15-2. ジイソプロピルナフタレンの催奇形性試験

LPT Report No. 7252/92 "Examination of the influence of di-isopropyl naphthalene(KMC) on the pregnant rat and the fetus by oral administration" (1993)

Type	:	Two generation study
Species	:	rat
Sex	:	gavage
Strain	:	Sprague-Daeley
Route of admin.	:	gavage
Exposure period	:	Day 6 to 15 of gestation
Frequency of treatm.	:	Once Daily
Duration of test	:	3 month
Doses	:	0, 100, 250, 625 mg/kg/d
Control group	:	yes, concurrent vehicle
NOEL	:	= 100 mg/kg bw
Method	:	OECD Test-Guideline 414 "Teratogenicity"
Year	:	1993
GLP	:	yes

This study was conducted according to OECD and GLP guidelines.

In this study, the developmental toxicity of Di-isopropyl Naphahalene (DIPN) was evaluated in rats. Pregnant rats were given DIPN at 0, 100, 250, 625 mg/kg b.w. /day by gavage on days 6-15 of pregnancy.

No substance-related mortality was observed.

No clinical signs were observed in the substance-treated dams.

Body weight remained within the normal range at 100 mg, 250 mg and 625 mg DIPN /kg b.w. by gavage, body weight gain was not influenced at 100mg/kg b.w., either. Body weight gain was dose-related slightly to moderately inhibited between gestation days 6 and 9 in the intermediate- and high- dosed dams (250 mg and 625 mg/kg b.w., respectively). Differences from the controls were ~26% at the intermediate and ~70% at the highest dose, however, the results were not significantly different from the control at $p \leqq 0.01$. On the other hand there was an increase in body weight gain between the 12^{th} and 15^{th} day of pregnancy (+34% significant at $p \leqq 0.01$) but at the end of the study (20^{th} day of pregnancy) the net body weight change was lower in the controls. (Figure 1)

The food consumption was not impaired at DIPN dose of 100mg/kg b.w., by gavage. Food consumption showed a transient slight but significant reduction ($p \leqq 0.01$) at 250 mg/kg b.w. from the 6^{th} to 9^{th} gestation day (approx. ~15%). Decreased food consumption was dose-related more distinct and lasted for longer period at 625 mg/kg b.w.: the significant (at $p \leqq 0.01$) differences from the control were approx. ~34% (6^{th} to 9^{th} gestation day) and approx ~7% (12^{th} to 15^{th} gestation day). (Figure 2)

Treatment did not influence drinking-water consumption.

No substance related pathological changes were detected at autopsy.

No distinct influence on the prenatal development was detected. (Table 7-10)

The fetal incidence at the retardations seemed to be very slightly increased at the skeletal examination (staining of the skeleton according to DAWSON's method) for the intermediate and high dose-level groups, however, no significance was determined. All other fetal parameters were within the normal range of the control group.(Table 13)

External macroscopic inspection and examination of soft tissue (WILSON's method) revealed no substance-related variations and/or retardations.(Table 14)

A few malformed fetuses were detected in the control and substance-treated groups, all these malformation – in form of encephalocele, stump tail, crossed-legs, shifted and fused dorsal, lumber and coccygel vertebrae, cleft palate – possibly belong to the spontaneous range with reference to their type and number. There was no difference in their type and number. There was no difference in incidence and type between treated and untreated groups. (Table 11-12)

Under the present test conditions, the no-observed–effect level (NOEL) for the dams and for the fetal organism was 100mg DIPN/kg b.w., by gavage (treatment from the 6^{th} to 15^{th} day of pregnancy). 250mg/kg b.w. was within the beginning maternal and fetotoxic range. DIPN did not possess teratogenic properties.

FIGURE 1 EXAMINATION OF THE INFLUENCE OF Di-ISOPROPYL NAPHTHALENE ON THE PREGNANT RAT AND THE FETUS BY ORAL ADMINISTRATION

