Table 5-76

Pre-post SEA Counts and Rates of Chromosomal Anomalies

Variable: Chromosomal Anomalies
Restrictions: All Children of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	Time of Conception Relative to the Father's Duty in SEA: Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	p-Value
a) D>10 ppt (n=1208)	Low	249	0	0.0	106	0	0.0	
	Medium	338	2	5.9	245	0	0.0	
	High	113	0	0.0	157	1	6.4	
b) D>5 ppt (n=1748)	Low	286	0	0.0	155	1	6.5	
	Medium	616	2	3.2	308	0	0.0	
	High	156	0	0.0	227	1	4.4	

Chromosomal Anomalies (All Children)

Model 2: Children of Ranch Hands - Log_2(Current Dioxin) and Time

There is insufficient data (Table 5-77) to assess the significance of variation in the association between chromosomal anomalies and current dioxin with time since duty in SEA and time of conception among children of Ranch Hands.

Table 5-77

Pre-post SEA Counts and Rates of Chromosomal Anomalies

Variable: Chromosomal Anomalies
Restrictions: All Children of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

Ranch Hands - Log_2(Current Dioxin), Time - Unadjusted

Exposure Restriction	Time of Conception	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	p-Value
a) D>10 ppt (n=1210)	Pre-SEA	≤18.6	0.0 (0/137)	10.9 (2/183)	0.0 (0/37)	
		>18.6	0.0 (0/95)	0.0 (0/171)	0.0 (0/78)	
	Post-SEA	≤18.6	0.0 (0/62)	0.0 (0/134)	0.0 (0/72)	
		>18.6	0.0 (0/40)	0.0 (0/108)	10.8 (1/93)	
b) D>5 ppt (n=1748)	Pre-SEA	≤18.6	0.0 (0/157)	6.4 (2/313)	0.0 (0/66)	
		>18.6	0.0 (0/150)	0.0 (0/270)	0.0 (0/102)	
	Post-SEA	≤18.6	11.1 (1/90)	0.0 (0/174)	0.0 (0/110)	
		>18.6	0.0 (0/63)	0.0 (0/136)	8.5 (1/117)	

Chromosomal Anomalies (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

There is insufficient data (Table 5-78) to assess the significance of variation in the association between chromosomal anomalies and categorized current dioxin with time of conception.

Table 5-78

Pre-post SEA Counts and Rates of Chromosomal Anomalies

Variable: Chromosomal Anomalies
Restrictions: All Children of Ranch Hands and Comparisons
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 3: Categorized Current Dioxin

Categorized Current Dioxin - Unadjusted

Time of Conception Relative to the Father's Duty in SEA

Exposure Category	Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	Odds Ratio	Category Contrast	p-Value
Background	1459	2	1.4	981	3	3.1		All Exp Categ	
Unknown	582	0	0.0	282	3	10.6		Unk vs Bkgd	
Low	290	2	6.9	174	0	0.0		Low vs Bkgd	
High	168	0	0.0	227	1	4.4		High vs Bkgd	
Total	2499			1664					

Chromosomal Anomalies (Full Siblings)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

There is insufficient data (Table 5-79) to assess the significance of variation in the association between chromosomal anomalies and initial dioxin with time of conception among full sibling children of Ranch Hands.

Table 5-79

Pre-post SEA Counts and Rates of Chromosomal Anomalies

Variable: Chromosomal Anomalies
Restrictions: Full Siblings of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	Time of Conception Relative to the Father's Duty in SEA: Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	p-Value
a) D>10 ppt (n=1030)	Low	231	0	0.0	78	0	0.0	
	Medium	276	1	3.6	206	0	0.0	
	High	103	0	0.0	136	1	7.4	
b) D>5 ppt (n=1489)	Low	252	0	0.0	114	1	8.8	
	Medium	545	1	1.8	245	0	0.0	
	High	135	0	0.0	198	1	5.1	

Chromosomal Anomalies (Full Siblings)

Model 2: Children of Ranch Hands - Log_2(Current Dioxin) and Time

There is insufficient data (Table 5-80) to assess the significance of variation in the association between chromosomal anomalies and current dioxin with time since duty in SEA and time of conception among full sibling children of Ranch Hands.

Table 5-80

Pre-post SEA Counts and Rates of Chromosomal Anomalies

Variable: Chromosomal Anomalies
Restrictions: Full Siblings of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

Ranch Hands - Log_2(Current Dioxin), Time - Unadjusted

Exposure Restriction	Time of Conception	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	p-Value
a) D>10 ppt (n=1032)	Pre-SEA	≤18.6	0.0 (0/124)	6.5 (1/155)	0.0 (0/35)	
		>18.6	0.0 (0/85)	0.0 (0/143)	0.0 (0/69)	
	Post-SEA	≤18.6	0.0 (0/47)	0.0 (0/115)	0.0 (0/64)	
		>18.6	0.0 (0/28)	0.0 (0/92)	13.3 (1/75)	
b) D>5 ppt (n=1489)	Pre-SEA	≤18.6	0.0 (0/126)	3.6 (1/276)	0.0 (0/60)	
		>18.6	0.0 (0/145)	0.0 (0/237)	0.0 (0/88)	
	Post-SEA	≤18.6	16.9 (1/59)	0.0 (0/144)	0.0 (0/98)	
		>18.6	0.0 (0/53)	0.0 (0/106)	10.3 (1/97)	

Chromosomal Anomalies (Full Siblings)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

There is insufficient data (Table 5-81) to assess the significance of variation in the association between chromosomal anomalies and categorized current dioxin with time of conception among full siblings.

Table 5-81

Pre-post SEA Counts and Rates of Chromosomal Anomalies

Variable: Chromosomal Anomalies
Restrictions: Full Siblings of Ranch Hands and Comparisons
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 3: Categorized Current Dioxin

Categorized Current Dioxin - Unadjusted

Time of Conception Relative to the Father's Duty in SEA

Exposure Category	Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	Odds Ratio	Category Contrast	p-Value
Background	1250	2	1.6	812	3	3.7		All Exp Categ	
Unknown	514	0	0.0	221	3	13.6		Unk vs Bkgd	
Low	244	1	4.1	148	0	0.0		Low vs Bkgd	
High	148	0	0.0	195	1	5.1		High vs Bkgd	
Total	2156			1376					

Other and Unspecified Anomalies (All Children)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

There is insufficient data (Table 5-82) to assess the significance of variation in the association between other and unspecified anomalies and initial dioxin with time of conception among children of Ranch Hands.

Table 5-82

Pre-post SEA Counts and Rates of Other and Unspecified Anomalies

Variable: Other and Unspecified Anomalies
Restrictions: All Children of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	Time of Conception Relative to the Father's Duty in SEA: Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	p-Value
a) D>10 ppt (n=1208)	Low	249	0	0.0	106	1	9.4	
	Medium	338	4	11.8	245	2	8.2	
	High	113	0	0.0	157	0	0.0	
b) D>5 ppt (n=1748)	Low	286	1	3.5	155	1	6.5	
	Medium	616	1	1.6	308	3	9.7	
	High	156	3	19.2	227	0	0.0	

Other and Unspecified Anomalies (All Children)

Model 1: Children of Ranch Hands - Log_2(Current Dioxin)

There is insufficient data (Table 5-83) to assess the significance of variation in the association between other and unspecified anomalies and current dioxin with time since duty in SEA and time of conception among children of Ranch Hands.

