

TABLE 8-12. (Continued)

## Analysis of Visual Fields

Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
c) Minimal						
(n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	1.7 (58)	0.0 (132)	0.0 (77)	--	--
d) Maximal						
(n=741)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (78)	0.6 (179)	0.0 (104)	--	--

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

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

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

Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)

Under both the minimal and maximal assumptions there were only three ocular movement abnormalities. For the minimal cohort, they were all in the medium initial dioxin category; for the maximal cohort, three were in the medium initial dioxin category and one was in the low category. The association with initial dioxin was not significant in either cohort (Table 8-14 [a-d]:  $p > 0.90$  for the unadjusted and adjusted analyses).

Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time

The interaction between current dioxin and time since tour could not be analyzed because no Ranch Hands with a later tour had an abnormal ocular movement. The association between current dioxin and ocular movement was not significant for Ranch Hands with an early tour in the unadjusted analyses (Table 8-14 [e]:  $p = 0.783$  for the minimal analysis; Table 8-14 [f]:  $p = 0.818$  for the maximal analysis). Adjusted analyses were not done due to the sparseness of the data.

## Model 3: Ranch Hands and Comparisons by Current Dioxin Category

The prevalence of abnormal ocular movement did not differ significantly among the current dioxin categories in either the unadjusted (Table 8-14 [g]:  $p = 0.165$ ) or adjusted (Table 8-14 [h]:  $p = 0.170$ ) analysis.

TABLE 8-12. (Continued)

## Analysis of Visual Fields

## e) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	782	0.8	All Categories		0.313
Unknown	343	0.3	Unknown vs. Background	0.38 (0.05,3.15)	0.636
Low	196	0.0	Low vs. Background	--	0.520
High	187	0.0	High vs. Background	--	0.550
Total	1,508				

--: Relative risk and confidence interval not given due to the absence of abnormalities.

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

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

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

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

was significant ( $p=0.636$ ) in the unadjusted analysis. No adjusted analysis was done due to sparse data.

## **Light Reaction**

### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

Initial dioxin was not associated significantly with the prevalence of light reaction abnormalities under both the minimal and maximal assumptions (Table 8-13 [a-d]:  $p>0.30$  for the unadjusted and adjusted analyses).

### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

The interaction between current dioxin and time since tour was not evaluated under the minimal assumption because only one Ranch Hand with an early tour had an abnormal light reaction. He was in the high current dioxin category. The unadjusted minimal analysis did not find a significant association between current dioxin and light reaction for Ranch Hands with a later tour (Table 8-13 [e]:  $p=0.943$ ). The current dioxin-by-time interaction was not significant in the unadjusted maximal analysis of light reaction (Table 8-13 [f]:  $p=0.432$ ). No adjusted analysis was done because of the sparse number of abnormalities.

### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

The prevalence of light reaction abnormalities did not differ significantly among the four current dioxin categories in the unadjusted analysis (Table 8-13 [g]:  $p=0.565$ ). The overall contrast remained nonsignificant after adjustment for age (Table 8-13 [h]:  $p=0.287$ ).

## **Ocular Movement**

### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

Under both the minimal and maximal assumptions there were only three ocular movement abnormalities. For the minimal cohort, they were all in the medium initial dioxin category; for the maximal cohort, three were in the medium initial dioxin category and one was in the low category. The association with initial dioxin was not significant in either cohort (Table 8-14 [a-d]:  $p>0.90$  for the unadjusted and adjusted analyses).

### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

The interaction between current dioxin and time since tour could not be analyzed because no Ranch Hands with a later tour had an abnormal ocular movement. The association between current dioxin and ocular movement was not significant for Ranch Hands with an early tour in the unadjusted analyses (Table 8-14 [e]:  $p=0.783$  for the minimal analysis; Table 8-14 [f]:  $p=0.818$  for the maximal analysis). Adjusted analyses were not done due to the sparseness of the data.

### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

The prevalence of abnormal ocular movement did not differ significantly among the current dioxin categories in either the unadjusted (Table 8-14 [g]:  $p=0.165$ ) or adjusted (Table 8-14 [h]:  $p=0.170$ ) analysis.

TABLE 8-13.

## Analysis of Light Reaction

Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
a) Minimal (n=521)	Low	130	0.8	1.49 (0.67,3.30)	0.346
	Medium	260	0.0		
	High	131	1.5		
b) Maximal (n=741)	Low	184	1.6	0.98 (0.54,1.77)	0.950
	Medium	371	0.3		
	High	186	1.1		
Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>		p-Value	Covariate Remarks	
c) Minimal (n=521)	1.42 (0.61,3.29)		0.435	AGE (p=0.541)	
d) Maximal (n=741)	0.99 (0.54,1.82)		0.990	AGE (p=0.815)	

<sup>a</sup>Relative risk for a twofold increase in dioxin.

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

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



TABLE 8-13. (Continued)

## Analysis of Light Reaction

Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Low	Medium	High		
e) Minimal (n=521)	≤18.6	1.4 (72)	0.0 (128)	1.9 (54)	0.95 (0.25,3.64)	0.943 <sup>b</sup>
	>18.6	0.0 (58)	0.0 (132)	1.3 (77)	--	--
f) Maximal (n=741)	≤18.6	1.9 (106)	0.5 (191)	1.2 (83)	0.83 (0.34,1.99)	0.432 <sup>†</sup> 0.671 <sup>b</sup>
	>18.6	1.3 (78)	0.0 (179)	1.0 (104)	1.35 (0.57,3.17)	0.494 <sup>b</sup>

<sup>a</sup>Relative risk for a twofold increase in dioxin.<sup>b</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

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

<sup>†</sup>Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-13. (Continued)

## Analysis of Light Reaction

## g) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	782	1.0	All Categories		0.565
Unknown	343	0.9	Unknown vs. Background	0.85 (0.23,3.24)	0.999
Low	196	0.0	Low vs. Background	--	0.332
High	187	1.1	High vs. Background	1.05 (0.22,4.97)	0.999
Total	1,508				

## h) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	782	All Categories		0.287	AGE (p=0.309)
Unknown	343	Unknown vs. Background	0.84 (0.22,3.18)	0.794	
Low	196	Low vs. Background	--	--	
High	187	High vs. Background	1.20 (0.25,5.87)	0.819	
Total	1,508				

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

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

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

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

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

**TABLE 8-14.**

**Analysis of Ocular Movement**

Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
a) Minimal (n=521)	Low	130	0.0	0.97 (0.37,2.53)	0.958
	Medium	260	1.2		
	High	131	0.0		
b) Maximal (n=741)	Low	184	0.5	1.02 (0.51,2.08)	0.944
	Medium	371	0.8		
	High	186	0.0		

Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
c) Minimal (n=521)	1.01 (0.38,2.68)	0.988	AGE (p=0.781)
d) Maximal (n=741)	1.00 (0.49,2.07)	0.988	AGE (p=0.779)

<sup>a</sup>Relative risk for a twofold increase in dioxin.

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

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

TABLE 8-14. (Continued)

## Analysis of Ocular Movement

Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Low	Medium	High		
e) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	2.3 (132)	0.0 (77)	0.82 (0.20,3.41)	0.783 <sup>b</sup>
f) Maximal (n=741)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	1.3 (78)	1.7 (179)	0.0 (104)	0.88 (0.31,2.52)	0.818 <sup>b</sup>

<sup>a</sup>Relative risk for a twofold increase in dioxin.<sup>b</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

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

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

**TABLE 8-14. (Continued)**

**Analysis of Ocular Movement**

**g) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted**

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	0.5	All Categories		0.165
Unknown	343	0.3	Unknown vs. Background	0.57 (0.06,5.11)	0.999
Low	196	1.5	Low vs. Background	3.03 (0.67,13.63)	0.296
High	187	0.0	High vs. Background	--	0.848
Total	1,509				

**h) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted**

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	783	All Categories		0.170	AGE (p=0.455)
Unknown	343	Unknown vs. Background	0.59 (0.07,5.31)	0.636	
Low	196	Low vs. Background	3.01 (0.67,13.56)	0.150	
High	187	High vs. Background	--	--	
Total	1,509				

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

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

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

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

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



## Facial Sensation

### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

Under both the minimal and maximal assumptions, initial dioxin was not associated significantly with the prevalence of facial sensation abnormalities in either the unadjusted or adjusted analyses (Table 8-15 [a-d]:  $p > 0.60$  for all analyses). There were only three assayed Ranch Hands with an abnormal facial sensation.

### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

The interaction between current dioxin and time since tour was not investigated because there was only one Ranch Hand with an early tour who had a facial sensation abnormality. Under both the minimal and maximal assumptions, current dioxin was not associated significantly with facial sensation for Ranch Hands with a later tour (Table 8-15 [e] and [f]:  $p = 0.454$  and  $p = 0.203$ , in the unadjusted analyses, respectively). No adjusted analysis was done because of sparse data.

### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

The prevalence of facial sensation abnormalities did not differ significantly among the current dioxin categories in both the unadjusted and adjusted categorized current dioxin analyses (Table 8-15 [g] and [h]:  $p = 0.543$  and  $p = 0.313$ , respectively).

## Smile

### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

Initial dioxin was not significantly associated with the prevalence of smile abnormalities under both the minimal and maximal assumptions (Table 8-16 [a-d]:  $p > 0.10$  for the unadjusted and adjusted analyses). Only three Ranch Hands in the minimal cohort and five Ranch Hands in the maximal cohort had an abnormal smile.

### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

The current dioxin-by-time since tour interaction was not analyzed because only one Ranch Hand with a later tour had a smile abnormality. For Ranch Hands with an early tour, current dioxin was marginally associated with smile in the unadjusted minimal analysis (Table 8-16 [e]: Est. RR=2.53,  $p = 0.059$ ), but there was no significant association in the unadjusted maximal analysis (Table 8-16 [f]:  $p = 0.668$ ). For the minimal analysis, both Ranch Hands with a later tour who had a smile abnormality were in the high current dioxin category. No adjusted analyses were done because of sparse data.

### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

The categorized current dioxin analyses of smile did not reveal a significant contrast in either the unadjusted or adjusted analysis (Table 8-16 [g] and [h]:  $p > 0.35$  for all contrasts).

TABLE 8-15.

## Analysis of Facial Sensation

Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
a) Minimal (n=521)	Low	130	0.8	0.87 (0.31,2.40)	0.779
	Medium	260	0.4		
	High	131	0.8		
b) Maximal (n=741)	Low	184	0.0	1.21 (0.57,2.58)	0.628
	Medium	371	0.5		
	High	186	0.5		

Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Adjusted			
Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
c) Minimal (n=521)	0.77 (0.26,2.25)	0.619	AGE (p=0.365)
d) Maximal (n=741)	1.12 (0.51,2.44)	0.776	AGE (p=0.394)

<sup>a</sup>Relative risk for a twofold increase in dioxin.

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

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

**TABLE 8-15. (Continued)**

**Analysis of Facial Sensation**

**Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Unadjusted**

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Low	Medium	High		
e) Minimal						
(n=521)	≤18.6	0.0 (72)	0.8 (128)	1.9 (54)	1.55 (0.49,4.88)	0.454 <sup>b</sup>
	>18.6	1.7 (58)	0.0 (132)	0.0 (77)	--	--
f) Maximal						
(n=741)	≤18.6	0.0 (106)	0.5 (191)	1.2 (83)	1.88 (0.71,4.97)	0.203 <sup>b</sup>
	>18.6	0.0 (78)	0.6 (179)	0.0 (104)	--	--

<sup>a</sup>Relative risk for a twofold increase in dioxin.

<sup>b</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

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

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

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

**TABLE 8-15. (Continued)**

**Analysis of Facial Sensation**

**g) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted**

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	0.6	All Categories		0.543
Unknown	343	0.0	Unknown vs. Background	--	0.334
Low	196	0.5	Low vs. Background	0.80 (0.09,6.87)	0.999
High	187	0.5	High vs. Background	0.84 (0.10,7.20)	0.999
Total	1,509				

**h) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted**

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	783	All Categories		0.313	AGE (p=0.809)
Unknown	343	Unknown vs. Background	--	--	
Low	196	Low vs. Background	0.80 (0.09,6.87)	0.836	
High	187	High vs. Background	0.80 (0.09,7.10)	0.842	
Total	1,509				

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

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

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

Low (Ranch Hands):  $15 \text{ ppt} < \text{Current Dioxin} \leq 33.3 \text{ ppt}$ .

High (Ranch Hands): Current Dioxin  $> 33.3 \text{ ppt}$ .

TABLE 8-16.

## Analysis of Smile

Ranch Hands - Log<sub>2</sub> (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
a) Minimal (n=521)	Low	130	0.0	1.87 (0.88,3.98)	0.124
	Medium	260	0.4		
	High	131	1.5		
b) Maximal (n=741)	Low	184	1.1	1.24 (0.69,2.21)	0.485
	Medium	371	0.3		
	High	186	1.1		

Ranch Hands - Log<sub>2</sub> (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
c) Minimal (n=521)	1.88 (0.88,4.02)	0.124	AGE (p=0.889)
d) Maximal (n=741)	1.18 (0.65,2.15)	0.588	AGE (p=0.518)

<sup>a</sup>Relative risk for a twofold increase in dioxin.

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

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



**TABLE 8-16. (Continued)**

**Analysis of Smile**

**Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Unadjusted**

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Low	Medium	High		
e) Minimal (n=521)	≤18.6	0.0	0.8	0.0	--	--
		(72)	(128)	(54)		
	>18.6	0.0	0.0	2.6	2.53 (0.96,6.66)	0.059 <sup>b</sup>
		(58)	(132)	(77)		
f) Maximal (n=741)	≤18.6	0.0	0.5	0.0	--	--
		(106)	(191)	(83)		
	>18.6	2.6	0.0	1.9	1.15 (0.60,2.19)	0.668 <sup>b</sup>
		(78)	(179)	(104)		

<sup>a</sup>Relative risk for a twofold increase in dioxin.

<sup>b</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

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

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

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

**TABLE 8-16. (Continued)**

**Analysis of Smile**

**g) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted**

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	1.2	All Categories		0.711
Unknown	343	0.6	Unknown vs. Background	0.51 (0.11,2.35)	0.384
Low	196	0.5	Low vs. Background	0.44 (0.06,3.51)	0.439
High	187	1.1	High vs. Background	0.93 (0.20,4.34)	0.927
Total	1,510				

**h) Ranch Hands and Comparisons by Current Dioxin Category - Adjusted**

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	784	All Categories		0.671	AGE (p=0.190)
Unknown	343	Unknown vs. Background	0.49 (0.11,2.30)	0.369	
Low	196	Low vs. Background	0.45 (0.06,3.55)	0.445	
High	187	High vs. Background	1.11 (0.23,5.30)	0.898	
Total	1,510				

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

## **Palpebral Fissure**

### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

Under both the minimal and maximal assumptions, the initial dioxin analyses did not find a significant association with palpebral fissure (Table 8-17 [a-d]:  $p > 0.35$  in the unadjusted and adjusted analyses).

### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

The interaction between current dioxin and time since tour was not significant for the minimal and maximal analyses of palpebral fissure (Table 8-17 [e-h]:  $p > 0.20$  in the unadjusted and adjusted analyses).

### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

The percentages of participants with an abnormal palpebral fissure did not differ significantly among the current dioxin categories in the unadjusted analysis (Table 8-17 [i]: 1.3%, 1.2%, 2.0%, and 1.6% for the background, unknown, low, and high current dioxin categories,  $p = 0.850$ ). After adjustment for age, the overall contrast remained nonsignificant (Table 8-17 [j]:  $p = 0.803$ ).

## **Balance**

### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

Under both the minimal and maximal assumptions, initial dioxin was not significantly associated with balance in the unadjusted analyses (Table 8-18 [a] and [b]:  $p = 0.871$  and  $p = 0.479$ ). No adjusted analyses were done because only two assayed Ranch Hands had an abnormal balance (one in the medium initial dioxin category and one in the high category under both assumptions).

### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

The current dioxin-by-time since tour interaction could not be evaluated because no Ranch Hands with a later tour had an abnormal balance. Under both the minimal and maximal assumptions, current dioxin was not significantly associated with balance in the unadjusted analyses for Ranch Hands with an early tour (Table 8-18 [c] and [d]:  $p = 0.921$  and  $p = 0.770$ , respectively). No adjusted analyses were done because of sparse data.

### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

The unadjusted categorized current dioxin analysis of balance did not show a significant overall contrast (Table 8-18 [e]:  $p = 0.117$ ). There were no abnormalities in the background or unknown current dioxin categories and there was one abnormality in both the low and high current dioxin categories.

TABLE 8-17.

## Analysis of Palpebral Fissure

Ranch Hands - Log<sub>2</sub> (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
a) Minimal (n=521)	Low	130	0.8	1.27 (0.76,2.14)	0.376
	Medium	260	1.5		
	High	131	2.3		
b) Maximal (n=741)	Low	184	1.6	1.13 (0.75,1.70)	0.564
	Medium	371	1.1		
	High	186	2.2		

Ranch Hands - Log<sub>2</sub> (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
c) Minimal (n=519)	1.22 (0.71,2.08)	0.483	AGE (p=0.582) DIAB*INS (p=0.040)
d) Maximal (n=741)	1.12 (0.74,1.71)	0.598	AGE (p=0.857)

<sup>a</sup>Relative risk for a twofold increase in dioxin.

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

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

TABLE 8-17. (Continued)

## Analysis of Palpebral Fissure

Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Low	Medium	High		
e) Minimal (n=521)	≤18.6	0.0	1.6	0.0	0.79 (0.18,3.43)	0.552 <sup>b</sup>
		(72)	(128)	(54)		0.758 <sup>c</sup>
	>18.6	1.7	1.5	3.9	1.25 (0.70,2.23)	0.451 <sup>c</sup>
		(58)	(132)	(77)		
f) Maximal (n=741)	≤18.6	1.9	1.1	0.0	0.67 (0.25,1.81)	0.228 <sup>b</sup>
		(106)	(191)	(83)		0.427 <sup>c</sup>
	>18.6	1.3	1.7	2.9	1.26 (0.78,2.02)	0.347 <sup>c</sup>
		(78)	(179)	(104)		

Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
g) Minimal (n=519)			0.453 <sup>b</sup>	AGE (p=0.744)
	≤18.6	0.74 (0.18,3.08)	0.681 <sup>c</sup>	DIAB*INS (p=0.038)
	>18.6	1.27 (0.71,2.26)	0.423 <sup>c</sup>	
h) Maximal (n=741)			0.229 <sup>b</sup>	AGE (p=0.700)
	≤18.6	0.66 (0.24,1.76)	0.403 <sup>c</sup>	
	>18.6	1.22 (0.75,2.00)	0.420 <sup>c</sup>	

<sup>a</sup>Relative risk for a twofold increase in dioxin.<sup>b</sup>Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).<sup>c</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.



**TABLE 8-17. (Continued)**  
**Analysis of Palpebral Fissure**

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	1.3	All Categories		0.850
Unknown	343	1.2	Unknown vs. Background	0.91 (0.28,2.93)	0.879
Low	196	2.0	Low vs. Background	1.61 (0.50,5.20)	0.424
High	187	1.6	High vs. Background	1.26 (0.34,4.63)	0.726
Total	1,510				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	784	All Categories		0.803	AGE (p=0.211)
Unknown	343	Unknown vs. Background	0.90 (0.28,2.88)	0.853	
Low	196	Low vs. Background	1.63 (0.50,5.25)	0.416	
High	187	High vs. Background	1.45 (0.39,5.42)	0.584	
Total	1,510				

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

TABLE 8-18.

## Analysis of Balance

Ranch Hands - Log<sub>2</sub> (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
a) Minimal (n=521)	Low	130	0.0	1.10 (0.36,3.30)	0.871
	Medium	260	0.4		
	High	131	0.8		
b) Maximal (n=741)	Low	184	0.0	1.39 (0.58,3.34)	0.479
	Medium	371	0.3		
	High	186	0.5		

<sup>a</sup>Relative risk for a twofold increase in dioxin.

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

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

TABLE 8-18. (Continued)

## Analysis of Balance

Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Low	Medium	High		
c) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.8 (132)	1.3 (77)	0.92 (0.18,4.70)	0.921 <sup>b</sup>
d) Maximal (n=741)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (78)	0.6 (179)	1.0 (104)	1.21 (0.34,4.24)	0.770 <sup>b</sup>

<sup>a</sup>Relative risk for a twofold increase in dioxin.<sup>b</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).

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

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

Background (Comparisons): Current Dioxin ≤10 ppt.

Unknown (Ranch Hands): Current Dioxin ≤10 ppt.

Low (Ranch Hands): 15 ppt &lt; Current Dioxin ≤33.3 ppt.

High (Ranch Hands): Current Dioxin &gt;33.3 ppt.

TABLE 8-18. (Continued)

## Analysis of Balance

## e) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	0.0	All Categories		0.117
Unknown	343	0.0	Unknown vs. Background	--	--
Low	196	0.5	Low vs. Background	--	0.400
High	187	0.5	High vs. Background	--	0.386
Total	1,509				

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

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

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

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

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

## Speech

### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

No initial dioxin analyses were done for speech because only one Ranch Hand had a speech abnormality under both the minimal and maximal assumptions. Table 8-19 shows that he was in the medium initial dioxin category.

### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

No current dioxin and time since tour analyses were done because there was only one speech abnormality.

### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

For the categorized current dioxin analyses, there was one speech abnormality in the background category and one in the low current dioxin category. Neither the overall contrast nor the low versus background contrast was significant in the unadjusted analysis (Table 8-19 [e]:  $p=0.421$  and  $p=0.720$ , respectively). No adjusted analysis was done due to sparse data.

## Neck Range of Motion

### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

The unadjusted initial dioxin analyses of neck range of motion did not find a significant association under both the minimal (Table 8-20 [a]:  $p=0.748$ ) and maximal (Table 8-20 [b]:  $p=0.356$ ) assumptions. The adjusted minimal analysis revealed two significant initial dioxin-by-covariate interactions—initial dioxin-by-race (Table 8-20 [c]:  $p=0.001$ ) and initial dioxin-by-diabetic class ( $p=0.008$ ). Separate analyses were done for Blacks and non-Blacks to explore the interactions. The analyses for Blacks found that only one Black Ranch Hand had an abnormal range of motion and he was in the low initial dioxin category.

The initial dioxin-by-diabetic class interaction was significant for non-Blacks. Further stratification by diabetic class showed a significant association between initial dioxin and range of motion for non-Black diabetics (Appendix Table G-1: Adj. RR=2.20,  $p=0.002$ ; % abnormal: 7.7%, 17.2%, and 21.1% for the low, medium, and high initial dioxin categories). Initial dioxin was not associated significantly with range of motion for either diabetically impaired non-Blacks (Adj. RR=0.52,  $p=0.221$ ) or for normal non-Blacks (Adj. RR=1.20,  $p=0.267$ ). After excluding the initial dioxin-by-covariate interactions, the relative risk was marginally more than 1 in the adjusted minimal analysis (Table 8-20 [c]: Adj. RR=1.24,  $p=0.087$ ).

The initial dioxin-by-diabetic class interaction was also significant in the adjusted maximal analysis (Table 8-20 [d]:  $p=0.004$ ). Stratified findings were consistent with the results of the adjusted minimal analysis for non-Blacks. For diabetic Ranch Hands, initial dioxin was associated significantly with range of motion (Appendix Table G-1: Adj. RR=1.85,  $p=0.004$ ; % abnormal: 10.0%, 12.2%, and 19.4% for the low, medium, and high initial dioxin categories), but the association was not significant for either diabetically impaired (Adj. RR=0.61,  $p=0.122$ ) or normal Ranch Hands (Adj. RR=1.01,  $p=0.956$ ). After excluding



TABLE 8-19.