body weight of female animals

daily mean value of 20 animals each

treatment from 6th – 15th day of pregnancy

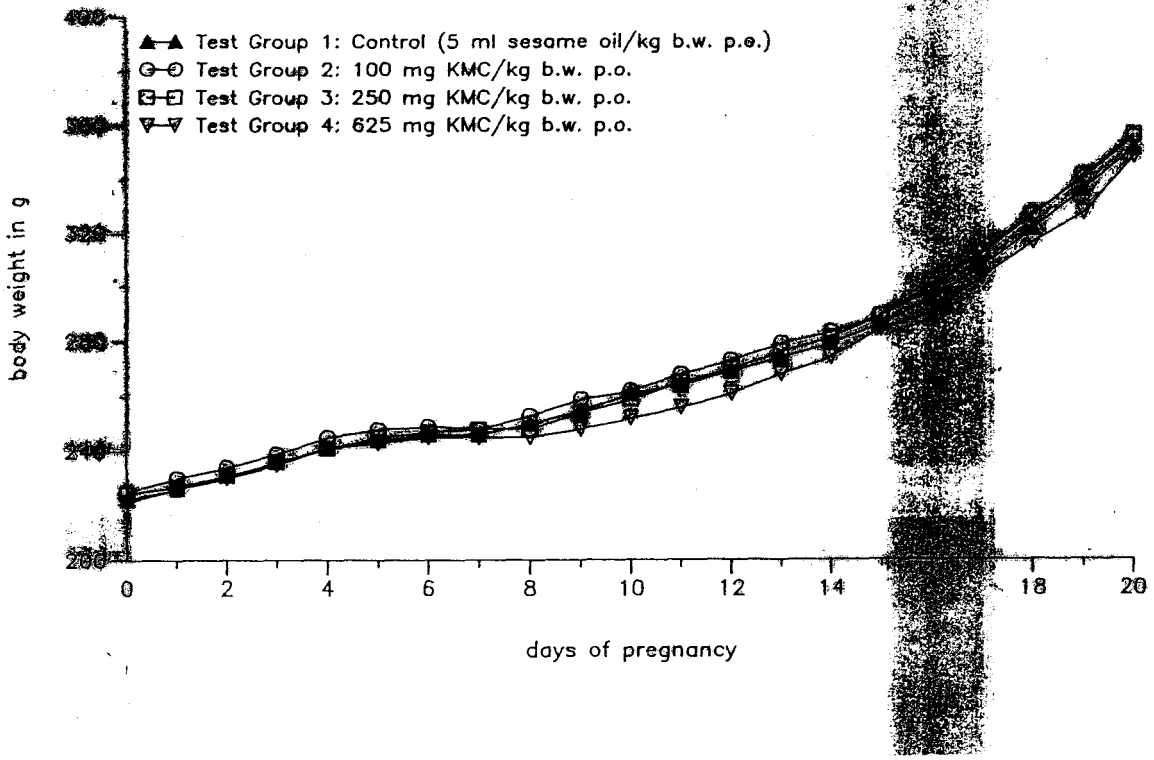
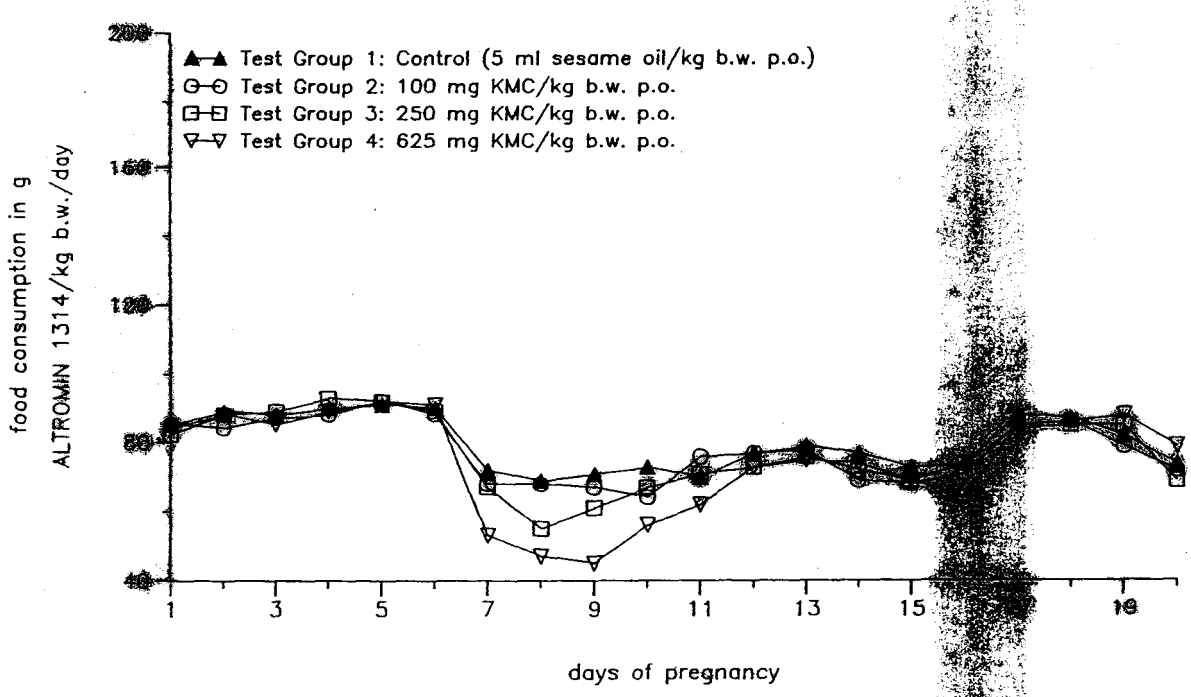