Table 5-83

Pre-post SEA Counts and Rates of Other and Unspecified Anomalies

Variable: Other and Unspecified Anomalies
Restrictions: All Children of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

Ranch Hands - Log_2(Current Dioxin), Time - Unadjusted

Exposure Restriction	Time of Conception	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	p-Value
a) D>10 ppt (n=1210)	Pre-SEA	≤18.6	0.0 (0/137)	0.0 (0/183)	0.0 (0/37)	
		>18.6	0.0 (0/95)	23.4 (4/171)	0.0 (0/78)	
	Post-SEA	≤18.6	0.0 (0/62)	7.5 (1/134)	0.0 (0/72)	
		>18.6	25.0 (1/40)	9.3 (1/108)	0.0 (0/93)	
b) D>5 ppt (n=1748)	Pre-SEA	≤18.6	0.0 (0/157)	0.0 (0/313)	0.0 (0/66)	
		>18.6	6.7 (1/150)	11.1 (3/270)	9.8 (1/102)	
	Post-SEA	≤18.6	0.0 (0/90)	5.7 (1/174)	0.0 (0/110)	
		>18.6	15.9 (1/63)	14.7 (2/136)	0.0 (0/117)	

Other and Unspecified Anomalies (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

There is insufficient data (Table 5-84) to assess the significance of variation in the association between other and unspecified anomalies and categorized current dioxin with time of conception.

Table 5-84

Pre-post SEA Counts and Rates of Other and Unspecified Anomalies

Variable: Other and Unspecified Anomalies
Restrictions: All Children of Ranch Hands and Comparisons
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 3: Categorized current dioxin

Categorized Current Dioxin - Unadjusted

Time of Conception Relative to the Father's Duty in SEA

Exposure Category	Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	Odds Ratio	Category Contrast	p-Value
Background	1459	3	2.1	981	2	2.0		All Exp Categ	
Unknown	582	2	3.4	282	1	3.5		Unk vs Bkgd	
Low	290	3	10.3	174	2	11.5		Low vs Bkgd	
High	168	1	6.0	227	0	0.0		High vs Bkgd	
Total	2499			1664					

Other and Unspecified Anomalies (Full Siblings)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

There is insufficient data (Table 5-85) to assess the significance of variation in the association between other and unspecified anomalies and initial dioxin with time of conception among full sibling children of Ranch Hands.

Table 5-85

Pre-post SEA Counts and Rates of Other and Unspecified Anomalies

Variable: Other and Unspecified Anomalies
Restrictions: Full Siblings of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	Time of Conception Relative to the Father's Duty in SEA: Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	p-Value
a) D>10 ppt (n=1030)	Low	231	0	0.0	78	0	0.0	
	Medium	276	2	7.2	206	1	4.9	*
	High	103	0	0.0	136	0	0.0	
b) D>5 ppt (n=1489)	Low	252	1	4.0	114	1	8.8	
	Medium	545	1	1.8	245	1	4.1	
	High	135	1	7.4	198	0	0.0	

Other and Unspecified Anomalies (Full Siblings)

Model 2: Children of Ranch Hands - Log_2(Current Dioxin) and Time

There is insufficient data (Table 5-86) to assess the significance of variation in the association between other and unspecified anomalies and current dioxin with time since duty in SEA and time of conception among full sibling children of Ranch Hands.

Table 5-86

Pre-post SEA Counts and Rates of Other and Unspecified Anomalies

Variable: Other and Unspecified Anomalies
Restrictions: Full Siblings of Ranch Hands
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

Ranch Hands - Log_2(Current Dioxin), Time - Unadjusted

Exposure Restriction	Time of Conception	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	p-Value
a) D>10 ppt (n=1032)	Pre-SEA	≤18.6	0.0 (0/124)	0.0 (0/155)	0.0 (0/35)	
		>18.6	0.0 (0/85)	14.0 (2/143)	0.0 (0/69)	
	Post-SEA	≤18.6	0.0 (0/47)	0.0 (0/115)	0.0 (0/64)	
		>18.6	0.0 (0/28)	10.9 (1/92)	0.0 (0/75)	
b) D>5 ppt (n=1489)	Pre-SEA	≤18.6	0.0 (0/126)	0.0 (0/276)	0.0 (0/60)	
		>18.6	6.9 (1/145)	4.2 (1/237)	11.4 (1/88)	
	Post-SEA	≤18.6	0.0 (0/59)	0.0 (1/144)	0.0 (0/98)	
		>18.6	18.9 (1/53)	9.4 (1/106)	0.0 (0/97)	

Other and Unspecified Anomalies (Full Siblings)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

There is insufficient data (Table 5-87) to assess the significance of variation in the association between other and unspecified anomalies and categorized current dioxin with time of conception among full siblings.

Table 5-87

Pre-post SEA Counts and Rates of Other and Unspecified Anomalies

Variable: Other and Unspecified Anomalies
Restrictions: Full Siblings of Ranch Hands and Comparisons
Categories: Time of Conception Relative to the Father's Duty in SEA
Model 3: Categorized Current Dioxin

Categorized Current Dioxin - Unadjusted

Time of Conception Relative to the Father's Duty in SEA

Exposure Category	Pre-SEA n	Pre-SEA Abn	Pre-SEA Rate	Post-SEA n	Post-SEA Abn	Post-SEA Rate	Odds Ratio	Category Contrast	p-Value
Background	1250	3	2.4	812	2	2.5		All Exp Categ	
Unknown	514	2	3.9	221	1	4.5		Unk vs Bkgd	
Low	244	1	4.1	148	1	6.8		Low vs Bkgd	
High	148	1	6.8	195	0	0.0		High vs Bkgd	
Total	2156			1376					

5.10 Conclusion

Throughout this section, nonsignificant results are indicated by NS, borderline significant results are indicated by NS*. Dioxin by covariate interactions with a with p-value greater than or equal to 0.01 and less than 0.05 are indicated with a preceding double asterisk (**). Four asterisks (****) indicate the presence of an interaction between dioxin and a covariate with a p-value less than 0.01. The p-value is replaced by a double hyphen (--) when the analysis was not carried out due to sparse data.

At baseline, the significance of changes in the association between reported birth defect (yes,no) and the father's group membership (Ranch Hand, Comparison) with time of birth of the child relative to the father's SEA tour of duty was assessed with a chi-square test and was found significant (p=0.04). The finding was that the Ranch Hand birth defect rate was less than that of the Comparisons in children born before the father's SEA duty and greater than the Comparison rate in children born after the father's SEA duty. That analysis motivated the full verification of all reproductive outcomes.

The baseline analysis used a different definition of birth defect than that used in this report. The baseline definition included all the anomalies specified in the CDC definition and an additional 12 anomalies not included in the CDC definition of birth defect.

Because the databases have been subjected to additional quality control since the baseline report, the baseline analysis was repeated using current data. Additionally, a series of 6 analyses were carried out under various combinations of birth defect definition (baseline, CDC), source (unverified mother's report, verified), restriction (children born during or prior to the fathers baseline physical examination, none) and adjustment (dioxin, none), to explain differences, if any, between current and baseline results. Table 5-88 summarizes the overall findings of each of these 6 analyses. The p-value in Table 5-88 expresses the significance of the birth defect by group by time of birth interaction of the baseline approach. In that table, the CDC definition includes all congenital anomalies.

This series of analyses demonstrates that the baseline finding still holds with current data but is not significant when the mother's reports are restricted to those that could be verified or when the CDC birth defect definition is used.

Table 5-88

Baseline Analyses with Different Birth Defect Definitions Data Sources, Restrictions and Adjustments

Birth Defect Definition	Source	Restriction	Adjustment	p-Value
Baseline	Mother's Report	None	None	0.001
Baseline	Mother's Report	Children Born Before Baseline	Dioxin	0.038
Baseline	Mother's Report and also Verified	Children Born Before Baseline	None	0.032
Baseline	Mother's Report and also Verified	Children Born Before Baseline	Dioxin	NS
CDC	Verified	Children Born Before Baseline	None	NS
CDC	Verified	None	None	NS

Because the baseline approach exhibited a significant result when using the baseline definition of birth defect but not when using the CDC definition, a series of analyses was carried out to determine whether the baseline finding could be attributed to a particular CDC category of birth defects. Each analysis was carried out twice, first with restriction to children born before the baseline examination then without this restriction. The results are summarized in Table 5-89. In Table 5-89 the p-value refers to the birth defect (yes, no) by group (Ranch Hand, Comparison) by time of birth (pre-SEA, post-SEA) interaction. All of the birth defect determinations used in Table 5-89 were verified.

