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westward to the shoreline to include isolated TCDD "hotspots" and this identical area was used for estimating 2,4-D and 2,4,5-T emissions (Figure 2.1).

Individual sample blocks with nondetectable measurements of the compounds (labelled "ND") were each assigned a value of one-half the detection level (EPA, 1989), whereas missing values within the fenceline were assigned the median value for all plots sampled and analyzed at the site (Figure 3.2, 3.3, and 3.4). Finally, for purposes of modeling point emission sources across the surface of the soil sampling grid, a point source was located at the center of each four-plot sampling area. The soil concentration of TCDD, 2,4-D, and 2,4,5-T for each point source was calculated by averaging the four measured concentrations (ppb) associated with the set of four adjacent sample plots (see Figures 3.5, 3.6, and 3.7).

Methods developed by EPA for estimating exposures to TCDD (EPA, 1986a; Hwang and Falco, 1986) were used to calculate time-averaged compound vapor-phase emission rates for TCDD as well as 2,4-D and 2,4,5-T. It is important to note that environmental fate processing (e.g., photolysis, microbial degradation) which reduce the concentration of these compounds in soil over time are not accounted for using this estimation procedure; thus, the emission rate estimates represent overestimates for long exposure durations (e.g., greater than approximately 10 years). These emission rates (N_D), expressed as grams per cm^2 per second, were estimated for each four-plot average soil concentration as follows:

$$N_D = (2D_i)\,(e^{\frac{4}{3}})\,(K_{ai})\,\frac{(C_{ai})}{\sqrt{3.14\alpha T}} \qquad \text{(3-1)}$$

Figure 3-2. TCDD (Dioxin) Surface Soil Concentrations (ppb): Measured and Estimated Values

	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
06					0.8	0.8	0.8	0.8	0.005	8.7	0.005	0.005	0.1	0.1	0.1	0.1	31	0.005	0.005	0.1	1.3	0.005	7.0	0.005	0.005	0.8	0.4	0.005	0.005	0.005	0.005	0.005
07		0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.3	0.005	1.5	3.0	1.4	17	13	24	27	5.0	6.8	0.1	2.5	45	0.8	20	19	18	1.4	13	6.4	57	0.8	0.005
08		0.8	0.8	0.8	0.8	0.6	0.8	0.8	136	163	91	20	6.7	0.8	1.1	0.3	0.1	9.5	0.005	0.1	0.005	0.2	3.1	0.2	0.005	0.2	1.9	61	0.2	0.2	32	39
09	0.8	0.8	9.6	0.8	0.8	0.8	0.8	0.8	26	50	46	21	7.7	0.5	9.4	0.005	0.2	0.005	0.005	0.005	0.1	19	0.5	0.005	0.005	9.8	0.5	0.6	2.6	25	1.7	0.1
10	0.8	0.8	77	0.8	0.8	0.8	0.8	0.8	0.9	26	59	25	7.2	0.8	0.8	0.3	0.1	0.4	1.3	0.2	0.3	0.005	1.4	0.005	0.005	18	1.6	1.1	20	8.5	0.4	0.2
11	0.8	0.8	0.8	0.8	0.8	0.8	0.2	0.8	0.2	5.0	18	1.8	0.005	0.1	12	61	0.5	12	0.8	0.8	1.9	1.2	31	0.4	34	0.3	5.2	1.7	0.9	10	6.6	0.3
12	0.8	36	0.8	0.8	0.8	0.8	0.8	0.2	0.7	0.3	2.2	0.005	0.005	0.005	0.005	0.005	0.005	5.6	2.7	1.3	0.4	18	53	0.6	7.1	29	1.5	0.1	4.2	22	43	0.005
13	23	0.8	0.8	0.8	0.8	0.6	0.8	0.8	0.1	0.005	0.005	0.005	0.3	0.005	0.1	0.005	0.1	29	0.005	0.7	1.0	0.005	0.005	0.2	43	3.9	32	0.005	0.1	0.3	0.4	0.3
14	0.8	0.8	0.8	0.8	0.8	1.0	0.8	0.8	0.2	0.8	0.4	1.4	21	1.8	0.2	0.005	0.005	0.005	0.2	2.2	0.6	18	0.2	0.005	0.5	1.7	1.0	3.1	5.1	1.6	0.2	1.8
15	0.8	0.8	2.8	0.8	1.1	12	13	59	0.5	0.4	6.0	35	27	0.005	0.6	15	10	0.2	0.3	43	9.7	24	0.005	1.4	55	27	3.5	3.1	24	9.0	0.2	0.005
16	1.1	0.8	0.8	0.8	1.1	1.2	0.5	0.3	35	19	4.7	0.3	0.1	0.005	0.4	0.1	0.9	0.005	2.7	0.9	1.1	0.005	0.1	0.6								
17	0.8	0.8	0.8	0.8	27	26	10	9.7	0.1	0.3	0.4	0.5	11	14	16	0.2	4.9	0.4	17	0.8	2.9	1.7	0.9	0.005								
18	9.0	0.8	0.8	0.8	0.5	21	0.005	0.5	0.3	0.4	0.005	0.4	0.8	0.2	61	0.005	0.005	17	1.8	18	0.005	17	28	0.005								
19	0.8	0.8	0.7	0.2	0.9	148	6.0	0.005	59	2.8	1.2	0.8	0.7	0.005	3.5	5.2	0.3	0.1	2.1	0.1	0.1	0.1	0.005	0.005								
20	0.8	0.8	0.8	0.8	0.2	1.5	13	0.4	0.1	0.2	0.4	0.4	0.9	0.1	7.1	0.6	0.005	0.005	0.005	0.1	0.1	1.5	0.2	0.005								
21	1.9	0.8	0.8	0.8	0.4	6.7	46	53	0.005	41	23	27	0.005	0.005	1.3	22	0.4	61	0.6	0.2	0.6	0.005	0.005	0.005								
22	0.8	0.8	0.8	0.8	0.005	0.2	0.5	2.7	0.9	21	1.6	12	0.005	0.1	14	0.4	0.005	22	24	42	11	132	11	0.9								
23	0.8	0.8	0.8	0.8	0.1	0.1	0.3	0.1	5.5	3.7	0.4	0.7	0.1	0.1	0.2	0.005	0.005	1.3	1.0	0.7	0.1	0.3	0.005	0.005								
24	0.8	0.8	0.8	0.8	2.4	0.8	9.0	10	0.3	0.1	0.1	5.4	0.2	0.1	25	10	51	1.5	1.8	0.1	0.1	0.1	0.1	0.8								
25	0.8	0.8	0.8	0.8	37	0.005	0.005	0.005	0.1	2.3	38	13	43	18	20	0.3	4.8	9.0	2.1	0.3	42	42	7.2	0.5								

Figure 3-3. 2,4-D Surface Soil Concentrations (ppb): Measured and Estimated Values

	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
06					372.5	372.5	372.5	372.5	372.5	231235	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5
07		372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	350	372.5	372.5	372.5	372.5	372.5	372.5
08		372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	17729	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5
09	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5
10	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5
11	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	189	372.5	372.5	372.5	372.5	372.5
12	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5
13	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	42	372.5	372.5	372.5	372.5	372.5	372.5	372.5
14	372.5	372.5	372.5	372.5	372.5	372.5	2.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	161	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5
15	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5
16	372.5	372.5	372.5	.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5								
17	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5								
18	372.5	86647	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5								
19	372.5	372.5	372.5	372.5	372.5	395	372.5	372.5	372.5	372.5	372.5	372.5	281330	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5								
20	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5								
21	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	80506	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5								
22	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	672	372.5	372.5								
23	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5								
24	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	53	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5								
25	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	294	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5	372.5								

Figure 3-4. 3,4,5-T Surface Soil Concentrations (ppb): Measured and Estimated Values

	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
04					956	956	956	956	956	237155	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956
05		956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	1040	956	956	956	956	956	956	956
06		956	956	956	956	956	956	956	956	956	53291	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956
07	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956
08	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956
09	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956
10	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956
11	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	518	956	956	956	956	956
12	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956
13	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	101	956	956	956	956	956	956	956
14	956	956	956	956	956	956	221	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	387	956	956	956	956	956	956	956	956	956
15	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956
16	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956								
17	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956								
18	956	152492	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956								
19	956	956	956	956	956	1087	956	956	956	956	956	956	180363	956	956	956	956	956	956	956	956	956	956	956								
20	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956								
21	956	956	956	956	956	956	956	956	956	956	956	956	956	56528	956	956	956	956	956	956	956	956	956	956								
22	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	872	956	956								
23	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956	956								
24	956	956	956	956	956	956	956	956	956	956	956	956	53	956	956	956	956	956	956	956	956	956	956	956								
25	956	956	956	956	956	956	956	956	956	956	956	956	956	606	956	956	956	956	956	956	956	956	956	956								

Figure 3-5. TCDD (Dioxin) Surface Soil Concentrations (ppb): Aggregated Cells

	04	06	08	10	12	14	16	18	20	22	24	26	28	30	32	34
06	0.80	0.80	0.80	0.80	2.25	0.88	4.65	9.50	15.75	1.75	12.20	6.95	9.45	3.70	15.85	0.20
08	0.80	3.00	0.75	0.80	93.75	44.50	3.93	2.70	2.45	0.03	4.83	0.95	2.50	11.05	7.00	18.20
10	0.80	19.85	0.80	0.65	8.03	25.95	2.03	18.53	3.25	0.78	0.85	8.20	13.08	2.40	9.85	1.88
12	15.15	0.80	0.75	0.65	0.28	0.55	0.08	0.03	8.68	1.18	4.85	13.45	20.75	8.40	6.65	10.85
14	0.80	1.30	3.73	18.40	0.48	5.70	12.45	3.95	2.55	11.43	13.08	0.40	21.05	2.68	9.93	0.55
16	0.88	0.80	13.83	5.13	13.60	1.48	6.28	4.18	1.55	5.35	1.43	0.40				
18	2.85	0.63	42.60	1.13	15.62	0.60	0.43	17.43	4.35	5.50	4.30	7.00				
20	1.08	0.80	2.25	28.10	10.33	12.70	0.25	7.75	15.35	0.23	0.55	0.05				
22	0.80	0.80	0.10	0.90	7.78	3.68	0.08	3.65	5.83	16.93	35.85	2.98				
24	0.80	0.80	10.05	4.75	0.70	14.13	15.33	13.83	16.58	1.20	21.05	2.15				

Figure 3-6. 2,4-D Surface Soil Concentrations (ppb): Aggregated Cells

	04	06	08	10	12	14	16	18	20	22	24	26	28	30	32	34
06	372.50	372.50	372.50	372.50	58088.13	372.50	372.50	372.50	372.50	372.50	372.50	372.50	366.88	372.50	372.50	372.50
08	372.50	372.50	372.50	372.50	372.50	4711.63	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50
10	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	326.63	372.50	372.50
12	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	289.88	372.50	372.50	372.50
14	372.50	372.50	372.50	280.00	372.50	372.50	372.50	372.50	372.50	372.50	372.50	319.63	372.50	372.50	372.50	372.50
16	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50				
18	21941.13	372.50	378.13	372.50	372.50	372.50	70611.88	372.50	372.50	372.50	372.50	372.50				
20	372.50	372.50	372.50	372.50	372.50	372.50	20405.88	372.50	372.50	372.50	372.50	372.50				
22	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	372.50	497.38	372.50				
24	372.50	372.50	372.50	372.50	372.50	372.50	273.00	372.50	372.50	372.50	372.50	372.50				

Figure 3-7. 2,4,5-T Surface Soil Cencentrations (ppb): Aggregated Cells

	04	06	08	10	12	14	16	18	20	22	24	26	28	30	32	34
06	956.00	956.00	956.00	956.00	60005.75	956.00	956.00	956.00	956.00	956.00	956.00	956.00	977.00	956.00	956.00	956.00
08	956.00	956.00	956.00	956.00	956.00	14039.75	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00
10	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	846.50	956.00	956.00
12	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	742.25	956.00	956.00	956.00
14	956.00	956.00	956.00	772.25	956.00	956.00	956.00	956.00	956.00	956.00	956.00	813.75	956.00	956.00	956.00	956.00
16	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00				
18	38840.00	956.00	989.75	956.00	956.00	956.00	45807.75	956.00	956.00	956.00	956.00	956.00				
20	956.00	956.00	956.00	956.00	956.00	956.00	14849.00	956.00	956.00	956.00	956.00	956.00				
22	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	956.00	935.00	956.00				
24	956.00	956.00	956.00	956.00	956.00	956.00	662.75	956.00	956.00	956.00	956.00	956.00				

where, D_i = molecular diffusivity of the vapor-phase compound in air (i.e., for TCDD, $D_i = 4.7 \times 10^{-2}$ cm^2/s; for 2,4-D, $D_i = 6.2 \times 10^{-2}$ cm^2/s; for 2,4,5-T, $D_i = 5.91 \times 10^{-2}$ cm^2/s)[3];

ε = porosity of soil (i.e., approximately 0.35 for the calcium carbonate soil at JI);

K_{as} = air/soil partition coefficient (mg/cm^3 air)/(mg/g soil)[4];

C_{so} = initial compound concentration in soil (g/g); and

T = exposure duration (i.e., 25 years in units of seconds[5]).

Using the parameters defined above, alpha (α) is expressed as follows:

$$\alpha = \frac{(D_i)\ (\varepsilon^{\frac{4}{3}})}{[\varepsilon + \frac{\rho_s(1 - \varepsilon)}{K_{as}}]} \qquad (3\text{-}2)$$

where, ρ_s = soil density (i.e., approximately 1.76 g/cm^3 for the calcium carbonate soil at JI).

To convert the area emission rate to a point source emission rate for this modeling analysis, each compound emission rate was divided by the area of the four plots equal to 1,600 ft^2 (1.5×10^6cm^2). Receptors were placed along the border, or fenceline, of the storage area at intervals of 20 feet (104 receptors total) which

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[3] D_i values for 2,4-D and 2,4,5-T were obtained from R. Coutant, Batelle Memorial Institute Columbus, based on formulas cited in Fuller, Schettler, and Giddings. 1966. Title. Ind. Eng. Chem. 58:19, and A. Bondi. 1968. Physical properties of molecular crystals, liquids, and glasses. Wiley and Sons. New York.

[4] $K_{as} = 41\ H_c / K_d$. For TCDD $H_c = 5.00 \times 10^{-5}$, $K_d = 3.65 \times 10^6$. For 2,4-D, $H_c = 1.02 \times 10^{-8}$, $K_d = 1.66 \times 10^1$. For 2,4,5-T, $H_c = 8.68 \times 10^{-9}$, $K_d = 1.22 \times 10^1$.

[5] It was assumed that the HO site would exist for no longer than twenty-five years before remediation is conducted; thus, the longest potential exposure duration would be twenty-five years.

correspond to the original study area sampling grid. These receptors enclosed the entire perimeter of the storage area.

The ISC model was used to calculate a 1- and 8-hour average ambient air concentration (g/m^3) at each receptor for each wind direction. In order to convert this value to an annual average concentration, each model-predicted concentration was multiplied by a conversion factor of 9.925 (EPA, 1990). It should be noted that there is an unknown measure of uncertainty associated with this factor, as applied in this analysis, because it was developed using data for elevated point source releases.

Tables B-1 through B-9 (see Appendix B) present results of the atmospheric dispersion modeling, i.e., g of vapor-phase compound (TCDD, 2,4-D, and 2,4,5,-T) per m^3 of ambient air at the fenceline receptor sites. The receptor sites are presented as x,y coordinates which have their origin (i.e., x = 0 and y = 0) at the lower, southwest corner of the HO site (Figure 2.1) and proceed clockwise around the fenceline of the entire site. Air concentrations were estimated as 1-hr and 8-hr averages, as well as annual averages.

Given the fenceline receptor concentrations, the next step involved determination of the plausible "zone of impact" or zone where potential human inhalation exposure might occur. As discussed in Section 3.1.4, human activities near the HO site are assumed to be almost entirely confined to short durations (approximately 1 hour) at locations south and west of the HO site. Cross-referencing these locations with a wind rose for JI (Figure 2.1), reveals that, on an annual basis, the prevailing frequency of winds (i.e., greater than 95 percent) are from the 40 to 110 degree wind direction sector; therefore, it is plausible that inhalation exposure may occur for individuals working at downwind locations (e.g., burn pit, fire training area). Thus, to estimate reasonable maximum exposure (EPA 1989b), the maximum 1-hr average concentration occurring along the prevailing, downwind side of the HO site's fenceline (i.e., the north, south, and west sides) was selected. This ambient air

concentration was considered to represent the reasonable maximum ambient air concentration which an individual may breath while in the zone of impact.

TABLE 3.2

Maximum 1-hour average vapor-phase concentrations (mg/m^3) of TCDD, 2,4-D, and 2,4,5-T estimated to occur for the TMEI and AMEI at the perimeter of the HO site.

Chemical	TMEI	AMEI
TCDD	1.01×10^{-8}	1.01×10^{-8}
2,4-D	1.81×10^{-4}	6.79×10^{-5}
2,4,5-T	2.00×10^{-4}	1.27×10^{-4}

Table 3.2 presents the selected maximum 1-hr average ambient air concentrations (mg/m^3) of vapor-phase TCDD, 2,4-D, and 2,4,5-T estimated to occur for TMEI and the AMEI at the fenceline of the site and in the zone of impact. These ambient air concentrations were then used in the following equation to estimate the daily absorbed dose (EPA 1988b, 1989b, 1989c):

$$AbsorbedDose\ (mg/kg\text{-}day) = \frac{CA \times IR \times ET \times EF \times ED \times ABS}{BW \times AT} \qquad (3\text{-}3)$$

where,

CA = contaminant ambient air concentration (mg/m^3);

IR = inhalation rate (i.e., 2.1 m^3/hour for an average adult engaged in a moderate activity level);

ET = exposure time (i.e., 1 hour/day for persons engaged in activities in the zone of impact);

EF = exposure frequency (i.e., 250 days/year);

ED = exposure duration [i.e., 0.68 years (250 days/365 days)];

ABS = absorption fraction (0.75, EPA, 1988b);

BW = body weight (i.e., 70 kg for an average adult); and

AT = averaging time [i.e., 250 days for noncarcinogenic effects; 25,550 days (365 days/year x 70 years) for carcinogenic effects].

