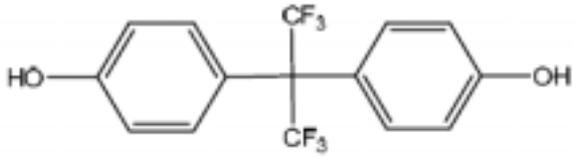


## Combined Repeated Dose Toxicity Study with the Reproduction/ Developmental Toxicity Screening Test(OECD TG422) -Data Sheet-

MITI No.	4-1335	CAS No.	1478-61-1
Test substance	Chemical name	: 4,4'-(1,1,1,3,3,3-Hexafluoropropane-2,2-diyl)diphenol	
	Synonym	: 4,4'-(Hexafluoroisopropylidene)diphenol	
	Molecular weight	: 366.23	
	Molecular formula	: C <sub>15</sub> H <sub>10</sub> F <sub>6</sub> O <sub>2</sub>	
	Structural formula	:	
			
Appearance	White powder		
Solubility	<2 wt% (in water, 100 degC, DuPont TI)		
Biodegradation	No data is available in the existing chemicals survey program.		
Bioconcentration	No data is available in the existing chemicals survey program.		
Purity	99.69%		
Range finding study	Dose level	0, 100, 400, (1,000→350) mg/kg/day	
	Dosing period	14 days	
	Results	<p>1,000→350 (Day 5 and thereafter): Killed in extremis (M 2/3), Found dead (F 1/3), Body weight ↓ (M, F), Food consumption ↓ (M, F), Water consumption ↑ (M, F), Clinical signs (tip toe gait, hunchback position, lethargy, emaciation, dehydration, diarrhea, piloerection, salivation, noisy respiration, staining around mouth or anogenital regions) (M, F), Atrophy of the spleen (M), Whiteish kidney, enlargement of the kidney and hydronephrosis (M), White patches in the forestomach epithelium, reddish urinary bladder, and atrophy of the seminal vesicle (M), Atrophy of the uterus (F)</p> <p>400: Body weight ↓ (M, F), Food consumption ↓ (M, F), Water consumption ↑ (M, F), Salivation (M, F), Distention of the gastrointestinal tract (F)</p> <p>100: Body weight ↓ (F), Food consumption ↓ (M, F), Water consumption ↑ (M), Salivation (M, F)</p> <p>Found dead/ killed in extremis 1,000→350: Distention of the gastrointestinal tract, brittle forestomach, dark red region of the granular gastric epithelium, small spleen, reddened pancreas, hydronephrosis, pallor of the kidney, thickened urinary bladder, white fluid-filled urinary bladder (M, F)</p>	
<b>Combined Repeated Dose Toxicity Study with the Reproduction/ Developmental Toxicity Screening Test(OECD TG422)</b>			
Experimental Method	Test animals	CrI:CD (SD) male and female rats, 9 weeks old (initiation of dosing)	
	Administration	Oral gavage    Vehicle: Arachis oil	
	Dose level	0, 30, 100, 300 mg/kg/day,    Recovery 0, 300 mg/kg/day (R300)	

	Dosing period	M: 42days F: 42 - 55 days (from 14 days before mating to day 4 of lactation)
Results of Repeated dose toxicity	Clinical signs	M: Salivation (30, 100, 300), Staining around mouth (30, 100, 300) F: Salivation (30, 100, 300), Staining around mouth (30, 100, 300), Staining anogenital region (300)
	FOB	M: NE F: NE
	Body weight	M: Body weight gain ↓ (100, 300) F: Body weight ↓ (300), Body weight gain ↓ (100)
	Food consumption	M: Food consumption ↓ (100, 300), Food efficiency ↓ (100, 300) F: Food consumption ↓ (30, 100, 300)
	Urinalysis	M: NE F: NE
	Hematology	M: RBC ↓ (300, R300), Hgb ↓ (300), RET ↓ (Day 14, 300), Hct ↓ (tendency) (300), MCV ↑ (R300), MCHC ↑ (R300) F: NE
	Blood chemistry	M: Alb ↓ (100, 300), ALT ↑ (100, 300), BUN ↑ (300), T-Cho ↓ (30, 100, 300) F: Alb ↓ (100, 300), A/G ↓ (100, 300), ALT ↑ (300), Cl ↓ (300), T-Cho ↓ (30, 100, 300)
	Organ weight	M: Liver R ↑ (300), Adrenal R ↑ (300, R300), Epididymides A,R ↓ (300), Testes A ↓ (300) F: NE
	Necropsy	M: Small seminal vesicle (300), Small prostate (300), Small testis (100, R300), Small epididymis (100, R300) F: NE
	Histopathology	M: Centrilobular hepatocyte enlargement (30, 100, 300), Basophilic tubules and tubular dilatation in the kidney (300), Decrease in incidence of cortical vacuolation in the adrenal (100, 300, R300), Decrease in incidence and grade of groups of alveolar macrophages in the lung (300), Leydig cell atrophy in the testis (300), Reduced secretory content and smaller size of the seminal vesicle and coagulating gland (100, 300, R300), Reduced secretory content and smaller size of the prostate (100, 300), Tubuloalveolar differentiation of mammary gland (30, 100, 300, R300), Decrease in incidence and grade of vacuolation of pars anterior cells in the pituitary (300, R300) F: Centrilobular hepatocyte enlargement (100, 300), Decrease in incidence and grade of groups of alveolar macrophages in the lung (100, 300), Glandular hyperplasia in the mammary gland (300), Follicular cyst in the ovary (300, R300)
	Target organ	Testis, Seminal vesicle, Prostate, Mammary gland
Results of Reproduction and developmental toxicity	Parent	M: Fertility ↓ (30, 100, 300) F: Irregular estrus cycle (300), Gestation index ↓ (30, 100, 300)
	Offspring	NE
NOAEL		Repeated dose toxicity: M less than 30, F 30 Reproductive and developmental toxicity: less than 30
	Basis for NOAEL	Repeated dose toxicity: M 30: Tubuloalveolar differentiation of mammary gland F 100: Body weight gain ↓  Reproductive and developmental toxicity: M 30: Fertility ↓ F 30: Gestation index ↓

NOEL		Repeated dose toxicity: M less than 30, F less than 30 Reproductive and developmental toxicity: less than 30
	Basis for NOEL	Repeated dose toxicity: M 30: Centrilobular hepatocyte enlargement, Tubuloalveolar differentiation of mammary gland F 30: Food consumption ↓, T-Cho ↓  Reproductive and developmental toxicity: M 30: Fertility ↓ F 30: Gestation index ↓
Note		

↑; increase, ↓; decrease

M; male, F; female

A; absolute organ weight, R; relative organ weight

**The data was reviewed by Hazard-Data Evaluation Committee of National Institute of Technology and Evaluation in fiscal 2010.**