APPENDIX K: SUMMARY OF HUMAN HEALTH EFFECTS DATA FOR PARAQUAT

Tables from HED New Use Risk Assessment 2006

Table 3.1.a. Acute Toxicity Profile – Paraquat Dichloride

Guideline No.	Study Type [species]	MRID(s)	Results [a]	Toxicity Category
870.1100	Acute oral [rat]	00054573	LD50 = 189 (M) or 125 (F) mg/kg	II
870.1200	Acute dermal [rabbit]	00054574	LD50 = 174 mg/kg (M)	I
870.1300	Acute inhalation [rat]	00046105	LC50 = 1 µg/L (M/F)	I
870.2400	Acute eye irritation [rabbit]	00054575	Severe irritation	I
870.2500	Acute dermal irritation [rabbit]	00054576	Slight to severe irritation; PIS = 2.1	III
870.2600	Skin sensitization [guinea pig]	00155289	Negative	--

[a] The test material used in the acute inhalation study was crystalline paraquat dichloride. Purity was not specified, but the purity of crystalline paraquat dichloride used in other studies was 99.9%. The test material used in the other studies was paraquat dichloride in the form of ORTHO Paraquat Concentrate 3 (end use product containing 34.4% paraquat cation). Results are expressed in terms of paraquat dichloride rather than paraquat cation.

Table 3.1.b. Subchronic, Chronic and Other Toxicity Profile		
Guideline No./ Study Type	**MRID No. (year)/ Classification/Doses**	**Results**
870.3150 90-Day oral toxicity Beagle dog	MRID 00072416 (1981) Acceptable/guideline 0, 7, 20, 60, or 120 ppm (estimated to be 0, 0.2, 0.5, 1.5, and 3 mg/kg/day)	NOAEL = 0.5 mg/kg/day LOAEL = 1.5 mg/kg/day, based on increased lung weight and incidence of alveolitis in both sexes
870.3200 21-Day dermal toxicity New Zealand White rabbit	MRID # not provided (Accession # 260635) (1986) Acceptable/guideline 0, 0.50, 1.15, 2.60, or 6.00 mg/kg/day	Dermal NOAEL = 1.15 mg/kg/day. Dermal LOAEL = 2.60 mg/kg/day, based on small scabs at the treatment site in both sexes and epidermal erosis/ulceration, surface exudation, acanthosis, and/or inflammation in males Systemic NOAEL = 6 mg/kg/day Systemic LOAEL = not observed
870.3465 21-Day inhalation toxicity Sprague-Dawley rat	MRID 00113718 (1979) Acceptable/guideline 0, 0.012, 0.112, 0.487, and 1.280 µg/L	NOAEL = 0.012 µg/L. LOAEL = 0.112 µg/L, based on squamous keratinizing metaplasia and hyperplasia of the epithelium of the larynx.
870.3700a Prenatal developmental Wistar rat	MRID 00113714 (1978) (initial study) Acceptable/guideline 0, 1, 5, or 10 mg/kg/day	Maternal NOAEL = 1 mg/kg/day. Maternal LOAEL = 5 mg/kg/day, based on mortality, clinical signs of toxicity (piloerection, hunched posture, respiratory distress), microscopic lesions in the lungs and kidney, and decreased body weight gain (BWG). Developmental NOAEL = 1 mg/kg/day. Developmental LOAEL = 5 mg/kg/day, based on slightly decreased fetal body weights and on delayed ossification.
870.3700a Prenatal developmental Wistar rat	MRID 43964701 (1992) (subsequent study) Acceptable/guideline 0, 1, 3, or 8 mg/kg/day	Maternal NOAEL = 8 mg/kg/day (highest dose tested). Maternal LOAEL = not observed. Developmental NOAEL = 8 mg/kg/day (highest dose tested). Developmental LOAEL = not observed.

Table 3.1.b. Subchronic, Chronic and Other Toxicity Profile		
Guideline No./ Study Type	**MRID No. (year)/ Classification/Doses**	**Results**
870.3700a Prenatal developmental SPR Alderley Park mice	MRID 00096338 (1978) (initial study) Acceptable/guideline 0, 1, 5, or 10 mg/kg/day	Maternal NOAEL = 1 mg/kg/day. Maternal LOAEL = 5 mg/kg/day based on decreased body weight gains. Developmental NOAEL = 10 mg/kg/day. Developmental LOAEL = not observed.
870.3700a Prenatal developmental Crl:CD-1 (ICR) BR mice	MRID 43949902 (1992) (subsequent study) Acceptable/guideline 0, 7.5, 15, or 25 mg/kg/day	Maternal NOAEL =15 mg/kg/day. Maternal LOAEL = 25 mg/kg/day based on mortality, clinical signs of toxicity (piloerection, labored respiration, hunched posture, hypothermia, hypoactivity, and/or pale extremities and eyes), decreased body weights and body weight gains, increased lung weights, and gross lesions in the lung. Developmental NOAEL = 15 mg/kg/day. Developmental LOAEL = 25 mg/kg/day based on retardation of the skeleton and decreased fetal body weights.
870.3800 Reproduction and fertility effects (3-generation) Wistar rat	MRID 00126783, 00149748, and 00149749 (1982) Acceptable/guideline 0, 25, 75, or 150 ppm (approximately equivalent to 0, 1.25, 3.75, and 7.5 mg/kg/day)	NOAEL = 1.25 mg/kg/day LOAEL for parental toxicity = 3.75 mg/kg/day, based on increased incidences of alveolar histiocytes. Offspring NOAEL = 7.5 mg/kg/day. Offspring LOAEL = not observed. Reproductive NOAEL = 7.5 mg/kg/day. Reproductive LOAEL = not observed.
870.4100b Chronic toxicity Beagle dog	MRID 00132472 (1983) Acceptable/guideline 0/0, 0.45/0.48, 0.93/1.00, or 1.51/1.58 mg/kg/day in males/females	NOAEL = 0.45/0.48 mg/kg/day in males/females LOAEL = 0.93/1.00 mg/kg/day in males/females, based on increased severity of chronic pneumonitis and gross lung lesions in both sexes, and focal pulmonary granulomas in males
870.4200b Carcinogenicity mouse	MRID 00087924 (1981) Acceptable/guideline 0, 0 (two controls), 12.5, 37.5, or 100/125 ppm (estimated to be 0, 0, 1.9, 5.6, and 15.0/18.8 mg/kg/day)	NOAEL = 1.9 mg/kg/day. LOAEL = 5.6 mg/kg/day, based on decreased body weights and food consumption in females, and increased incidences of renal tubular necrosis, tubular dilatation, and interstitial nephritis in males No evidence of carcinogenicity