Table 3.3 presents the estimated lifetime average daily absorbed dose for TCDD, and average daily dose for TCDD, 2,4-D, and 2,4,5-T resulting from vapor-phase inhalation exposure.

TABLE 3.3

Estimated lifetime average daily absorbed dose (LADD) and average daily absorbed doses (ADD) expressed as mg/kg/day for TCDD, 2,4-D, and 2,4,5-T resulting from vapor-phase inhalation exposure to the TMEI and the AMEI.

Chemical	TMEI		AMEI	
	LADD	ADD	LADD	ADD
TCDD	5.6×10^{-11}	2.3×10^{-10}	5.6×10^{-11}	2.3×10^{-11}
2,4-D		4.1×10^{-6}		1.5×10^{-6}
2,4,5-T		4.5×10^{-6}		2.9×10^{-6}

3.3.3 Inhalation of Contaminated Soil

Inhalation of contaminated airborne particles emitted from the HO site represents a plausible exposure pathway resulting from potent[illegible] future uses as discussed in Section 3.2.3. Although data collected by Helsel et al. (1987) suggested that virtually no particle-associated TCDD exposure (via inhalation) was occurring

as the result of airborne particulate originating from the undisturbed site, disturbances to the site may result in dispersion of contaminated soil particles and thus, present the potential for inhalation exposure to downwind receptors. The following Sections (3.3.3.1 through 3.3.3.3) present the methods for estimating potential particle-associated inhalation exposures resulting from persons being engaged in activities in the zone of impact during two distinct future-use activities at the HO site: (1) excavation of contaminated soil; and (2) construction of a cement cover over the existing site. To estimate the compound concentration in soil which is disturbed during site activities associated with these figure-use scenarios, first, the median value of the subsurface concentrations for each verticle profile (see Section 2.0) was calculated, and then the grand median of these median values was calculated. Thus, the grand median values for TCDD, 2,4-D, and 2,4,5-T were 0.42, 25.8, and 93 ppb, respectively.

3.3.3.1 Wind Erosion

Wind erosion was evaluated with respect to its contribution to airborne particulates emitted from the site as the result of disturbances to contaminated soil during either excavation or construction of a cement cover. The flux of dust particles less than 10 gm in diameter from surfaces with an "unlimited reservoir"[6] of erodible particles can be estimated as follows (Cowherd *et al.* 1985; EPA, 1988b):

$$E = 0.036\ (1-V)\ \frac{(U_m)}{(U_t)}\ F(x) \qquad \textbf{(3-4)}$$

where,

E = total dust flux of <10 gm diameter particles ($g/m^2/hr$);

[6] Soil surfaces that are exposed to the wind, uncrusted, and which consist of finely divided particles (EPA, 1988b).

V = fraction of vegetation (i.e., assumed to be 0.20 on the HO site at JI);

U_m = mean annual wind speed (i.e., 6.75 m/s at JI);

U_t = threshold wind speed (i.e., assumed to be 8.2 m/s, see EPA 1988c); and

F(x) = model function (i.e., 1.5, based on a comparison of $(U_t/U_m)0.886$ versus F(x) as presented in Cowherd *et al.*, 1985).

Then, the total dust flux (E), is converted to an emission rate using the following relationship (Cowherd *et al.* 1985):

$$Q = (C_s)\ (E)\ (A)\ \frac{(1\ hr)}{(3{,}600\ seconds)} \qquad \textbf{(3-5)}$$

where,

Q = compound emission rate (ng/second);

C_s = compound concentration in soil (ng/g); and

A = surface area of the site disturbed per day (i.e., 86 m^2/day during excavation and 173 m^2/day during cement cover construction).

Thus, the particle-associated compound emission rate estimates (g/hr) for wind erosion from either excavation or construction of cement cover were calculated as follows:

Chemical	Emission Rate (g/hr)	
	Excavation	Cement Cover
TCDD	1.4×10^{-11}	2.9×10^{-11}
2,4-D	8.9×10^{-10}	1.8×10^{-9}
2,4,5-T	3.2×10^{-9}	6.5×10^{-9}

3.3.3.2 Vehicular Traffic

The emissions of soil-associated TCDD, 2,4-D, and 2,4,5-T which may result from vehicular traffic on the HO site for either future use scenario (i.e., excavation or cement cover construction) can be estimated from an emission factor. The derivation of this factor is contained in EPA (1985, 1988b), and takes the form of:

$$E_v = k[1.7(\frac{s}{12})] \ (\frac{S}{48}) \ (\frac{W}{2.7})^{0.7} \ (\frac{w}{4})^{0.5} \ (365-\frac{p}{365})$$

where,

	E_v	=	Emission factor (kg/vehicle kilometer traveled);
	k	=	Particle size multiplier (i.e., 0.36 to 0.45, EPA, 1983);
	s	=	Silt content of road surface material (i.e., 0.2, EPA, 1988b);
	S	=	Mean vehicle speed (i.e., 8 km/hr);
	W	=	Mean vehicle weight (i.e., approximately 45 Mg for front-end loader and dump truck used during excavation and 35 Mg for loaded cement truck used during construction of cement cover);
	w	=	Mean number of wheels (i.e., 20 during excavation using at least two vehicles, and 10 during cement covering using one vehicle); and
	p	=	Number of days with at least 0.254 mm (0.01 in) of precipitation per year (i.e., 162 at JI).

This emission factor is provided in units of kg particulate emitted per vehicle kilometer traveled (kg/VKT). The particle size multiplier (k) varies with aerodynamic particle size range. Of particular interest is the respirable particle size range, because particles in this range may be inhaled and retained in the respiratory tract allowing for possible desorption from the surface of the particles and subsequent absorption through the capillaries (Paustenbach *et al.*, 1986). For unpaved surfaces,

U.S. EPA (1983) has estimated k to be 0.45 for aerodynamic particle diameters less than 10 μm; whereas, for soil loading and unloading operations and maintenance of outdoor storage piles, k is estimated to be 0.36 for aerodynamic particle diameters less than 10 μm.

Thus, the compound emission rate estimates (g/hr) associated with particle emissions from vehicular traffic involved in excavation or construction of cement cover were calculated as follows:

Chemical	Emission Rate (g/hr)	
	Excavation	Cement Cover
TCDD	8.0×10^{-9}	6.0×10^{-9}
2,4-D	4.9×10^{-7}	3.6×10^{-7}
2,4,5-T	1.8×10^{-6}	1.3×10^{-6}

3.3.3.3 Loading and Unloading Operations

The emission of particle-associated TCDD, 2,4-D, and 2,4,5-T during excavation activities (e.g., loading and unloading of contaminated soil) can be estimated from an emission factor described in Cowherd *et al.* (1985) and EPA (1988b):

$$E = k\,(0.0018)\,\left[\frac{(\frac{S}{5})\,(\frac{U}{5})\,(\frac{H}{5})}{(\frac{M}{2})^2\,(\frac{Y}{6})^{0.33}}\right] \qquad (3\text{-}7)$$

where,

E = Emission factor (lb emission per ton of soil moved);

k = Particle size multiplier (i.e., 0.36, EPA 1988b);

s = Silt content (i.e., 0.2, EPA 1988b);

U = Mean wind speed (i.e., 15.1 mph at JI);

H = Drop height (i.e., 12 ft);

M = Soil moisture content (i.e., 0.09, Crockett et al., 1986); and

Y = Dumping device capacity (i.e., 4 yd^3).

The particle-associated emission rate values were estimated as follows:

Chemical	Emission Rate (g/hr)
	Excavation
TCDD	5.6×10^{-8}
2,4-D	3.4×10^{-6}
2,4,5-T	1.2×10^{-5}

3.3.3.4 Estimated Emission Rates of Compounds Associated with Soil During Excavation or Construction of a Cement Cover and Estimated Inhalation Exposure and Absorbed Doses for Exposed Individuals

The estimated emission rates of particle-associated TCDD, 2,4-D, and 2,4,5-T for wind erosion and vehicular traffic associated with excavation and cement cover construction, and loading and unloading operations associated with excavation, were summed to provide an estimate of the total emission expected per hour, which results from these activities. Thus, during construction of the cement cover, it was assumed that both wind erosion and vehicular traffic would contribute to particle-associated compound emissions; therefore, their respective compound-specific emission rates were summed. Loading and unloading operations were not considered to be necessary for construction of the cement cover. However, for the excavation scenario,

compound-specific emission rates associated with particle emissions due to wind erosion, vehicular traffic and loading and unloading operations were summed.

The total emission rates for both excavation and construction of a cement cover were then used as input rates for the atmospheric dispersion model described in Section 3.3.2. The emissions of the particle-associated compounds were assumed to originate from the center of the soil sampling grid for purposes of dispersion modeling. The modeling provided estimates of 1-hr and 8-hr concentrations (g/m^3) of the particle-associated compounds across the same receptor perimeter as described above (Section 3.3.2) for the vapor-phase ambient air concentrations estimates.

The duration of exposure was assumed to be 243 days (0.67 years) for excavation and 120 days (0.33 years) for construction of a cement cover. Tables B-10 through B-15 and B-16 through B-20 (see Appendix B) present the estimated particle-associated ambient air concentrations (g/m^3) of TCDD, 2,4-D, and 2,4,5-T resulting from excavation and cement cover construction, respectively.

Absorbed inhalation doses were then calculated for both the TMEI and AMEI using equation 3 described above. The pulmonary absorption of the particle-associated compounds was assumed to be 3.0 percent for all three compounds; whereas, vapor-phase pulmonary absorption was assumed to be 75 percent for all three compounds (EPA, 1988b). In addition to particle-associated compound inhalation, it was assumed that vapor-phase inhalation could also occur simultaneously; thus, the vapor-phase absorbed doses estimated in Section 3.3.2 (see Table 3.2) were summed with the particle-associated absorbed doses to yield a total absorbed dose for both the excavation and cement cover construction scenarios. These total absorbed dose estimates are provided in Table 3.4. It is important to note that the TMEI and AMEI were selected based on the highest possible concentration resulting from the sum of both the vapor-phase concentration and the particle-associated concentration for each receptor location.

TABLE 3.4

Estimated Lifetime Average Daily Dose (LADD) and Average Daily Dose (ADD) expressed as mg/kg/day for TCDD, 2,4-D, and 2,4.5-T resulting from vapor-phase and particle-associated inhalation exposure to the TMEI and the AMEI during excavation and construction of a cement cover.

EXCAVATION

Chemical	TMEI		AMEI	
	LADD	ADD	LADD	ADD
TCDD	1.5×10^{-12}	1.6×10^{-10}	1.5×10^{-12}	1.6×10^{-10}
2,4-D	----	2.7×10^{-6}	----	1.2×10^{-6}
2,4,5-T	----	3.0×10^{-6}	----	1.9×10^{-6}

CEMENT COVER CONSTRUCTION

Chemical	TMEI		AMEI	
	LADD	ADD	LADD	ADD
TCDD	3.5×10^{-13}	7.5×10^{-11}	3.5×10^{-13}	7.5×10^{-11}
2,4-D	----	1.3×10^{-6}	----	5.0×10^{-7}
2,4,5-T	----	1.5×10^{-6}	----	9.4×10^{-7}

3.3.4 Ingestion of Contaminated Fish

A review of Table 2.1 shows that there is TCDD fish contamination in certain areas. The contamination appears to be restricted to the area adjacent to the former HO storage site, which is off-limits to fishing. Walsh III (1984) states that many coral reef fishes are strongly site-attached, and therefore move about only in relatively small areas. However, he points out that other coral reef fish can undergo

extensive daily movements. These large movements are usually restricted to adults. Randall (1961) studied the Convict Tang and noted that adults could move up to 300 yards in several hours. Walsh studied these movements in several Hawaiian fish species that are also present on JA. Table 2.1 indicates that these authors have identified the following species of fish as potentially having large daily movements:

Achilles Tang
Bluelined Surgeonfish
Bullethead Parrotfish
Convict Tang
Goldring Surgeonfish
Parrotfish
Spectacled Parrotfish
Threadfin Butterflyfish

Some of these fish species have been found to have TCDD contamination. If they migrate into the fishing areas near the former HO storage site, (Zones 5 and 10, Figure 3.1), then there is a potential for JI inhabitants to consume contaminated fish. For the fish that showed positive TCDD values, the migratory fish species had the lowest values. These values may be low because these fish may not spend all of their time in the contaminated area. It is not possible to quantify this potential exposure because the fishermen's catches have not been sampled. The potential for exposure may be low, but sampling of the fishermen's catches should be performed to confirm this. Sampling at the west wharf has revealed no contaminated fish, and this may be an indication of the low probability of catching a contaminated fish.

3.4 Uncertainties Associated with the Assessment of Exposure

There are many input values that must be selected along the path to developing a quantitative estimate of potential exposure. They involve making assumptions about the chemicals, the environment in which they are located, and the potential for human contact with them. In addition, input values, whether selected

by assumption or by existing empirical evidence, are all associated with some individual variability to a lesser or greater degree. In the aggregate, the use of assumptions and the variability underlying input values both create an element of uncertainty that is important to keep in mind when considering quantitative estimates of exposure and risk. Where the uncertainties are large, bounding them with statistical measures and sensitivity analyses can place quantitative limits on their range. This procedure was considered to be beyond the scope of this investigation because the risk assessment is screening-level and missing a lot of needed information. Instead, a qualitative description of the uncertainties is presented below.

Future use scenarios for HO site. The two future use scenarios were chosen to represent situations where site disruption was either minimal (concrete cover without remediation) or maximal (excavation of contaminated soil). As such, these are hypothetical scenarios that may not necessarily reflect the actual future use. This in itself creates an elements of uncertainty about the true risks at the site. Further, it is expected that paving this site would not occur without some form of prior treatment to stabilize the contaminated soil.

Assumptions in calculating exposure to chemicals at the HO site. There are two classes of assumptions that were necessary to have made in the estimation of exposure: those associated with human receptors and those associated with the calculation of emission factors. The *human receptor assumptions* include use of the TMEI or AMEI (the AMEI is more realistic), body weight, inhalation rate, and pulmonary deposition rate. It is important to recognize that under typical conditions, EPA recommends calculation of risk for the TMEI. However, at the HO site, locations that would normally produce a TMEI are inaccessible, making the AMEI a more viable alternative for prediction of exposure and risk. The *emission factor assumptions* associated with the excavation and paving scenarios include construction vehicle weight, number of wheels, duration of excavation scenario, duration of cement

covering scenario, physical parameters of soil (moisture content, density, pH, carbon content), threshold wind velocity, diffusion coefficients (computer estimates) and air-soil partition coefficients, concentrations of chemicals in soil (missing values, invalid values, unknown spatial distribution of 2,4-D and 2,4,5-T on surface and in vertical profiles), and QA issues. The first three are assumed to be of low variability; the rest are assumed to be of higher variability. In addition, the levels of particle-association inhalation exposure prior to the soil sampling study conducted by Crockett et al. (1986) are unknown. During this period, i.e., 1972 to 1986 (the period when Agent Orange storage began until the first soil sampling study was conducted) it was assumed that the average inhalation exposure levels estimated to occur over the lifetime exposure period (i.e., 25 years), which were based on the 1986 soil sampling study (Crockett et al. 1986), were representative of inhalation exposures levels occurring prior to 1986.

In addition, there are several variables *unaccounted for in this analysis*. These include:

- Transience of the potentially exposed population (transience implies that duration is variable);
- Differences in exposure between males and females;
- Other chemicals of concern at the site (e.g., other isomers of dioxin);
- Other chemicals on the Island (e.g., solvents, radiation, combustion products);

- Prior or concurrent occupational or environmental exposures to TCDD, 2,4-D, or 2,4,5-T, or other substances affecting the same target organs from the HO site or other sources:

Dedrumming operation	TCDD, 2,4-D, 2,4,5-T
Smoking	PIC (especially PAHs)[7]
Fire training area	TCDD and other PIC
JACADS stack plumes	TCDD, TCDFs[8], and other PIC
Fish consumption	Potential TCDD contamination
Launch area	Plutonium and progeny

  and other occupational hazards on JI involving in particular solvents or metals;

- Atmospheric transformation and soil photodegradation of TCDD, 2,4-D, and 2,4,5-T;

- Confounding exposure presented by accidental release of CW from JACADS; and

- Groundwater contamination and its relation to exposure of marine biota.

Uncertainty in dispersion modeling. The uncertainty in model predictions is a function of (1) "inherent" uncertainty; (2) uncertainties in model input variables; and (3) model physics errors. The inherent uncertainty arises from the random nature of the turbulent flow in which the plume is embedded (i.e., its variation from

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[7] PIC = Products of incomplete combustion; for example, polynuclear aromatic hydrocarbons (PAHs).

[8] TCDFs = Tetrachlorinated dibenzo furans.

one realization (i.e., observation) to the next) and the finite averaging time of the concentrations. Almost without exception, existing air quality models predict the ensemble-averaged concentration field (i.e., the mean concentration at any location over a large number of realizations of the same experiment). Overall, based on comparisons of model predictions to observations, the deviation between the predicted ensemble-average and an individual realization is large (i.e., of the order of the prediction).

