≤ 18.6	> 18.6	C*T	≤ 18.6	> 18.6	
Malignant Systemic Neoplasms by Location/Site (continued)							
Brain	--	--	--	--	--	--	--
Thymus and Mediastinum	--	--	--	--	--	--	--
Thyroid Gland	--	--	--	--	--	--	--
Bronchus and Lung	--	--	--	--	--	--	--
Colon and Rectum	--	--	--	--	--	--	--
Kidney and Bladder	--	--	ns	--	--	ns	--
Prostate	--	--	--	--	--	--	--
Testicles	--	--	--	--	--	--	--
Ill-Defined Sites	--	--	--	--	--	--	--
Carcinoma In Situ of Penis	--	--	--	--	--	--	--
Carcinoma In Situ of Other and Unspecified Sites	--	--	--	--	--	--	--
Hodgkin's Disease	--	--	--	--	--	--	--
Leukemia	--	--	--	--	--	--	--
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue	--	--	--	--	--	--	--
Skin and Systemic Neoplasms							
All	NS	ns	NS	NS	NS	NS	NS

+: C*T: Relative risk for ≤ 18.6 category less than relative risk for > 18.6 category.

≤ 18.6 and > 18.6 : Relative risk 1.00 or greater.

-: ≤ 18.6 and > 18.6 : Relative risk less than 1.00.

NS/ns: Not significant ($p > 0.10$).

NS*/ns*: Marginally significant ($0.05 < p \leq 0.10$).

--: Analysis not performed due to sparse data.

Note: P-value given if $p \leq 0.05$.

A capital "NS" denotes relative risk for ≤ 18.6 category less than relative risk for > 18.6 category or relative risk 1.00 or greater. A lowercase "ns" denotes relative risk for ≤ 18.6 category greater than relative risk for > 18.6 category or relative risk less than 1.00.

TABLE 7-22.
Summary of Categorical Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)

Variable	Verification Status	All	Unadjusted				
			Unknown versus Background	Low versus Background	High versus Background		
Skin Neoplasms							
Behavior							
All	V VS	NS NS	NS* NS*	NS NS	ns ns		
Malignant	V VS	NS NS	NS NS	NS NS	ns ns		
Benign (Non-Blacks only)	V	NS	NS	NS	NS		
Benign (Blacks Included)	V	NS	NS	NS	NS		
Uncertain Behavior or Unspecified Nature	V VS	-- --	NS NS	-- ns	-- ns		
Cell Type							
Basal Cell Carcinoma							
All Sites Combined	V	NS	NS	NS	ns		
Ear, Face, Head, and Neck	V	0.019	NS	NS	-0.032		
Trunk	V	NS	NS	NS	NS		
Upper Extremities	V	NS	NS	NS	ns		
Lower Extremities	V	--	--	--	--		
Other Sites and NOS	V	0.011	ns	NS*	NS		

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Unadjusted		
			Unknown versus Background	Low versus Background	High versus Background
Sun Exposure-Related Malignant Skin Neoplasms					
All Sites Combined	V	NS	NS	NS	ns
Ear, Face, Head, and Neck	V	0.026	NS	NS	-0.050
Trunk	V	NS	NS	ns	NS
Upper Extremities	V	NS	NS	NS	NS
Lower Extremities	V	--	--	--	--
Other Sites and NOS	V	0.011	ns	NS*	NS
Melanoma					
All Sites Combined	V	--	ns	ns	ns
Ear, Face, Head, and Neck	V	--	NS	--	--
Trunk	V	--	ns	ns	ns
Upper Extremities	V	--	--	--	--
Lower Extremities	V	--	--	--	--
Other Sites and NOS	V	--	--	--	--
Squamous Cell Carcinoma					
	V	NS	NS	NS	NS

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Unadjusted		
			Unknown versus Background	Low versus Background	High versus Background
Basal Cell Carcinoma by Occupation					
Officer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	ns
Officer - Other Sites vs. None	V	NS	NS	NS	ns
Enlisted Flyer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	ns
Enlisted Flyer - Other Sites vs. None	V	0.003	ns	NS	+0.020
Enlisted Groundcrew - Ear, Face, Head, and Neck vs. None	V	NS*	NS	NS	ns*
Enlisted Groundcrew - Other Sites vs. None	V	NS*	ns	NS	ns
Sun Exposure-Related Malignant Skin Neoplasm by Occupation					
Officer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	ns
Officer - Other Sites vs. None	V	NS	NS	NS	ns