Table 5-89

P-Value Summary of Birth Defect by Time of Conception (Pre-SEA, Post-SEA) by Group (Ranch Hand, Comparison) Analyses Unadjusted for Covariates

a) Restricted to Children Born Prior to the Father's AFHS Baseline Examination

Birth Defect Category	p-Value
Total Congenital	NS
Total Congenital	NS
Circulatory System and Heart	NS
Digestive System	NS
Genital	NS
Urinary	NS*
Musculoskeletal	NS
Skin	NS

b) Without the Restriction to Children Born Prior to the Father's AFHS Baseline Examination

Birth Defect Category	p-Value
Total Congenital	0.028
Nervous System	NS
Eye	NS
Ear, Face and Neck	NS
Circulatory System and Heart	NS
Respiratory System	0.028
Digestive System	NS
Genital	NS
Urinary	0.036
Musculoskeletal	NS
Skin	NS
Chromosomal Abnormality	NS
Other and Unspecified	NS

With restriction to children born during or prior to the father's baseline physical examination, no significant birth defect by group by time of birth interactions were found with birth defects restricted to any of the categories listed in Table 5-89 (a). The analysis of urinary anomalies found a borderline significant interaction, caused by the Ranch Hand rate (11.4 per 1000) being less than the Comparisons rate (11.8 per 1000) in pre-SEA children with the situation reversed in post-SEA children (Ranch Hand: 18.3 per 1000, Comparison 7.7 per 1000).

With all children being considered [Table 50-89 (b)], significant changes in relative risk were found for total congenital anomalies (p=0.028), respiratory system anomalies (p=0.028) and urinary anomalies (p=0.036). All three of these findings were caused by the Ranch Hand rate being less the Comparisons rate in pre-SEA children and greater than the Comparison rate in post-SEA children.

A series of analyses were carried out with Models 1, 2 and 3 to determine whether any of the previously noted odds ratio changes were associated with the father's dioxin level. Verified birth defects satisfying the definition of each of the 13 CDC categories were assessed in all children and again in full siblings (without restriction to those born prior to the father's baseline examination) without adjustment for covariates. The results are summarized in Tables 5-90, 5-91 and 5-92.

Table 5-90

P-Value Summary of Pre-Post Initial Dioxin (Model 1) Analyses of Birth Defects (Children of Ranch Hands)

a) All Children

Variable	Unadjusted D>10 ppt	Unadjusted D>5 ppt
Total Congenital Anomalies	NS	NS
Nervous System Anomalies	--	--
Eye Anomalies	--	--
Ear, Face and Neck Anomalies	--	--
Circulatory System and Heart Anomalies	NS*	NS
Respiratory System Anomalies	--	--
Digestive System Anomalies	NS	NS
Genital Anomalies	NS	NS
Urinary System Anomalies	NS	NS
Musculoskeletal Deformities	NS	NS
Anomalies of the Skin	NS	NS
Chromosomal Anomalies	--	--
Other and Unspecified Anomalies	--	--

Table 5-90 (Continued)

b) Full Siblings

Variable	Unadjusted D>10 ppt	Unadjusted D>5 ppt
Total Congenital Anomalies	NS	NS
Nervous System Anomalies	--	--
Eye Anomalies	--	--
Ear, Face and Neck Anomalies	--	--
Circulatory System and Heart Anomalies	NS	NS
Respiratory System Anomalies	--	--
Digestive System Anomalies	NS	NS
Genital Anomalies	NS	NS
Urinary System Anomalies	NS	NS
Musculoskeletal Deformities	NS	NS
Anomalies of the Skin	NS	NS
Chromosomal Anomalies	--	--
Other and Unspecified Anomalies	--	--

Table 5-91

P-Value Summary of Pre-Post Current Dioxin and Time (Model 2) Analyses of Birth Defects (Children of Ranch Hands)

a) All Children

Variable	Unadjusted D>10 ppt	Unadjusted D>5 ppt
Total Congenital Anomalies	NS	NS
Nervous System Anomalies	--	--
Eye Anomalies	--	--
Ear, Face and Neck Anomalies	--	--
Circulatory System and Heart Anomalies	NS	NS
Respiratory System Anomalies	--	--
Digestive System Anomalies	0.030	NS*
Genital Anomalies	NS	NS
Urinary System Anomalies	NS	NS
Musculoskeletal Deformities	0.017	NS
Anomalies of the Skin	NS	NS
Chromosomal Anomalies	--	--
Other and Unspecified Anomalies	--	--

Table 5-91 (Continued)

b) Full Siblings

Variable	Unadjusted D>10 ppt	Unadjusted D>5 ppt
Total Congenital Anomalies	NS	NS
Nervous System Anomalies	--	--
Eye Anomalies	--	--
Ear, Face and Neck Anomalies	--	--
Circulatory System and Heart Anomalies	NS	NS
Respiratory System Anomalies	--	--
Digestive System Anomalies	0.030	NS*
Genital Anomalies	NS	NS
Urinary System Anomalies	NS	NS
Musculoskeletal Deformities	0.019	NS
Anomalies of the Skin	NS	NS
Chromosomal Anomalies	--	--
Other and Unspecified Anomalies	--	--

Table 5-92

P-Value Summary of Pre-Post Categorized Current Dioxin (Model 3) Analyses of Birth Defects (Children of Ranch Hands and Comparisons)

a) All Children

Variable	All	Unadjusted Contrasts with Background Unknown	Low	High
Total Congenital Anomalies	NS	NS	NS	NS
Nervous System Anomalies	--	--	--	--
Eye Anomalies	--	--	--	--
Ear, Face and Neck Anomalies	--	--	--	--
Circulatory System and Heart Anomalies	NS	NS	NS	NS
Respiratory System Anomalies	--	--	--	--
Digestive System Anomalies	NS	NS	NS	NS
Genital Anomalies	NS	NS	NS	NS
Urinary System Anomalies	NS	NS	NS	NS
Musculoskeletal Deformities	NS	NS	NS	NS
Anomalies of the Skin	NS	NS	NS	NS
Chromosomal Anomalies	--	--	--	--
Other and Unspecified Anomalies	--	--	--	--

Table 5-92 (Continued)

b) Full Siblings

Variable	All	Unadjusted Contrasts with Background Unknown	Low	High
Total Congenital Anomalies	NS	NS	NS*	NS
Nervous System Anomalies	--	--	--	--
Eye Anomalies	--	--	--	--
Ear, Face and Neck Anomalies	--	--	--	--
Circulatory System and Heart Anomalies	NS*	NS	NS	NS
Respiratory System Anomalies	--	--	--	--
Digestive System Anomalies	NS	NS	NS	NS
Genital Anomalies	NS	NS	NS	NS
Urinary System Anomalies	NS	NS	NS*	NS
Musculoskeletal Deformities	NS	NS	NS	NS
Anomalies of the Skin	NS	NS	NS	NS
Chromosomal Anomalies	--	--	--	--
Other and Unspecified Anomalies	--	--	--	--

The only significant results in these analyses were the Model 2 assessments of digestive system anomalies and musculoskeletal deformities in children of Ranch Hands having more than 10 ppt current dioxin. The digestive system findings were caused by high post-SEA rates in children of Ranch Hands with late tours and high dioxin level and in children of Ranch Hands with early tours and intermediate dioxin levels. The musculoskeletal findings were caused by decreasing post-SEA rates in children of Ranch Hands with early tours, opposite to a corresponding increasing trend in pre-SEA rates. These findings are inconsistent, lack credible biologic explanation, and therefore appear unrelated to dioxin.