## Analysis of Speech

Ranch Hands - Log<sub>2</sub> (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.)	p-Value
a) Minimal (n=521)	Low	130	0.0	--	--
	Medium	260	0.4		
	High	131	0.0		
b) Maximal (n=741)	Low	184	0.0	--	--
	Medium	371	0.3		
	High	186	0.0		

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

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

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

TABLE 8-19. (Continued)

## Analysis of Speech

Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.)	p-Value
		Low	Medium	High		
c) Minimal (n=521)	≤18.6	0.0 (72)	0.0 (128)	0.0 (54)	--	--
	>18.6	0.0 (58)	0.8 (132)	0.0 (77)	--	--
d) Maximal (n=741)	≤18.6	0.0 (106)	0.0 (191)	0.0 (83)	--	--
	>18.6	0.0 (78)	0.6 (179)	0.0 (104)	--	--

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

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

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

The initial dioxin-by-diabetic class interaction was significant for non-Blacks. Further stratification by diabetic class showed a significant association between initial dioxin and range of motion for non-Black diabetics (Appendix Table G-1: Adj. RR=2.20, p=0.002; % abnormal: 7.7%, 17.2%, and 21.1% for the low, medium, and high initial dioxin categories). Initial dioxin was not associated significantly with range of motion for either diabetically impaired non-Blacks (Adj. RR=0.52, p=0.221) or for normal non-Blacks (Adj. RR=1.20, p=0.267). After excluding the initial dioxin-by-covariate interactions, the relative risk was marginally more than 1 in the adjusted minimal analysis (Table 8-20 [c]: Adj. RR=1.24, p=0.087).

The initial dioxin-by-diabetic class interaction was also significant in the adjusted maximal analysis (Table 8-20 [d]: p=0.004). Stratified findings were consistent with the results of the adjusted minimal analysis for non-Blacks. For diabetic Ranch Hands, initial dioxin was associated significantly with range of motion (Appendix Table G-1: Adj. RR=1.85, p=0.004; % abnormal: 10.0%, 12.1%, and 19.4% for the low, medium, and high initial dioxin categories), but the association was not significant for either diabetically impaired (Adj. RR=0.61, p=0.122) or normal Ranch Hands (Adj. RR=1.01, p=0.956). After excluding

TABLE 8-19. (Continued)

## Analysis of Speech

## e) Ranch Hands and Comparisons by Current Dioxin Category - Unadjusted

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	0.1	All Categories		0.421
Unknown	343	0.0	Unknown vs. Background	--	0.999
Low	196	0.5	Low vs. Background	4.01 (0.25,64.40)	0.720
High	187	0.0	High vs. Background	--	0.999
Total	1,509				

--: Relative risk and confidence interval not given due to the absence of abnormalities.

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

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

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

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

TABLE 8-20.

## Analysis of Neck Range of Motion

Ranch Hands - Log<sub>2</sub> (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
a) Minimal (n=521)	Low	130	9.2	1.04 (0.82,1.31)	0.748
	Medium	260	11.2		
	High	131	9.2		
b) Maximal (n=741)	Low	184	14.1	0.92 (0.78,1.10)	0.356
	Medium	371	11.3		
	High	186	8.6		

Ranch Hands - Log<sub>2</sub> (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
c) Minimal (n=519)	1.24 (0.97,1.59)***	0.087***	INIT*RACE (p=0.001) INIT*DIAB (p=0.008) AGE (p<0.001)
d) Maximal (n=739)	1.05 (0.87,1.27)***	0.597***	INIT*DIAB (p=0.004) AGE*RACE (p=0.003)

<sup>a</sup>Relative risk for a twofold increase in dioxin.

\*\*\*Log<sub>2</sub> (initial dioxin)-by-covariate interaction (p≤0.01); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

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

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

INIT: Log<sub>2</sub> (initial dioxin).

TABLE 8-20. (Continued)

## Analysis of Neck Range of Motion

Ranch Hands - Log <sub>2</sub> (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Low	Medium	High		
e) Minimal (n=521)	≤18.6	8.3 (72)	12.5 (128)	1.9 (54)	0.74 (0.47,1.18)	0.110 <sup>b</sup> 0.207 <sup>c</sup>
	>18.6	6.9 (58)	12.1 (132)	13.0 (77)	1.14 (0.86,1.52)	0.359 <sup>c</sup>
f) Maximal (n=741)	≤18.6	16.0 (106)	11.0 (191)	6.0 (83)	0.71 (0.52,0.96)	0.024 <sup>b</sup> 0.024 <sup>c</sup>
	>18.6	11.5 (78)	11.2 (179)	11.5 (104)	1.08 (0.86,1.34)	0.516 <sup>c</sup>
Ranch Hands - Log <sub>2</sub> (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) <sup>a</sup>		p-Value	Covariate Remarks	
g) Minimal (n=521)	≤18.6	1.06 (0.65,1.71)		0.257 <sup>b</sup> 0.824 <sup>c</sup>	AGE*RACE (p=0.003)	
	>18.6	1.45 (1.07,1.96)		0.017 <sup>c</sup>		
h) Maximal (n=741)	≤18.6	0.83 (0.59,1.16)		0.026 <sup>b</sup> 0.270 <sup>c</sup>	AGE*RACE (p=0.004)	
	>18.6	1.30 (1.03,1.65)		0.029 <sup>c</sup>		

<sup>a</sup>Relative risk for a twofold increase in dioxin.<sup>b</sup>Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).<sup>c</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.



TABLE 8-20. (Continued)

## Analysis of Neck Range of Motion

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	784	11.7	All Categories		0.692
Unknown	343	12.2	Unknown vs. Background	1.05 (0.71,1.55)	0.808
Low	196	12.2	Low vs. Background	1.05 (0.65,1.69)	0.843
High	187	9.1	High vs. Background	0.75 (0.44,1.30)	0.305
Total	1,510				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	782	All Categories		0.830**	DXCAT*DIAB (p=0.039) AGE (p<0.001)
Unknown	342	Unknown vs. Background	0.97 (0.63,1.47)**	0.867**	RACE (p=0.004)
Low	194	Low vs. Background	1.11 (0.66,1.86)**	0.703**	DIAB*INS (p=0.025)
High	187	High vs. Background	1.28 (0.71,2.32)**	0.413**	
Total	1,505				

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

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

the interaction, the adjusted maximal analysis did not find a significant association (Table 8-20 [d]:  $p=0.597$ ).

#### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

The unadjusted current dioxin and time since tour analyses of range of motion did not find a significant current dioxin-by-time interaction under the minimal assumption (Table 8-20 [e]:  $p=0.110$ ), but under the maximal assumption, the interaction was significant (Table 8-20 [f]:  $p=0.024$ ). The relative risk was significantly less than 1 for Ranch Hands in the maximal cohort with a later tour (time $\leq$ 18.6: Est. RR=0.71,  $p=0.024$ ; % abnormal: 16.0%, 11.0%, and 6.0% for the low, medium, and high current dioxin categories). The relative risk was more than 1, but not significant, for Ranch Hands in the maximal cohort with an early tour (time $>$ 18.6: Est. RR=1.08,  $p=0.516$ ; % abnormal: 11.5%, 11.2%, and 11.5% for the low, medium, and high current dioxin categories).

In the adjusted minimal analysis, the current dioxin-by-time interaction remained nonsignificant (Table 8-20 [g]:  $p=0.257$ ), but the relative risk for Ranch Hands with an early tour became significant (time $>$ 18.6: Adj. RR=1.45,  $p=0.017$ ) after adjustment for the age-by-race interaction. The interaction between current dioxin and time remained significant in the adjusted maximal analysis (Table 8-20 [g]:  $p=0.026$ ), but the significance of the within time strata results changed. After adjustment for the age-by-race interaction, the relative risk became nonsignificant for Ranch Hands with a later tour (time $\leq$ 18.6: Adj. RR=0.83,  $p=0.270$ ), and it became significantly more than 1 for Ranch Hands with an early tour (time $>$ 18.6: Adj. RR=1.30,  $p=0.029$ ).

#### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

The prevalence of range of motion abnormalities did not differ significantly among current dioxin categories in the unadjusted analysis (Table 8-20 [i]: 11.7%, 12.2%, 12.2%, and 9.1% for the background, unknown, low, and high current dioxin categories,  $p=0.692$ ). The adjusted analysis found a significant interaction between categorized current dioxin and diabetic class (Table 8-20 [j]:  $p=0.039$ ). Appendix Table G-1 presents stratified results that show a marginally significant difference among the percentages of abnormalities within the diabetic stratum (15.2%, 10.5%, 5.9%, and 22.6% for the background, unknown, low, and high current dioxin categories,  $p=0.094$ ). However, none of the three Ranch Hand versus background contrasts was significant ( $p>0.10$  for each contrast). The overall contrast was not significant in either the diabetically impaired stratum ( $p=0.240$ ) or in the normal stratum ( $p=0.631$ ). After excluding the interaction, the adjusted analysis was not significant (Table 8-20 [j]:  $p>0.40$  for all contrasts).

### **Cranial Nerve Index**

#### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

The unadjusted initial dioxin analyses of the cranial nerve index were not significant under both the minimal (Table 8-21 [a]:  $p=0.812$ ) and maximal (Table 8-21 [b]:  $p=0.467$ ) assumptions. However, after adjustment for the age-by-race interaction, the relative risk became marginally more than 1 under the minimal assumption (Table 8-21 [c]: Adj. RR=1.21,  $p=0.090$ ). The percentages of participants in the minimal cohort with an abnormal

TABLE 8-21.

## Analysis of Cranial Nerve Index

Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
a) Minimal (n=513)	Low	128	12.5	1.03 (0.83,1.26)	0.812
	Medium	256	15.2		
	High	129	12.4		
b) Maximal (n=732)	Low	183	17.5	0.95 (0.81,1.10)	0.467
	Medium	367	15.0		
	High	182	11.5		
Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>		p-Value	Covariate Remarks	
c) Minimal (n=513)	1.21 (0.97,1.50)		0.090	AGE*RACE (p=0.010)	
d) Maximal (n=730)	1.05 (0.89,1.23)**		0.591**	INIT*DIAB (p=0.034) AGE*RACE (p=0.033)	

<sup>a</sup>Relative risk for a twofold increase in dioxin.

\*\*Log<sub>2</sub> (initial dioxin)-by-covariate interaction (0.01<p≤0.05); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

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

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

TABLE 8-21. (Continued)

## Analysis of Cranial Nerve Index

Ranch Hands - Log <sub>2</sub> (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Low	Medium	High		
e) Minimal (n=513)	≤18.6	10.0 (70)	16.8 (125)	3.8 (53)	0.76 (0.51,1.14)	0.114 <sup>b</sup> 0.186 <sup>c</sup>
	>18.6	12.1 (58)	16.0 (131)	17.1 (76)	1.11 (0.86,1.43)	0.424 <sup>c</sup>
f) Maximal (n=732)	≤18.6	20.0 (105)	14.4 (187)	7.4 (81)	0.74 (0.57,0.97)	0.021 <sup>b</sup> 0.027 <sup>c</sup>
	>18.6	14.1 (78)	15.6 (179)	14.7 (102)	1.09 (0.89,1.32)	0.411 <sup>c</sup>
Ranch Hands - Log <sub>2</sub> (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) <sup>a</sup>		p-Value	Covariate Remarks	
g) Minimal (n=513)	≤18.6	1.00 (0.65,1.52)		0.225 <sup>b</sup> 0.986 <sup>c</sup>	AGE*RACE (p=0.012)	
	>18.6	1.34 (1.02,1.74)		0.033 <sup>c</sup>		
h) Maximal (n=732)	≤18.6	0.84 (0.63,1.12)		0.023 <sup>b</sup> 0.236 <sup>c</sup>	AGE*RACE (p=0.029)	
	>18.6	1.25 (1.02,1.54)		0.034 <sup>c</sup>		

<sup>a</sup>Relative risk for a twofold increase in dioxin.<sup>b</sup>Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).<sup>c</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.



**TABLE 8-21. (Continued)**

**Analysis of Cranial Nerve Index**

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	773	16.0	All Categories		0.338
Unknown	341	14.7	Unknown vs. Background	0.90 (0.63,1.28)	0.559
Low	194	17.5	Low vs. Background	1.11 (0.73,1.69)	0.617
High	183	11.5	High vs. Background	0.68 (0.41,1.11)	0.123
Total	1,491				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	773	All Categories		0.665	AGE (p<0.001) RACE (p=0.063)
Unknown	341	Unknown vs. Background	0.84 (0.58,1.22)	0.356	
Low	194	Low vs. Background	1.14 (0.73,1.77)	0.558	
High	183	High vs. Background	0.98 (0.58,1.64)	0.931	
Total	1,491				

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



cranial nerve index were 12.5, 15.2, and 12.4 percent for the low, medium, and high initial dioxin categories.

The initial dioxin-by-diabetic class interaction was significant in the adjusted maximal analysis (Table 8-21 [d]:  $p=0.034$ ). Stratified results parallel the findings for range of motion. Appendix Table G-1 shows that there was a significant increased risk of cranial nerve index abnormalities associated with initial dioxin for diabetic Ranch Hands (Adj.  $RR=1.69$ ,  $p=0.009$ ; % abnormal: 10.0%, 12.2%, and 22.6% for the low, medium, and high initial dioxin categories). The relative risk was not significant for both diabetically impaired (Adj.  $RR=0.89$ ,  $p=0.603$ ) and normal Ranch Hands (Adj.  $RR=0.99$ ,  $p=0.916$ ). After excluding the interaction the adjusted maximal analysis was not significant (Table 8-21 [d]: Adj.  $RR=1.05$ ,  $p=0.591$ ).

### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

The current dioxin and time since tour analyses for the cranial nerve index displayed findings similar to the corresponding analyses for range of motion. In the unadjusted analyses, the current dioxin-by-time interaction was not significant under the minimal assumption (Table 8-21 [e]:  $p=0.114$ ), but it was significant under the maximal assumption (Table 8-21 [f]:  $p=0.021$ ). There was a significant decreased risk of cranial nerve index abnormalities for Ranch Hands in the maximal cohort with a later tour (time>18.6: Est.  $RR=0.74$ ,  $p=0.027$ ; % abnormal: 20.0%, 14.4%, and 7.4% for the low, medium, and high current dioxin categories) that contrasted with a nonsignificant increased risk for Ranch Hands in the maximal cohort with an early tour (time≤18.6: Est.  $RR=1.09$ ,  $p=0.411$ ).

After adjusting for the age-by-race interaction, the relative risk became significantly more than 1 for Ranch Hands in the minimal cohort with an early tour (Table 8-21 [g]: Adj.  $RR=1.34$ ,  $p=0.033$ ), although the current dioxin-by-time interaction remained nonsignificant ( $p=0.225$ ). In the adjusted maximal analysis, the current dioxin-by-time interaction remained significant (Table 8-21 [h]:  $p=0.023$ ). As in the adjusted minimal analysis, the adjusted maximal analysis found a relative risk significantly more than 1 for Ranch Hands with an early tour (time>18.6: Adj.  $RR=1.25$ ,  $p=0.034$ ). After adjustment, the relative risk became nonsignificant for Ranch Hands in the maximal cohort with a later tour (time≤18.6: Adj.  $RR=0.84$ ,  $p=0.236$ ).

### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

The unadjusted categorized current dioxin analysis did not find a significant difference in the prevalence of cranial nerve index abnormalities among the four categories (Table 8-21 [i]: 16.0%, 14.7%, 17.5%, and 11.5% for the background, unknown, low, and high current dioxin categories,  $p=0.338$ ). The overall contrast remained nonsignificant (Table 8-21 [j]:  $p=0.665$ ) after adjustment for age and race.

## **Cranial Nerve Index Without Range of Motion**

### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

Under both the minimal and maximal assumptions, the cranial nerve index without range of motion was not associated significantly with initial dioxin (Table 8-22 [a-d]:  $p>0.65$  for all unadjusted and adjusted analyses).