FIGURE 2 EXAMINATION OF THE INFLUENCE OF Di-ISOPROPYL NAPHTHALENE (ISOMERS) ON THE PREGNANT RAT AND THE FETUS BY ORAL ADMINISTRATION

food consumption of female animals

daily mean value of 20 animals each

treatment from 6th – 15th day of pregnancy



Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration
TABLE 7 Summary of Reproduction Data

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Females mated (1)	n =	25	25	25	25
surplus, not evaluated	n =	4	5	4	5
pregnant, evaluated (2)	n =	20	20	20	20
aborted	n =	0	0	0	0
premature births	n =	0	0	0	0
Dams with viable fetuses	n =	20	20	20	20
Dams with complete resorptions	n =	0	0	0	0
Female mortality	n =	0	0	0	0
	%	0.0	0.0	0.0	0.0

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Di-isopropyl Naphthalene (KMC)
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TABLE 7 Summary of Reproduction Data

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Pregnant at Caesarean-section	n =	20	20	20	20
	%	100.0	100.0	100.0	100.0
Corpora lutea	M	13.7	12.8	14.4	14.2
	SD	0.9	3.1	1.7	1.6
	total	274	256	287	284
Implantation sites	M	13.6	12.7	13.8	13.8
	SD	0.9	3.0	2.4	2.4
	total	272	253	276	275
Pre-implantation loss	mean %	0.7	1.0	4.5	3.7
	SD	2.2	3.4	9.7	12.2
Post-implantation loss	mean %	11.9	5.8	10.1	9.4
	SD	21.5	7.6	15.3	11.5

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TABLE 7 Summary of Reproduction Data

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Pregnant at Caesarean-section	n =	20	20	20	20
Resorptions:					
total	M	1.7	0.8	1.1	1.4
	SD	3.1	1.1	1.2	1.7
	total	33	16	22	27
	mean %	11.9	5.8	9.8	9.4
	SD	21.5	7.6	15.2	11.5
early	total	28	15	17	18
	mean %	10.1	5.4	7.5	6.3
	SD	19.6	7.7	12.4	9.3
late	total	5	1	5	9
	mean %	1.7	0.4	2.3	3.1
	SD	3.8	1.6	4.5	8.5
Dead fetuses	n =	0	0	1	0
	M	0.0	0.0	0.05	0.0

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		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Dams with viable fetuses	n =	20	20	20	20
Live fetuses	M	12.0	11.9	12.7	12.4
	SD	3.0	2.8	3.2	2.6
	total	239	237	253	248
	mean %	88.1	94.2	89.9	90.6
	SD	21.5	7.6	15.3	11.5
	left % #	50.2	45.6	50.4	51.2
	right %	49.8	54.4	49.6	48.8
Females	total	122	130	124	126
	mean %	52.1	57.3	51.5	51.3
	SD	19.1	21.0	19.2	18.2
Males	total	117	107	129	122
	mean %	47.9	42.7	48.5	48.7
	SD	19.9	21.0	19.2	18.2

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distribution in the uterine horns

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Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration
TABLE 7 Summary of Reproduction Data

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Litters evaluated	n =	20	20	20	20
Fetuses evaluated	n =	239	237	254	248
live	n =	239	237	253	248
dead	n =	0	0	1	0
Total malformations (skeletal, soft tissue and external observation)					
fetal incidence	n =	6	3	1	4
(malformation rate)	%	2.5	1.3	0.4	1.6
litter incidence	n =	3	1	1	1
	%	15.0	5.0	5.0	5.0
Total variations incl. retardations (skeletal and soft tissue observation)					
fetal incidence	n =	160	138	166	163
(variation rate)	%	66.9	58.2	65.4	65.7
litter incidence	n =	19	20	20	20
	%	95.0	100.0	100.0	100.0

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Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration
TABLE 7 Summary of Reproduction Data

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Total variations (soft tissue)					
Fetuses evaluated	n =	119	118	127	124
fetal incidence	n =	38	27	35	33
	%	31.9	22.9	27.6	26.6
litter incidence	n =	18	16	17	15
	%	90.0	80.0	85.0	75.0
Total variations (skeletal observations)					
Fetuses evaluated	n =	120	119	127	124
fetal incidence	n =	29	26	28	28
	%	24.2	21.8	22.0	22.6
litter incidence	n =	17	13	12	11
	%	85.0	65.0	60.0	55.0