In summary, a repetition of the baseline analysis with verified birth defect data revealed a significant reversal in birth defect rates with time of birth of the child relative to the father's duty in SEA, with the Ranch Hand rate being less than the Comparison rate among pre-SEA children and greater than the Comparison rate among post-SEA children. However, after accounting for paternal dioxin level, we found no evidence that this effect was confined to a specific birth defect category and we found no significant association between this change in risk and dioxin. We conclude that this change in relative risk over time is unrelated to dioxin.

6. POST-SEA BIRTH DEFECTS

6.1 Post-SEA Exposure Analyses

The association between paternal dioxin and birth defects, grouped by CDC category, among children conceived during or after the father's duty in SEA were assessed with Models 1, 2 and 3. Each analysis was carried out twice, first with no restriction on sibship and again with the restriction to full siblings. The results are shown in Tables 6-1 through 6-78. When the data were not too sparse, analyses were carried out without and then with adjustment for covariates.

Listings of post-SEA children with anomalies in any of the 12 CDC categories are shown in Appendix Table D-1. Table D-1 also gives the father's current categorized dioxin level; children with multiple anomalies are listed for each anomaly.

Throughout this section, rates are computed as the number of occurrences of a birth defect per 1000 children.

Total Congenital Anomalies (All Children)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

Without adjustment for covariates (Table 6-1 [a] and [b]), there is no significant association between initial dioxin and total congenital anomalies among children of Ranch Hands with more that 10 ppt (p=0.362) or more than 5 ppt current dioxin (p=0.861).

After adjustment for covariates (Table 6-1 [c]), there is no significant association between total congenital anomalies and initial dioxin in the children of Ranch Hands with more than 10 ppt current dioxin (p=0.261).

After adjustment for covariates (Table 6-1 [d]), the association between initial dioxin level and total congenital anomalies in children of Ranch Hands with more than 5 ppt current dioxin varies significantly with the father's race (p=0.020). This changing association is displayed in Appendix Table D-2. The significance is caused by a low relative risk (OR=0.35 95% CI 0.11-1.15, p=0.077) among children of Black fathers. The relative risk among children of nonblack fathers was not significantly different from 1.0.

Table 6-1

Post-SEA Counts and Rates of Total Congenital Anomalies

Variable: Total Congenital Anomalies
Restrictions: All Children of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	n	Abnormal Number	Abnormal Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=508)	Low	106	20	188.7	0.92(0.77,1.10)	0.362
	Medium	245	68	277.6		
	High	157	31	197.5		
b) D>5 ppt (n=690)	Low	155	35	225.8	0.99(0.87,1.12)	0.861
	Medium	308	72	233.8		
	High	227	49	215.9		

Ranch Hands - Log_2(Initial Dioxin) - Adjusted

Exposure Restriction	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=458)	0.90(0.75,1.08)	0.261	RACE(p=0.028) OCC(p=0.062)
d) D>5 ppt (n=616)	0.93(0.80,1.08)***	0.358***	RACE*DIOXIN(p=0.020) OCC(p=0.003) F-AGE(p=0.033)

Total Congenital Anomalies (All Children)

Model 2: Children of Ranch Hands - Log_2(Current Dioxin) and Time

Without adjustment for covariates (Table 6-2 [a]), there is no significant variation in the association between total congenital anomalies and current dioxin and time since duty in SEA among children of Ranch Hands having more than 10 ppt current dioxin (p=0.818). The relative risks among children of Ranch Hands with late (p=0.638) and early (p=0.389) tours are not significant.

Without adjustment for covariates (Table 6-2 [b]), there is no significant variation in the association between total congenital anomalies and current dioxin and time since duty in SEA among children of Ranch Hands with more than 5 ppt current dioxin (p=0.274). The relative risks among children of Ranch Hands with late (p=0.604) and early (p=0.303) tours were not statistically significant.

After adjustment for covariates (Table 6-2 [c]), there is significant variation in the association between total congenital anomalies and current dioxin and time since duty in SEA and the mother's drinking (p=0.018) among children of Ranch Hands having more than 10 ppt current dioxin. The basis for this variation in displayed in Appendix Table D-2. For the mothers who did not drink during pregnancy, there is no significant variation in the association between total congenital anomalies and current dioxin and time since duty in SEA (p=0.857). Furthermore the relative risks among children of Ranch Hands with late (p=0.289) or early (p=0.155) tours are not significantly different from 1. There was insufficient data to make similar comparisons in the other strata.

After adjustment for covariates (Table 6-2 [d]), there is significant variation in the association between total congenital anomalies and current dioxin with time since duty in SEA tour and the father's age at the time of conception (p=0.033) among children of Ranch Hands having more than 5 ppt current dioxin. The basis for this variation in displayed in Appendix Table D-2. For the fathers less than 30 years of age at time of conception, there is no significant variation in the association between the congenital anomalies and current dioxin and time since duty SEA (p=0.720). In that stratum, the relative risks among children of Ranch Hands with late (p=0.294) or early (p=0.202) tours are not significantly different from 1. For the fathers 30 years or older at the time of conception, there is a significant variation in the association between total congenital anomalies and current dioxin with time since duty in SEA (p=0.046). In that stratum, the negative relative risk among children of Ranch Hands with late tours was significantly less than 1 (p=0.014) while the risk for the early tours is not different from 1 (p=0.739).

If this variation in risk is ignored, there is no significant overall association between total congenital anomalies and current dioxin and time since duty in SEA (p=0.241). Furthermore, the association between total congenital anomalies and current dioxin is not significant among children whose father had a late (p=0.194) or early (p=0.819) tour.

Table 6-2

Post-SEA Counts and Rates of Total Congenital Anomalies

Variable: Total Congenital Anomalies
Restrictions: All Children of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

Ranch Hands - Log_2(Current Dioxin), Time - Unadjusted

Exposure Restriction	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=509)						0.818
	≤18.6	193.5 (12/62)	253.7 (34/134)	236.1 (17/72)	0.94(0.71,1.23)	0.638
	>18.6	275.0 (11/40)	250.0 (27/108)	204.3 (19/93)	0.90(0.70,1.15)	0.389
b) D>5 ppt (n=690)						0.274
	≤18.6	266.7 (24/90)	252.9 (44/174)	209.1 (23/110)	0.95(0.79,1.15)	0.604
	>18.6	95.2 (6/63)	279.4 (38/136)	179.5 (21/117)	1.10(0.92,1.32)	0.303

Table 6-2 (Continued)

Ranch Hands - Log_2(Current Dioxin), Time - Adjusted

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=459)			0.902***	RACE(p=0.012) SMOKE(p=0.110)
	≤18.6	0.90(0.67,1.20)***	0.465***	OCC(p=0.027) DRINK*TIME*
	>18.6	0.92(0.71,1.18)***	0.518***	DIOXIN(p=0.018)
d) D>5 ppt (n=616)			0.241***	OCC(p=0.001) F-AGE*TIME*
	≤18.6	0.87(0.70,1.08)***	0.194***	DIOXIN(p=0.033)
	>18.6	1.02(0.84,1.25)***	0.819***	

Total Congenital Anomalies (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 6-3 [a]), there is a borderline significant overall association between total congenital anomalies and categorized current dioxin (p=0.072). The total congenital anomaly rate in children of Ranch Hands in the Low category is significantly greater than that in children of Comparisons in the Background category (OR=1.58, 95% CI 1.10-2.27, p=0.013). The total congenital anomaly rates among children of Ranch Hands in the High (p=0.636), and Unknown (p=0.831) categories are not significantly different from the rate among children of Comparisons in the Background category.