TABLE 7-22. (Continued)
Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)

Variable	Verification Status	All	Unadjusted		
			Unknown versus Background	Low versus Background	High versus Background
<u>Sun Exposure-Related Neoplasms by Occupation (continued)</u>					
Enlisted Flyer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	ns
Enlisted Flyer - Other Sites vs. None	V	0.010	ns	NS	+0.049
Enlisted Groundcrew - Ear, Face, Head, and Neck vs. None	V	NS	NS	NS	ns
Enlisted Groundcrew - Other Sites vs. None	V	NS*	ns	NS	ns
<u>Basal Cell Carcinoma (Number)</u>					
One vs. None	V	NS	NS	NS	ns
Multiple vs. None	V	NS*	NS*	NS	ns
Systemic Neoplasms					
All	V	NS*	ns*	NS	NS
	VS	NS*	ns*	NS	NS
Malignant	V	0.001	ns	+0.016	ns
Benign	V	0.044	ns	ns	+0.043
Uncertain Behavior or Unspecified Nature	V	NS	ns	ns	ns
	VS	NS	ns	ns	ns

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Unadjusted		
			Unknown versus Background	Low versus Background	High versus Background
Malignant Systemic Neoplasms by Location/Site					
Ear, Face, Head, and Neck	V	--	ns	ns	ns
Oral Cavity, Pharynx, and Larynx	V	--	ns	ns	ns
Brain	V	--	--	--	--
Thymus and Mediastinum	V	--	NS	--	--
Thyroid Gland	V	--	--	--	--
Bronchus and Lung	V	--	NS	NS	--
Colon and Rectum	V	--	ns	ns	ns
Kidney and Bladder	V	0.006	NS	+0.033	ns
Prostate	V	--	ns	NS	ns
Testicles	V	--	--	NS*	--
Ill-Defined Sites	V	--	--	--	--
Carcinoma In Situ of Penis	V	--	ns	ns	ns
Carcinoma In Situ of Other and Unspecified Sites					
Hodgkin's Disease	V	--	ns	ns	ns
Leukemia	V	--	--	NS	--
Other Sites and NOS					

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	Unadjusted			High versus Background		
		All	Unknown versus Background	Low versus Background			
<u>Malignant Systemic Neoplasms by Location/Site (continued)</u>							
Other Malignant Neoplasms of Lymphoid and Histiocytic Tissue							
None	V	NS	NS	NS	ns		
<u>Skin and Systemic Neoplasms</u>							
All	V	NS	NS	NS	NS		
Enlisted Groundcrew	VS	NS	NS	NS	NS		
Ear, Face, Head, and Neck							

+: Relative risk 1.00 or greater.

-: Relative risk less than 1.00.

V: Verified neoplasms only.

VS: Verified and suspected neoplasms.

NS/ns: Not significant ($p>0.10$).

NS*/ns*: Marginally significant ($0.05 < p \leq 0.10$).

--: Analysis not performed due to sparse data.

Note: P-value given if $p \leq 0.05$.

A capital "NS" denotes relative risk 1.00 or greater; a lowercase "ns" denotes relative risk less than 1.00; a capital "NS" under the "All" column does not imply directionality.

Multiple ^{20s}	None	ns	ns	ns	ns
<u>Systemic Neoplasms</u>					
All	V	NS	NS	ns	ns
Malignant	NS	V	0.001	ns	ns
Benign	V	0.001	ns	ns	ns
Uncertain Behavior or Unspecified Nature	V	NS	ns	ns	ns
	VS	NS	ns	ns	ns

TABLE 7-22. (Continued)
Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)