For the horizontal scale of distance for this application, the principal cause of inherent uncertainty is three-dimensional boundary layer turbulence. This category of turbulence arises in ideal, homogeneous terrain and is caused by the stochastic nature of turbulence in the boundary layer; it is dominant over distances of less than approximately 20 km.

Model input variables that introduce uncertainty to the concentration estimate include (but may not be limited to) wind speed, wind direction, temperature, and emission rate. For this analysis, conservative meteorological parameters (in terms of plume dispersion) were used in the modeling; therefore, in terms of a peak model-predicted impact, the uncertainty introduced by the prescribed meteorological data should be small compared to the uncertainty introduced by the estimate of emissions for the emission area. The uncertainty in the emission estimates may be on the order of several magnitudes. Because the model-predicted impact is directly proportional to the emission rate, the uncertainty in the impacts may also be on the order of several magnitudes. Uncertainty contributed by errors in the representation of atmospheric physical processes in the model may also be large; however, quantification of this uncertainty for a particular model is a complicated process.

4.0 Toxicity Assessment

This section provides a review of the toxicological properties of TCDD, 2,4-D, and 2,4,5-T. These chemicals, which are present at the HO site, have been identified in Section 2.0 as having the potential for exposure in humans. The toxicity assessment of these chemicals examines the weight-of-evidence available regarding their ability to cause adverse health effects in exposed individuals. This evaluation also includes an estimation of the relationship between the extent of exposure to these compounds and the likelihood and severity of adverse effects.

4.1 Toxicological Profile for 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD)

4.1.1 Chemical Characteristics

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) is one of 75 compounds that are referred to as dioxins. TCDD is a man-made chemical with no known natural sources. It is not intentionally manufactured except for research purposes. This chemical is produced as a byproduct in the manufacture and/or use of herbicides containing 2,4,5-trichlorophenoxy acids; 2,4,5-trichlorophenol in wood preservatives;

hexachlorophene in germicides; and pulp and paper plants. TCDD can also be produced during incineration of municipal or certain industrial wastes; transformer/capacitor fires involving chlorinated benzenes and biphenyls; and the burning of wood in the presence of chlorine. A summary of the physical-chemical properties of TCDD can be found in Table 3.1. Much of the toxicological information in this review was extracted from three key documents, definitive reviews in their own rights: ATSDR (1989), IARC (1977), and IARC (1986). Primary citations acknowledged in these documents were also used as citations in this review.

4.1.2 Pharmacokinetics

4.1.2.1 Absorption

There are no data on the absorption of TCDD via inhalation. For oral and dermal absorption, the vehicle used to administer the compound has a great influence on its absorption. Lipophilic vehicles enhance the absorption of this chemical, while soil, fly ash, and activated carbon greatly reduce its bioavailability. One human study (Poiger and Schlatter, 1986), showed that >87% of the dose was absorbed after ingestion of the compound in a corn oil vehicle. Animal studies have shown a 50 to 80% absorption in a lipophilic vehicle when given by gavage (Nolan et al., 1979; Olson et al., 1980; Piper et al., 1973), and a 50 to 60% absorption when administered in the diet (Fries and Marrow, 1975). McConnell et al. (1984) and Lucier et al. (1986), investigated the difference in TCDD gastric absorption when two different vehicles were used, corn oil and soil. The soil vehicle was discovered to reduce the bioavailability of TCDD by 50%. Paustenbach et al. (1986) reviewed several papers on the oral bioavailability of TCDD from soil. The reviewed papers reported bioavailabilities ranging from 0.5% to 85%. The authors stated that several factors could influence the oral bioavailability of TCDD from soil, these include: bolus size of dose; method for calculating bioavailability; and organic content of the soil. These authors concluded that the upper estimate for the oral bioavailability of TCDD in soil

would be 30%. Dermal absorption of TCDD is also greatly influenced by the dosing vehicle. When applied on rat skin with methanol (Poiger and Schlatter, 1980), TCDD was 40% absorbed, whereas with an acetone-carbon disulfide mixture it was 77% absorbed (Driver et al., 1990). When bound to soil, Driver et al. (1990) showed that TCDD after 24 hours was less than 1% absorbed.

4.1.2.2 Distribution

There are no data on the distribution of TCDD following inhalation. In a human study Poiger and Schlatter (1986) discovered that approximately 90% of the absorbed dose was sequestered in the fat after an oral dose of TCDD in corn oil. Rats and mice preferentially sequestered TCDD in the liver and then adipose, whereas in guinea pigs this trend was reversed this (EPA, 1985). In studies with mice, Gasiewicz et al. (1983a,b) and Birnbaum et al. (1986), demonstrated that inducible mouse strains sequestered more TCDD in their livers than non-inducible strains. Weber and Birnbaum (1985) and Krowke (1986), demonstrated that TCDD crosses the mouse placenta and 75% of the total fetal body burden is located in the liver. Nau et al. (1986), further revealed that the mouse pup was also exposed via the mother's milk.

4.1.2.3 Metabolism

The only metabolic data available are either from in vitro studies or oral animal studies. Poiger et al. (1982) analyzed the bile of dogs to determine the possible metabolites of TCDD. They found five phenolic compounds: 1,3,7,8-tetrachloro-2-methoxydibenzo-p-dioxin; 2,7,8-trichloro-3-methoxydibenzo-p-dioxin; trichloro-dimethoxydibenzo-p-dioxins; tetrachloro-dimethoxy diphenylether; and 1,2-dichloro-4,5-dimethoxybenzene. Isolated rat hepatocytes were studied by Sawahata et al. (1982), and they identified 1-hydroxy-2,3,7,8-tetra-chlorodibenzo-p-dioxin and 8-hydroxy-2,3,7-trichlorodibenzo-p-dioxin as the metabolites in this study. Mason and

Safe (1986a,b) demonstrated that these metabolites had less biological activity than TCDD. Several authors have studied the differences in TCDD metabolism between species to attempt to explain the wide difference in species sensitivity to TCDD (Olson and Wroblewski, 1985; Poiger and Schlatter, 1985; and Wroblewski and Olson 1985). Pretreatment with TCDD in dogs (*in vivo*) and rats (*in vitro*) resulted in a greatly increased rate of metabolism of a subsequent dose, 100 and 320% respectively, but no increase was noted with the same experiment in guinea pigs. These results may partly explain why guinea pigs are 25 times more sensitive than rats to the effects of TCDD.

4.1.2.4 Excretion

Excretion data following inhalation or dermal exposure to TCDD are not available. Poiger and Schlatter (1986), investigated the elimination of TCDD in a human volunteer. They discovered that 11% of the dose was eliminated in the feces in the first three days, but during days 7 through 125 only 3.5% of the dose was eliminated. This led to a half-life calculation for this study of 2,120 days. In contrast, laboratory animals have a much shorter half-life: guinea pigs, 22 to 30 days; rats, 17 to 31 days; and mice, 11 to 24 days. Rats and guinea pigs eliminated 91 to 99% in the feces, mice, 54 to 72%; and 59% was eliminated in the hamster feces (EPA 1985).

4.1.2 Noncancer Toxicity

The noncancer toxicity of TCDD following inhalation exposure is not available. The summary of the oral R_fD values can be found in Table 4.6. This compound has shown to be lethal at very low concentrations in all laboratory animals tested, but there is a wide range of LD50 values between species. Oral administration of TCDD in lipophilic solvents has resulted in the following LD_{50} values: 0.6 to 2.1 ug/kg in guinea pigs (Schwetz et al., 1973), 20 to 60 ug/kg in rats, 100 to 600 ug/kg in mice,

and 1,000 to 5,000 ug/kg in hamsters (EPA, 1985; McConnell, 1985). One dermal study by Schwetz et al. (1973), with TCDD in acetone on New Zealand white rabbits produced an LD_{50} of 142 to 531 ug/kg. Death in all of the above experiments was delayed, and was not observed until 5 to 40 days after TCDD administration.

Toxicity data for humans are difficult to interpret because no one has been exposed to pure TCDD. Humans have been exposed to TCDD only as a minor contaminant in mixtures of other chlorinated aromatics or phenolics, and in the case of pesticide formulations various solvents are also present. It is not always known if the effects seen are from TCDD or from the other chemicals present, or a combination of the chemicals in the mixture. Many of the toxic effects described below have been reported in humans, but no confirmation linking these effects solely to TCDD can be made because of the confounding factors, including adequate exposure data, involved in the epidemiological studies. Therefore, the only data available on pure TCDD exposure are in laboratory animals.

TCDD is a potent inducer of chloracne in both humans and animals. Greig (1984) and Puhvel et al. (1982), produced chloracne lesions in hairless mice by both oral administration and dermal application respectively of TCDD. A threshold dose is not available since both investigations used only one dose level. Both children and adults developed chloracne lesions after the Seveso accident, with a greater prevalence showing in children. The higher frequency in children may have due to their greater activity patterns with soil (Suskind, 1985; Taylor, 1979).

In laboratory animals, a characteristic effect seen with both acute and long term studies, and usually seen with lethal doses, is the wasting syndrome. Weight loss and/or severely limited weight gain can begin to appear within 24 hours after TCDD administration, and continues until death 15 to 30 days after exposure (EPA, 1985; Peterson et al., 1984). Lu et al. (1986) showed that this syndrome is not entirely caused by a loss of appetite. Guinea pigs' weights when fed were stable until

a few days before death, but at that time weight loss began and was observed until death. This study did show that most of the observed weight loss can be attributed to appetite loss, but not all of it. This syndrome has not been reported in humans (ATSDR 1989).

Rats and mice are sensitive to the hepatic effects of TCDD, but guinea pigs and monkeys do not appear to be quite as sensitive (EPA, 1985). Types of lesions include necrosis, proliferative changes, cellular membrane alterations, bile duct proliferation, altered lipid metabolism, and excess amounts of porphyrin. Turner and Collins (1983), noted mild changes in guinea pig livers following a single gavage dose ranging from 0.1 to 20 ug/kg. Changes included hypertrophy, steatosis, focal necrosis, and hyalin-like bodies. A LOAEL of 0.001 ug/kg/day for liver effects in rats and mice was determined by EPA (1985) after a review of the literature (Kociba et al., 1979; NTP, 1982b).

Rats, mice, and guinea pigs are all very sensitive to the immunotoxic effects of TCDD. Reviews by EPA (1985, 1988a) and Knutsen (1984) revealed minimum effective oral doses of 1 ug/kg/week for mice, 5 ug/kg/week for rats, and 0.04 ug/kg/week for guinea pigs. Strain differences in mice have been observed to segregate with the Ah locus response (Dencker et al., 1985). C57B1/6 mouse thymus cultures, which are Ah-responsive, proved to be very sensitive to the immunotoxic effects of TCDD, whereas DBA/2J mouse thymus cultures, which are not Ah responsive, showed no effects. Luster et al. (1982) demonstrated that Fischer rat pups and B6C3F1 mice pups were sensitive to the immunotoxic effects of TCDD following in utero and postnatal lactation exposure.

The teratogenic effects of TCDD have been extensively studied, and rats and mice have been shown to be sensitive to these effects. Cleft palate and hydronephrotic kidney were the effects seen in mice after an oral dose of only 1 µg/kg (Courtney, 1976; Moore et al., 1973; Neubert and Dillmann, 1972; Smith et al., 1976).

Gavage administration of 0.125 to 0.25 µg/kg to rats during organogenesis produced hemorrhage of internal organs and subcutaneous edema (Sparschu et al., 1971a,b; Khera and Ruddick, 1973). As with hepatic effects, the teratogenic effects were only seen in Ah-responsive C57B1/6J mice (Poland and Glover, 1980; Dencker and Pratt, 1981).

The fetotoxicity of TCDD has been seen in rats, mice, and monkeys, with the monkey being the most sensitive species. In studies reviewed by EPA (1985, 1988a), fetal death and vaginal bleeding was seen at oral doses between 2 and 9 ug/kg/day. Murray et al. (1979), conducted a three-generation dietary study with Sprague-Dawley rats. Doses of 0.01 and 0.1 ug/kg/day resulted in decreased litter size, decreased fetal survival, and decreased neonatal survival. A decrease in fertility was observed at the 0.1 ug/kg/day dose. McNulty (1984, 1985) reported a high incidence of spontaneous abortions in Rhesus monkeys at total oral doses of 0.2 and 1.0 µg/kg on days 20 to 40 of gestation. Khera and Ruddick (1973) reported a decrease in male Wistar rat reproductive performance after oral administration of TCDD.

Several epidemiological studies have been conducted to determine if there is a correlation between TCDD exposure and birth defects (Aldred, 1978; Bisanti et al., 1980; Bonaccorsi et al., 1978; Department of Health, New Zealand, 1980; McQueen et al., 1977; Nelson et al., 1979; Reggiani, 1980; Smith et al., 1982; and Thomas, 1980). All of theses studies failed to demonstrate a correlation between birth defects and possible exposure to TCDD. Erickson et al. (1984) conducted a case control study of Vietnam veterans to determine if the offspring of these men had an increased risk of birth defects. This study showed that when all types of defects were combined there was not an increase in risk to birth defects among Vietnam veterans. They did find an increase in certain types of defects which include spina bifida, cleft palate, and certain congenital tumors. The authors noted that these increased risks may have been due to several factors including, unmeasured confounding factors, chance, or some other experience in Vietnam. The increased risks were low.

4.1.3 Carcinogenicity

The genotoxicity data for this compound have yielded conflicting results. Many of the studies have given negative results, while the positive tests showed weak response. The results of these studies can be found in Tables 4.1 and 4.2. The insolubility and high toxicity of TCDD has caused problems in some of these test systems. More testing must be done to resolve the conflicting data obtained so far (ATSDR, 1989).

As with noncancer effects, there are no inhalation carcinogenic data available. Several studies have shown that TCDD is carcinogenic by oral administration, the key studies being NTP (1982b) and Kociba et al. (1978a,b). A summary of the results of these studies can be found in Tables 4.3 and 4.4. In contrast to the oral studies, dermal studies have demonstrated limited or conflicting results. In the NTP (1982a) study, female Swiss mice had an increase incidence of fibrosarcomas in the integumentary system (but not the males). Berry et al. (1978) and Slaga and Nesnow (1985), reported no promotion or weak promoting activity in CD-1 mice and Sencar mice, respectively, when TCDD was applied to the skin. On the other hand, Poland et al. (1982) showed promotion in CD-1 mice, and that promotion was affected by genetic differences in the mice. These inconsistencies have not been resolved yet.

Human data on the genotoxicity and carcinogenicity of TCDD are inconclusive because of the previously described confounding factors involved in the epidemiological studies. There appears to be limited evidence that there may be an increased risk of soft-tissue sarcomas and lymphomas from exposure to phenoxyacetic acid herbicides and/or chlorophenols contaminated with TCDD (EPA, 1985). A recent retrospective cohort study (Fingerhut et al., 1991) found an increased risk of soft-tissue sarcomas in workers exposed for over one year to chemicals contaminated with TCDD, with a latency period of over 20 years. Limitations of this study were the

TABLE 4.1 Genotoxicity of 2,3,7,8-TCDD *in vitro*

End point	Species (test system)	Results	References
Gene mutation	*Salmonella typhimurrum* (reverse mutation)	—/—	McCann, 1978 Gilbert et al., 1980 Geiger and Neal, 1981 Mortelmans et al., 1984
	S. typhimurium (reverse mutation)	Not tested/+	Hussain et al., 1972 Seiler, 1973
	Escherichia coli (reverse mutation)	Not tested/+	Hussain et al., 1972
	Saccharomyces cerevisiae (reversion)	+/—	Bronzetti et al., 1983
	L5178Y mouse lymphoma cells (forward mutation)	Not tested/+, and not tested/—	Rogers et al., 1982
Cytogenetic	*S. cerevisiae* (gene conversion)	+/—	Bronzetti et al., 1983
	S. cerevisiae (host mediated)	+/NA[a]	Bronzetti et al., 1983
	Chinese hamster cells (sister chromatid exchange)	Not tested/—	Toth et al., 1984
Cell transformation	Baby hamster kidney cells - BHK	Not tested/+	Hay, 1982
	C3H/10T1/2 cells	Not tested/—	Abernathy et al., 1985

[a] Not available.

Source: ATSDR, 1989.

TABLE 4.2 Genotoxicity of 2,3,7,8-TCDD *in vivo*

End point	Species (test system)	Results	References
Gene mutation	*Drosophila* (sex-linked recessive lethal)	—	Zimmering et al., 1985
Cytogenetic	*Drosophila* (sister chromatid exchange)	—	Zeiger, 1983
	Drosophila (structural aberration)	—	Zeiger, 1983
	Rat (sister chromatid exchange)	—	Lundgren et al., 1986
	Rat - marrow cells (structural aberration)	—	Green and Moreland, 1975
	Rats - marrow cells (structural aberration)	+	Green et al., 1977
	Mouse - marrow cells (structural aberration)	+	Loprieno et al., 1982
	Mouse - marrow cells (sister chromatid exchange)	—	Meyne et al., 1985
	Mouse - marrow cells (structural aberration)	—	Meyne et al., 1985
	Mouse - marrow cells (micronucleus)	—	Meyne et al., 1985

Source: ATSDR, 1989.