After adjustment for covariates (Table 6-3 [b]), there is significant variation in the association between total congenital anomalies and categorized current dioxin with the father's military occupation (p=0.002). This changing association is displayed in Appendix Table D-2. The significance is primarily caused by the changes in the Low versus Background contrasts with occupation (officer OR=0.17, p=0.087; enlisted flyers OR=2.58, p=0.037, enlisted ground OR=1.72, p=0.022).

Table 6-3

Post-SEA Counts and Rates of Total Congenital Anomalies

Variable: Total Congenital Anomalies
Restrictions: All Children of Ranch Hands and Comparisons Children Conceived during or after the Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) Current Dioxin (Categorized Within Group) - Unadjusted

Exposure Category	n	Abnormal Number	Abnormal Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	981	204	208.0	All Exp Categ		0.072
Unknown	282	57	202.1	Unk vs Bkgd	0.96(0.69,1.34)	0.831
Low	174	51	293.1	Low vs Bkgd	1.58(1.10,2.27)	0.013
High	227	44	193.8	High vs Bkgd	0.92(0.64,1.32)	0.636
Total	1664					

b) Current Dioxin (Categorized Within Group) - Adjusted

Exposure Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	843	All Exp Categ	****	****	DIOXIN*OCC (p=0.002)
Unknown	246	Unk vs Bkgd			
Low	156	Low vs Bkgd			
High	203	High vs Bkgd			
Total	1448				

Total Congenital Anomalies (Full Siblings)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

Without adjustment for covariates (Table 6-4 [a] and [b]), there is no significant association between total congenital anomalies and initial dioxin among full sibling children of Ranch Hands with more than 10 ppt (p=0.259) or more than 5 ppt (p=0.684) current dioxin.

After adjustment for covariates (Table 6-4 [c]), there is no association between total congenital anomalies and initial dioxin among full sibling children of Ranch Hands with more than 10 ppt current dioxin (p=0.219).

After adjustment for covariates (Table 6-4 [d]), there is no significant association between total congenital anomalies and initial dioxin among full sibling children of Ranch Hands with more than 5 ppt current dioxin (p=0.494).

Table 6-4

Post-SEA Counts and Rates of Total Congenital Anomalies

Variable: Total Congenital Anomalies
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	n	Abnormal Number	Abnormal Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=420)	Low	78	16	205.1	0.89(0.74,1.09)	0.259
	Medium	206	57	276.7		
	High	136	27	198.5		
b) D>5 ppt (n=557)	Low	114	20	175.4	1.03(0.89,1.19)	0.684
	Medium	245	58	236.7		
	High	198	44	222.2		

Ranch Hands - Log_2(Initial Dioxin) - Adjusted

Exposure Restriction	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=390)	0.88(0.72,1.08)	0.219	None
d) D>5 ppt (n=513)	0.94(0.79,1.12)	0.494	M-AGE(p=0.072) OCC(p=0.033)

Total Congenital Anomalies (Full Siblings)

Model 2: Children of Ranch Hands - Log_2(Current Dioxin) and Time

Without adjustment for covariates (Table 6-5 [a]), there is no significant variation in the association between total congenital anomalies and current dioxin with time since duty in SEA among full sibling children of Ranch Hands with more than 10 ppt current dioxin (p=0.786). Furthermore, there is no significant association between total congenital anomalies and current dioxin among children of Ranch Hands with late (p=0.529) or early (p=0.291) tours.

Without adjustment for covariates (Table 6-5 [b]), there is no significant variation in the association between total congenital anomalies and current dioxin with time since duty in SEA among full sibling children of Ranch Hands with more than 5 ppt current dioxin (p=0.532). Furthermore, there is no significant association between total congenital anomalies and current dioxin among children of Ranch Hands late (p=0.904) or early (p=0.312) tours.

After adjustment for covariates (Table 6-5 [c]), there is no significant variation in the association between total congenital anomalies and current dioxin with time since duty in SEA among full sibling children of Ranch Hands with more than 10 ppt current dioxin (p=0.643) and there is no significant association between total congenital anomalies and the father's current dioxin among children of Ranch Hands with late (p=0.561) or early (p=0.200) tours.

After adjustment for covariates (Table 6-5 [d]), there is no significant variation in the association between total congenital anomalies and current dioxin level with time since duty in SEA (p=0.618) among full sibling children of Ranch Hands with more than 5 ppt current dioxin. Furthermore, there is no significant association between total congenital anomalies and the father's current dioxin among children of Ranch Hands with late (p=0.541) or early (p=0.988) tours.

Table 6-5

Post-SEA Counts and Rates of Total Congenital Anomalies

Variable: Total Congenital Anomalies
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

Ranch Hands - Log_2(Current Dioxin), Time - Unadjusted

Exposure Restriction	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=421)						0.786
	≤18.6	234.0 (11/47)	234.8 (27/115)	265.6 (17/64)	0.91(0.68,1.22)	0.529
	>18.6	285.7 (8/28)	260.9 (24/92)	186.7 (14/75)	0.86(0.65,1.14)	0.291
b) D>5 ppt (n=557)						0.532
	≤18.6	203.4 (12/59)	263.9 (38/144)	214.3 (21/98)	1.01(0.82,1.25)	0.904
	>18.6	75.5 (4/53)	292.5 (31/106)	164.9 (16/97)	1.11(0.91,1.36)	0.312

Table 6-5 (Continued)

Ranch Hands - Log_2(Current Dioxin), Time - Adjusted

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=391)			0.643	None
	≤18.6	0.92(0.68,1.23)	0.561	
	>18.6	0.83(0.62,1.10)	0.200	
d) D>5 ppt (n=513)			0.618	M-AGE(p=0.059) OCC(p=0.038)
	≤18.6	0.93(0.72,1.19)	0.541	
	>18.6	1.00(0.80,1.25)	0.988	

Total Congenital Anomalies (Full Siblings)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 6-6 [a]), there is a borderline significant association between total congenital anomalies and categorized dioxin level among full siblings (p=0.060). Children of Ranch Hands in the Low current dioxin category are at significantly greater risk of total congenital anomalies than children of Comparisons in the Background category (OR=1.55, 95% CI 1.05-2.29, p=0.028). The risks of congenital anomaly among children of Ranch Hands in the Unknown (p=0.351) and High (p=0.450) categories are not significantly different from that of children of Comparisons in the Background category.

After adjustment for covariates (Table 6-6 [b]), the overall association between total congenital anomalies and categorized current dioxin varies significantly with the father's military occupation among full siblings (p=0.012). This changing association is displayed in Appendix Table D-2. The children of the Ranch Hands in the Low dioxin category were at greater risk of congenital anomalies than children of Comparisons in the Background category in both the enlisted flyer (p=0.091) and enlisted ground (p=0.032) strata. In the officer stratum there is a borderline significantly lower risk of congenital anomalies among children of Ranch Hands in the Unknown category (p=0.103) relative to that in children of Comparisons in the Background category.

Table 6-6

Post-SEA Counts and Rates of Total Congenital Anomalies

Variable: Total Congenital Anomalies
Restrictions: Full Siblings of Ranch Hands and Comparisons
Children Conceived during or after the Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) Unadjusted

Exposure Category	n	Abnormal Number	Abnormal Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	812	174	214.3	All Exp Categ		0.060
Unknown	221	41	185.5	Unk vs Bkgd	0.84(0.57,1.22)	0.351
Low	148	44	297.3	Low vs Bkgd	1.55(1.05,2.29)	0.028
High	195	37	189.7	High vs Bkgd	0.86(0.58,1.28)	0.450
Total	1376					

b) Adjusted

Exposure Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	715	All Exp Categ	****	****	RACE(p=0.083)
Unknown	199	Unk vs Bkgd			OCC*DIOXIN
Low	137	Low vs Bkgd			(p=0.012)
High	180	High vs Bkgd			
Total	1231				

Nervous System Anomalies (All Children)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

Without adjustment for covariates (Table 6-7 [a] and [b]), there is no significant association between nervous system anomalies and initial dioxin among children of Ranch Hands with more that 10 ppt current dioxin (p=0.501) or more than 5 ppt (p=0.149) current dioxin.