Table 3.1.b. Subchronic, Chronic and Other Toxicity Profile		
Guideline No./ Study Type	**MRID No. (year)/ Classification/Doses**	**Results**
870.4200b Carcinogenicity JCL:ICR mice	MRID 40202403 (1982) Acceptable/guideline 0, 2, 10, 30, or 100 ppm (estimated to be 0, 0.3, 1.5, 4.5, and 15 mg/kg/day)	NOAEL = 4.5 mg/kg/day. LOAEL = 15 mg/kg/day, based on mortality in females No evidence of carcinogenicity
870.4300 Chronic/Carcino-genicity Wistar rat	MRID 40218001 (1982) Acceptable/guideline 0, 6, 30, 100, or 300 ppm (equivalent to 0/0, 0.25/0.30, 1.26/1.50, 4.15/5.12, or 12.25/15.29 mg/kg/day in males/females)	NOAEL = 4.15/5.12 mg/kg/day (M/F) LOAEL = 12.25/15.29 mg/kg/day (M/F), based on mortality No evidence of carcinogenicity
870.4300 Chronic/Carcino-genicity Fischer 344 rat	MRIDs 00138637, 00153223, 40202401, 40202402, and 41317401 (1983) Acceptable/guideline 0, 0 (two controls), 25, 75, or 150 ppm (estimated to be 0, 0, 1.25, 3.75, or 7.5 mg/kg/day)	NOAEL = 1.25 mg/kg/day. LOAEL =3.75 mg/kg/day, based on ocular opacity in females corroborated by lenticular changes observed microscopically. No evidence of carcinogenicity
Gene Mutation 870.5100 Bacterial Gene Mutation	00100440 (1977) Unacceptable/guideline 1.0, 3.3, 10, 33, 100, 333, or 1000 μg/plate	There was no evidence of induced mutant colonies over background.
Gene Mutation 870.5100 Bacterial Gene Mutation	00100441 (1977) Acceptable/guideline 0.16, 0.8, 4, 20, 100, 500, 2500, or 5000 μg/plate	There was no evidence of induced mutant colonies over background.
Cytogenetics 870.5375 *In Vitro* Chromosome Aberration	00152692 (1985) Acceptable/guideline 0.75 to 3500 μg/mL	There was slight evidence of chromosome aberrations induced over background in the presence and absence of S9-activation

Table 3.1.b. Subchronic, Chronic and Other Toxicity Profile		
Guideline No./ Study Type	**MRID No. (year)/ Classification/Doses**	**Results**
Cytogenetics 870.5385 *In Vivo* Chromosome Aberration	40202405 (1987) Acceptable/guideline 15, 75, or 150 mg/kg (33% paraquat ion)	There was no evidence of chromosome aberration induced over background.
Other Effects 870.5550 Unscheduled DNA Synthesis	00152693 (1985) Acceptable/guideline 10^{-9}, 10^{-8}, 10^{-7}, 10^{-6}, 10^{-5}, 10^{-4}, 10^{-3}, or 10^{-2} M	There was no evidence that unscheduled DNA synthesis, as determined by radioactive tracer procedures [nuclear silver grain counts] was induced.
Other Effects 870.5550 Unscheduled DNA Synthesis	40202404 (1987) Acceptable/guideline 45, 75, or 120 mg/kg (33% paraquat ion)	There was no evidence that unscheduled DNA synthesis, as determined by radioactive tracer procedures [nuclear silver grain counts] was induced.
Other Effects 870.5450 Dominant Lethal Assay	00100442 (year not reported) Acceptable/guideline 0.04, 0.4, or 4 mg/kg/day (23.8% paraquat ion)	There was no time-related positive response of increased pre- or post-implantation loss compared to controls.
Other Effects 870.5915 *In Vivo* Sister Chromatid Exchange	00152695 (1985) Acceptable/guideline 1.2, 2.5, 12.4, 24.7, 124, 247, 1240, or 2470 µg/mL	There was a concentration-related positive response of SCE induced over background in the presence of S9-activation. A positive response of SCE induced over background was also observed in the absence of S9-activation; however, there was no clear dose-response.
Special studies Rhesus monkey and humans	MRIDs 00126096-00126099 (1982) Acceptable/non-guideline 607 µg intramuscular injection in monkeys or approximately 9 µg paraquat/cm^2 to the skin of humans (70.0 cm^2)	Monkeys eliminated 43.5-51.5% of the administered radioactivity in the urine within 24 hours after intramuscular injection and 52.3-72.3% within 7 days post-dose. Following dermal application to humans, total urinary excretion of the applied doses was 0.052-0.702% (corrected for incomplete urinary excretion with a rhesus monkey parenteral excretion factor of 58.6%). This result suggests that the compound is poorly absorbed through the skin in humans. Peak excretion occurred during the first 24 hours post-dose.