TABLE 4.3 Summary of the oral carcinogenicity bioassay of Kociba et al. (1978 a,b)

Animal	Sex	Drug tested	Tumor type	Incidence
Sprague-Dawley rats	M	Control	Squamous cell carcinoma of the tongue, adenoma of the adrenal cortex, and squamous cell carcinoma of tyhe hard palate	0/85
		0.001	Squamous cell carcinoma of the tongue	1/50
		0.01	Squamous cell carcinoma of the tongue	1/50
			Squamous cell carcinoma of the adrenal cortex	2/50
		0.1	Squamous cell carcinoma of the tongue	3/50
			Adenoma of the adrenal cortex	5/50
			Squamous cell carcinoma of the hard palate	4/50
	F	Control	Hepatocellular carcinoma	1/86
		0.001	Hepatocellular carcinoma	0/50
		0.01	Hepatocellular carcinoma	2/50
			Squamous cell carcinoma of the hard palate	1/50
		0.1	Hepatocellular carcinoma	11/49
			Squamous cell carcinoma of the hard palate	4/49
			Squamous cell carcinoma of the lung	7/49

Source: ATSDR, 1989.

TABLE 4.4 Other Oral Studies Supporting the Conclusion that 2,3,7,8-TCDD is an Animal Carcinogen

Method of Exposure	Animal	Sex/ number	Doses tested	Tumor type	References
Diet	Sprague-Dawley rats	M/10	0.01, 0.005, 0.05, 0.5, 1.0, or 5 ppb	Increase in total tumor incidence	Van Miller et al., 1977a,b
Gavage	Osborne-Mendel rats	M/50	0.01, 0.05, or 0.5 µg/kg/ week	Follicular-cell adenomas and carcinomas of the liver	NTP, 1982b
	Osborne-Mendel rats	F/50	0.01, 0.05, or 0.5 µg/kg/ week	Neoplastic nodules and hepatocellular carcinomas of the liver	NTP, 1982b
	B6C3Fl mice	M/50	0.01, 0.05, or 0.5 µg/kg/ week	Hepatocellular carcinomas	NTP, 1982b
	B6C3Fl mice	F/50	0.01, 0.05, or 0.5 µg/kg/ week	Hepatocellular carcinoma and follicular-cell adenomas of the thyroid	NTP, 1982b
	Swiss mice	M/44	0.007, 0.7, or 7.0 µg/kg/ week	Hepatomas and hepatocellular carcinomas	Toth et al., 1979

Source: ATSDR, 1989.

limited number of cases, and the misclassification of soft-tissue sarcomas. A summary of the unit cancer risk values can be found in Table 4.9.

4.2 Toxicological Profile for 2,4-Dichlorophenoxyacetic Acid (2,4-D)

The purpose of this toxicological profile is to describe the known behavior of 2,4-D by using the most current and related information available. It is important to note that the n-butyl esters of 2,4-dichlorophenoxyacetic acid can hydrolyzed in biological and aquatic systems. Therefore, the behavior of the pure acid and their salts are pertinent and will be discussed in the following paragraphs along with studies on the esters when they are available (USAF, 1974).

4.2.1 Chemical Characteristics

2,4-Dichlorophenoxyacetic acid (2,4-D[9]) is a man-made chemical with no known natural sources. The chemical is produced by the interaction of 2,4-dichlorophenol, with the sodium salt of monochloroacetic acid, typically followed by an acid treatment to convert the 2,4-D salt to an acid (Sittig, 1980, 1986).

2,4-D is a systemic herbicide used for the control of broad leaf weeds in cereal crops, sugar cane, turf, pastures and other non-cropland (Weed Science Society of America, 1974). It is also used to control the ripening of bananas and citrus fruits (WHO, 1975). An estimated 27 million kg of 2,4-D acid equivalent, in the form of esters and salts, were used in the US in 1975 (IARC, 1977). 2,4-D was used as a jungle defoliant during the Vietnam War in the mid-1960's, where it was a component of "Agent Orange" (a 50:50 mixture of the n-butyl esters of 2,4-D and 2,4,5-trichlorophenoxyacetic acid). About 40 million liters of "Agent Orange" were sprayed

[9] 2,4-D refers to the acid derivative unless otherwise stated.

in South Vietnam between 1965-1971 (Committee on the Effects of Herbicides in Vietnam, 1974).

Various physical and chemical properties of 2,4-D are discussed in Section 4.5.

4.2.2 Pharmacokinetics

The differences in toxic effects caused by the various salts, amines and esters of 2,4-D can be explained on a pharmacometric basis. The concentrations of chemicals at the receptor sites in an organism depends on the absorption and distribution rates in relation to rates of metabolism and excretion. The rate of absorption in animals or plants is based on the route of entry and rate of membrane transport. Specific membrane transport rates depend upon the characteristics of the membrane in relation to the size, shape, polarity and lipid solubility of the particular molecule considered (USAF, 1974).

4.2.2.1 Absorption

The most common route of exposure to herbicides in mammals is via ingestion, although exposure via inhalation and cutaneous routes is possible. The literature indicates that gastric absorption of 2,4-D, its amines and alkali salts occur readily as would be predicted from the Henderson-Hasselbalch relationships (USAF, 1974). The gastro-intestinal absorption of 2,4-D esters may be incomplete (Erne, 1966 as cited in USAF, 1974).

Frank et al. (1985) calculated that a maximum of 4.5% of the amount of 2,4-D deposited on the bare skin of a person directly sprayed with 2,4-D was absorbed. Among those occupationally exposed, dermal exposure appears to be the most important route of absorption.

4.2.2.2 Distribution

After oral administration of 2,4-D to sheep and cattle, analyses of muscle, fat, liver and kidney showed the presence of 2,4-dichlorophenol (Clark et al., 1975 as cited in USDIFWS, 1978). There are no data concerning distribution after other relevant routes of administration.

4.2.2.3 Metabolism

Most studies indicate that 2,4-D is rapidly eliminated via the kidneys by active tubular secretion into the urine. Cattle and rabbits excrete 2,4-D in their urine mostly unchanged (USAF, 1974). Erne (1966) as cited in USAF (1974), found that 2,4-D had a half-life from three to twelve hours and that urinary excretion was the primary route of elimination in the rat, rabbit, calf and chicken. Berndt and Koschier (1973), as cited in USAF (1974), concluded that renal tubular transport by the organic anion mechanism may account for the relatively rapid disappearance of 2,4-D and that might account for 2,4-D's low toxicity.

4.2.2.4 Excretion

In a study on the kinetics of 2,4-D, five male volunteers were administered a dose of 5 mg/kg bw. Absorption was nearly complete, as indicated by the recovery of 88-100% of the dose in the urine within 144 h. Approximately 80% of the 2,4-D was excreted unchanged in the urine. The additional 20% was excreted as an acid-labile conjugate (Sauerhoff et al., 1977a). Extensive and rapid gastrointestinal absorption of 2,4-D was also observed by Kohli et al. (1974b).

Maximum concentrations of 2,4-D were detected in urine three days after dermal exposure (Feldman and Maibach, 1974).

4.2.3 Toxicity

Toxicity data for humans are difficult to obtain because people are rarely exposed to pure 2,4-D. Most occupational exposure studies are difficult to evaluate because of the combined exposures of many workers to more than one herbicide or greater than one derivative of a single herbicide.

4.2.3.1 Noncancer Toxicity

Most of the data derived from acute toxicity studies indicate that 2,4-D has low toxicity. In the rat, the single dose LD_{50} is 620 mg/kg for the butyl ester derivative of 2,4-D and 100 mg/kg for the dog in the 2,4-D acid derivative (Rowe et al., 1954; Edson et al., 1964 as cited in USAF, 1974).

Groups of 3 male and 3 female beagle dogs were fed 10, 50, 100, or 500 mg/kg of diet 2,4-D for 2 years, beginning at 6-8 months of age. Twenty-eight dogs survived the 2 year period and were clinically normal. No adverse effects related to 2,4-D were observed (Hansen et al., 1971).

Results of teratological studies are variable; teratogenic effects are observed with doses close to maternal toxicity. In a study by Bjorklund and Erne (1966), Sprague-Dawley rats were given 1000 mg/l 2,4-D (50 mg/kg) in the drinking water during pregnancy and for an additional 10 months after that, and 2,4-D was administered to the second generation for up to 2-years. Pregnancy and parturition were normal, the litter size was not significantly reduced, and no malformations were noted in the young. Except for retarded growth and increased mortality in the second generation, no clinical or morphological changes were seen.

In a three-generation study, Osborne-Mendel rats were orally administered 100 or 500 µg/kg (4 µg/kg or 20 µg/kg) of diet 2,4-D. No adverse effects were observed.

Diets containing 1500 µg/kg (60 µg/kg) 2,4-D significantly reduced the percentage of pups surviving to weaning and their weights (Hansen et al., 1971).

No significant increases in embryonic effects were noted when 2,4-D was orally administered to hamsters at doses up to 100 mg/kg on days 6-10 of gestation (Collins and Williams, 1971).

An Oral Reference Dose (Oral R_fD), of 0.01 mg/kg/day has been set by EPA (IRIS, 1991). This is based on data from Dow Chemical Co. (1983). Hematologic, hepatic and renal toxicity were demonstrated in Fisher 344 rats during a subchronic feeding. 2,4-D was fed to the rats for 91 days at doses calculated to be 0, 1, 5, 15, or 45 mg/kg/day. There were a total of 200 animals in the study. Criteria examined to determine toxicity were survival, daily examination for clinical symptomology, weekly change in body weights and clinical, gross and histopathologic alterations. The results demonstrated statistically significant reductions in mean hemoglobin (both sexes), mean hematocrit and red blood cell levels (both sexes), and mean reticulocyte levels (males only) at the 5 mg/kg/day dose or higher after 7 weeks. There were also significant reductions in liver enzymes LDH, SGOT, SGPT, and alkaline phosphatase at week 14 in animals treated at the 15 mg/kg/day or higher doses. Kidney weights (absolute and relative) showed significant increases in all animals at the 15 mg/kg/day dose or higher at the end of the experimental protocol. Histopathologic examinations correlated well with kidney organ weight changes showing cortical and subcortical pathology. The dose used to derive the R_fD_o was 1 mg/kg/day (IRIS, 1991). The R_fD_o was set at 0.01 mg/kg bw/day by using a total uncertainty factor of 100 to account for uncertainty in the interspecies and interhuman variability in the toxicity of 2,4-D in regard to these specific data (IRIS, 1991). Because the analysis of the 90-day and a follow up 1-year interim study, results suggest that the NOAEL would also be relevant for the full 2-year duration. Inclusion of the subchronic-to-chronic uncertainty factor is not warranted (IRIS, 1991). The EPA has medium confidence (tending towards high) in this oral R_fD (IRIS, 1991). Confidence

in the study is medium because of a reasonable number of animals were used of both sex, the four doses were given, and a generous number of parameters were examined (IRIS, 1991). Confidence in the data base is medium because several studies support both the observation of critical toxic effects and the levels at which they occur (IRIS, 1991).

Critical noncarcinogenic toxicity values for 2,4-D are discussed in Section 4.5.

4.2.3.2 Carcinogenicity

Osborne-Mendel rats were orally administered 5, 25, 125, 625, or 1250 mg/kg (0.2, 1.0, 5.0, 25.0, or 50 mg/kg) 2,4-D for 2 years. A significant increase in tumors was seen only in the highest dose group, but tumors were randomly distributed and were typical of those found in aging rats of this strain (Hansen et al., 1971). Because of the limitations of this study (including the small number of animals used) no evaluation of carcinogenicity could be made based on the available studies (IARC, 1987).

IARC (1987 and 1977) state that the evidence for carcinogenicity in animals is inadequate for 2,4-D.

4.2.3.3 Additional Data

The genotoxicity data for 2,4-D have yielded fairly inconsistent results overall. Many *in vitro* studies have given positive results in absence of metabolic activation, but a few negative results have been noted. The results of these studies can be found in Tables 4.5 (*in vitro* data) and 4.6 (*in vivo* data).

TABLE 4.5 Genotoxicity of 2,4-D *in vitro*

End point	Species (test system)	Results	References
Gene Mutation	*Salmonella typhimurium* (reverse mutation)	-/-[a]	Nishimura et al., 1982 Mortelmans et al., 1984
	S. typhimurium (reverse mutation)	0[b]/-	Anderson and Styles, 1978
	S. typhimurium (reverse mutation)	-/0	Zetterberg et al., 1977 Anderson et al., 1972
	Saccharomyces cerevisiae (reverse mutation)	+/0	Zetterberg, 1978
Cytogenetic	*S. cerevisiae* (gene conversion)	+/0	Zetterberg et al., 1977
	S. cerevisiae (gene conversion)	(+)[c]/0	Siebert and Lemperle, 1974
	Chinese hamster cells (sister chromatid exchange)	-/-	Linnainmaa, 1984
	Human lymphocytes (sister chromatic exchange)	+/0	Korte and Jalal, 1982
	Human lymphocytes (chromosomal aberration)	+/0	Pilinskaya, 1974 Mustonen et al., 1986

[a] In presence of metabolic activation/absence of metabolic activation
[b] Not tested
[c] Weakly positive

Source: IARC, 1987.

TABLE 4.6 Genotoxicity of 2,4-D *in vivo*

End point	Species (test system)	Results	References
Gene mutation	*Drosophila melanogaster* (sex-linked recessive lethal)	-	Vogel and Chandley, 1974 Zimmering et al., 1985
	Drosophila melanogaster (sex-linked recessive lethal)	+	Magnusson et al., 1977
Cytogenetic	*Drosophila melanogaster* (somatic mutation/ recombination)	+	Rasmuson and Svahlin, 1978
	Drosophila melanogaster (aneuploidy)	-	Ramel and Magnusson, 1979 Magnusson et al., 1977 Woodruff et al., 1983
	Mouse (micronucleus test)	-	Seiler, 1978 Jenssen and Renberg, 1976
	Mouse (dominant lethal test)	-	Epstein et al., 1972
	Human lymphocytes (sister chromatid exchange)	-	Linnainmaa, 1983
	Human lymphocytes (sister chromatid exchange)	(+)[a]	Crossen et al., 1978
	Human lymphocytes (chromosome aberration)	-	Mustonen et al., 1986
	Human lymphocytes (chromosome aberration)	(-)[b]	Hoegstedt et al., 1980

[a] Weakly positive
[b] Weakly negative

Source: IARC, 1987.

4.3 Toxicological Profile for 2,4,5-Trichlorophenoxyacetic Acid (2,4,5-T)

The purpose of this toxicological profile is to describe the known behavior of 2,4,5-T by using the most current and related information available. It is important to note that the n-butyl esters of 2,4,5-trichlorophenoxyacetic acid can be hydrolyzed in biological and aquatic systems. Therefore, the behavior of the pure acid and their salts are pertinent and will be discussed along with studies on the esters when they are available (USDAF, 1974).

4.3.1 Chemical Characteristics

2,4,5-Trichlorophenoxyacetic acid (2,4,5-T[10]) is a man-made chemical with no known natural sources. The chemical is currently produced by the reaction of 2,4,5-trichlorophenol with the sodium salt of monochloroacetic acid, typically followed by an acid treatment to convert the 2,4,5-T salt to an acid (Sittig, 1980).

2,4,5-T was used as a jungle defoliant during the Vietnam War in the mid-1960s, where it was a component of "Agent Orange" (a 50:50 mixture of the n-butyl esters of 2,4,5-T and 2,4-dichlorophenoxyacetic acid). About 40 million liters of "Agent Orange" were sprayed in South Vietnam between 1965-1971 (Committee on the Effects of Herbicides in Vietnam, 1974).

Various physical and chemical properties of 2,4,5-T are discussed in Section 4.5.

[10] 2,4,5-T refers to the acid derivative unless otherwise stated.

4.3.2 Pharmacokinetics

The differences in toxic effects caused by the various salts, amines and esters of 2,4,5-T can be explained on a pharmacometric level. The concentrations of chemicals at the receptor sites in an organism depends upon the absorption and distribution rates in relation to rates of metabolism and excretion. The rate of absorption in animals or plants is dependent on the route of entry and the rate of membrane transport. Specific membrane transport rates depend upon the characteristics of the membrane in relation to the size, shape, polarity and lipid solubility of the particular molecule considered (USDAF, 1974).

4.3.2.1 Absorption

The most common route of exposure to herbicides in mammals is via ingestion, although exposure via inhalation and cutaneous routes is possible. The literature indicates that gastric absorption of 2,4,5-T and its amines and alkali salts occur readily as would be predicted from the Henderson-Hasselbalch relationships (USDAF, 1974). There is no information in the available literature about the absorption of 2,4,5-T via the skin or inhalation.

4.3.2.2 Distribution

There was no available information on the distribution of 2,4,5-T.

4.3.2.3 Metabolism and Excretion

Most studies indicate that animals rapidly eliminate 2,4,5-T via the kidney by active tubular secretion into the urine. Cattle and rabbits excrete 2,4,5-T in their urine mostly unchanged (USDAF, 1974). Erne (1966), as cited in USDAF (1974), found that 2,4,5-T had a half-life from three to twelve hours and that urinary

excretion was the primary route of elimination in the rat, rabbit, calf and chicken. Berndt and Koschier (1973), as cited in USDAF (1974), concluded that renal tubular transport by the organic anion mechanism may account for the relatively rapid disappearance of 2,4,5-T, which may account for 2,4,5-T's low toxicity.

[1-^{14}C]2,4,5-T was administered to pregnant and non-pregnant rats by stomach tube in a study by Fang et al. (1973), as cited in USDIFWS (1978). The rate of elimination for both groups was the same. Ninety to 95% of the label was eliminated in the form of unchanged 2,4,5-T in the urine. In addition, two non-polar and one water soluble metabolite were observed. Acid hydrolysis of the water soluble metabolite produced 2,4,5-T suggests potential ester formation.

Studies in humans confirm the results observed in animals. Gerring et al. (1973) orally administered 2,4,5-T directly or in milk in 5 human male volunteers. An average of 88% of the dose was excreted in the urine within 96 hours of administration, and renal clearance was 180 to 260 ml/min. The ingested 2,4,5-T was eliminated unchanged into the urine (USDAF, 1974). There was no free trichlorophenol detected in the urine. Clearance from the plasma and excretion both followed first-order kinetics with a half-life of 23 hours. Fecal excretion was <1% of the dose (Gerring et al., 1973).