There is insufficient data (Table 6-7 [c] and [d]) to assess the significance of the association between nervous system anomalies and initial dioxin with adjustment for covariates.

Table 6-7

Post-SEA Counts and Rates of Nervous System Anomalies

Variable: Nervous System Anomalies
Restrictions: All Children of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	n	Abnormal Number	Abnormal Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=508)	Low	106	1	9.4	1.28(0.63,2.61)	0.501
	Medium	245	2	8.2		
	High	157	2	12.7		
b) D>5 ppt (n=690)	Low	155	0	0.0	1.55(0.85,2.82)	0.149
	Medium	308	2	6.5		
	High	227	3	13.2		

Ranch Hands - Log_2(Initial Dioxin) - Adjusted

Exposure Restriction	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=458)	No adjusted analyses, only 5 defects total		
d) D>5 ppt (n=616)	No adjusted analyses, only 5 defects total		

Nervous System Anomalies (All Children)

Model 2: Children of Ranch Hands - Log_2(Current Dioxin) and Time

There is insufficient data (Table 6-8) to assess the significance of variation in the association between nervous system defects and current dioxin with time since duty in SEA among children of Ranch Hands with more than 10 ppt or more than 5 ppt current dioxin.

Table 6-8

Post-SEA Counts and Rates of Nervous System Anomalies

Variable: Nervous System Anomalies
Restrictions: All Children of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

Ranch Hands - Log_2(Current Dioxin), Time - Unadjusted

Exposure Restriction	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=509)						
	≤18.6	0.0 (0/62)	7.5 (1/134)	13.9 (1/72)	No analyses, only 5 defects total	
	>18.6	25.0 (1/40)	9.3 (1/108)	10.8 (1/93)		
b) D>5 ppt (n=690)						
	≤18.6	0.0 (0/90)	0.0 (0/174)	18.2 (2/110)	No analyses, only 5 defects total	
	>18.6	0.0 (0/63)	14.7 (2/136)	8.5 (1/117)		

Ranch Hands - Log_2(Current Dioxin), Time - Adjusted

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=459)	No adjusted analyses, only 5 defects total			
d) D>5 ppt (n=616)	No adjusted analyses, only 5 defects total			

Nervous System Anomalies (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 6-9 [a]), the overall association between nervous system anomalies and categorized current dioxin level is not significant (p=0.136). The nervous system anomaly rate among children of Ranch Hands in the High current dioxin category (13.2 per 1000) is borderline significantly greater than the rate among children of Comparisons in the Background current dioxin category (3.1 per 1000); OR=4.37, 95% CI 0.87-21.8, p=0.072. The nervous system anomaly rate among children of Ranch Hands in the Low category is not significantly different from that of children of Comparisons in the Background category.

There is insufficient data to assess the association between nervous system anomalies and categorized dioxin with adjustment for covariates (Table 13-9 [b]).

Table 6-9

Post-SEA Counts and Rates of Nervous System Anomalies

Variable: Nervous System Anomalies
Restrictions: All Children of Ranch Hands and Comparisons
Children Conceived during or after the Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) Unadjusted

Exposure Category	n	Abnormal Number	Abnormal Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	981	3	3.1	All Exp Categ		0.136
Unknown	282	0	0.0	Unk vs Bkgd	-- -- --	--
Low	174	1	5.7	Low vs Bkgd	1.88(0.20,18.3)	0.584
High	227	3	13.2	High vs Bkgd	4.37(0.87,21.8)	0.072
Total	1664					

Table 6-9 (Continued)

b) Adjusted

Exposure Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	843	No adjusted analyses, only 7 defects total			
Unknown	246				
Low	156				
High	203				
Total	1448				

Nervous System Anomalies (Full Siblings)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

Without adjustment for covariates (Table 6-10 [a] and [b]), there is no significant association between nervous system anomalies and initial dioxin among full sibling children of Ranch Hands with more than 10 ppt (p=0.214) while there is a borderline significant association among children of Ranch Hands with more than 5 ppt (p=0.073) current dioxin.

There is insufficient data to assess the significance of the association between nervous system anomalies and initial dioxin among full sibling children of Ranch Hands with adjustment for covariates (Table 6-10 [c] and [d]).

Table 6-10

Post-SEA Counts and Rates of Nervous System Anomalies

Variable: Nervous System Anomalies
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	n	Abnormal Number	Abnormal Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=420)	Low	78	0	0.0	1.65(0.76,3.59)	0.214
	Medium	206	2	9.7		
	High	136	2	14.7		
b) D>5 ppt (n=557)	Low	114	0	0.0	1.85(0.93,3.69)	0.073
	Medium	245	1	4.1		
	High	198	3	15.2		

Ranch Hands - Log_2(Initial Dioxin) - Adjusted

Exposure Restriction	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=390)	No adjusted analyses, only 4 defects total		
d) D>5 ppt (n=513)	No adjusted analyses, only 4 defects total		

Nervous System Anomalies (Full Siblings)

Model 2: Children of Ranch Hands - Log_2(Current Dioxin) and Time

There is insufficient data (Table 6-11) to assess variation in the association between nervous system anomalies and current dioxin with time since duty in SEA among full sibling children of Ranch Hands.

Table 6-11

Post-SEA Counts and Rates of Nervous System Anomalies

Variable: Nervous System Anomalies
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

Ranch Hands - Log_2(Current Dioxin), Time - Unadjusted

Exposure Restriction	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=421)						
	≤18.6	0.0 (0/47)	8.7 (1/115)	15.6 (1/64)	No analyses, only 4 defects total	
	>18.6	0.0 (0/28)	10.9 (1/92)	13.3 (1/75)		
b) D>5 ppt (n=557)						
	≤18.6	0.0 (0/59)	0.0 (0/144)	20.4 (2/98)	No analyses, only 4 defects total	
	>18.6	0.0 (0/53)	9.4 (1/106)	10.3 (1/97)		

Ranch Hands - Log_2(Current Dioxin), Time - Adjusted

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=391)		No adjusted analyses, only 4 defects total		
d) D>5 ppt (n=513)		No adjusted analyses, only 4 defects total		

Nervous System Anomalies (Full Siblings)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 6-12 [a]), there is no overall association between nervous system anomalies and categorized current dioxin among full sibling children (p=0.153). However, the nervous system anomaly rate among children of Ranch Hands in the High current dioxin category (15.4 per 1000) is borderline significantly greater than that of children of Comparisons in the Background category (3.7 per 1000); OR=4.21, 95% CI 0.84-21.1, p=0.080. The low versus background (p=0.600) contrast is not statistically significant.

There is insufficient data (Table 6-12 [b]) to assess the significance of the association between nervous system anomalies and categorized current dioxin among full sibling children with adjustment for covariates.

