1 物質番号

通し番号	C-1001
整理番号	1
MITI番号	
CAS番号	51-03-6
物質名	ピペロニルブトキシド
英名	Piperonyl butoxide

2 発がん性分類

機関名	分類結果	評価年	評価書引用文献
IARC	3	1987	●National Technical Information service (1968) Evaluation of carcinogenic, Teratogenic and mutagenic Activities of selected pesticides and Industrial Chemicals, Vol. 1, Carcinogenic study (PB－223159) ●National cancer Institute (1979) Bioassay of Piperonyl Butoxide for possible carcinogenicity (Tech. Rep. ser. NO. 120; DHEW publ No.(NIH)79－1375) ●Sarles, M.P. & vandegrift, W.B. (1952) chronic oral toxicity and related studies on anlmals with the insecticide and pyrethrum synergist, piperonyl butoxide.Am. J. trop. Med. Hyg., 1, 862－883 ●Epstein, SS. Joshi, S., Andrea, J, Clapp, P., Falk, H. & Mantel, N. (1967) synergistic toxicity and carcinogenicity of 'Freons' and piperonyl butoxide. Nature, 214, 526-528
EPA	×	－	－
NTP	×	－	－
ACGIH	×	－	－
産衛学会	×	－	－
EU	×	－	－

3 発がん性に関する追加文献（動物試験、疫学調査）

追加文献の有無	有

（1）動物試験

#1	試験概要	試験物質		試験の種類	ガイドライン	GLP適用状況	試験実施年	試験実施者
				chronic test			1997	Tokyo Metropolitan Research Laboratory of Public Health
	試験条件	動物種	系統	動物数/性別/群	投与経路	用量/濃度	単位	投与/暴露期間
		mouse	Crj:CD-1	control：52(M)/51(F), 0.6%diet：53(M)/52(F), 1.2%diet：100(M)/106(F)	feeding	0, 0.6, 1.2	%	52 weeks
	試験結果概要	発がん影響	Hepatocellular adenomas and carcinomas were induced by piperonyl butoxide-treatment in a dose-related manner in males, with a 5-fold increase with a doubling of the dose, while they were found only in the 1.2% group of females. A sex difference was observed in hepatocarcinogenicity with females being less sensitive to piperonyl butoxide than males.				
		非発がん影響	Kidneys were black-colored in several treated male mice and were dose-dependent. Edema and hemorrhage of ovary were observed in all groups of female mice. Hemorrhages in many organs were found especially in the dead male mice of the 1.2% group.				
		結論	Piperonyl butoxide is a hepatocarcinogen to mice.				
	文献名	O. Takahashi , S. Oishi, T. Fujitani, T. Tanaka, M. Yoneyama , ″Chronic toxicity studies of piperonyl butoxide in CD-1 mice:Induction of hepatocellular carcinoma″ Toxicology 124 (1997) 95-103						

#2

試験概要	試験物質		試験の種類	ガイドライン	GLP適用状況	試験実施年	試験実施者
			chronic toxicity study			1994	Tokyo Metropolitan Research Laboratory of Public Health

試験条件	動物種	系統	動物数/性別/群	投与経路	用量/濃度	単位	投与/暴露期間
	mouse	Crj:CD-1	male control:52, 0.6%diet:53, 1.2%diet:100	diet	0, 0.6, 1.2	%	12 months

試験結果概要	
発がん影響	Hepatocellular carcinoma was induced in treated groups in a dose-deoendant manner but not in the control groups. The incidences of hepatocellular carcinoma were 11.3 and 52.0% in mice given 0.6 and 1.2% piperonyl butoxide, indicating that piperonyl butoxide can cause hepatocellular carcinoma in mice .
非発がん影響	
結論	In conclusion, the present results clearly indicate that Piperonyl butoxide can induce hepatocellular carcinoma in mice.

文献名	
	Takahashi O, Oishi S, Fujitani T, Tanaka T, Yoneyama M "Piperonyl butoxide induces hepatocellular carcinoma in male CD-1 mice." Arch Toxicol. 1994;68(7):467-9.

#3

試験概要	試験物質		試験の種類	ガイドライン	GLP適用状況	試験実施年	試験実施者
			chronic toxicity study			1994	Tokyo Metropolitan Research Laboratory of Public Health

試験条件	動物種	系統	動物数/性別/群	投与経路	用量/濃度	単位	投与/暴露期間
	rat	F344	30 animals/dose/sex, 2.4%: 33 animals/sex	diet	0, 0.6, 1.2, 2.4	%	nearly 2 years

試験結果概要	
発がん影響	Piperonyl butoxide induced hepatocellular carcinoma in both sexes in a dose-dependent manner. Hepatocellular carcinoma was found even in the 1.2% treated male group (incidence, 26.7%), and incidences in the 2.4% groups of males and females were 80.0 and 57.7% respectively of all those surviving. Piperonyl butoxide also caused essential thrombocythemia with a dose-response relationship.
非発がん影響	Beginning at about 40 weeks, 10 rats in the 1.2% treated male group died due to cecal hemorrhages. Piperonyl butoxide also caused essential thrombocythemia with a dose-response relationship. Hemorrhages in stomach and cecum, anemia, degenerative lesions of alveoli, and nephrotoxicity were also observed related to exposure.
結論	These results indicate that piperonyl butoxide is a hepatocarcinogen to the rat.

文献名	
	Takahashi O, Oishi S, Fujitani T, Tanaka T, Yoneyama M. "Chronic toxicity studies of piperonyl butoxide in F344 rats: induction of hepatocellular carcinoma." Fundam Appl Toxicol. 1994 Feb;22(2):293-303.