In a similar study, 2,4,5-T was administered orally at 2, 3, or 5 mg/kg bw. Maximum plasma concentrations were detected 7 to 24 hours after administration. Following the 5 mg/kg bw dose, the half-life averaged 19 hours. For all of the doses examined, an average of 63 to 79% of the dose was recovered in the urine within 96 h of administration (Kohli et al., 1974a).

4.3.3 Toxicity

Toxicity data for humans are difficult to obtain because people are rarely exposed to pure 2,4,5-T. In the majority of cases, the available data do not distinguish between the possible effects of exposure to 2,4,5-T and those of exposure to associated chemicals or more toxic contaminants such as TCDD.

4.3.3.1 Noncancer Toxicity

Most of the data derived form acute toxicity studies indicate that 2,4,5-T has low toxicity. In the mice, the single dose LD_{50} was 940 mg/kg for the butyl ester derivative for 2,4,5-T and 500 mg/kg in the rat for the 2,4,5-T acid derivative (Rowe and Hymas, 1954 as cited in USDAF, 1974).

Dogs fed 2,4,5-T 5 times a week for 90 days at a dosage level of 2, 5, or 10 mg/kg bw exhibited no adverse effects. Daily doses of 20 mg/kg bw resulted in deaths 11-75 days after the first dosing (Drill and Hiratzka, 1953).

Results of teratology studies in animals are variable. 2,4,5-T (containing less than 0.02 mg/kg TCDD) orally administered on days 6-15 of gestation was embryotoxic to NMRI mice. The frequency of cleft palate was significantly increased when doses of greater than 20 mg/kg bw were administered. Reductions in fetal weight were found with doses of 10-15 mg/kg bw, but there was no increase in embryolethality over controls. Cleft palates were produced following a single oral dose of 150-300 mg/kg bw. 2,4,5-T butyl ester was found to have similar embryopathic effects as 2,4,5-T following administration on days 6-15 of gestation (Neubert and Dillmann, 1972).

To the contrary, 2,4,5-T (containing 0.5 mg/kg TCDD) was neither teratogenic or fetotoxic when orally administered to CD rats at doses ranging from 1-80 mg/kg

bw (Courtney and Moore, 1971), or in Sprague-Dawley rats at doses ranging from 1-24 mg/kg bw (Emerson et al., 1971) on days 6-15 of gestation. The butyl ester of 2,4,5-T had no effect when orally dosed at 50 or 150 mg/kg bw in Wistar rats, but 2,4,5-T (containing less than 0.5 mg/kg) did induce skeletal anomalies following single daily doses of 100-150 mg/kg bw on days 6-15 of gestation (Khera and McKinley, 1972).

Sjoden and Soderberg (1977), reported that prenatal exposure to 2,4,5-T may lead to behavioral abnormalities and changes in thyroid activity as well as brain serotonin levels in the progeny. Crampton and Rogers (1983) reported that prenatal exposure to 2,4,5-T has long-term effects on behavior in rats. After exposure to a single dose of 2,4,5-T (6 mg/kg) on day 8 of gestation, abnormalities were observed in tests for novelty responses.

An oral Reference Dose (oral R_fD), of 0.01 mg/kg/day has been set by EPA (IRIS, 1991). This is based on data from two well conducted studies (Kociba et al., 1979; Smith et al., 1981). Kociba et al. (1979) maintained Sprague-Dawley rats (50/sex) on diets supplying 0, 3, 10, or 30 mg 2,4,5-T/kg bw/day for 2 years. Toxicological endpoints measured were body weight, food consumption, tumorigenicity, hematology, urinalysis, serum chemistry, and histopathology. No effects were seen at 3 mg/kg/day. An increase in urinary excretion of coproporphyrin (at 4 months only) was reported for males at 10 and 30 mg/kg/day and for females at the 30 mg/kg bw dose level. A mild dose-related increase in the incidence of mineralized deposits in the renal pelvis was reported for females after 2 years. Smith et al. (1981) conducted a three generation reproduction study. Rats were fed levels of 2,4,5-T corresponding to 0, 3, 10, or 30 mg 2,4,5-T/kg bw/day. No effects were observed at the lower doses. Reduced neonatal survival was observed at both higher doses. The dose used to derive the R_fD_o was 3 mg/kg/day (IRIS, 1991). The R_fD_o was set at 0.01 mg/kg bw/day by using a total uncertainty factor of 300 to account for uncertainty in the extrapolation of dose levels from laboratory animals to humans

(10), uncertainty in the threshold for sensitive humans (10), and uncertainty because of deficiencies in the chronic toxicity data base (3) (IRIS, 1991). The EPA has medium confidence (tending towards high) in this oral R_fD (IRIS, 1991). There is high confidence in the studies used to determine the R_fD_o because of the completeness of the studies and the data base is supportive of the magnitude of the reproductive effect. The relative weakness of the chronic toxicity data base precludes a higher overall confidence level (IRIS, 1991).

Critical noncarcinogenic toxicity values for 2,4,5-T are discussed in Section 4.5.

4.3.3.2 Carcinogenicity

2,4,5-T has been tested in mice by oral administration. In a study by Mutanyi-Kjovacs et al. (1976), 20 male and 19 female 6-week old inbred XVBII/G mice were given 100 mg/l (5 mg/kg) 2,4,5-T (containing less than 0.05 mg/kg chlorinated dibenzodioxins) in the drinking water for 2 months. Subsequently, 2,4,5-T was fed orally at a concentration of 80 mg/kg (3.2 mg/kg) of diet for lifespan. No significant increase was noted in the incidence of tumors. In a similar study by the same authors, C3HF mice were treated in the same manner. The treated female mice showed a significant increase in the total number of tumors. Although an increased incidence of tumors at various sites were observed in this study, no evaluation of carcinogenicity of 2,4,5-T could be made because of the limitations of this study (small number of animals used) (IARC, 1987).

IARC (1987, 1977) state that the evidence for carcinogenicity in animals is inadequate for 2,4,5-T.

4.3.3.3 Additional Data

The genotoxicity data suggest that 2,4,5-T is not likely to effect genetic material. Most studies have given negative results, while the positive studies had only weak responses. The results of these studies can be found in Tables 4.7 (*in vitro* data) and 4.8 (*in vivo* data).

TABLE 4.7 Genotoxicity of 2,4,5-T *in vitro*

End point	Species (test system)	Results	References
Gene mutation	*Salmonella typhimurium* (reverse mutation)	-/-[a]	Herbold et al., 1982 Nishimura et al., 1982 Mortelmans et al., 1984
	Salmonella typhimurium (reverse mutation)	0[b]/-	Anderson and Styles, 1978
	Salmonella typhimurium (reverse mutation)	-/0	Andersen et al., 1972
	Saccharomyces cerevisiae (reverse mutation)	+/0	Zetterberg, 1978

[a] In presence of metabolic activation/absence of metabolic activation
[b] Not tested

Source: IARC, 1987.

TABLE 4.8 Genotoxicity of 2,4,5-T *in vivo*

End point	Species (test system)	Results	References
Gene mutation	*Drosophila melanogaster* (sex-linked recessive lethal)	+	Majumdar and Golia, 1974
	Drosophila melanogaster (sex-linked recessive lethal)	(+)[a]	Magnusson et al., 1977
	Drosophila melanogaster (sex-linked recessive lethal)	-	Zimmering et al., 1985
Cytogenetic	*Drosophila melanogaster* (somatic mutation/recombination)	-	Rasmuson and Svahlin, 1978
	Drosophila melanogaster (aneuploidy)	-	Ramel and Magnusson, 1979 Magnusson et al., 1977
	Mouse (micronucleus test)	-	Jenssen and Renberg, 1976
	Mouse (dominant lethal test)	-	Buselmaier et al., 1972
	Rat (dominant lethal test)	-	Herbold et al., 1982
	Human lymphocytes (sister chromatid exchange)	(+)	Crossen et al., 1978

[a] Weakly positive

Source: IARC, 1987.

4.4 Toxicity Profile for the Mixtures of 2,4,5-Trichlorophenoxyacetic Acid (2,4,5-T), 2,4-Dichlorophenoxyacetic Acid (2,4-D), and 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) as Chlorophenoxy Herbicides

4.4.1 Toxicity

Toxicity data for humans are difficult to obtain because people are rarely exposed to pure 2,4,5-T, 2,4-D or TCDD. Most occupational exposure studies are difficult to evaluate because of the combined exposures of many workers to more than one herbicide or greater than one derivative of a single herbicide. In the majority of cases, the available data do not distinguish between the possible effects of exposure to 2,4,5-T or 2,4-D and the exposure to associated chemicals such as TCDD. Many studies involve the occupational exposure to the general category of chlorophenoxy herbicides.

4.4.2 Noncancer Toxicity

4.4.2.1 Chloracne

In a reaction incident with exposure to 2,4,5-T and its contaminant TCDD in 1949, workers were who were exposed were followed for 4 years. Directly after exposure, workers had complaints including chloracne and respiratory tract, liver and nervous system disorders. By 1953, liver and nervous system problems subsided, but chloracne still persisted in some cases (Suskind, 1985).

4.4.2.2 Reproduction and Prenatal Toxicity

Effects on reproduction and prenatal toxicity have been addressed in several studies in humans. A study in Arkansas, USA, divided the state into low, medium and high 2,4,5-T use areas on the basis of rice acreage. No significant differences in

rates of facial cleft were found among the different areas between 1943 and 1974 (Nelson et al., 1979). The USEPA investigated spontaneous abortion rates in areas of Oregon, USA, in relation to 2,4,5-T spray rates between 1972 and 1977. Significantly higher spontaneous abortion rates were noted in areas in which 2,4,5-T was used. IARC (1986) noted that some of the methods in the study were inadequate.

A study of the pregnancy outcomes of wives of professional herbicide (2,4,5-T) sprayers was conducted in New Zealand (Smith et al., 1981). There were a total of 1172 births among families in the exposed group (1969-1979 for spraying of 2,4,5-T; 1960-1979 for spraying of any pesticide) and 1122 births in a control group. Major congenital defects were reported in 2% (24) of births to applicator families and 1.6% (18) of births to the control group; the difference was not significant. Similar rates were observed for the two groups for stillbirths and miscarriages. In further analysis, the pregnancy outcomes associated with spraying of 2,4,5-T by the father in the same year or in the previous year of the birth were selected and compared to the control group. The relative risk for congenital defects in children of exposed fathers was 1.19 and for miscarriages 0.89 (Smith et al., 1982b). These results were not statistically significant.

4.4.3 Cancer

4.4.3.1 Case-Control Studies

4.4.3.1.1 Soft-Tissue Sarcomas

Hardell and Sandstrom (1979), conducted a case-control study of 52 male patients with soft-tissue sarcoma and 220 matched controls. A person was classified as being exposed if he had at least one full day of exposure more than 5 years before a tumor was diagnosed. Of the 52 cases, 13 cases were exposed to chlorophenoxy herbicides (12 had been exposed to 2,4,5-T or 2,4-D, and one to 4-chloro-2-methyl-

phenoxy acetic acid (MCPA) alone; combined exposure to 2,4,5-T and 2,4-D was reported in 9 cases). A significant association was observed (odds ratio = 5.3; 95% CI, 2.4 to 11.5) with prior exclusion of exposure cases to chlorophenol. Latency from first exposure was 10 to 20 years. The average duration of exposure was three to four months (range, 2 days to 49 months).

Eriksson et al. (1981) undertook a case-control study with 110 cases with soft-tissue sarcomas and 220 matched controls in an area of Sweden where MCPA and 2,4-D had been widely used in agriculture. A significant association was observed (odds ration = 8.5) for exposure to chlorophenoxy herbicides alone for more than 30 days (7 cases), and 5.7 for exposures of less than or equal to 30 days (7 cases). The odds ratio for exposure to chlorophenoxy herbicides other than 2,4,5-T was 4.2 (95% CI, 1.3 to 15.8).

An initial analysis of occupations recorded with the National New Zealand Center Registry between 1976 and 1980 did not find and excess of soft-tissue sarcoma cases in agricultural and forestry workers (Smith et al., 1982). After this preliminary analysis, nearly 90% of the cases (or next of kin) were interviewed regarding past occupations and actual exposure to chlorophenoxy herbicides. A significant association was observed (odds ratio = 1.6; 90% CI, 0.7 to 3.3) was calculated for those who had probably or definitely been exposed for more than one day greater than 5 years prior to the diagnosis of the tumor. None of the cases was of a professional applicator. The possibility of recall bias based on the previous study was noted.

In a study by Smith et al. (1984) 82 persons with soft-tissue sarcomas and 92 controls (with other types of cancers) were interviewed for a case-control study. For those potentially exposed to phenoxyherbicides for more than one day not in the 5 years prior to cancer diagnosis, no significant association was observed (odds ratio = 1.3; 90% CI, 0.6 to 2.5). In addition, no significant association was observed for

chlorophenol exposure (odds ratio = 1.5; 90% CI. 0.5 to 4.5). The authors concluded that further studies were needed to clarify whether human exposure to these chemicals increase the risk of soft-tissue sarcoma.

4.4.3.1.2 Malignant Lymphomas

A case-control study of 169 cases of malignant lymphoma was undertaken with 338 matched controls (Hardell et al., 1981). The study design, including determination of exposure, was similar to the Swedish soft-tissue sarcoma studies (see Hardell and Sandstorm, 1979). A significant association (odds ratio = 4.8; 95% CI, 2.9 to 8.1) was obtained for exposure to chlorophenoxy herbicides, excluding cases and controls exposed to chlorophenols. Stratifying by duration of exposure, the relative risk estimate was 4.3 for less than 90 days and 7.0 for 90 days or more exposure to chlorophenoxy herbicides. The majority of chlorophenoxy herbicide-exposed cases reported exposure to both 2,4,5-T and 2,4-D (25 cases), two reported exposure to 2,4,5-T, 2,4-D and MCPA, seven to 2,4-D alone and 5 to MCPA alone (Hardell, 1981a).

An analysis of reported occupations appearing on the New Zealand Cancer Registry indicated an excess of malignant lymphoma and multiple myeloma among men in agricultural occupations during 1977-1981. The main findings of a subsequent case-control study concerned 88 cases of malignant lymphoma (covering non-Hodgkin's lymphoma other than lymphosarcoma and reticulosarcoma), classified as ICD 202, and 352 matched controls. A subsequent study with 83 cases of ICD 202 suggested that exposure to chlorophenoxy herbicides was not associated, since the odds ratio of 1.3 (90% CI. 0.7 to 2.5) was obtained when controls were people with other cancers were used, and an odds ratio of 1.0 (90% CI. 0.5 to 2.1) when the controls were the general population (Pearce et al., 1986).

4.4.3.1.3 Nasal and Nasopharyngeal Cancer

Hardell et al. (1982), described an odds ratio of 2.1 (95% CI, 0.9 to 4.7) for exposure to chlorophenoxy herbicides.

4.5 Conclusion and Summary

There is limited evidence that occupational exposures to chlorophenoxy herbicides are carcinogenic to humans (IARC, 1986). Benchmark values for all relevant toxicological indicators, carcinogenic and noncarcinogenic, are presented in Tables 4.9 and 4.10, respectively.

TABLE 4.9
Critical Carcinogenic Toxicity Values for Indicator Chemicals
Herbicide Orange Storage Area
Johnston Island, Johnston Atoll

Chemical Name	Slope Factor (SF) $(mg/kg\text{-}day)^{-1}$	Weight of Evidence Classification	Type of Cancer	SF Basis/ SF Source
Oral Route				
2,3,7,8-Tetrachlorodibenzo-p-Dioxin[a]	1.56×10^5	B1[a]	Lung, liver, hard palate, nasal turbinates	Food/ATSDR (June 1989)
2,4-Dichlorophenoxy acetic acid[b] (n-butyl ester)	No data	No data	No data	No data
2,4,5-Trichlorophenoxy acetic acid[b] (n-butyl ester)	No data	No data	No data	No data
2,4,5-Trichlorophenoxy acetic acid[b] (Iso-octyl ester)	No data	No data	No data	No data
Inhalation Rate	No data	No data	No data	No data

[a] When associated with phenoxy herbicides and/or chlorophenols, B2 when considered alone.

TABLE 4.10
Critical Noncarcinogenic Toxicity Values for Indicator Chemicals
Herbicide Orange Storage Area
Johnston Island, Johnston Atoll

Chemical Name	Chronic R_fD (mg/kg-day)	Confidence Level[a]	Critical Effect	R_fD Basis/ R_fD Source	Uncertainty and Modifying Factors[b]
Oral Route					
2,3,7,8-Tetrachlorodibenzo-p-Dioxin	1×10^{-9}	No data	Primary: Fetal survival Secondary: Renal	No data/ ATSDR	UF=100 for A, L MF=10
2,4-Dichlorophenoxy acetic acid (n-butyl ester)	1×10^{-2}[c]	Medium	Primary: Renal Secondary: Hematologic, hepatic	Food/ IRIS	UF=100 for H, A MF=1
2,4,5-Trichlorophenoxy acetic acid (n-butyl ester)	1×10^{-2}[d]	Medium	Primary: Neonatal survival Secondary: Increased urinary coproporphyrin	Food/ IRIS	IF=300 for H, A, D MF=1
Inhalation Route	No data	No data	No data	No data	No data

[a] Confidence level from IRIS, either high, medium, or low.
[b] Uncertainty adjustments: H=variation in human sensitivity; A=animal to human extrapolation; and D=deficiencies in toxicity data.
[c] R_fD value for acid, n-butyl ester value not available.
[d] R_fD value for acid, n-butyl ester and iso-octyl ester values not available.

