	Grouping	Ref.	OECD TG (level)	Lines of evidence	Species	Exposure weeks	Route of Exposure	Effect dose	Tested doses	MTD	Observed effect (+ and -)	Assessment of each line of evidence	Assessment of the integrated line of evidence	Modality
Evidence of general toxicity		[redacted] 1998b	OECD 408 (level 4)	Liver weight	Rat	13 weeks (+ 4 weeks recovery)	Oral	5000, 20000 ppm	0, 50, 200, 5000, 20000 ppm	>20000 ppm	Statistically significant increase in absolute and relative liver weight.	The liver was identified as a target organ following repeated exposure with liver enzyme induction and severe liver toxicity. Hepatocellular adenoma has been observed in rats and mice and hepatocellular carcinoma and hepatoblastoma in mice in the presence of high liver toxicity, including cell damage and hypertrophy. Additional in vitro and in vivo mechanistic studies studies in rats and mice demonstrated that benthiavalicarb-isopropyl is not a tumour initiator but acts as a tumour promoter mediated by the activation of CAR/PXR.	/	/
		[redacted] 2001a	OECD 453 (level 4)		Rat	104 weeks	Oral	5000, 10000 ppm	0, 50, 200, 5000, 10000 ppm	5000 ppm	Statistically significant increase in absolute and relative liver weight in males and females at 5000 and 10000 ppm at all sacrifice times.			
		[redacted], 2002c			Rat	8 weeks	Oral	10000 ppm	0, 200, 10000 ppm		Statistically significant increase in absolute and relative liver weight at 10000 ppm after 8 weeks.			
		[redacted], 2002a			Rat	2 weeks	Oral	10000 ppm	0, 200, 10000 ppm		Statistically significant increase in absolute and relative liver weight at 10000 ppm after 2 weeks.			
		[redacted], 1999	OECD 416 (level 4)		Rat	2-gen reprotox	Oral	1000, 10000 ppm	0, 100, 1000, 10000 ppm		Statistically significant increase in relative and absolute liver weight in males and females at 10000 ppm and in relative liver weight in males at 1000 ppm of the F0 generation. Statistically significant increase in absolute and relative liver weight in males and females at 10000 ppm of the F1 and F2 generation.			
		[redacted] 2004	OECD 414 (level 4)		Rat	GD5-19	Oral	1000 mg/kg bw/day	0, 10, 100, 1000 mg/kg bw/day		Statistically significant increase in relative weight at 1000 mg/kg bw/day.			
		[redacted] 2000a	OECD 414 (level 4)		Rat	GD7-19	Oral		0, 10, 100, 1000 mg/kg bw/day		Statistically significant increase in absolute and relative liver weight at 1000 mg/kg bw/day.			
		[redacted] 1998a	~ OECD 408 (level 4)		Mouse	13 weeks	Oral	7000, 20000 ppm	0, 50, 200, 7000, 20000 ppm	7000 ppm	Statistically significant increase in absolute and relative liver weight.			
		[redacted] 2001b	OECD 451 (level 4)		Mouse	104 weeks	Oral	2500, 5000 ppm	0, 20, 100, 2500, 5000 ppm	≥2500 ppm	Statistically significant increase in absolute and relative liver weight in males and females at 2500 and 5000 ppm.			
		[redacted], 2002b			Mouse	2 weeks	Oral	5000 ppm	0, 100, 5000 ppm		Statistically significant increase in absolute and relative liver weight at 5000 ppm after 1 and 2 weeks.			
		[redacted], 2018a			Mouse	4 weeks	Oral		0, 500, 5000 ppm		Statistically significant increase in absolute and relative liver weight at 5000 ppm after 1 and 4 weeks.			
		[redacted] 2000b	OECD 414 (level 4)		Rabbit	GD6-28	Oral	40 mg/kg/day	0, 10, 20, 40 mg/kg bw/day		Statistically significant increase in relative liver weight at 40 mg/kg bw/day.			
		[redacted], 1998	~ OECD 407 (level 4)		Dog	4 weeks	Oral	300 and 1000 mg/kg bw/day	0, 100, 300, 1000 mg/kg bw/day		Increase in absolute and relative liver weight.			
		[redacted] 1999	OECD 409 (level 4)		Dog	13 weeks	Oral	200 and 1000 mg/kg bw/day	0, 40, 200, 1000 mg/kg bw/day	>1000 mg/kg bw	Statistically significant increase in absolute liver weight in males and females at 1000 mg/kg bw/day. Statistically significant increase in relative liver weight in males at 1000 mg/kg bw/day and in females at 200 and 1000 mg/kg bw/day.			