TABLE 8-22.

## Analysis of Cranial Nerve Index Without Range of Motion

Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
a) Minimal (n=513)	Low	128	3.9	1.05 (0.75,1.48)	0.760
	Medium	256	4.3		
	High	129	5.4		
b) Maximal (n=732)	Low	183	4.4	1.06 (0.82,1.37)	0.653
	Medium	367	3.8		
	High	182	5.0		
Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>		p-Value	Covariate Remarks	
c) Minimal (n=513)	1.04 (0.73,1.48)		0.829	AGE (p=0.826) INS (p=0.085)	
d) Maximal (n=732)	1.05 (0.81,1.37)		0.692	AGE (p=0.833)	

<sup>a</sup>Relative risk for a twofold increase in dioxin.

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

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

TABLE 8-22. (Continued)

## Analysis of Cranial Nerve Index Without Range of Motion

Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Low	Medium	High		
e) Minimal (n=513)	≤18.6	2.9 (70)	4.0 (125)	3.8 (53)	0.89 (0.46,1.72)	0.620 <sup>b</sup> 0.725 <sup>c</sup>
	>18.6	5.2 (58)	4.6 (131)	6.6 (76)	1.08 (0.72,1.63)	0.716 <sup>c</sup>
f) Maximal (n=732)	≤18.6	4.8 (105)	3.7 (187)	2.5 (81)	0.93 (0.59,1.46)	0.509 <sup>b</sup> 0.750 <sup>c</sup>
	>18.6	3.9 (78)	5.0 (179)	4.9 (102)	1.12 (0.81,1.55)	0.499 <sup>c</sup>

Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
g) Minimal (n=513)	≤18.6	0.87 (0.44,1.71)	0.612 <sup>b</sup> 0.687 <sup>c</sup>	AGE (p=0.978) INS (p=0.087)
	>18.6	1.06 (0.69,1.63)	0.783 <sup>c</sup>	
h) Maximal (n=732)	≤18.6	0.92 (0.58,1.44)	0.509 <sup>b</sup> 0.710 <sup>c</sup>	AGE (p=0.736)
	>18.6	1.10 (0.79,1.54)	0.562 <sup>c</sup>	

<sup>a</sup>Relative risk for a twofold increase in dioxin.<sup>b</sup>Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).<sup>c</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-22. (Continued)

## Analysis of Cranial Nerve Index Without Range of Motion

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	773	5.1	All Categories		0.320
Unknown	341	2.9	Unknown vs. Background	0.57 (0.28,1.15)	0.117
Low	194	5.7	Low vs. Background	1.13 (0.57,2.25)	0.725
High	183	3.8	High vs. Background	0.75 (0.33,1.70)	0.489
Total	1,491				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	773	All Categories		0.277**	DXCAT*INS (p=0.018) AGE (p=0.018)
Unknown	341	Unknown vs. Background	0.53 (0.26,1.09)**	0.084**	
Low	194	Low vs. Background	1.09 (0.54,2.19)**	0.807**	
High	183	High vs. Background	0.84 (0.36,1.93)**	0.674**	
Total	1,491				

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

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

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

Low (Ranch Hands):  $15 \text{ ppt} < \text{Current Dioxin} \leq 33.3 \text{ ppt}$ .

High (Ranch Hands): Current Dioxin  $> 33.3 \text{ ppt}$ .



### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

The association between current dioxin and the cranial nerve index without range of motion did not differ significantly between time since tour strata under both the minimal and maximal assumptions (Table 8-22 [e-h]:  $p > 0.50$  for each unadjusted and adjusted analysis).

### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

The prevalence of cranial nerve index abnormalities, excluding range of motion abnormalities, did not differ significantly among current dioxin categories in the unadjusted categorized current dioxin analysis (Table 8-22 [i]: 5.1%, 2.9%, 5.7%, and 3.8% for the background, unknown, low, and high current dioxin categories,  $p = 0.320$ ).

The adjusted analysis detected a significant categorized current dioxin-by-insecticide exposure interaction (Table 8-22 [j]:  $p = 0.018$ ). Stratified results showed a marginally significant overall contrast for participants who had never been exposed to insecticides (Appendix Table G-1:  $p = 0.056$ ). The percentages of abnormalities were 2.7, 2.0, 9.8, and 7.5 percent for the background, unknown, low, and high current dioxin categories in this stratum. Relative to the background category, there was a significant increased risk of an abnormality for Ranch Hands in the low current dioxin category (Adj. RR=3.76, 95% C.I.: [1.20, 11.76],  $p = 0.023$ ) and a marginally significant increased risk for Ranch Hands in the high current dioxin category (Adj. RR=3.34, 95% C.I.: [0.98, 11.34],  $p = 0.053$ ). The overall contrast was not significant for Ranch Hands who had been exposed to insecticides ( $p = 0.113$ ), although the adjusted relative risk was marginally less than 1 for the unknown versus background contrast (Adj. RR=0.46, 95% C.I.: [0.21, 1.02],  $p = 0.056$ ). In this stratum, the prevalences for the background, unknown, low, and high current dioxin categories were 6.8, 3.3, 4.2, and 2.3 percent.

After excluding the interaction, the overall contrast was not significant in the adjusted analysis (Table 8-22 [j]:  $p = 0.277$ ), although there was a marginally significant decreased risk for Ranch Hands in the unknown category relative to the background category (Adj. RR=0.53, 95% C.I.: [0.26, 1.09],  $p = 0.084$ ).

## **Pin Prick**

### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

The unadjusted initial dioxin analyses did not find a significant association with pin prick under both the minimal (Table 8-23 [a]:  $p = 0.941$ ) and maximal (Table 8-23 [b]:  $p = 0.632$ ) assumptions. Under both assumptions, the adjusted analyses detected a significant initial dioxin-by-diabetic class interaction (Table 8-23 [c] and [d]:  $p = 0.032$  in the minimal analysis and  $p = 0.042$  in the maximal analysis). Stratified results under the minimal assumption showed a marginally significant increased risk of pin prick abnormalities for diabetic Ranch Hands (Appendix Table G-1: Adj. RR=1.58,  $p = 0.069$ ). In this stratum, the percentages of abnormalities were 7.7, 6.9, and 21.1 percent for the low, medium, and high initial dioxin categories. The relative risk was less than 1, but not significant in both the diabetically impaired (Adj. RR=0.20,  $p = 0.175$ ) and normal strata (Adj. RR=0.92,  $p = 0.682$ ). Stratified results under the maximal assumption showed that initial dioxin was marginally associated with a decreased risk of a pin prick abnormality for diabetically impaired Ranch Hands (Adj.



TABLE 8-23.

## Analysis of Pin Prick

Ranch Hands - Log<sub>2</sub> (Initial Dioxin) - Unadjusted

Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
a) Minimal (n=512)	Low	128	9.4	1.01 (0.76,1.34)	0.941
	Medium	255	5.9		
	High	129	6.2		
b) Maximal (n=729)	Low	183	6.0	1.05 (0.85,1.30)	0.632
	Medium	363	6.6		
	High	183	7.1		

Ranch Hands - Log<sub>2</sub> (Initial Dioxin) - Adjusted

Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
c) Minimal (n=510)	1.07 (0.80,1.44)**	0.633**	INIT*DIAB (p=0.032) AGE*RACE (p=0.036)
d) Maximal (n=727)	1.10 (0.89,1.37)**	0.390**	INIT*DIAB (p=0.042) AGE*RACE (p=0.022)

<sup>a</sup>Relative risk for a twofold increase in dioxin.

\*\*Log<sub>2</sub> (initial dioxin)-by-covariate interaction (0.01<p≤0.05); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.