5.0 *Risk Characterization*

Characterization of risk is based on the results of the exposure assessment (as summarized in Table 3.12) and the benchmark toxicity values (presented in Table 4.10). The basic algorithm for calculation of risk for carcinogenicity is:

$$Risk = Lifetime\ Average\ Daily\ Dose\ (mg/kg/day) \times unit\ cancer\ risk\ (mg/kg/day) \quad (5\text{-}8)$$

and for systemic toxicity (as the hazard quotient) is:

$$Noncancer\ hazard\ quotient = \frac{Average\ Daily\ Dose\ (ADD)}{Reference\ Dose\ (R_fD)} \quad (5\text{-}9)$$

Among the chemicals of concern, TCDD is the only known carcinogen. The Unit Cancer Risk (UCR) on which risk was calculated is 1.56×10^5. TCDD, 2,4-D, and 2,4,5-T are all systemic toxicants. It is important to note that, in the case of systemic

toxicity, hazard quotients are *not* additive for different chemicals where their respective R_fD's are based on different target organs. R_fD's and their bases are listed in Table 4.10 as the primary effect on which each chemical's R_fD is based. For TCDD the primary effect is fetotoxicity; for 2,4-D it is renal toxicity; and for 2,4,5-T it is reduced neonatal survival. As a result, hazard quotients are presented separately for all three chemicals and are not added into a single hazard index.

The noncancer hazard quotient assumes that there is a level of exposure (i.e., R_fD) below which it is unlikely for even sensitive populations to experience adverse health effects. If the exposure level (i.e., average daily intake) exceeds this threshold (i.e., if the hazard quotient exceeds unity), there may be concern for potential noncancer effects. It is important to note that the level of concern does not increase linearly as the R_fD is approached or exceeded because R_fDs do not have equal accuracy or precision and are not based on the same severity or toxic effects. Thus, the slopes of the dose response curve in excess of the R_fD can range widely depending on the substance (EPA, 1989c).

For all three compounds (i.e., TCDD, 2,4-D, and 2,4,5-T) inhalation, only oral R_fDs were available, and only an oral cancer potency factor (or UCR) was available for TCDD. Therefore, it was necessary to adjust these toxicity benchmark values, which were based on exposure (administered) dose to account for absorption. This route-to-route extrapolation method as been described by EPA (1989c) and is used to express the toxicity expected from an absorbed dose. Additionally, these adjusted toxicity benchmark values must then be used with inhalation exposure values which have also been adjusted to estimate absorbed dose. The uncertainties associated with this method include the fact that "point-of-entry" toxicity (i.e., in the lungs) cannot be estimated from oral toxicity data. Furthermore, unlike orally administered compounds, inhaled chemicals would not be subjected to first-pass hepatic metabolism before reaching the systemic circulation. Therefore, a toxic effect attributable to an active metabolite might be more pronounced if the compound was administered

orally. Conversely, the pulmonary absorption of a toxic parent compound that undergoes little or no first-pass metabolism may result in a greater dose of the toxic moiety entering the systemic circulation than if the compound was absorbed orally.

5.1 Quantitative Assessment of Risk

All parameters used in calculations leading to the expression of carcinogenic and systemic toxicity risks are presented in Table 5.1 for the current scenario and Table 5.2 for the two future use scenarios. Although all media were considered in the analysis, lack of or inadequate monitoring data on water and marine biota reduced multimedia considerations to air only. For this medium, both vapor phase and chemical-bound particulate were factored into the calculations.

For the *current scenario*, the cancer risk from exposure to TCDD is 3×10^{-5} for the TMEI and 3×10^{-5} for the AMEI. The hazard quotient from exposure to TCDD is 0.76 for the TMEI and 0.76 for the AMEI. The hazard quotient from exposure to 2,4-D is 0.0014 for the TMEI and 0.00051 for the AMEI. The hazard quotient from exposure to 2,4,5-T is 0.0015 for the TMEI and 0.00095 for the AMEI.

For the *future-use scenario involving excavation (Scenario 1)*, the cancer risk from exposure to TCDD is 8×10^{-7} for the TMEI and 8×10^{-7} for the AMEI. The hazard quotient from exposure to TCDD is 0.52 for the TMEI and 0.52 for the AMEI. The hazard quotient from exposure to 2,4-D is 0.00090 for the TMEI and 0.00034 for the AMEI. The hazard quotient from exposure to 2,4,5-T is 0.0010 for the TMEI and 0.00063 for the AMEI.

For the *future-use scenario involving paving (Scenario 2)*, the cancer risk from exposure to TCDD is 2×10^{-7} for the TMEI and 2×10^{-7} for the AMEI. The hazard quotient from exposure to TCDD is 0.25 for the TMEI and 0.25 for the AMEI. The hazard quotient from exposure to 2,4-D is 0.00045 for the TMEI and 0.00017 for the

Table. 5.1 Estimated Lifetime Average Daily Absorbed Dose a, i
Average Daily Absorbed Dose and Subsequent Risk from Inhalation of Vapor-Phase TCDD, 2,4-D, and 2,4,5-T within the Impact Zone of the Existing Herbicide Orange Site.

Compound	Ambient Air Conc (mg/m^3) (1hr avg)	Inhalation Rate (m^3/hr)	Exposure time (hr/d)	Exposure Freq (d/yr)	Exposure Duration (yr)	Absorption Fraction (vapor)	Body Weight (kg)	Avg. Time (d)	ABS. DOSE (mg/kg/day)	CANCER RISK	CHRONIC RfD (Adjusted) (mg/kg/day)	HAZARD RATIO (DOSE/RfD)
TMEI												
TCDD-c	1.01E-08	2.1	1	250	25	0.75	70	25550	5.55E-11	2.89E-05		
TCDD-nc	1.01E-08	2.1	1	250	1	0.75	70	250	2.27E-10		3.00E-10	7.56E-01
2,4-D	1.81E-04	2.1	1	250	1	0.75	70	250	4.06E-06		3.00E-03	1.35E-03
2,4,5-T	2.00E-04	2.1	1	250	1	0.75	70	250	4.51E-06		3.00E-03	1.50E-03
AMEI												
TCDD-c	1.01E-08	2.1	1	250	25	0.75	70	25550	5.55E-11	2.89E-05		
TCDD-nc	1.01E-08	2.1	1	250	1	0.75	70	250	2.27E-10		3.00E-10	7.56E-01
2,4-D	6.79E-05	2.1	1	250	1	0.75	70	250	1.53E-06		3.00E-03	5.09E-04
2,4,5-T	1.27E-04	2.1	1	250	1	0.75	70	250	2.85E-06		3.00E-03	9.50E-04

Table. 5.2 Estimated Lifetime Average Daily Absorbed Dose and Average Daily Absorbed Dose and Subsequent Risk from Inhalation of Vapor-Phase and Particle-Associated TCDD, 2,4-D, and 2,4,5-T within the Impact Zone During either Excavation or Construction of a Cement Cover.

SCENARIO 1: Excavation

Compound	Ambient Air Conc (mg/m^3) (1hr avg; adjusted for absorption)	Inhalation Rate (m^3/hr)	Exposure time (hr/d)	Exposure Freq (d/yr)	Exposure Duration (yr)	Absorption Fraction	Body Weight (kg)	Avg. Time (d)	ABS DOSE (mg/kg/day)	CANCER RISK	CHRONIC RfD (Adjusted) (mg/kg/day)	HAZARD RATIO (DOSE/RfD)
TMEI												
TCDD-c	7.80E-09	2.1	1	243	0.67	1	70	25550	1.48E-12	7.70E-07		
TCDD-nc	7.80E-09	2.1	1	243	0.67	1	70	243	1.56E-10		3.00E-10	5.19E-01
2,4-D	1.35E-04	2.1	1	243	0.67	1	70	243	2.70E-06		3.00E-03	9.01E-04
2,4,5-T	1.50E-04	2.1	1	243	0.67	1	70	243	3.00E-06		3.00E-03	1.00E-03
AMEI												
TCDD-c	7.80E-09	2.1	1	243	0.67	1	70	25550	1.48E-12	7.70E-07		
TCDD-nc	7.80E-09	2.1	1	243	0.67	1	70	243	1.56E-10		3.00E-10	5.19E-01
2,4-D	5.09E-05	2.1	1	243	0.67	1	70	243	1.02E-06		3.00E-03	3.39E-04
2,4,5-T	9.5E-05	2.1	1	243	0.6658	1	70	243	1.9E-06		3.00E-03	6.33E-04

SCENARIO 2: Construction of Cement Cover

Compoun	Ambient Air Conc (mg/m^3) (1hr avg; adjusted for absorption)	Inhalation Rate (m^3/hr)	Exposure time (hr/d)	Exposure Freq (d/yr)	Exposure Duration (yr)	Absorption Fraction	Body Weight (kg)	Avg. Time (d)	ABS DOSE (mg/kg/day)	CANCER RISK	CHRONIC RfD (Adjusted) (mg/kg/day)	HAZARD RATIO (DOSE/RfD)
TMEI												
TCDD-c	7.58E-09	2.1	1	120	0.33	1	70	25550	3.51E-13	1.83E-07		
TCDD-nc	7.58E-09	2.1	1	120	0.33	1	70	120	7.48E-11		3.00E-10	2.49E-01
2,4-D	1.35E-04	2.1	1	120	0.33	1	70	120	1.34E-06		3.00E-03	4.45E-04
2,4,5-T	1.50E-04	2.1	1	120	0.33	1	70	120	1.48E-06		3.00E-03	4.94E-04
AMEI												
TCDD-c	7.58E-09	2.1	1	120	0.33	1	70	25550	3.51E-13	1.83E-07		
TCDD-nc	7.58E-09	2.1	1	120	0.33	1	70	120	7.48E-11		3.00E-10	2.49E-01
2,4-D	5.09E-05	2.1	1	120	0.33	1	70	120	5.02E-07		3.00E-03	1.67E-04
2,4,5-T	9.50E-05	2.1	1	120	0.33	1	70	120	9.37E-07		3.00E-03	3.12E-04

AMEI. The hazard quotient from exposure to 2,4,5-T is 0.00049 for the TMEI and 0.00031 for the AMEI.

5.2 Uncertainties

As in exposure assessment (see Section 3.4), there are uncertainties associated with the dose-response component of risk assessment. The EPA is now considering new evidence to suggest that TCDD may be a threshold carcinogen dependent on receptor-mediated (aryl hydroxylase) binding into a ligand-receptor complex for all dioxin-induced effects, and that this binding is rate-limiting. Furthermore, the complex must undergo activation and translocation into the nucleus as a prerequisite for effect. The Agency is now considering lowering the slope factor by two-fold, which would have an impact on the ultimate expression of risk. At this time of report preparation, the IRIS file on TCDD has been pulled while deliberations are underway on this issue.

As recorded in Table 4.10, the level of confidence in the studies used to develop RfD's for all three chemicals can be highly variable for a great variety of reasons having to do with the quality of available science. No level of confidence is presented for TCDD; levels of confidence for 2,4-D and 2,4,5-T are described as medium, creating a margin of uncertainty.

Susceptibility to chemical toxicity among potential human receptors can also be highly variable due to preexisting general morbidity of residents on the Island, particular sensitivities among individuals (e.g., pregnant women), and such other factor as genetic predisposition to cancer.

Determination of carcinogenic risk from exposure to TCDD is typically amortized over a lifetime of 70 years. While exposure for the current scenario was assumed to have a maximum duration of 25 years (based on first exposure in 1972

and paving, excavation, or some other modification to the site in 1997), for some individuals, lifetime may be fewer or greater than 70 years, creating an element of uncertainty in the risk calculation.

Section 4.0 included a discussion on the toxicity of HO as a mixture. However there is insufficient evidence to formulate either a composite R_fD or additive hazard quotients. As a result, any synergistic, potentiative, or antagonistic effects posed by exposure to the three chemicals in combination could alter the benchmark values used to calculate risk. These toxicological phenomena could not be accounted for in this analysis.

Finally, the uncertainties posed by dose-response data and the toxicity benchmark values derived from them for the determination of risk are compounded on top of the uncertainties associated with exposure assessment, as expressed in Section 3.4. Together they may result in a risk determination that can be off by as many as two orders of magnitude.

6.0 Ecological Effects

Johnston Island is a coral atoll occupying 626 acres in the Pacific Ocean, 717 nautical miles southwest of Honolulu. The island was expanded from an area of 60 acres by the deposition of local dredged material in 1942. The marine ecosystem in the waters surrounding the Johnston Atoll is typical of a diverse tropical Indo-Pacific reef community. One hundred ninety-three fish species and 164 invertebrate species have been identified (Amerson and Shelton, 1976). The terrestrial fauna at the Johnston Atoll comprises about 40 species of birds, many of which brood on the nearby Sand Island. Relative to the marine community, the terrestrial ecosystem is less diverse since the island is arid, only seven feet above sea level, and has no tropical forest. No information was available on other terrestrial fauna and flora. Most of the land on the island is taken up by a 9,000 foot runway and military buildings associated with the chemical agent disposal system and, therefore, would provide poor habitat for most species.

As part of the investigation of contaminant effects at JI, this section describes the sampling and analysis of TCDD in sediments and biota, analyzes possible exposure of ecological receptors (fish, invertebrates, and birds) to dioxin, and assesses

risks. Risks to the ecological community resulting from exposure to 2,4-D and 2,4,5-T have not been assessed because these substances were not monitored in the present study.

6.1 Sampling Data

From 1985 through 1988, sediments were sampled from four areas of JI. Areas 1 through 3 are near the inner reef in the vicinity of the HO site, while Area 4 is on the opposite side of the Island (Figure 1). While a total of 38 samples were collected (Table 1), only 26 were identified by sampling area. In Area 1, dioxin was detected in one of 11 samples at a concentration of 160 parts per trillion (ppt). In Area 2, dioxin was detected in one of seven samples at a concentration of 190 ppt. Dioxin was not detected in the four Area 3 samples or the two Area 4 samples.

Samples were collected from a variety of fish, invertebrate, and bird species from 1984 through 1989 (Table 2). A total of 199 tissue samples (44 fish species, 13 invertebrate species, 2 bird species) were analyzed for dioxin. Samples of aquatic species were collected from Areas 1 through 4, Area 5 (inner reef), and Area 6 (outer reef) (see Figure 1). Samples of birds were collected on land near the Formal HO Storage Area.

A total of 32/199 tissue samples contained detectable concentrations of dioxin. Frequency of detection for the fish, invertebrate, and bird samples from each area is listed in Table 2.1. Analysis of the fish and invertebrate tissue data is complicated by the use of different organs (liver, muscle, and unspecified organs) for various samples. In addition, differences in habitat and feeding strategies are likely to result in variable uptake. Nevertheless, for the purpose of summarizing the data, all fish (whole body, muscle, or unspecified), crab, snail, octopus, and sea cucumber data have been summarized for each area.

A total of three bird samples were analyzed. TCDD was not detected in any of the samples which included one liver sample and two unspecified organ samples.

6.2 Toxicological Profile for TCDD

The toxicity of dioxin to fish and wildlife was reviewed by Eisler (1986). Dioxin is toxic to fish at low and sub-ng/L levels which makes it one of the most toxic compounds tested in aquatic organisms. Mehrle et al. (1988) reported significant increases in mortality and decreases in growth in rainbow trout (*Oncorhynchus mykiss*) exposed for 28 days to 0.038 ng/L followed by a 28-day observation period. Recently, Wisk and Cooper (1990) exposed Japanese medaka (*Oryzias latipes*) embryos to dioxin beginning on the day of fertilization and continuing until hatch (11 to 14 days). A statistically significant increase in the incidence of lesions occurred at 0.4 ng/L. Eisler's (1986) review stated that the highest tested concentration that did not produce adverse effects was 0.01 ng/L.

Due to its low water solubility, estimated at less than 20 ng/L (Marple et al., 1986), releases of dioxin to the aquatic environment tend to result in accumulations in sediments and biota (Eisler, 1986). Eisler (1986) cited studies in which higher levels of dioxin were found in bottom-feeding versus top-feeding fish, indicating the likely importance of sediments as a source. Dietary uptake may also contribute to body burdens as substantial levels of dioxin were measured in fish gut contents (Young and Cockerham, 1985; as cited in Eisler, 1986). Mehrle et al. (1988) estimated a bioconcentration factor (steady state fish muscle concentration divided by water concentration) of 39,000. Monitoring studies have identified measurable levels of dioxin in field samples of fish and crab tissues (e.g., Belton et al., 1985; Ryan et al., 1984). Studies in New Jersey have resulted in closure of the Passaic River to the harvesting of fish and shellfish because dioxin was frequently found in fish and crabs at concentrations exceeding the FDA levels of concern (Belton et al., 1985).

Several studies were found linking tissue residues with toxic effects. The Mehrle et al. (1988) study, which reported increased mortality and decreased growth, measured mean whole body dioxin concentrations of 0.74 ng/g (=740 ppt). Branson et. al. (1985) exposed rainbow trout to 0.107 ng/L dioxin for 6 hours and monitored elimination over 139 days. Dioxin body burdens at the end of the study were 650 ppt in whole fish, 260 ppt in muscle, and 2710 in liver. In these fish, there was reduced growth relative to controls and evidence of fin rot. The embryo exposure study of Wisk and Cooper (1990) reported that lesions were reported in embryos containing 240 ppt dioxin.

Dioxin is known to bioaccumulate in fish-eating birds (reviewed by Walker, 1990). Braune and Norstrom (1989) measured dioxin concentrations in herring gulls (*Larus argentatus*) and alewife, which comprise a major portion of their diet, from Lake Ontario. Mean whole body dioxin concentrations were 127 ppt in gulls and 4 ppt in fish. A biomagnification factor (whole body bird/whole body alewife concentration) of 32 was calculated. Egg levels may be similar to whole body levels; mean dioxin levels in herring gull eggs and whole body tissues were 83 and 127 ppt, respectively.