		[redacted] 2001	OECD 452 (level 4)		Dog	52 weeks	Oral	400 mg/kg bw/day	0, 4, 40, 400 mg/kg bw/day	>400 mg/kg bw	Statistically significant increase in absolute liver weight in males and females at 400 mg/kg bw/day but not in relative liver weight.			
		[redacted] 1998b	OECD 408 (level 4)	Liver histopathology	Rat	13 weeks (+ 4 weeks recovery)	Oral	20000 ppm	0, 50, 200, 5000, 20000 ppm	>20000 ppm	Statistically significant increase in hepatocytic hypertrophy.			/
		[redacted] 2001a	OECD 453 (level 4)		Rat	104 weeks	Oral	5000, 10000 ppm	0, 50, 200, 5000, 10000 ppm	5000 ppm	Statistically significant increase in hepatocellular adenoma in males at 10000 ppm after 104 weeks. Statistically significant increase in spongiosis hepatitis, hepatocytic hypertrophy and foci of cellular alteration in males and fatty change, hepatocytic hypertrophy and bile duct proliferation in females at 5000 and/or 10000 ppm after 104 weeks.			
		[redacted], 1999	OECD 416 (level 4)		Rat	2-gen reprotox	Oral	10000 ppm	0, 100, 1000, 10000 ppm		Hepatocellular hypertrophy at 10000 ppm in males and females of F0 and F1 generations.			
		[redacted], 2018a			Mouse	4 weeks	Oral	500, 5000 ppm	0, 500, 5000 ppm		Statistically significant increase in the activity of T4 glucuronidation at 500 and 5000 ppm after 4 weeks.			
		[redacted] 1998a	~ OECD 408 (level 4)		Mouse	13 weeks	Oral	7000 and 20000 ppm	0, 50, 200, 7000, 20000 ppm	7000 ppm	Statistically significant increase in anisonucleosis (males), fatty change (males), hepatocytic hypertropphy (males and females), multinucleated giant cells (males), single cell necrosis (males and females) and bile duct proliferation (males and females).			
		[redacted] 2001b	OECD 451 (level 4)		Mouse	104 weeks	Oral	2500, 5000 ppm	0, 20, 100, 2500, 5000 ppm	2500 ppm	Statistically significant increase in the incidence of hepatocellular adenoma and carcinoma and hepatoblastoma in males and hepatocellular adenoma in females at 2500 and 5000 ppm after 104 weeks. Statistically significant increase in anisonucleosis, fatty change, hepatocytic hypertrophy, multinucleated cells, necrosis and foci of cellular alteration in males and anisonucleosis, fatty change, hepatocytic hypertrophy and necrosis in females at 2500 and/or 5000 ppm.			
		[redacted], 1998	~ OECD 407 (level 4)		Dog	4 weeks	Oral	1000 mg/kg bw/day	0, 100, 300, 1000 mg/kg bw/day		Hepatocytic hypertrophy.			
		[redacted] 1999	OECD 409 (level 4)		Dog	13 weeks	Oral	1000 mg/kg bw/day	0, 40, 200, 1000 mg/kg bw/day	>1000 mg/kg bw	Hepatocytic hypertrophy and pigment deposition in males and females.			

		[redacted] 2001	OECD 452 (level 4)		Dog	52 weeks	Oral	/	0, 4, 40, 400 mg/kg bw/day	>400 mg/kg bw	No substance related effect at any of the doses tested.			
		[redacted] 1998b	OECD 408 (level 4)	Kidney weight	Rat	13 weeks (+ 4 weeks recovery)	Oral	5000 and 20000 ppm	0, 50, 200, 5000, 20000 ppm	>20000 ppm	Statistically significant increase in absolute kidney weight in females at 5000 and 20000 ppm and statistically significant increase in relative kidney weight in males at 20000 ppm.	No consistent effect on kidney weight after repeated exposure.	/	/
		[redacted] 2001a	OECD 453 (level 4)		Rat	104 weeks	Oral	5000, 10000 ppm	0, 50, 200, 5000, 10000 ppm	5000 ppm	Statistically significant increase in absolute and relative kidney weight in males and females at 5000 and 10000 ppm at all sacrifice times.			
		[redacted], 1999	OECD 416 (level 4)		Rat	2-gen reprotox	Oral	1000, 10000 ppm	0, 100, 1000, 10000 ppm		Statistically significant increase in absolute and relative kidney weight in females of the F0 generation at 1000 ppm without dose effect relationship. Statistically significant increase in relative kidney weight in males of the F1 generation at 10000 ppm.			