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

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

TABLE 8-23. (Continued)

## Analysis of Pin Prick

Ranch Hands - Log <sub>2</sub> (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Low	Medium	High		
e) Minimal (n=512)	≤18.6	12.7 (71)	6.4 (125)	5.6 (54)	0.80 (0.50,1.29)	0.123 <sup>b</sup> 0.363 <sup>c</sup>
	>18.6	7.0 (57)	3.9 (130)	8.0 (75)	1.28 (0.88,1.87)	0.194 <sup>c</sup>
f) Maximal (n=729)	≤18.6	3.8 (105)	8.5 (189)	6.2 (81)	1.06 (0.77,1.45)	0.971 <sup>b</sup> 0.743 <sup>c</sup>
	>18.6	7.7 (78)	5.8 (174)	6.9 (102)	1.06 (0.80,1.42)	0.676 <sup>c</sup>
Ranch Hands - Log <sub>2</sub> (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) <sup>a</sup>		p-Value	Covariate Remarks	
g) Minimal (n=506)	≤18.6	0.89 (0.55,1.46)**		0.184**b 0.649**c	CURR*TIME*DRKYR (p=0.019) AGE*RACE (p=0.039)	
	>18.6	1.33 (0.91,1.95)**		0.137**c		
h) Maximal (n=720)	≤18.6	1.12 (0.80,1.57)**		0.970**b 0.500**c	CURR*TIME*DRKYR (p=0.029) AGE*RACE (p=0.030)	
	>18.6	1.13 (0.84,1.52)**		0.406**c		

<sup>a</sup>Relative risk for a twofold increase in dioxin.<sup>b</sup>Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).<sup>c</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).<sup>\*\*</sup>Log<sub>2</sub> (current dioxin)-by-time-by-covariate interaction (0.01<p≤0.05); adjusted relative risk, confidence interval, and p-value derived from a model fitted after deletion of this interaction.Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.CURR: Log<sub>2</sub> (current dioxin).

TIME: Time since tour.

TABLE 8-23. (Continued)

## Analysis of Pin Prick

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	771	5.8	All Categories		0.925
Unknown	339	5.3	Unknown vs. Background	0.90 (0.52,1.59)	0.727
Low	194	5.2	Low vs. Background	0.88 (0.43,1.77)	0.714
High	183	6.6	High vs. Background	1.13 (0.59,2.19)	0.712
Total	1,487				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	769	All Categories		0.878	DIAB (p=0.010) AGE*INS (p=0.035)
Unknown	338	Unknown vs. Background	0.97 (0.54,1.71)	0.902	
Low	192	Low vs. Background	0.84 (0.40,1.77)	0.643	
High	183	High vs. Background	1.22 (0.61,2.42)	0.571	
Total	1,482				

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

RR=0.44,  $p=0.093$ ) that contrasted with nonsignificant increased risks for diabetic (Adj. RR=1.40,  $p=0.111$ ) and normal (Adj. RR=1.06,  $p=0.678$ ) Ranch Hands.

Under both assumptions, the adjusted initial dioxin analyses were not significant after excluding the interaction with diabetic class (Table 8-23 [c] and [d]:  $p=0.633$  in the minimal analysis and  $p=0.390$  in the maximal analysis).

### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

In the unadjusted analyses of pin prick, the interaction between current dioxin and time since tour was not significant under both the minimal (Table 8-23 [e]:  $p=0.123$ ) and maximal (Table 8-23 [f]:  $p=0.971$ ) assumptions. Under both assumptions, the adjusted analyses detected a significant current dioxin-by-time-by-lifetime alcohol history interaction (Table 8-23 [g] and [h]:  $p=0.019$  in the minimal analysis and  $p=0.029$  in the maximal analysis). Lifetime alcohol history was dichotomized to explore the interaction. Appendix Table G-1 shows that the current dioxin-by-time interaction was significant for Ranch Hands in the minimal cohort who had 40 drink-years or less ( $p=0.013$ ). In this stratum, pin prick was associated significantly with current dioxin for Ranch Hands with an early tour ( $\leq 40$  drink-years,  $\text{time} > 18.6$ : Adj. RR=1.81,  $p=0.011$ ; % abnormal: 2.6%, 4.3%, and 10.7% for the low, medium, and high current dioxin categories). By contrast, the relative risk was less than 1, but not significant for Ranch Hands with a later tour ( $\leq 40$  drink-years,  $\text{time} \leq 18.6$ : Adj. RR=0.73,  $p=0.337$ ). The current dioxin-by-time interaction was not significant for Ranch Hands in the minimal cohort who had more than 40 drink-years ( $p=0.108$ ).

Stratified results under the maximal assumption found that the interaction between current dioxin and time was not significant for Ranch Hands who had 40 drink-years or less ( $p=0.203$ ), but it was significant for Ranch Hands who had more than 40 drink-years ( $p=0.022$ ). In both lifetime alcohol history strata, current dioxin was marginally associated with pin prick for Ranch Hands with an early tour, but the direction of the results differed. The relative risk was marginally more than 1 for those who had 40 drink-years or less (Adj. RR=1.39,  $p=0.055$ ; % abnormal: 6.3%, 4.1%, and 9.2% for the low, medium, and high current dioxin categories), while it was marginally less than 1 for those who had more than 40 drink-years (Adj. RR=0.42,  $p=0.089$ ; % abnormal: 15.4%, 10.0%, and 0.0% for the low, medium, and high current dioxin categories). For Ranch Hands with a later tour, the relative risk was not significant in either lifetime alcohol history stratum.

After excluding the interaction with lifetime alcohol history, the adjusted analyses did not find a significant current dioxin-by-time interaction under both the minimal (Table 8-23 [g]:  $p=0.184$ ) and maximal (Table 8-23 [h]:  $p=0.970$ ) assumptions.

### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

Both the unadjusted and adjusted categorized current dioxin analyses of pin prick did not find a significant contrast (Table 8-23 [i] and [j]:  $p>0.55$  for all contrasts).



## **Light Touch**

### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

The unadjusted initial dioxin analyses did not find a significant association with light touch under both the minimal (Table 8-24 [a]:  $p=0.928$ ) and maximal (Table 8-24 [b]:  $p=0.940$ ) assumptions. The adjusted analyses were also not significant (Table 8-24 [c] and [d]:  $p=0.951$  for the minimal analysis and  $p=0.938$  for the maximal analysis).

### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

Under the minimal assumption, the association between current dioxin and light touch differed significantly between time since tour strata in the unadjusted analysis (Table 8-24 [e]:  $p=0.023$ ), although the association was not significant within both time strata. The relative risk was more than 1 for Ranch Hands with an early tour ( $\text{time}>18.6$ : Est. RR=1.43,  $p=0.111$ ) and it was less than 1 for Ranch Hands with a later tour ( $\text{time}\leq 18.6$ : Est. RR=0.59,  $p=0.129$ ). The current dioxin-by-time interaction was not significant under the maximal assumption in the unadjusted analysis (Table 8-24 [f]:  $p=0.401$ ).

The adjusted analyses supported the unadjusted findings. The interaction between current dioxin and time was significant under the minimal assumption (Table 8-24 [g]:  $p=0.048$ ), although neither within time stratum result was significant ( $\text{time}>18.6$ : Adj. RR=1.39,  $p=0.182$ ;  $\text{time}\leq 18.6$ : Adj. RR=0.62,  $p=0.207$ ). Under the maximal assumption, the adjusted analysis did not find a significant current dioxin-by-time interaction (Table 8-24 [h]:  $p=0.397$ ).

### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

The prevalence of light touch abnormalities did not differ significantly among current dioxin categories in the unadjusted analysis (Table 8-24 [i]:  $p=0.994$ ). The adjusted analysis was also not significant (Table 8-24 [j]:  $p=0.989$ ).

## **Muscle Status**

### ***Model 1: Ranch Hands - Log<sub>2</sub> (Initial Dioxin)***

Under both the minimal and maximal assumptions, the initial dioxin analyses of muscle status did not find a significant association (Table 8-25 [a-d]:  $p>0.35$  for all unadjusted and adjusted analyses).

### ***Model 2: Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time***

The association between current dioxin and muscle status did not differ significantly between time since tour strata in the unadjusted analyses (Table 8-25 [e] and [f]:  $p=0.869$  for the minimal analysis and  $p=0.629$  for the maximal analysis). The current dioxin-by-time interaction remained nonsignificant after covariate adjustment (Table 8-25 [g] and [h]:  $p=0.710$  for the minimal analysis and  $p=0.422$  for the maximal analysis).