Elliott et al. (1989) reported that population declines in great blue herons (*Ardea herodias*) in British Columbia coincided with a tripling of dioxin levels in eggs from 66 to 210 ppb. These researchers cited studies in which colonial waterbird population declines occurred when dioxin levels exceeded 2000 ppt and began to recover when levels decreased to below 500 ppt. These field studies have not established causal relationships; controlled laboratory studies are required. Eisler (1986) cited a laboratory study in which chick edema disease (pericardial, subcutaneous, and peritoneal edema accompanied by liver enlargement and necrosis) occurred in domestic chickens fed dioxin at 1 or 10 ppb for 21 days. This disease was frequently lethal.

6.3 Risk Assessment

Releases of HO have exposed fish and invertebrates and possibly birds to dioxin. Only a rough estimate of risk is possible given the limitations of the data. When possible, risks were assessed by comparing body burdens with levels associated with toxic effects.

6.3.1 Aquatic life

The highest concentration of dioxin was reported in the crown squirrelfish. Squirrelfishes tend to remain close to the bottom and do not travel long distances (Migdalski and Fichter, 1976). These behaviors may increase their exposure to localized sources of dioxin in sediments. Out of four samples (three Area 1; one Area 2), TCDD was detected in one sample from Area 1 at 352 ppt and in one sample from Area 2 at 472 ppt. These concentrations exceed the 260 ppt measured in rainbow trout muscle that was associated with decreased growth and fin lesions (Branson et al., 1985).

The only other fish species with concentrations exceeding 100 ppt was the yellowfin goatfish. Three samples were collected in Area 1, where concentrations were 11, 85, and 102 ppt. TCDD was not detected in single samples of this species from Areas 2 and 5. Goatfishes are bottom feeders (Migdalski and Fichter, 1976), which may account for their enhanced body burdens. The maximum reported concentration is nearly one-half the 260 ppt reported as toxic by Branson et al. (1985).

Several invertebrate samples were detected at levels between 14 and 28 ppt. The only invertebrate sample detected at greater than 100 ppt was a "snails" sample from Area 2 measured at 120 ppt. No data linking tissue concentrations with effects in snails could be located.

Uncertainties in the analysis result from the collection of a small number (usually less than five) samples of each species in each area. In addition, in some samples either the species or organ that was analyzed or the collection site was not reported.

6.3.2 Birds

In three samples of birds, there were no detectable concentrations of dioxin. Further sampling is recommended to more adequately characterize risks.

6.4 Regulatory Concentrations

EPA has not issued ambient water quality criteria for the protection of aquatic life from exposure to dioxin (F. Gostomski, EPA, personal communication, January 22, 1991). FDA advisory levels are for the protection of human health rather than aquatic species. No sediment quality criteria have been published or proposed for dioxin.

7.0 *Data Requirements Assessment*

The EPA (1989) recommends that the data needs for the RI/FS be addressed at the site scoping meetings. Developing a comprehensive sampling and analysis plan (SAP) during the scoping meeting allows all of the data needs for the RI/FS, including the risk assessment, to be met. The data needs are identified by determining the type and duration of possible exposures (e.g., acute, chronic), potential exposure routes (e.g., fish ingestion, dust inhalation), and key exposure points (e.g., work areas) for each medium. These same types of considerations are also important for the ecological risk assessment. Data needs may have to be addressed before a more comprehensive risk assessment can be performed.

While there is always a need for better empirical data on toxicity, dispersion modeling, and general methodologies for expressing risk, monitoring data is usually site-specific and can be tailored to specific features of the site. There has not been a systematic effort in collecting the needed monitoring data at the HO site. To date, the most definitive data-collection activity has been the soil characterization study by Crockett et al. (1986). Data that can be obtained to convert this risk assessment into a more realistic multimedia approach are presented below. Many of these needs

were presented in the trip report for the site visit (Appendix C). Although the indicated supplemental data collection would provide the complete range of information needed for a full baseline risk assessment, there are some pieces of information that are more important than others, so that the individual needs may need to be ranked in priority order. This may preclude the necessity of having to perform all recommended procedures.

7.1 Air Sampling

The risk assessment used estimated values for the particulate and vapor phase emissions from the site. Air sampling would characterize the particulates and vapors coming from the site. Particle size distribution will enable determination of the percentage of respirable dust. To determine the wind erosion around the site several Hi-Vol samplers, equipped with particulate traps, could be placed downwind around the fence line. At the southwestern fenceline the odor of 2,4-D was detectable during the site visit, indicating that there may be significant vapor emissions from the site. Organic vapor phase samplers capable of collecting dioxins, 2,4-D, and 2,4,5-T can be placed around the site to characterize ambient air concentrations. There are other potential sources of dioxin on JI, including JACADS, the burn pit, and the fire training area. Sampling would permit source apportionment of dioxin from each of these sites.

7.2 Soil Sampling

The characteristics of the soil can have an influence on the bioavailability of dioxins and the other chemicals. Soil moisture content, organic content, and particle size distribution are missing elements that are important for lowering the uncertainty in the soil exposure calculations. It was originally planned to vertically sample the TCDD hot spots, but sample results were not available in time to accomplish this, and, therefore, some hot spots were missed in the vertical soil sampling. These hot

spots could now be sampled vertically for all three compounds, TCDD, 2,4-D, and 2,4,5-T. Only 15 plots were sampled for 2,4-D and 2,4,5-T, presenting a spacial distribution for these compounds inadequate for risk assessment. More plots could be sampled for these two compounds. One method that can be used to accomplish this is to revisit the 48 plots that were originally vertically sampled. These 48 plots could be sampled for all three chemicals of concern. This sample design would have two benefits: (1) better knowledge of the spacial distribution for 2,4-D and 2,4,5-T; and (2) knowledge of the fate of these chemicals over time.

7.3 Sediment Sampling

Channell and Stoddart (1984) found positive sediment samples near the western shore, prior to construction of the seawall in that area. This area could be revisited to determine if the seawall is performing according to its intended function. More sediment samples are needed to better characterize the spacial pattern of contamination. A grid pattern similar to the soil sampling protocol would help to characterize the spacial contamination pattern. These samples should include areas close to the shoreline.

7.4 Water Sampling

7.4.1 Seawater Sampling

No seawater sampling has been conducted off the former HO site. The U.S. Fish and Wildlife (1987) report that TCDD levels of 38 pg/l are toxic to fish. Toxic endpoints include severe adverse effects on survival, growth, and behavioral responses. With this potency, seawater sampling may be important.

7.4.2 Groundwater Sampling

The groundwater under the former HO site has never been sampled and may be a vital link in any discovery of HO site-related fish contamination. Groundwater sampling could proceed as described in Appendix C.

7.5 Biological Sampling

More sampling can to be performed within Site 3 to determine if contaminated fish are in this area. No biological samples have been analyzed for 2,4-D or 2,4,5-T. It is not possible to assess the potential impact from fish ingestion for these two chemicals if this analysis is not performed. Walsh III (1984) and Randall (1961) demonstrated that several adult fish species can have large movements. A study could be performed to ascertain if these migratory fish species are moving from the waters adjacent to the former HO site into fishing waters (e.g., Zones 5 and 10 in Figure 3.1). Sampling and analysis of fishermen's catches can be easily used to determine if humans are consuming contaminated fish. This is the only study that would demonstrate if the fish being consumed are contaminated.

7.6 Ecological Risk Sampling Recommendations

Further field investigations may be needed to adequately characterize the ecological risks at JI. Any additional research should be coordinated with the work underway by Dr. John Labelle of the Woods Hole Oceanographic Institute in support of the JACADS monitoring program. Additional sampling programs could be designed so that statistical comparisons can be made between concentrations in the different areas. In such an investigation sediment sampling would be expanded to allow better characterization of the spatial pattern of contamination. Biota samples would be focussed on species whose behavior may lead to greater levels of contamination (e.g., bottom feeding resident species). Organisms that are important

parts of marine food chains (e.g., small invertebrates such as marine worms) would be sampled. Based on the available data, the crown squirrelfish, yellowfin goatfish, snails, and crabs are good candidates for further sampling. Increased sampling of birds may be required to determine whether populations are at risk due to consumption of contaminated prey (e.g., fish and snails). Sampling could focus on one or two bird species that tend to be localized on the Island.

Although the contaminant studies should remain focussed on dioxin, it would be useful to examine several fish samples for 2,4-D. This compound has been measured at levels as high as 281 ppm in soil samples on the Island (Crockett et al. 1986). Although it is not bioaccumulated to the same extent as dioxin, measurable residues have been reported in fish from lakes treated with the compound (Frank et al. 1987) and toxicity data are available (e.g., Cope et al., 1970).

8.0 *Summary*

Scope of the study and physical setting. This report contains the results of a screening-level risk assessment conducted for the Air Force Occupational and Environmental Health Laboratory concerning the Herbicide Orange (HO) storage site at Johnston Island (JI). The risk assessment is part of the remedial investigation and feasibility study (RI/FS) process established by the U.S. EPA for characterizing the nature and extent of risks posed by hazardous waste sites and for developing and evaluating remedial options. This process is being conducted in the context of the U.S. Department of Defense (DoD) Installation Restoration Program (IRP).

JI is currently used for three purposes:

1. In the late 1950's and early 1960's, the island was used to launch missiles for atmospheric testing of nuclear weapons. During 1962, three missile aborts caused transuranic contamination on parts of the island. Launch and support facilities at JI are maintained in a caretaker status in case testing is deemed necessary for national defense.

2. JI has been designated as a chemical warfare destruction site and the Department of the Army maintains the Johnston Atoll Chemical Agent Disposal System (JACADS) on the Island. JACADS is involved in active thermal destruction of CW agents.

3. Johnston Atoll, including JI, is a National Bird Refuge, largely because of bird populations on nearby Sand Island. Among the few species of animal life swimming in waters off JI is the green sea turtle, currently classified as an endangered species. The Island is also used as a chemical munitions storage site.

The Island is inhabited with military personnel and civilian employees of DoD support contractors. The tour of duty for military personnel has generally run 1 to 2 years. Civilian personnel have generally been on the Island for longer periods of time (5 years but as many as 15 years or more). No children reside on the Island, although there is a potential for fetal exposures.

Site characterization. During the period from 1972 to 1977, JI was also used for temporary storage of Herbicide Orange (HO). A total of 1.37 million gallons of HO in 26,300 fifty-five gallon drums were transferred to JI from South Vietnam in 1972. The drums were stored on a 4-acre site on the northwest corner of the Island. The HO was successfully incinerated at sea in 1977. Corrosion of drums while in storage resulted in HO leakage at a rate of approximately 20 to 70 drums per week. Approximately 49,000 pounds of HO are estimated to have escaped into the environment annually during the storage period. The site is now contaminated with the active ingredients of HO: 2,3,7,8-tetrachloro-dibenzodioxin (TCDD); the n-butyl ester of 2,4-dichlorophenoxy acetic acid (2,4-D); and the n-butyl ester of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T).

For this risk assessment, the chemicals of primary concern are TCDD, 2,4-D, and 2,4,5-T. The site is bounded by a seawall to the west-northwest, an open area and storage area to the east-southeast, a roadway to the south, and several limited-use operations to the west: a transformer, beacon building, Hi-Vol sampler associated with JACADS, fire training area, and burn pit. Access to the site itself is restricted by a fence on all landlocked sides. Soil on the site is contaminated with the three chemicals of concern. Soil samples taken in 1986 contained surface residues of TCDD (nondetect at 0.1 ppb to 163 ppb), 2,4-D (2.5 to 281,330 ppb), and 2,4,5-T (53 to 237,155 ppb). Soil samples also contained subsurface residues of TCDD (nondetect to 510 ppb), 2,4-D (nondetect to 365,202 ppb), and 2,4,5-T (nondetect to 682,247 ppb). Measurement of these substances in air, groundwater, seawater, and sediments have not been conducted. Analysis of marine biota for TCDD has revealed residues ranging from nondetect to 472 ppb. Subsurface soil and marine biota samples were limited to the point of greatly confining the scope of the exposure and risk assessments.

Exposure assessment. The potential for exposure to TCDD, 2,4-D, and 2,4,5-T for persons engaged in activities proximal to the HO site is dependent on numerous factors including the physical setting of the site (i.e., climate, vegetation, soil type, and hydrology), as well as features of the potentially exposed populations. The frequency and duration of potential exposure depends on population demographics and human activities patterns associated with land-use around the site.

The site is currently not in use, is dormant, and has limited access by a surrounding fence. However, potential avenues of human exposure include volatilization of the contaminants into the air, suspension of particle-associated compounds into the air due to wind erosion, and consumption of edible marine life that have become contaminated in the waters adjacent to the site. For purposes of assessing current or "baseline" risk from exposures related to the HO site, only the air pathway was evaluated. Wind erosion was judged to be non-significant for the

undisturbed site, whereas, ingestion of contaminated marine biota, while considered plausible, could not be performed to due the lack of sufficient data.

For exposure through the air medium, important human activities include, but are not necessarily limited to, occupational operations associated with the seawall, the electrical transformer, the Hi-Vol sampler, the beacon building in the immediate area, the fire training area, the rip-rap area used as a boat-launch site, and the burn pit at an intermediate distance.

Two future scenarios that would alter exposure potential from that presented by current land conditions which were considered in this report are: (1) remediation through excavation; and (2) covering of the site with cement. For purposes of assessing potential inhalation exposures due to the release of particle-associated compounds resulting from future-use activities, emission rates were estimated for each activity (i.e., unloading and loading of contaminated soil, vehicular traffic, wind erosion) within each scenario (i.e., excavation or cement cover construction).

For both vapor-phase inhalation potentially occurring during the current scenario, as well as vapor-phase and particle-associated inhalation potentially occurring during the two future-use scenarios, exposure was estimated for the Theoretical Most Exposed Individual (TMEI), as well as an Alternate Most Exposed Individual (AMEI). The TMEI was assumed to have access to the entire perimeter of the HO site; whereas, the AMEI has access to only the fenceline (southern side of the site).

To estimate the air concentrations (g/m^3) of both vapor-phase and particle-associated TCDD, 2,4-D, and 2,4,5-T, a screening-level atmospheric dispersion modeling analysis was conducted to estimate one-hour, eight-hour, and annual average concentrations of these compounds around the perimeter of the HO site. These predicted air concentrations were then used to estimate inhalation exposures

and lifetime average and average daily absorbed doses to the TMEI and the AMEI. The estimated absorbed doses where then used to assess cancer and noncancer risks, respectively.

Toxicity assessment. For noncarcinogenic toxic endpoints, TCDD appears to be approximately seven orders of magnitude more potent than either 2,4-D or 2,4,5-T, with oral R_fD's of 1×10^{-9}, 1×10^{-2}, and 1×10^{-2}, respectively. The primary critical effect seen for TCDD was fetal survival and the secondary critical effect seen was renal damage. The primary critical effect seen for 2,4-D was renal damage and the secondary critical seen was hematologic and hepatic effects. The R_fD for 2,4-D was based on studies producing a medium level of confidence. For 2,4,5-T the primary critical effect was neonatal survival, and the secondary critical effect was increased urinary coproporphyrin excretion. The R_fD for this chemical was based on studies producing a medium level of confidence.

For both 2,4-D and 2,4,5-T an evaluation of their carcinogenicity cannot be made on the limited animal data available. TCDD is classified as a B1 carcinogen when associated with phenoxy herbicides and/or chlorophenols. In animal studies TCDD has been shown to be a potent carcinogen with an oral slope factor of 1.56×10^5 $(mg/kg/day)^{-1}$. Increased incidences of cancer have been observed in lungs, liver, hard palate, and nasal turbinates. Epidemiological studies have produced only a potential correlation of an increased risk of soft-tissue sarcomas for chemicals contaminated with TCDD.

Human health risk assessment. Characterization of risk based on the results of the exposure assessment for inhalation of vapor-phase TCDD revealed that current or baseline lifetime excess cancer risk associated with the undisturbed HO site was approximately 3×10^{-5} for both the TMEI and the AMEI. This is equivalent to 3 excess cancer cases occurring among 10,000 individuals exposed for a period of 25 years during their lifetime. TCDD-associated estimated cancer risks resulting from

excavation and cement cover construction activities were 8×10^{-7} and 2×10^{-7}, respectively, for both the TMEI and the AMEI. The magnitude of these cancer risk estimates are within the Superfund site remediation goals (i.e., cancer risk range of 10^{-4} to 10^{-7}); however, it is plausible that additional lifetime excess cancer risk may be present due to ingestion of contaminated marine biota. This exposure pathway has not been adequately characterized and was not included in the risk characterization.

For the current scenario, noncancer risks, as measured by hazard quotients from exposure of the TMEI to TCDD, 2,4-D, and 2,4,5-T, were 0.76, 0.0014, and 0.0015, respectively; whereas, the hazard quotients from exposure of the AMEI to TCDD, 2,4-D, and 2,4,5-T were 0.76, 0.00051, and 0.00095, respectively.

For the future excavation scenario, noncancer risks, as measured by the hazard quotients from exposure of the TMEI to TCDD, 2,4-D, and 2,4,5-T, were 0.52, 0.00090, and 0.0010, respectively; whereas, the hazard quotients from exposure of the AMEI to TCDD, 2,4-D, and 2,4,5-T were 0.52, 0.00034, and 0.00063, respectively.