Variable	Verification Status	All	Adjusted				
			Unknown versus Background	Low versus Background	High versus Background		
Skin Neoplasms							
<i>by Occupation</i>							
<u>Behavior</u>							
All	V VS	NS NS	NS NS	NS NS	ns ns		
Malignant	V VS	NS NS	NS NS	NS NS	ns ns		
Benign (Non-Blacks only)	V	NS	NS	NS	NS		
Benign (Blacks Included)	V	NS	NS	NS	NS		
Uncertain Behavior or Unspecified Nature	V VS	-- --0.023	-- --	-- --	-- --		
<i>Enlisted Groundcrew</i>							
<u>Cell Type</u>							
Basal Cell Carcinoma							
All Sites Combined	V	NS	NS	NS	ns		
Ear, Face, Head, and Neck	V	NS*	NS	NS	ns*		
Trunk	V	NS	NS	NS	NS		
Upper Extremities	V	NS	NS	NS	--		
Lower Extremities	V	--	--	--	--		
Other Sites and NOS	V	0.035	ns	+0.024	NS		

TABLE 7-22. (Continued)
Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)

Variable	Adjusted		Adjusted		
	Verification Status	All	Unknown versus Background	Low versus Background	High versus Background
Sun Exposure-Related Malignant Skin Neoplasms					
All Sites Combined	V	NS	NS	NS	ns
Ear, Face, Head, and Neck	V	NS	NS	NS	ns
Trunk	V	NS	NS	ns	NS
Upper Extremities	V	NS	NS	NS	NS
Lower Extremities	V	--	--	--	--
Other Sites and NOS	V	0.035	--	+0.024	NS
Melanoma					
All Sites Combined	V	--	ns	--	--
Ear, Face, Head, and Neck	V	--	--	--	--
Trunk	V	--	--	--	--
Upper Extremities	V	--	--	--	--
Lower Extremities	V	--	--	--	--
Other Sites and NOS	V	--	--	--	--
Squamous Cell Carcinoma					
	V	NS	NS	NS	NS

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Adjusted		
			Unknown versus Background	Low versus Background	High versus Background
<u>Basal Cell Carcinoma by Occupation</u>					
Officer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	--
Officer - Other Sites vs. None	V	NS	NS*	NS	--
Enlisted Flyer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	ns
Enlisted Flyer - Other Sites vs. None	V	0.028	--	NS	+0.017
Enlisted Groundcrew - Ear, Face, Head, and Neck vs. None	V	0.048	NS	NS	ns
Enlisted Groundcrew - Other Sites vs. None	V	NS*	--	NS	ns
<u>Sun Exposure-Related Malignant Skin Neoplasm by Occupation</u>					
Officer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	--
Officer - Other Sites vs. None	V	NS	NS	NS	--
Other Malignant Neoplasms of Lymphoid and and Histiocytic Tissue	V	NS	NS	NS	--

TABLE 7-22. (Continued)
Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)

Variable	Verification Status	All	Adjusted		
			Unknown versus Background	Low versus Background	High versus Background
<u>Sun Exposure-Related Malignant Skin Neoplasm by Occupation (continued)</u>					
Enlisted Flyer - Ear, Face, Head, and Neck vs. None	V	NS	NS	ns	ns
Enlisted Flyer - Other Sites vs. None	V	NS*	--	NS	+0.028
Enlisted Groundcrew - Ear, Face, Head, and Neck vs. None	V	NS	NS	NS	ns
Enlisted Groundcrew - Other Sites vs. None	V	NS*	--	NS	ns
<u>Basal Cell Carcinoma (Number)</u>					
One vs. None	V	NS	NS	NS	ns
Multiple vs. None	V	NS*	+0.039	+0.038	ns
Systemic Neoplasms					
All	V	0.021	ns*	NS	NS*
Other Sites and NOS	VS	0.022	-0.050	NS	NS*
Malignant	V	0.002	ns	+0.004	--
Benign	V	0.011	ns	ns	+0.010
Uncertain Behavior or Unspecified Nature	V VS	NS NS	ns ns	ns ns	ns ns

TABLE 7-22. (Continued)

As shown in Table 7-22, the various analyses of the 1000+ neoplasms were evaluated from sex, behavior or unspecified behavior, anatomical location/site, cell type by specified cell type by specified anatomical location/site, and cell type by anatomical location/site by occupation.