Table 6-12

Post-SEA Counts and Rates of Nervous System Anomalies

Variable: Nervous System Anomalies
Restrictions: Full Siblings of Ranch Hands and Comparisons
Children Conceived during or after the Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) **Unadjusted**

Exposure Category	n	Abnormal Number	Abnormal Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	812	3	3.7	All Exp Categ		0.153
Unknown	221	0	0.0	Unk vs Bkgd	-- -- --	--
Low	148	1	6.8	Low vs Bkgd	1.83(0.19,17.8)	0.600
High	195	3	15.4	High vs Bkgd	4.21(0.84,21.1)	0.080
Total	1376					

Table 6-12 (Continued)

b) Adjusted

Exposure Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	715	No adjusted analyses, only 7 defects total			
Unknown	199				
Low	137				
High	180				
Total	1231				

Anomalies of the Eye (All Children)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

Without adjustment for covariates (Table 6-13 [a] and [b]), there is no significant association between eye anomalies and initial dioxin among children of Ranch Hands with more than 10 ppt (p=0.534) or more than 5 ppt (p=0.872) current dioxin.

There is insufficient data to assess the significance of the association between eye anomalies and initial dioxin among children of Ranch Hands with adjustment for covariates (Table 6-13 [c] and [d]).

Table 6-13

Post-SEA Counts and Rates of Eye Anomalies

Variable: Eye Anomalies
Restrictions: All Children of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	n	Abnormal Number	Abnormal Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=508)	Low	106	0	0.0	1.26(0.62,2.56)	0.534
	Medium	245	3	12.2		
	High	157	2	12.7		
b) D>5 ppt (n=690)	Low	155	2	12.9	1.04(0.62,1.76)	0.872
	Medium	308	2	6.5		
	High	227	3	13.2		

Ranch Hands - Log_2(Initial Dioxin) - Adjusted

Exposure Restriction	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=458)	No adjusted analyses, only 5 defects total		
d) D>5 ppt (n=616)	No adjusted analyses, only 7 defects total		

Anomalies of the Eye (All Children)

Model 2: Children of Ranch Hands - Log_2(Current Dioxin) and Time

Without adjustment for covariates (Table 6-14 [a]), there is no significant variation in the association between eye anomalies and current dioxin with time since duty in SEA among children of Ranch Hands with more than 10 ppt current dioxin (p=0.428). Furthermore there is no significant association between eye anomalies and current dioxin among children of Ranch Hands with late (p=0.352) or early (p=0.819) tours.

Without adjustment for covariates (Table 6-14 [b]), there is no significant variation in the association between eye anomalies and current dioxin with time since duty in SEA among children of Ranch Hands with more than 5 ppt current dioxin (p=0.868). Furthermore there is no significant association between eye anomalies and current dioxin among children of Ranch Hands with late (p=0.851) or early (p=0.730) tours.

There is insufficient data to assess the significance in variation in the association between eye anomalies and current dioxin with time since duty in SEA with adjustment for covariates (Table 6-14 [c] and [d]).

Table 6-14

Post-SEA Counts and Rates of Eye Anomalies

Variable: Eye Anomalies
Restrictions: All Children of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

Ranch Hands - Log_2(Current Dioxin), Time - Unadjusted

Exposure Restriction	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=509)						0.428
	≤18.6	0.0 (0/62)	14.9 (2/134)	13.9 (1/72)	1.62(0.58,4.49)	0.352
	>18.6	25.0 (1/40)	0.0 (0/108)	10.8 (1/93)	0.87(0.26,2.83)	0.819
b) D>5 ppt (n=690)						0.868
	≤18.6	11.1 (1/90)	11.5 (2/174)	18.2 (2/110)	1.07(0.54,2.10)	0.851
	>18.6	0.0 (0/63)	7.4 (1/136)	8.5 (1/117)	1.18(0.47,2.95)	0.730

Table 6-14 (Continued)

Ranch Hands - Log_2(Current Dioxin), Time - Adjusted

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=459)	No adjusted analyses, only 5 defects total			
d) D>5 ppt (n=616)	No adjusted analyses, only 7 defects total			

Anomalies of the Eye (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 6-15 [a]), there is no significant overall association between eye anomalies and categorized current dioxin (p=0.622). Contrasts of children of Ranch Hands in the High (p=0.370), Low (p=0.839) and Unknown (p=0.271) categories with children of Comparisons in the Background category were not statistically significant.

There is insufficient data to assess the significance of the association between eye anomalies and categorized current dioxin with adjustment for covariates (Table 6-15 [b]).

Table 6-15

Post-SEA Counts and Rates of Eye Anomalies

Variable: Eye Anomalies
Restrictions: All Children of Ranch Hands and Comparisons Children Conceived during or after the Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) Unadjusted

Exposure Category	n	Abnormal Number	Abnormal Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	981	7	7.1	All Exp Categ		0.622
Unknown	282	4	14.2	Unk vs Bkgd	2.00(0.58,6.89)	0.271
Low	174	1	5.7	Low vs Bkgd	0.80(0.10,6.59)	0.839
High	227	3	13.2	High vs Bkgd	1.86(0.48,7.27)	0.370
Total	1664					

b) Adjusted

Exposure Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	843	No adjusted analyses, only 15 defects total			
Unknown	246				
Low	156				
High	203				
Total	1448				

Anomalies of the Eye (Full Siblings)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

Without adjustment for covariates (Table 6-16 [a] and [b]), there is no significant association between eye anomalies and initial dioxin among full sibling children of Ranch Hands having more than 10 ppt (p=0.597) or more than 5 ppt (p=0.518) current dioxin.

There is insufficient data to assess the association between eye anomalies and initial dioxin among full sibling children of Ranch Hands with adjustment for covariates (Table 6-16 [c] and [d]).

Table 6-16

Post-SEA Counts and Rates of Eye Anomalies

Variable: Eye Anomalies
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	n	Abnormal Number	Abnormal Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=420)	Low	78	0	0.0	1.22(0.59,2.49)	0.597
	Medium	206	3	14.6		
	High	136	2	14.7		
b) D>5 ppt (n=557)	Low	114	1	8.8	1.20(0.69,2.09)	0.518
	Medium	245	2	8.2		
	High	198	3	15.2		

Ranch Hands - Log_2(Initial Dioxin) - Adjusted

Exposure Restriction	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=390)	No adjusted analyses, only 5 defects total		
d) D>5 ppt (n=513)	No adjusted analyses, only 6 defects total		

Anomalies of the Eye (Full Siblings)

Model 2: Children of Ranch Hands - Log_2(Current Dioxin) and Time

There is insufficient data (Table 6-17) to assess the significance of variation in the association between eye anomalies and current dioxin with time since duty in SEA among full sibling children of Ranch Hands.

Table 6-17

Post-SEA Counts and Rates of Eye Anomalies

Variable: Eye Anomalies
Restrictions: Full Siblings of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

Ranch Hands - Log_2(Current Dioxin), Time - Unadjusted

Exposure Restriction	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=421)						
	≤18.6	0.0 (0/47)	17.4 (2/115)	15.6 (1/64)	No analyses, only 5 defects total	
	>18.6	35.7 (1/28)	0.0 (0/92)	13.3 (1/75)		
b) D>5 ppt (n=557)						
	≤18.6	0.0 (0/59)	13.9 (2/144)	20.4 (2/98)	No analyses, only 6 defects total	
	>18.6	0.0 (0/53)	9.4 (1/106)	10.3 (1/97)		

Ranch Hands - Log_2(Current Dioxin), Time - Adjusted

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=391)	No adjusted analyses, only 5 defects total			
d) D>5 ppt (n=513)	No adjusted analyses, only 6 defects total			

Anomalies of the Eye (Full Siblings)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 6-18 [a]) there is no significant overall association between eye anomalies and categorized current dioxin among full sibling children (p=0.253). However, the rate of eye anomalies among children of Ranch Hands in the High current dioxin category (15.4 per 1000) is borderline significantly greater than the corresponding rate among children of Comparisons in the Background category (OR=4.21, 95% CI 0.84-21.1, p=0.080). Contrasts of children of Ranch Hands in the Low (0.600) and Unknown (p=0.110) categories with children of Comparisons in the Background category were not statistically significant.