		[redacted] 2000a	OECD 414 (level 4)		Rat	GD7-19	Oral		0, 10, 100, 1000 mg/kg bw/day		No substance related effect at any of the doses tested.			
		[redacted] 1998a	~ OECD 408 (level 4)		Mouse	13 weeks	Oral	7000 and 20000 ppm	0, 50, 200, 7000, 20000 ppm	7000 ppm	Statistically significant decrease in absolute kidney weight at 7000 ppm (males) and 20000 ppm (males and females).			
		[redacted] 2001b	OECD 451 (level 4)		Mouse	104 weeks	Oral	2500, 5000 ppm	0, 20, 100, 2500, 5000 ppm	≥2500 ppm	Statistically significant decrease in absolute kidney weight in males and increase in females at 2500 and 5000 ppm after 104 weeks. No effect on relative kidney weight.			
		[redacted] 2000b	OECD 414 (level 4)		Rabbit	GD6-28	Oral	/	0, 10, 20, 40 mg/kg bw/day		No substance related effect on absolute and relative kidney weight at any of the doses tested.			
		[redacted], 1998	~ OECD 407 (level 4)		Dog	4 weeks	Oral	/	0, 100, 300, 1000 mg/kg bw/day		No substance related effect on absolute and relative kidney weight at any of the doses tested.			
		[redacted] 1999	OECD 409 (level 4)		Dog	13 weeks	Oral	1000 mg/kg bw/day	0, 40, 200, 1000 mg/kg bw/day	>1000 mg/kg bw	No substance related effect on absolute kidney weight at any of the doses tested. Statistically significant increase in relative kidney weight in males at 1000 mg/kg bw/day.			
		[redacted] 2001	OECD 452 (level 4)		Dog	52 weeks	Oral	/	0, 4, 40, 400 mg/kg bw/day	>400 mg/kg bw	No substance related effect on absolute and relative kidney weight at any of the doses tested.			
		[redacted] 1998b	OECD 408 (level 4)	Kidney histopathology	Rat	13 weeks (+ 4 weeks recovery)	Oral	/	0, 50, 200, 5000, 20000 ppm	>20000 ppm	No substance related effect at any of the doses tested.	Severe kidney pathology in the rat at and beyond the MTD after long term exposure.	/	/
		[redacted] 2001a	OECD 453 (level 4)		Rat	104 weeks	Oral	5000, 10000 ppm	0, 50, 200, 5000, 10000 ppm	5000 ppm	Statistically significant increase in calculus, chronic nephropathy, dilated tubules, hyaline droplets, fibrosis and transitional cell hyperplasia in males and glomerulosclerosis, calculus, hyaline casts, pigment deposition, hyaline droplets and lymphocyte infiltration in females at 5000 and/or 10000 ppm after 104 weeks.			
		[redacted], 1999	OECD 416 (level 4)		Rat	2-gen reprotox	Oral	/	0, 100, 1000, 10000 ppm		No substance related effect at any of the doses tested.			
		[redacted] 1998a	OECD 408 (level 4)		Mouse	13 weeks	Oral	/	0, 50, 200, 7000, 20000 ppm	7000 ppm	No substance related effect at any of the doses tested.			
		[redacted] 2001b	OECD 451 (level 4)		Mouse	104 weeks	Oral	/	0, 20, 100, 2500, 5000 ppm	2500 ppm	No substance related effect at any of the doses tested.			
		[redacted], 1998	~ OECD 407 (level 4)		Dog	4 weeks	Oral	/	0, 100, 300, 1000 mg/kg bw/day		No substance related effect at any of the dose levels tested.			
		[redacted] 1999	OECD 409 (level 4)		Dog	13 weeks	Oral	/	0, 40, 200, 1000 mg/kg bw/day	>1000 mg/kg bw	No substance related effect at any of the doses tested.			
		[redacted] 2001	OECD 452 (level 4)		Dog	52 weeks	Oral	/	0, 4, 40, 400 mg/kg bw/day	>400 mg/kg bw	No substance related effect at any of the doses tested.			
		[redacted] 2001a	OECD 453 (level 4)	Uterine histopathology	Rat	104 weeks	Oral	5000, 10000 ppm	0, 50, 200, 5000, 10000 ppm	≥5000 ppm	Statistically significant increase in uterus adenocarcinoma in females at 5000 and 10000 ppm. No substance related increase in pre-neoplastic or inflammatory lesions.	Adenocarcinoma of the uterus in the rat at and beyond the MTD without any non-neoplastic and pre-neoplastic pathology in the uterus. A MOA based on endocrine modulation (e.g. E/P ratio increase) could not be demonstrated. Other MOAs based on inflammation, oxidative stress and mutagenesis could be excluded with confidence.		