Variable	Verification Status	All	Adjusted		
			Unknown versus Background	Low versus Background	High versus Background
Malignant Systemic Neoplasms by Location/Site					
Ear, Face, Head, and Neck	V	--	--	--	--
Oral Cavity, Pharynx, and Larynx	V	--	--	--	--
Brain	V	--	--	--	--
Thymus and Mediastinum	V	--	--	--	--
Thyroid Gland	V	--	--	--	--
Bronchus and Lung	V	--	--	--	--
Colon and Rectum	V	--	--	--	--
Kidney and Bladder	V	0.041	NS	+0.014	--
Prostate	V	--	--	NS	--
Testicles	V	--	--	--	--
Ill-Defined Sites	V	--	--	--	--
Carcinoma In Situ of Penis	V	--	--	--	--
Carcinoma In Situ of Other and Unspecified Sites	V	--	--	--	--
Hodgkin's Disease	V	--	--	--	--
Leukemia	V	--	--	--	--
Other Malignant Neoplasms of Lymphoid and and Histiocytic Tissue					
	V	NS	NS	NS	--

TABLE 7-22. (Continued)

**Summary of Categorized Current Dioxin Analyses for
Malignancy Variables
(Ranch Hands and Comparisons)**

Variable	Verification Status	All	Adjusted		
			Unknown versus Background	Low versus Background	High versus Background
Skin and Systemic Neoplasms					
All Occupation (continued)	V VS	NS NS	NS NS	NS NS	NS NS
Enlisted Flyer					
--: Relative risk less than 1.00.					
+: Relative risk 1.00 or greater.					
V: Verified neoplasms only.					
VS: Verified and suspected neoplasms.					
NS/ns: Not significant ($p > 0.10$).					
NS*/ns*: Marginally significant ($0.05 < p \leq 0.10$).					
--: Analysis not performed due to sparse data.					
Note: P-value given if $p \leq 0.05$.					
A capital "NS" denotes relative risk 1.00 or greater; a lowercase "ns" denotes relative risk less than 1.00; a capital "NS" under the "All" column does not imply directionality.					
Enlisted Groundcrew					
Other Sites vs. None					
Basal Cell Cancer	NS	NS	NS	NS	NS
Number					
One vs. None					
Multiple vs. None					
Systemic Neoplasms					
All	V VS	0.021 0.022	V NS	V NS	NS
Malignant	V	0.002	V	V	0.004
Benign	V	0.011	V	V	0.010
Uncertain Behavior or Unspecified Nature	V VS	NS NS	ns ns	ns ns	ns

Skin Neoplasm Analyses

As shown in Table 7-1, the frequency of participants with skin neoplasms were evaluated from several different perspectives: behavior (i.e., malignant, benign, uncertain behavior or unspecified nature), cell type (i.e., basal cell or squamous cell carcinoma, melanoma, and sun exposure-related malignant skin neoplasm), cell type by specified anatomical location/site, and cell type and specified anatomical location/site by occupation.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

In general, the various analyses of the frequency of Ranch Hands having skin neoplasms did not indicate a positive association with initial dioxin. For the most part, the relative risks estimated from the unadjusted and adjusted models were less than 1 and nonsignificant. When significant or marginally significant relative risks were found they were usually less than 1. Significant relative risks greater than 1 were found in the occupation-specific analyses comparing the frequencies of Ranch Hand enlisted flyers with a basal cell carcinoma of other sites versus those Ranch Hand enlisted flyers without a basal cell carcinoma (unadjusted analysis: $p=0.050$ for the minimal assumption, $p=0.015$ for the maximal assumption; adjusted analysis: $p=0.039$ for maximal assumption). Significant or marginally significant relative risks greater than 1 were also found in the corresponding analyses of Ranch Hand enlisted flyers for sun exposure-related malignant skin neoplasms of other sites versus no sun exposure-related malignant skin neoplasm (unadjusted analysis: $p=0.052$ for minimal assumption, $p=0.015$ for maximal assumption; adjusted analysis: $p=0.049$ for maximal assumption). The comparable analyses for the other occupational groups had relative risks less than 1. These inconsistent results suggest that other factors may be involved in this increase in skin malignancy among enlisted flyers. Only a limited number of analyses for melanoma were performed due to sparse data.