For the future cement cover construction scenario, noncancer risks, as measured by the hazard quotients from exposure of the TMEI to TCDD, 2,4-D, and 2,4,5-T, were 0.25, 0.00045, and 0.00049, respectively; whereas the hazard quotients from exposure of the AMEI to TCDD, 2,4-D, and 2,4,5-T were 0.25, 0.00017, and 0.00031, respectively.

Similar to the cancer risk estimates for TCDD, these noncancer hazard quotients are within the Superfund site remediation goals (i.e., less than 1.0). However, noncancer risk resulting from ingestion of contaminated marine biota has not been evaluated.

Uncertainties associated with this analysis. There are several significant uncertainties associated with soil characterization, exposure assessment, and risk characterization. The two future-use scenarios, remedial excavation or surfacing with unknown pretreatment, are hypothetical and not necessarily reflective of actual future use. Many empirical and site-specific assumptions were made in the exposure assessment, including body weight, inhalation rate, pulmonary deposition rate, construction vehicle weight, number of wheels rolling over the site, duration of excavation, duration of the soil covering activity, physicochemical features of the soil, threshold wind velocity, diffusion and air-soil partition coefficients, and spatial distribution of 2,4-D and 2,4,5-T on the surface and in vertical profiles. In addition, other variables were unaccounted for in the analysis. They include population transience, male/female differences in exposure, presence of other isomers of dioxin and other chemicals on the Island and prior or concurrent exposures to them, atmospheric transformation and soil photodegradation of the chemicals of concern, groundwater contamination, and potential concurrent exposures from JACADS.

With regard to toxicity and dose-response parameters associated with the risk calculation, uncertainties include what is currently a rethinking of the mechanism of toxicity of TCDD in the scientific community (which would affect the benchmark toxicity value used in the risk calculation), medium levels of confidence in the R_fD values used, and the potential for sensitive individuals and those with preexisting morbidity to be exposed to chemicals at the HO site. In addition, the assumed periods of maximum exposure (25 years) and lifetime risk (70 years) may be incorrect. Lastly, synergistic or other toxicological phenomena caused by chemical interaction are unknown.

Ecological risk. A limited data base permitted only a preliminary ecological risk assessment. Sediment sampling indicates several locations of dioxin contamination. Among resident fish species sampled at the site, the crown squirrelfish had the highest dioxin levels in several samples (352 and 472 ppb).

These concentrations exceed levels reported to be associated with toxic effects in the rainbow trout. Further sampling of fish, invertebrates, birds, and sediments is needed to characterize the spatial pattern of contamination and to assess ecological risks.

Needs assessment. There is a fairly large uncertainty associated with the calculation of human health and ecological risks for the HO site because of a consistent lack of appropriate scientific information. It is recommended that uncertainty reduction be given a high priority in any future activities concerning HO site closure. With specific regard to the air component of the risk assessment, it is recommended that particulate and vapor-phase concentrations of TCDD, 2,4-D, and 2,4,5-T be conducted. Since ambient air concentrations of these chemicals is dependent on soil characteristics, it is recommended that additional soil sampling be performed to characterize soil moisture and organic content, particle size distribution, and spacial distributions of the chemical contaminants. Sediment and water sampling is recommended to determine which medium or media contain the potential source of the fish contamination. Further biological sampling is recommended to better characterize the potential for human exposure to contaminated fish, and (as a National Bird Sanctuary) the risks to the avian populations on the Atoll.

9.0 References

Abernathy, D.J., W.F. Greenlee, J.C. Hubard, and C.J. Boreiko. 1985. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) promotes the transformation of C3H/10T1/2 cells. *Carcinogenesis* 6:651-653.

Amerson, A.B., and P.C. Shelton. 1976. *The Natural History of Johnston Atoll, Central Pacific Ocean.* Atoll Research Bulletin No. 192. University of Kansas, Department of Systematics and Ecology, Lawrence, Kansas.

Anderson, D., and J.A. Styles. 1978. The bacterial mutation test. *Br. J. Cancer* 37:924-930.

Anderson, E., N. Browne, S. Duletsky, J. Ramig, and T. Warn. 1985. *Development of Statistical Distributions or Ranges of Standard Factors Used in Exposure Assessments. Final Report.* Report No. EPA/600/8-85/010, prepared by Technology Division, GCA Corporation, Chapel Hill, N.C. Washington, D.C.: U.S. Environmental Protection Agency, Office of Research and Development, Exposure Assessment Group. Available from National Technical Information Service, Springfield, Virginia, as PB85-242667.

ATSDR (Agency for Toxic Substances and Disease Registry). 1989. *Toxicological Profile for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin.* Report No. ATSDR/TP-88/23, prepared by Syracuse Research Corporation. Atlanta: Agency for Toxic Substances and Disease Registry. 138 pp. (available from National Technical Information Service, Springfield, Virginia, as PB89-214522).

Belton, T.J., R. Hazen, B.E. Ruppel, K. Lockwood, R. Mueller, E. Stevenson, and J.J. Post. 1985. *A Study of Dioxin (2,3,7,8-Tetrachlorodibenzo-p-Dioxin) Contamination in Select Finfish, Crustaceans and Sediments of New Jersey Waterways.* Office of Science and Research, New Jersey Department of Environmental Protection, Trenton, N.J.

Berry, D.L., J. DiGiovanni, M.R. Juchau, W.M. Bracken, G.L. Gleason, and T. J. Slaga. 1978. Lack of tumor-promoting ability of certain environmental chemicals in a two-stage system of mouse skin tumorigenesis: Potent anticarcinogenic effects. *Ann. N.Y. Acad. Sci.* 320:405-414.

Birnbaum, L.S., M.W. Harris, C.P. Miller, R.M. Pratt, and J.C. Lamb, IV. 1986. Synergistic interaction of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and hydrocortisone in the induction of cleft palate in mice. *Teratology* 33:29-35.

Branson, D.R., I.T. Takahashi, W.M. Parker, and G.E. Blau. 1985. Bioconcentration kinetics of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in rainbow trout. *Environ. Toxicol. Chem.* 4:779-788.

Braune, B.M., and R.J. Norstrom. 1989. Dynamics of organochlorine compounds in herring gulls: III. Tissue distribution and bioaccumulation in Lake Ontario gulls. *Environ. Toxicol. Chem.* 8:957-968.

Bronzetti, G., E. Zeiger, I. Lee, . . Suzuki, and H.V. Malling. 1983. Mutagenicity study of TCDD and ashes from urban incinerator "*in vitro*" and "*in vivo*" using yeast D7 strain. *Chemosphere* 12:549-553.

Channell, R.E., and T.L. Stoddart. 1984. *Herbicide Orange Monitoring Program: Interim Report, January 1980-December 1982.* Report No. ESL-TR-83-56. Engineering & Services Laboratory, Air Force Engineering & Services Center, Tyndall AFB, Florida. 58 pp.

Cope, O.B., E.M. Wood, and G.H. Wallen. 1970. Some chronic effects of 2,4-D on the bluegill (*Lepomis macrochirus*). *Trans. Am. Fish. Soc.* 99:1-12.

Courtney, K.D. 1976. Mouse teratology studies with chlorodibenzo-*p*-dioxins. *Bull. Environ. Contam. Toxicol.* 16(6):674-681.

Cowherd, C., Jr., G.E. Muleski, P.J. Englehart, and D.A. Gillette. 1985. *Rapid Assessment of Exposure to Particulate Emissions from Surface Contamination Sites.* Report No. EPA/600/8-85/002, prepared by Midwest Research Institute, Kansas City, Missouri. Washington, D.C.: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment. [159 pp.]

Crockett, A.B., A. Propp, and T. Kimes. 1986. *Soil Characterization of Former Herbicide Storage Site at Johnston Island.* Report No. ESL-TR-86-18 to U.S. Air Force Engineering and Services Center, Tyndall AFB, Florida. Idaho Falls: EG&G Idaho, Inc. 178 pp.

Dencker, L., and R.M. Pratt. 1981. Association between the presence of the Ah receptor in embryonic murine tissues and sensitivity to TCDD-induced cleft palate. *Terat. Carcinog. Mutag.* 1:399-406.

Dencker, L., E. Hassoun, R. D'Argy, and G. Alm. 1985. Fetal thymus organ culture as an *in vitro* model for the toxicity of 2,3,7,8-TCDD and its congeners. *Mol. Pharmacol.* 27:133-140.

Driver, J.H., G. Whitmyre, J.J. Konz, T.A. Roy, J.J. Yang, and A.J. Kreuger. 1990. Dermal exposure assessments for toxicants in soil: Soil adherence to skin and dermal bioavailability. In: *Total Exposure Assessment Methodology. A New Horizon.* Proceedings of the EPA/AandWMA Specialty Conference, November 1989, Las Vegas, Nevada.

Eisler, R. 1986. Dioxin hazards to fish, wildlife, and invertebrates: A synoptic review. *U.S. Fish Wildl. Serv. Biol. Rep.* 85(1.8).

Elliott, J.E., R.W. Butler, R.J. Norstrom, and P.E. Whitehead. 1989. Environmental contaminants and reproductive success of great blue herons *Ardea herodias* in British Columbia, 1986-87. *Environ. Pollut.* 59:91-114.

EPA (U.S. Environmental Protection Agency). 1977. *Compilation of Air Pollutant Emission Factors, 3rd ed. with Supplements 1-7. Parts A and B.* Report No. AP-42. Research Triangle Park, N.C.: U.S. Environmental Protection Agency, Office of Air and Waste Management and Office of Air Quality Planning and Standards. [477 pp.]

EPA (U.S. Environmental Protection Agency). 1979. *Water-Related Environmental Fate of 129 Priority Pollutants. Volume I.* Washington, D.C.: U.S. Environmental Protection Agency, Office of Water Planning and Standards. Report No. EPA-440/4-79-029a.

EPA (U.S. Environmental Protection Agency). 1983. *Methods for Assessing Exposure to Windblown Particulates.* Report No. EPA-600/4-83-007. Prepared by Enviro Control Division, Dynamac Corporation, for EPA Office of Solid Waste and Emergency Response. Washington, D.C.: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment. 65 pp.

EPA (U.S. Environmental Protection Agency). 1984. *Ambient Water Quality Criteria Document for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin.* Report No. EPA-440/5-84-007.

Washington, D.C.: U.S. Environmental Protection Agency, Office of Water Regulations and Standards.

EPA (U.S. Environmental Protection Agency). 1985. *Drinking Water Criteria Document for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin.* Report No. EPA 600/X-84-194-I. Cincinnati, Ohio: U.S. Environmental Protection Agency, Environmental Criteria and Assessment Office.

EPA (U.S. Environmental Protection Agency). 1987. *Industrial Source Complex (ISC) Dispersion Model User's Guide, Volumes 1 and 2,* 2nd ed. (revised). Report Nos. EPA-450/4-88-002a and 002b. Research Triangle Park, N.C.: U.S. Environmental Protection Agency.

EPA (U.S. Environmental Protection Agency). 1988a. *A Cancer Risk-Specific Dose Estimate for 2,3,7,8-TCDD.* Appendices A through F. Report No. EPA/600/6-88/007Ab (Draft). Washington, D.C.: U.S. Environmental Protection Agency, Office of Research and Development, Office of Health Effects Assessment.

EPA (U.S. Environmental Protection Agency). 1988b. *Estimating Exposures to 2,3,7,8-TCDD.* External review draft. Report No. EPA/600/6-88/005A. Washington, D.C.: Office of Health and Environmental Assessment. 368 pp.

EPA (U.S. Environmental Protection Agency). 1988c. *Superfund Exposure Assessment Manual.* Report No. EPA/540/1-88/001. Washington, D.C.: U.S. Environmental Protection Agency, Office of Remedial Response. 169 pp.

EPA (U.S. Environmental Protection Agency). 1989a. *Assessing Human Health Risks from Chemically Contaminated Fish and Shellfish: A Guidance Manual.* Report No. EPA-503/8-89-002. Washington, D.C.: U.S. Environmental Protection Agency, Office of Marine and Estuarine Protection and Office of Water Regulations and Standards. 136 pp.

EPA (U.S. Environmental Protection Agency). 1989b. *Exposure Factors Handbook.* Report No. EPA/600/8-89/043, prepared by Versar Inc., Springfield, Virginia. Washington, D.C.: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Exposure Assessment Group. [282 pp.]

EPA (U.S. Environmental Protection Agency). 1989c. *Risk Assessment Guidance for Superfund. Volume I. Human Health Evaluation Manual (Part A). Interim Final.* Report No. EPA/540/1-89-002. Washington, D.C.: U.S. Environmental Protection Agency, Office of Emergency and Remedial Response. [294 pp.]

EPA (U.S. Environmental Protection Agency). 1990. Background document to the integrated risk assessment for dioxins and furans from chlorine bleaching in pulp and

paper mills. Washington, D.C.: Office of Pesticides and Toxic Substances, Exposure Evaluation Division, Exposure Assessment Branch.

Fingerhut, M.A., W.E. Halperin, D.A. Marlow, L.A. Piagitelli, P.A. Honchar, M.H. Sweeney, A.L. Griefe, P.A. Dill, K. Steenland, and A.J. Suruda. 1991. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. *N. Eng. J. Med.* 324:212-218.

Forsell, D. 1987. Proposal for a Dioxin Sampling Program for Johnston Island, with cover letter to Elliott Eng, Chief, Ecology Function, U.S. Air Force Occupational & Environmental Health Laboratory, Brooks AFB, Texas. September 15, 1987. U.S. Department of the Interior, Fish and Wildlife Service. 5 pages.

Frank, R., A.G. Carpentier, and D.L. Mackenzie. 1987. Monitoring for 2,4-residues in fish species resident in treated lakes in east-central Ontario 1977-80. *Environ. Monit. Assess.* 9:71-82.

Fries, G.F., and G.S. Marrow. 1975. Retention and excretion of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin by rats. *J. Agric. Food Chem.* 23(2):265-269.

Gasiewicz, T.A., J.R. Olson, L.E. Geiger, and R.A. Neal. 1983a. Absorption, distribution and metabolism of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) in experimental animals. Pp. 495-525 in R.E. Tucker, A.L. Young, and A.P. Gray, Eds. *Human and Environmental Risk of Chlorinated Dioxins and Related Compounds.* New York: Plenum Press.

Gasiewicz, T.A., L. E. Geiger, G. Rucci, and R.A. Neal. 1983b. Distribution, excretion, and metabolism of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in C57BL/6J, DBA/2J, and B6D2F1/J mice. *Drug Metab. Dispos.* 11(5):397-403.

Geiger, L.E., and R.A. Neal. 1981. Mutagenicity testing of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in histidine auxotrophs of *Salmonella typhimurium*. *Toxicol. Appl. Pharmacol.* 59(1):125-129.

Gilbert, P., G. Saint-Ruf, F. Poncelet, and M. Mercier. 1980. Genetic effects of chlorinated anilines and azobenzenes on *Salmonella typhimurium*. *Arch. Environ. Contam. Toxicol.* 9(5):533-541.

Greig, J. 1984. Differences between skin and liver toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in mice. Pp. 391-397 in A. Poland and R.D. Kimbrough, Eds. *Biological Mechanisms of Dioxin Action.* Banbury Report 18. Cold Spring Harbor, New York: Cold Spring Harbor Laboratory.

Green, S., and F.S. Moreland. 1975. Cytogenetic evaluation of several dioxins in the rat. *Toxicol. Appl. Pharmacol.* 33:161.

Green, S., F.S. Morland, and C. Sheu. 1977. Cytogenic effect of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin on rat bone marrow cells. *FDA By-Lines* 6:292.

Hay, A. 1982. Toxicology of dioxins. Pp. 41-47 in *The Chemical Scythe: Lessons of 2,4,5-T and Dioxin.* New York, London: Plenum Press.

Helsel, R.W., J.N. Casanova, and R.W. Thomas. 1987. *Thermal Desorption / Ultraviolet Photolysis Process Research, Test and Evaluation Performed at Johnston Island for the USAF Installation Restoration Program, Vol. 1: Technical Report.* Final Report (July 1986 — August 1986) to Engineering & Services Laboratory, U.S. Air Force Engineering & Services Center, Tyndall Air Force Base, Florida, by EG&G Idaho, Idaho Falls. ESL Report No. TR-87-37, Vol. 1. Available from National Technical Information Service (NTIS), Springfield, Virginia, as AD-A195-595.

Holmes and Narver, Inc. 1990. RCRA B Permit Outline. Draft document. Honolulu: Holmes and Narver, Inc., Energy Support Division.

Holmes and Narver, Inc. 1989. Preliminary Assessment of Johnston Atoll. Report to U.S. Defense Nuclear Agency. Honolulu: Holmes and Narver, Inc. 61 pp.

Hussain, S., L. Ehrenberg, G. Lofroth, and T. Gejvail. 1972. Mutagenic effects of TCDD on bacterial systems. *Ambio* 1:32-33.

IARC (International Agency for Research on Cancer). 1977. *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man, Vol. 15.* Lyon, France: World Health Organization, International Agency for Research on Cancer.

IARC (International Agency for Research on Cancer. 1987. 2,4-D. Pp233-236 in *Genetic and Related Effects: An Updating of Selected IARC Monographs from Volumes 1 to 42. IARC Monographs of the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Supplement 6.* Lyon, France: World Health Organization, International Agency for Research on Cancer.

Irons, D.K., R.K. Kosaki, and J.D. Parrish. 1990. *Johnston Atoll Resource Survey: Final Report - Phase Six (21 Jul 89 - 20 Jul 90).* Report submitted by Hawaii Cooperative Fishery Research Unit, Honolulu, Hawaii, to U.S. Army Engineer District, Hononulu, Department of the Army, Fort Shafter, Hawaii. 59 pp.

Irwin, J. 1990. Internal memorandum to J. Tikvart, 19 June 1990. Research Triangle Park, N.C.: U.S. Environmental Protection Agency.