#4

試験概要	試験物質		試験の種類	ガイドライン	GLP適用状況	試験実施年	試験実施者
			Carcinogenicity Studies			1979	

試験条件	動物種	系統	動物数/性別/群	投与経路	用量/濃度	単位	投与/暴露期間
	rat	F344	control：20 animals/sex, 50 animals/dose/sex	feeding	5000, 10000	ppm	2 years

試験結果概要	
発がん影響	Although a statistically significant dose-related increase in the incidence of lymphoreticular neoplasia was associated with administration of the compound to females, the incidence of that class of neoplasm was higher in control males than in treated males.
非発がん影響	
結論	The finding of statistical significance in one sex is not considered by itself to constitute sufficient evidence of a biologic effect to justify an indictment of carcinogenic action.

文献名	
	Carcinogenesis bioassay of technical-grade piperonyl butoxide in F344 rats. Cardy RH, Renne RA, Warner JW, Cypher RL J Natl Cancer Inst. 1979 Mar;62(3):569-78

#5

試験概要	試験物質		試験の種類	ガイドライン	GLP適用状況	試験実施年	試験実施者
			Combined Chronic Toxicity / Carcinogenicity		yes	1998	Bio-Research Ltd Laboratory

試験条件	動物種	系統	動物数/性別/群	投与経路	用量/濃度	単位	投与/暴露期間
	rat	Sprague-Dawley	60/sex/dose	feeding	0, 30, 100, 500	mg/kg/day	104/105weeks

試験結果概要	
発がん影響	There was no increased incidence of neoplasia at any site.
非発がん影響	There was increased liver weights at 100 and 500 mg/kg/day associated with hepatocyte hypertrophy in both male and female rats. Hypertrophy and hyperplasia of thyroid follicles was observed at 500 mg/kg/day in both sexes
結論	There was no increased incidence of neoplasia at any site.

文献名	
	Butler WH, Gabriel KL, Osimitz TG, Preiss FJ. "Oncogenicity studies of piperonyl butoxide in rats and mice." Hum Exp Toxicol. 1998 Jun;17(6):323-30

#6	試験概要	試験物質		試験の種類	ガイドライン	GLP適用状況	試験実施年	試験実施者
				Carcinogenicity Studies		yes	1998	Bushy Run Research Center,
	試験条件	動物種	系統	動物数/性別/群	投与経路	用量/濃度	単位	投与/暴露期間
		mouse	CD1	60/sex/dose	feeding	0, 30, 100, 300	mg/kg/day	78weeks
	試験結果概要	発がん影響	At termination of the study in the mouse there was evidence of increased liver weights and an increased incidence of eosinophilic adenomas at 100 and 300 mg/kg/day in males and 300 mg/kg/day in females.					
		非発がん影響						
		結論	The observations reflect the expected changes related to the induction of the mixed function oxygenase group of enzymes. In the mouse the increased incidence of eosinophilic adenomas is not considered relevant for human risk evaluation.					
	文献名	Butler WH, Gabriel KL, Osimitz TG, Preiss FJ. "Oncogenicity studies of piperonyl butoxide in rats and mice." Hum Exp Toxicol. 1998 Jun;17(6):323-30						
#7	試験概要	試験物質		試験の種類	ガイドライン	GLP適用状況	試験実施年	試験実施者
		Technical-grade BP		Carcinogenicity Studies			1985	National Institute of Hyginic Sciences
	試験条件	rat	F344	46-49 animals/dose/sex	diet	0, 0.5, 1	%	2 years
	試験結果概要	発がん影響	Various tumours were detected in all groups, including the untreated control group, but no significant dose-related increase in the incidence of any tumour was found.					
		非発がん影響	Ileocaecal ulcers were found in animals of both sexes in both experimental groups and the incidence was dose related.					
		結論	It is concluded that under these experimental conditions piperonyl butoxide was not carcinogenic in F344 rats.					
	文献名	Maekawa A, Onodera H, Furuta K, Tanigawa H, Ogiu T, Hayashi Y. "Lack of evidence of carcinogenicity of technical-grade piperonyl butoxide in F344 rats: selective induction of ileocaecal ulcers." Food Chem Toxicol. 1985 Jul;23(7):675-82.						

#8	試験概要	試験物質		試験の種類	ガイドライン	GLP適用状況	試験実施年	試験実施者
				combined chronic/carcinogenic study				
	試験条件	動物種	系統	動物数/性別/群	投与経路	用量/濃度	単位	投与/暴露期間
		rat and mouse						
	試験結果概要	発がん影響	In a combined chronic/carcinogenic study in rats, positive carcinogenic effects were reported at doses where a high incidence of ileocecal ulcers were noticed in test mammals. Liver adenomas and carcinomas were reported in Fischer 344 rats only when tested at very high doses. A slight increase in thyroid follicular cell tumors was reported in Sprague-Dawley rats. A slight increase in thyroid follicular cell tumors was reported in Sprague-Dawley rats. A 1979 National Toxicology Program (NTP) study reported negative effects for carcinogenicity in the same strain of rats and in B6C3F1 mice. In CD-1 mice, PBO tested positive for liver tumor effects.(EPA REDより引用)					
		非発がん影響						
		結論	PBO is classified as a Group C –possible human carcinogen(EPA REDより引用)					
	文献名	EPA RED						

(2)疫学調査

#1	調査の種類	調査方法	結果の概要	調査実施年	調査実施者
	文献名				