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

In general, the unadjusted and the adjusted analyses of the various skin neoplasm variables found few significant interactions between current dioxin and time since tour. There were individual time strata with significant or marginally significant relative risks; the risks, in general, however, were less than 1. Similar to the analyses involving initial dioxin, Ranch Hand enlisted flyers with a basal cell carcinoma of other sites when contrasted with Ranch Hand enlisted flyers without a basal cell carcinoma displayed significant current dioxin-by-time interactions ($p<0.030$ for unadjusted and adjusted analyses under both assumptions). In both the unadjusted and the adjusted analyses, the relative risks were greater than 1 in each time stratum and were significant ($p<0.040$ for the unadjusted analysis under each assumption) or marginally significant ($p<0.060$ for the adjusted analysis under each assumption) for those Ranch Hand enlisted flyers with earlier tours (i.e., time since tour over 18.6 years). Corresponding analyses of Ranch Hand enlisted flyers with a sun exposure-related malignant skin neoplasm of other sites versus Ranch Hand enlisted flyers without a sun exposure-related malignant skin neoplasm also contained significant interactions between current dioxin and time and a relative risk greater than 1 in each time stratum. Ranch Hands in the earlier time stratum had a significant or marginally significant relative risk. As with the analysis using initial dioxin, only a limited number of analyses were performed for melanoma because of sparse data.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In general, the unadjusted and adjusted analyses for all skin neoplasms, all malignant skin neoplasms, benign skin neoplasms, and all skin neoplasms of uncertain behavior or unspecified nature exhibited nonsignificant overall and individual contrasts among Ranch Hands in the three current dioxin categories and the Comparisons in the background category. With the exception of the high versus background contrast for all skin neoplasms and the high versus background contrast for all malignant skin neoplasms, most of the individual Ranch Hand versus Comparison contrasts displayed relative risks that were greater than 1 and nonsignificant. For the high versus background contrasts of these analyses, the relative risks were less than 1 and nonsignificant.

The unadjusted and adjusted analyses for basal cell carcinoma of the ear, face, head, and neck exhibited significant ($p=0.019$) and marginally significant ($p=0.087$) overall contrasts, respectively. In the unadjusted analysis, the high versus background contrast had a relative risk significantly less than 1 ($p=0.032$). In the adjusted analysis, the relative risk for the high versus background contrast was less than 1 and marginally significant ($p=0.063$). The unadjusted analysis for sun exposure-related malignant skin neoplasms of the ear, face, head, and neck also exhibited a significant overall contrast ($p=0.026$) and a relative risk for the high versus background contrast that was less than 1 and significant ($p=0.050$); however, the adjusted analysis was not significant.

The unadjusted and adjusted analyses for basal cell carcinoma of other sites and sites NOS exhibited significant overall contrasts of the three Ranch Hand current dioxin categories and the Comparison background category ($p=0.011$ and $p=0.035$, respectively). The unadjusted and adjusted analyses had relative risks greater than 1 associated with the low versus background contrasts that were marginally significant ($p=0.053$) and significant ($p=0.024$), respectively. The other contrasts were nonsignificant.

In general, there was a sparse number of participants with melanoma. Therefore, only a limited number of analyses could be performed and no significant contrasts or relative risks were noted.

The unadjusted and the adjusted analyses exhibited significant overall contrasts for enlisted flyers with a basal cell carcinoma of other sites ($p=0.003$ and $p=0.028$, respectively). The high versus background contrast displayed a significant relative risk that was greater than 1 in the unadjusted analysis ($p=0.020$) and in the adjusted analysis ($p=0.017$). The analyses for the enlisted groundcrew contained significant or marginally significant overall contrasts; however, the associated Ranch Hand versus Comparison contrasts were usually nonsignificant. Enlisted flyers with a sun exposure-related malignant skin neoplasm of other sites also exhibited at least marginally significant overall contrasts and significant high versus background contrasts with relative risks greater than 1.

In the unadjusted and adjusted analyses for participants with multiple basal cell carcinoma versus no basal cell carcinoma, there were marginally significant overall contrasts in the unadjusted analysis ($p=0.053$) and the adjusted analysis ($p=0.078$). The unknown versus background contrast displayed a relative risk greater than 1 that was marginally significant in the unadjusted analysis ($p=0.060$) and significant in the adjusted analysis

($p=0.039$). In the unadjusted analyses, the relative risk for the low versus background contrast was greater than 1 but nonsignificant. The adjusted relative risk for this contrast was greater than 1 and significant ($p=0.038$). The high versus background contrasts had nonsignificant relative risks that were less than 1.