There is insufficient data to assess the significance of the association between anomalies of the eye and categorized dioxin with adjustment for covariates (Table 6-18 [b]).

Table 6-18

Post-SEA Counts and Rates of Eye Anomalies

Variable: Eye Anomalies
Restrictions: Full Siblings of Ranch Hands and Comparisons Children Conceived during or after the Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) Unadjusted

Exposure Category	n	Abnormal Number	Abnormal Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	821	3	3.7	All Exp Categ		0.253
Unknown	221	3	13.6	Unk vs Bkgd	3.71(0.74,18.5)	0.110
Low	148	1	6.8	Low vs Bkgd	0.83(0.19,17.8)	0.600
High	195	3	15.4	High vs Bkgd	4.21(0.84,21.1)	0.080
Total	1376					

Table 6-18 (Continued)

b) Adjusted

Exposure Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	715	No adjusted analyses, only 10 defects total			
Unknown	199				
Low	137				
High	180				
Total	1231				

Anomalies of the Ear, Face and Neck (All Children)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

Without adjustment for covariates (Table 6-19 [a] and [b]), there is no significant association between ear, face and neck anomalies and initial dioxin among children of Ranch Hands having more than 10 ppt (p=0.121) or having more than 5 ppt (p=0.781) current dioxin.

There is insufficient data to assess the significance of the association between ear, face and neck anomalies and initial dioxin among children of Ranch Hands with more than 10 ppt or more than 5 ppt current dioxin with adjustment for covariates (Table 6-19 [c] and [d]).

Table 6-19

Post-SEA Counts and Rates of Ear, Face and Neck Anomalies

Variable: Ear, Face and Neck Anomalies
Restrictions: All Children of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 1: Log_2(Initial Dioxin)

Ranch Hands - Log_2(Initial Dioxin) - Unadjusted

Exposure Restriction	Initial Dioxin	n	Abnormal Number	Abnormal Rate	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=508)	Low	106	0	0.0	1.61(0.89,2.91)	0.121
	Medium	245	4	16.3		
	High	157	3	19.1		
b) D>5 ppt (n=690)	Low	155	4	25.8	1.06(0.70,1.61)	0.781
	Medium	308	3	9.7		
	High	227	4	17.6		

Ranch Hands - Log_2(Initial Dioxin) - Adjusted

Exposure Restriction	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=458)	No adjusted analyses, only 7 defects total		
d) D>5 ppt (n=616)	No adjusted analyses, only 11 defects total		

Anomalies of the Ear, Face and Neck (All Children)

Model 2: Children of Ranch Hands - Log_2(Current Dioxin) and Time

Without adjustment for covariates (Table 6-20 [a]), there is no significant variation in the association between ear, face and neck anomalies and current dioxin with time since duty in SEA among children of Ranch Hands having more than 10 ppt current dioxin (p=0.534). There is a no significant association between ear, face and neck anomalies and current dioxin among children of Ranch Hands with late (p=0.820) or early (p=0.216) tours.

Without adjustment for covariates (Table 6-20 [b]), there is significant variation in the association between anomalies of the ear, face and neck and current dioxin with time since duty in SEA among children of Ranch Hands with more than 5 ppt current dioxin (p=0.005). This significance was caused by a borderline significant increase of ear, face and neck anomalies among children of Ranch Hands with early tours (OR=1.72, 95% CI 0.98-3.01, p=0.059) and a borderline significant decrease among children of Ranch Hands with late tours (OR=0.39, 95% CI 0.13-1.15, p=0.087).

There is insufficient data to assess variation in the association between ear, face and neck anomalies and current dioxin with time since duty in SEA among children of Ranch Hands with adjustment for covariates (Table 13-20 [c] and [d]).

Table 6-20

Post-SEA Counts and Rates of Ear, Face and Neck Anomalies

Variable: Ear, Face and Neck Anomalies
Restrictions: All Children of Ranch Hands
Children Conceived during or after the Father's Duty in SEA
Model 2: Log_2(Current Dioxin), Time

Ranch Hands - Log_2(Current Dioxin), Time - Unadjusted

Exposure Restriction	Time Since SEA (years)	Anomaly Rate (No./n) Current Dioxin Low	Medium	High	Est. Relative Risk (95% C.I.)	p-Value
a) D>10 ppt (n=509)						0.534
	≤18.6	0.0 (0/62)	7.5 (1/134)	0.0 (0/72)	0.79(0.11,5.96)	0.820
	>18.6	25.0 (1/40)	18.5 (2/108)	32.3 (3/93)	1.50(0.79,2.84)	0.216
b) D>5 ppt (n=690)						0.005
	≤18.6	33.3 (3/90)	11.5 (2/174)	0.0 (0/110)	0.39(0.13,1.15)	0.087
	>18.6	0.0 (0/63)	14.7 (2/136)	34.2 (4/117)	1.72(0.98,3.01)	0.059

Table 6-20 (Continued)

Ranch Hands - Log_2(Current Dioxin), Time - Adjusted

Exposure Restriction	Time Since SEA (years)	Adj. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
c) D>10 ppt (n=459)	No adjusted analyses, only 7 defects total			
d) D>5 ppt (n=616)	No adjusted analyses, only 11 defects total			

Anomalies of the Ear, Face and Neck (All Children)

Model 3: Children of Ranch Hands and Comparisons - Categorized Current Dioxin

Without adjustment for covariates (Table 6-21 [a]), there is no significant overall association between ear, face and neck anomalies and categorized current dioxin (p=0.786). There is no significant difference between the rate of ear, face and neck anomalies among children of Ranch Hands in the High (p=0.436), Low (p=0.974) or Unknown (p=0.393) categories with that in children of Comparisons in the Background category.

After adjustment for covariates (Table 6-21 [b]), there is no significant overall overall association between ear, face and neck anomalies and categorized current dioxin among children (p=0.720). There is no significant difference between the rate of ear, face and neck anomalies among children of Ranch Hands in the High (p=0.388), Low (p=0.920) or Unknown (p=0.322) current dioxin category and the rate in children of Comparisons in the Background current dioxin category.

Table 6-21

Post-SEA Counts and Rates of Ear, Face and Neck Anomalies

Variable: Ear, Face and Neck Anomalies
Restrictions: Full Siblings of Ranch Hands and Comparisons
Children Conceived during or after the Father's Duty in SEA
Model 3: Categorized Current Dioxin

a) Unadjusted

Exposure Category	n	Abnormal Number	Abnormal Rate	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value
Background	981	11	11.2	All Exp Categ		0.786
Unknown	282	5	17.7	Unk vs Bkgd	1.59(0.55,4.62)	0.393
Low	174	2	11.5	Low vs Bkgd	1.03(0.22,4.67)	0.974
High	227	4	17.6	High vs Bkgd	1.58(0.50,5.02)	0.436
Total	1664					

b) Adjusted

Exposure Category	n	Category Contrast	Est. Relative Risk (95% C.I.)	p-Value	Covariate Remarks
Background	843	All Exp Categ		0.720	DRINK(p=0.077)
Unknown	246	Unk vs Bkgd	1.73(0.58,5.11)	0.322	
Low	156	Low vs Bkgd	1.08(0.23,4.99)	0.920	
High	203	High vs Bkgd	1.67(0.52,5.40)	0.388	
Total	1448				

Anomalies of the Ear, Face and Neck (Full Siblings)

Model 1: Children of Ranch Hands - Log_2(Initial Dioxin)

Without adjustment for covariates (Table 6-22 [a] and [b]), there is no significant association ear, face and neck anomalies and initial dioxin among full sibling children of Ranch Hands having more than 10 ppt (p=0.150) or more than 5 ppt (p=0.540) current dioxin.