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Di-isopropyl Naphthalene (KMC)
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TABLE 7 Summary of Reproduction Data

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Total retardations (skeletal observation)					
Fetuses evaluated	n =	120	119	127	124
fetal incidence	n =	93	85	103	102
	%	77.5	71.4	81.1	82.3
litter incidence	n =	19	19	20	20
	%	95.0	95.0	100.0	100.0

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Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration
TABLE 8 Mean Placental and Fetal Body Weights

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Placental weights	Units: Grams				
of male fetuses	M	0.56	0.54	0.58	0.59
	SD	0.06	0.05	0.06	0.07
	n =	20	20	20	20
of female fetuses	M	0.55	0.60	0.57	0.59
	SD	0.06	0.27	0.08	0.08
	n =	20	20	20	20
Fetal weights	Units: Grams				
of male fetuses	M	3.73	3.75	3.74	3.63
	SD	0.25	0.23	0.26	0.26
	n =	20	20	20	20
of female fetuses	M	3.53	3.57	3.47	3.48
	SD	0.28	0.22	0.32	0.30
	n =	20	20	20	20

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Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration

TABLE 9 Mean Fetal Lengths

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Fetal lengths	Units: mm				
male + female fetuses	M	38.0	38.1	38.0	38.4
	SD	0.9	0.8	0.7	1.2
	n =	20	20	20	20

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Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration

TABLE 10 Summary of all Classified Fetal External Observations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Litters evaluated	n =	20	20	20	20
Fetuses evaluated	n =	239	237	254	248
live	n =	239	237	253	248
dead	n =	0	0	1	0
Total malformations					
fetal incidence	n =	6	3	1	4
	%	2.5	1.3	0.4	1.6
litter incidence	n =	3	1	1	1
	%	15.0	5.0	5.0	5.0
Total variations					
fetal incidence	n =	0	0	0	0
	%	0.0	0.0	0.0	0.0
litter incidence	n =	0	0	0	0
	%	0.0	0.0	0.0	0.0

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Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration
TABLE 11 Summary of Fetal External Malformations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Litters evaluated	n =	20	20	20	20
Fetuses evaluated	n =	239	237	254	248
live	n =	239	237	253	248
dead	n =	0	0	1	0
Encephalocele					
fetal incidence	n =	1	0	0	0
	%	0.4	0.0	0.0	0.0
litter incidence	n =	1	0	0	0
	%	5.0	0.0	0.0	0.0
Shifted and fused dorsal, lumbar and coccygeal vertebrae					
fetal incidence	n =	4	3	0	4
	%	1.7	1.3	0.0	1.6
litter incidence	n =	1	1	0	1
	%	0.5	0.5	0.0	0.5

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Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration
TABLE 11 Summary of Fetal External Malformations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Crossed legs, bilateral					
fetal incidence	n =	4	3	0	3
	%	1.7	1.3	0.0	1.2
litter incidence	n =	1	1	0	1
	%	0.5	0.5	0.0	0.5
Cleft palate					
fetal incidence	n =	0	0	1	0
	%	0.0	0.0	0.4	0.0
litter incidence	n =	0	0	1	0
	%	0.0	0.0	5.0	0.0
Stump tail					
fetal incidence	n =	5	3	0	4
	%	2.1	1.3	0.0	1.6
litter incidence	n =	2	1	0	1
	%	10.0	0.5	0.0	0.5

lanations and abbreviations see preface of the report

Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration

TABLE 12 Summary of Fetal External Variations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Litters evaluated	n=	20	20	20	20
Fetuses evaluated	n =	239	237	254	248
live	n =	239	237	253	248
dead	n =	0	0	1	0
fetal incidence	n =	0	0	0	0
	%	0.0	0.0	0.0	0.0
litter incidence	n =	0	0	0	0
	%	0.0	0.0	0.0	0.0

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Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration

TABLE 13 Summary of all Classified Fetal Skeletal Observations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Litters evaluated	n =	20	20	20	20
Fetuses evaluated	n =	120	119	127	124
live	n =	120	119	126	124
dead	n =	0	0	1	0
Total malformations					
fetal incidence	n =	0#	0#	0#	0#
	%	0.0	0.0	0.0	0.0
litter incidence	n =	0	0	0	0
	%	0.0	0.0	0.0	0.0
Total variations					
fetal incidence	n =	29	26	28	28
	%	24.2	21.8	22.0	22.6
litter incidence	n =	17	13	12	11
	%	85.0	65.0	60.0	55.0