Systemic Neoplasm Analyses

As Table 7-1 shows, the frequency of participants with systemic neoplasms were evaluated for two different characteristics: behavior and location/site.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

For both the unadjusted and the adjusted analyses of all systemic neoplasms (benign and malignant combined), significant relative risks greater than 1 were found under the maximal assumption ($p=0.009$ and $p=0.006$, respectively) and nonsignificant relative risks greater than 1 were found under the minimal assumption. The unadjusted analysis of Ranch Hands with a malignant systemic neoplasm under the minimal assumption yielded a relative risk less than 1 that was significant ($p=0.048$) with the relative risks from the other analyses also being less than 1 but nonsignificant. The unadjusted and the adjusted relative risks for Ranch Hands with a benign systemic neoplasm were significant and greater than 1 in both the minimal analysis ($p=0.022$ and $p=0.015$, respectively) and the maximal analysis ($p=0.001$ and $p<0.001$, respectively). In these analyses, the benign systemic neoplasms were predominantly lipomas (approximately 75 percent); also found, but with less frequency, were hemangiomas, dermoid cysts, fibromas, benign adenolymphoma, neurofibroma, facial fibroma, and adenoma. The unadjusted and adjusted analyses of the frequency of Ranch Hands with a systemic neoplasm of uncertain behavior or unspecified nature yielded nonsignificant relative risks.

For the most part, unadjusted and adjusted analyses of the systemic neoplasms could not be performed by location/site due to the sparse number of Ranch Hands with a systemic neoplasm at an individual location/site. For the few location/sites for which analyses were performed (kidney and bladder, prostate, testicles, and other malignant neoplasms of lymphoid and histiocytic tissue), the relative risks were nonsignificant.

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

The unadjusted and adjusted analyses of the frequency of Ranch Hands with systemic neoplasms (benign and malignant combined) exhibited nonsignificant interactions between current dioxin and time since tour. However, marginally significant relative risks greater than 1 were found under the maximal assumption (unadjusted, $p=0.098$; adjusted, $p=0.065$) for Ranch Hands with earlier tours (over 18.6 years). In the adjusted analysis, a significant relative risk greater than 1 ($p=0.036$) was found under the maximal assumption for Ranch Hands with later tours (i.e., 18.6 years or less).

For Ranch Hands with malignant systemic neoplasms, the interactions between current dioxin and time since tour were nonsignificant regardless of the analysis or assumption.

For Ranch Hands with benign systemic neoplasms, the interactions between current dioxin and time since tour were nonsignificant. However, under the minimal assumption, the

unadjusted and adjusted analyses for Ranch Hands with earlier tours exhibited significant relative risks greater than 1 ($p=0.035$ and $p=0.026$, respectively). Under the maximal assumption, the unadjusted analysis displayed a relative risk that was greater than 1 and marginally significant for Ranch Hands with later tours ($p=0.095$) and a relative risk greater than 1 and significant for Ranch Hands with earlier tours ($p=0.013$). In the adjusted analysis under the maximal assumption, the relative risks of both time strata were greater than 1 and significant (≤ 18.6 years, $p=0.030$; ≥ 18.6 years, $p=0.003$).

In general, the analyses by site of the frequency of Ranch Hands with a systemic neoplasm were limited because of the sparse number of Ranch Hands with a systemic neoplasm at a specified site/location.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

In the unadjusted analysis for Ranch Hands with a systemic neoplasm, the overall contrast of Ranch Hands in the three current dioxin categories and Comparisons in the background category was marginally significant ($p=0.087$); the relative risk for the unknown versus background contrast was less than 1 and also marginally significant ($p=0.072$). The other Ranch Hand versus Comparison contrasts had relative risks greater than 1 that were nonsignificant. The corresponding adjusted analyses contained a significant overall contrast ($p=0.021$), a relative risk for the unknown versus background contrast that was less than 1 and marginally significant ($p=0.057$), and a high versus background contrast with a marginally significant relative risk greater than 1 ($p=0.072$). The adjusted relative risk for the low versus background contrast was greater than 1 but nonsignificant. After including participants with suspected neoplasms in the analysis, similar results were produced.