### ***Model 3: Ranch Hands and Comparisons by Current Dioxin Category***

The unadjusted categorized current dioxin analysis did not find a significant difference in the prevalence of muscle status abnormalities among the four categories (Table 8-25 [i]:  $p=0.974$ ). The adjusted analysis detected a significant categorized current dioxin-by-diabetic



TABLE 8-24.

## Analysis of Light Touch

Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
a) Minimal (n=512)	Low	128	6.3	0.99 (0.69,1.40)	0.928
	Medium	255	3.9		
	High	129	3.9		
b) Maximal (n=729)	Low	183	4.4	1.01 (0.78,1.30)	0.940
	Medium	363	4.7		
	High	183	4.4		
Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>		p-Value	Covariate Remarks	
c) Minimal (n=504)	1.01 (0.69,1.50)		0.951	DIAB (p=0.039) AGE*RACE (p=0.017) AGE*DRKYR (p=0.043)	
d) Maximal (n=727)	0.99 (0.75,1.30)		0.938	DIAB (p=0.116) AGE*RACE (p=0.019)	

<sup>a</sup>Relative risk for a twofold increase in dioxin.

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

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

TABLE 8-24. (Continued)

## Analysis of Light Touch

Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Unadjusted

Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Low	Medium	High		
e) Minimal (n=512)	≤18.6	8.5 (71)	4.8 (125)	1.9 (54)	0.59 (0.30,1.17)	0.023 <sup>b</sup> 0.129 <sup>c</sup>
	>18.6	3.5 (57)	3.1 (130)	5.3 (75)	1.43 (0.92,2.22)	0.111 <sup>c</sup>
f) Maximal (n=729)	≤18.6	2.9 (105)	6.4 (189)	2.5 (81)	0.89 (0.59,1.35)	0.401 <sup>b</sup> 0.583 <sup>c</sup>
	>18.6	5.1 (78)	4.0 (174)	4.9 (102)	1.12 (0.80,1.56)	0.517 <sup>c</sup>

Ranch Hands - Log<sub>2</sub> (Current Dioxin) and Time - Adjusted

Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) <sup>a</sup>	p-Value	Covariate Remarks
g) Minimal (n=504)	≤18.6	0.62 (0.30,1.30)	0.048 <sup>b</sup>	DIAB (p=0.060)
	>18.6	1.39 (0.86,2.24)	0.207 <sup>c</sup>	AGE*RACE (p=0.029)
			0.182 <sup>c</sup>	AGE*DRKYR (p=0.035)
h) Maximal (n=727)	≤18.6	0.85 (0.54,1.36)	0.397 <sup>b</sup>	DIAB (p=0.135)
	>18.6	1.08 (0.77,1.53)	0.504 <sup>c</sup>	AGE*RACE (p=0.020)
			0.648 <sup>c</sup>	

<sup>a</sup>Relative risk for a twofold increase in dioxin.<sup>b</sup>Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).<sup>c</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.

TABLE 8-24. (Continued)

## Analysis of Light Touch

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	771	4.3	All Categories		0.994
Unknown	339	4.1	Unknown vs. Background	0.96 (0.51,1.82)	0.909
Low	194	4.1	Low vs. Background	0.96 (0.44,2.12)	0.923
High	183	3.8	High vs. Background	0.89 (0.39,2.04)	0.783
Total	1,487				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	769	All Categories		0.989	AGE (p=0.377) DIAB*INS (p=0.044)
Unknown	338	Unknown vs. Background	1.09 (0.57,2.09)	0.797	
Low	192	Low vs. Background	0.97 (0.42,2.27)	0.943	
High	183	High vs. Background	0.93 (0.39,2.22)	0.876	
Total	1,482				

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

TABLE 8-25.

## Analysis of Muscle Status

Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Unadjusted					
Assumption	Initial Dioxin	n	Percent Abnormal	Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
a) Minimal (n=521)	Low	130	0.8	1.03 (0.61,1.71)	0.922
	Medium	260	2.3		
	High	131	2.3		
b) Maximal (n=740)	Low	183	1.1	1.17 (0.79,1.72)	0.439
	Medium	371	1.9		
	High	186	1.6		
Ranch Hands - Log <sub>2</sub> (Initial Dioxin) - Adjusted					
Assumption	Adj. Relative Risk (95% C.I.) <sup>a</sup>		p-Value	Covariate Remarks	
c) Minimal (n=519)	1.09 (0.65,1.83)		0.747	AGE (p=0.175) DIAB (p=0.126)	
d) Maximal (n=729)	1.21 (0.80,1.83)		0.381	AGE (p=0.064) DIAB*DRKYR (p=0.005)	

<sup>a</sup>Relative risk for a twofold increase in dioxin.

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

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

TABLE 8-25. (Continued)

## Analysis of Muscle Status

Ranch Hands - Log <sub>2</sub> (Current Dioxin) and Time - Unadjusted						
Assumption	Time (Yrs.)	Percent Abnormal/(n) Current Dioxin			Est. Relative Risk (95% C.I.) <sup>a</sup>	p-Value
		Low	Medium	High		
e) Minimal (n=521)	≤18.6	0.0	3.9	1.9	1.07 (0.51,2.25)	0.869 <sup>b</sup>
		(72)	(128)	(54)		0.859 <sup>c</sup>
	>18.6	3.5	0.0	2.6	0.98 (0.44,2.15)	0.953 <sup>c</sup>
		(58)	(132)	(77)		
f) Maximal (n=740)	≤18.6	1.0	2.1	2.4	1.30 (0.75,2.25)	0.629 <sup>b</sup>
		(105)	(191)	(83)		0.348 <sup>c</sup>
	>18.6	1.3	1.1	1.9	1.07 (0.59,1.94)	0.835 <sup>c</sup>
		(78)	(179)	(104)		
Ranch Hands - Log <sub>2</sub> (Current Dioxin) and Time - Adjusted						
Assumption	Time (Yrs.)	Adj. Relative Risk (95% C.I.) <sup>a</sup>		p-Value	Covariate Remarks	
g) Minimal (n=519)	≤18.6	1.28 (0.59,2.79)		0.710 <sup>b</sup>	AGE (p=0.127)	
				0.533 <sup>c</sup>	DIAB (p=0.141)	
	>18.6	1.05 (0.48,2.31)		0.908 <sup>c</sup>		
h) Maximal (n=729)	≤18.6	1.55 (0.83,2.90)		0.422 <sup>b</sup>	AGE (p=0.041)	
				0.167 <sup>c</sup>	DIAB*DRKYR (p=0.005)	
	>18.6	1.10 (0.59,2.03)		0.766 <sup>c</sup>		

<sup>a</sup>Relative risk for a twofold increase in dioxin.<sup>b</sup>Test of significance for homogeneity of relative risks (current dioxin continuous, time categorized).<sup>c</sup>Test of significance for relative risk equal to 1 (current dioxin continuous, time categorized).Note: Minimal--Low: >10-14.65 ppt; Medium: >14.65-45.75 ppt; High: >45.75 ppt.Maximal--Low: >5-9.01 ppt; Medium: >9.01-33.3 ppt; High: >33.3 ppt.



TABLE 8-25. (Continued)

## Analysis of Muscle Status

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

Current Dioxin Category	n	Percent Abnormal	Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	783	2.2	All Categories		0.974
Unknown	342	1.8	Unknown vs. Background	0.80 (0.31,2.06)	0.650
Low	196	2.0	Low vs. Background	0.94 (0.31,2.82)	0.910
High	187	2.1	High vs. Background	0.98 (0.33,2.96)	0.978
Total	1,508				

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

Current Dioxin Category	n	Contrast	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	779	All Categories		0.945**	DXCAT*DIAB (p=0.019) AGE (p=0.014)
Unknown	338	Unknown vs. Background	0.77 (0.30,1.99)**	0.586**	DIAB*DRKYR (p=0.011)
Low	192	Low vs. Background	0.92 (0.30,2.81)**	0.884**	
High	183	High vs. Background	1.08 (0.34,3.45)**	0.893**	
Total	1,492				

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

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

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

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

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