The unadjusted and adjusted analyses for malignant systemic neoplasms indicated that the overall contrast of Ranch Hands in the unknown, low, and high current dioxin categories and Comparisons in the background category was significant ($p=0.001$ and 0.002 , respectively). The low versus background contrast had significant relative risks greater than 1 in the unadjusted analysis ($p=0.016$) and in the adjusted analysis ($p=0.004$). No Ranch Hands in the high current dioxin category had a malignant systemic neoplasm. The unknown versus background contrasts were nonsignificant.

For benign systemic neoplasms, the unadjusted and the adjusted analyses displayed significant overall contrasts among Ranch Hands in the three current dioxin categories and Comparisons in the background category ($p=0.044$ and $p=0.011$, respectively). The high versus background contrast exhibited a significant relative risk greater than 1 in the unadjusted analysis ($p=0.043$) and in the adjusted analysis ($p=0.010$).

For systemic neoplasms of uncertain behavior or unspecified nature, the overall contrast and individual Ranch Hand versus Comparison contrasts were nonsignificant in the unadjusted and the adjusted analyses.

In general, the analyses by site of the frequency of participants with a systemic neoplasm were limited because of the sparse numbers. The unadjusted and adjusted analyses of participants with a malignant systemic neoplasms of the kidney and bladder produced significant overall contrasts among the three Ranch Hand current dioxin categories

and the Comparison background category ($p=0.006$ and $p=0.041$, respectively). The low versus background contrast exhibited a significant relative risk greater than 1 in the unadjusted analysis ($p=0.033$) and in the adjusted analysis ($p=0.014$). No Ranch Hands in the high current dioxin category had a malignant systemic neoplasm of the kidney and bladder. The unknown versus background contrasts were nonsignificant.

Skin and Systemic Neoplasm Analysis

As Table 7-1 displays, study participants with either a skin or a systemic neoplasm were combined for analysis to investigate the association with initial dioxin, current dioxin and time since tour, and categorized current dioxin.

Model 1: Ranch Hands - Log₂ (Initial Dioxin)

The unadjusted and adjusted analyses of the frequency of Ranch Hands with a skin or systemic neoplasm produced nonsignificant relative risks.

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

Under each assumption, the unadjusted analysis and adjusted analysis of the frequency of Ranch Hands with a skin neoplasm or a systemic neoplasm displayed nonsignificant interactions between current dioxin and time since tour.

Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The unadjusted and adjusted analyses of participants with a skin or a systemic neoplasm indicated that the overall contrast of the three Ranch Hand current dioxin categories and the Comparison background category was nonsignificant, as were the individual Ranch Hand versus Comparison contrasts.

CONCLUSION

In summary, the analyses generally did not establish a significant positive association between dioxin and the presence of skin neoplasms. Significant relative risks were found for the skin neoplasm analyses; however, the relative risks were almost always less than 1. For the analyses focusing on enlisted flyers with a basal cell carcinoma of other sites (and sun exposure-related malignant skin neoplasms of other sites), relative risks were found to be significant and greater than 1. However, these results may be the result of a multiple-testing artifact, since they were not noted for the enlisted groundcrew who, as a group, had higher levels of serum dioxin than the enlisted flyers.

In general, the analyses using all systemic neoplasms combined produced some significant or marginally significant relative risks greater than 1. However, after performing the analyses separately by behavior (malignant neoplasms, benign neoplasms, and neoplasms of uncertain behavior and unspecified nature), the analyses of participants with a benign systemic neoplasm, such as lipomas, were found to have significant relative risks greater than 1 in contrast to the nonsignificant relative risks, which were often less than 1, for participants with a malignant systemic neoplasm.

The study provides no evidence of increased incidence for the neoplasms most commonly suspected as being associated with exposure to chlorophenols (HD, NHL, and

STS). However, the number of participants with these specific neoplasms was small; therefore, the statistical power to detect small or moderately elevated relative risks was low. There is no evidence in these data of a relationship between dioxin and either skin or systemic cancer. There is a suggestion of a dose-related relationship between dioxin and benign systemic neoplasms (lipomas) that will be explored in greater depth in the 1992 physical examination.

CHAPTER 7

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