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Di-isopropyl Naphthalene (KMC)
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TABLE 13 Summary of all Classified Fetal Skeletal Observations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Total retardations					
fetal incidence	n =	93	85	103	102
	%	77.5	71.4	81.1	82.3
litter incidence	n =	19	19	20	20
	%	95.0	95.0	100.0	100.0

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Di-isopropyl Naphthalene (KMC)
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TABLE 13 Summary of all Classified Fetal Skeletal Retardations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Litters evaluated	n =	20	20	20	20
Fetuses evaluated	n =	120	119	127	124
live	n =	120	119	126	124
dead	n =	0	0	1	0
Skull incompletely ossified					
fetal incidence	n =	40	29	31	22
	%	33.3	24.4	24.4	17.7
litter incidence	n =	15	12	13	11
	%	75.0	60.0	65.0	55.0
Hyoid bone incompletely ossified					
fetal incidence	n =	11	12	14	14
	%	9.2	10.1	11.0	11.3
litter incidence	n =	7	6	6	8
	%	35.0	30.0	30.0	40.0

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Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration
TABLE 13 Summary of all Classified Fetal Skeletal Retardations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Sternebra(e) not or incompletely ossified or reduced in size					
fetal incidence	n =	73	69	85	85
	%	60.8	58.0	66.9	68.5
litter incidence	n =	18	19	20	20
	%	90.0	95.0	100.0	100.0
Thoracic vertebral body/bodies dumb-bell-shaped, bipartite or incompletely ossified					
fetal incidence	n =	29	18	31	40
	%	24.2	15.1	24.4	32.3
litter incidence	n =	15	12	16	13
	%	75.0	60.0	80.0	65.0
Lumbar vertebral body/bodies dumb-bell-shaped					
fetal incidence	n =	2	0	3	3
	%	1.7	0.0	2.4	2.4
litter incidence	n =	2	0	2	3
	%	10.0	0.0	10.0	15.0

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Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration
TABLE 13 Summary of all Classified Fetal Skeletal Retardations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Metacarpalia (bilateral) not ossified					
fetal incidence	n =	4	1	1	8
	%	3.3	0.8	0.8	6.5
litter incidence	n =	4	1	1	2
	%	20.0	5.0	5.0	10.0
Coccygeal vertebral body/bodies dumb-bell-shaped					
fetal incidence	n =	0	0	1	0
	%	0.0	0.0	0.8	0.0
litter incidence	n =	0	0	1	0
	%	0.0	0.0	5.0	0.0

Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration
TABLE 13 Summary of all Classified Fetal Skeletal Variations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Litters evaluated	n =	20	20	20	20
Fetuses evaluated	n =	120	119	127	124
live	n =	120	119	126	124
dead	n =	0	0	1	0
Sternebra(e) misaligned					
fetal incidence	n =	9	9	8	9
	%	7.5	7.6	6.3	7.3
litter incidence	n =	8	8	6	7
	%	40.0	40.0	30.0	35.0
Accessory 14th rib(s)					
fetal incidence	n =	11	12	20	15
	%	9.2	10.1	15.7	12.1
litter incidence	n =	7	6	10	9
	%	35.0	30.0	50.0	45.0

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Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration
TABLE 13 Summary of all Classified Fetal Skeletal Variations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Rib(s) wavy					
fetal incidence	n =	10	7	2	6
	%	8.3	5.9	1.6	4.8
litter incidence	n =	6	6	2	2
	%	30.0	30.0	10.0	10.0
13th rib(s) reduced in size/missing (uni-/bilateral)					
fetal incidence	n =	1	0	1	0
	%	0.8	0.0	0.8	0.0
litter incidence	n =	1	0	1	0
	%	5.0	0.0	5.0	0.0
Sternebra(e) bipartite					
fetal incidence	n =	0	0	0	2
	%	0.0	0.0	0.0	1.6
litter incidence	n =	0	0	0	2
	%	0.0	0.0	0.0	10.0

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TABLE 14 Summary of all Classified Fetal Soft Tissue Observations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Litters evaluated	n =	20	20	20	20
Fetuses evaluated	n =	119	118	127	124
live	n =	119	118	127	124
dead	n =	0	0	0	0
Total malformations					
fetal incidence	n =	0#	0#	0#	0#
	%	0.0	0.0	0.0	0.0
litter incidence	n =	0	0	0	0
	%	0.0	0.0	0.0	0.0
Total variations					
fetal incidence	n =	38	27	35	33
	%	31.9	22.9	27.6	26.6
litter incidence	n =	18	16	17	15
	%	90.0	80.0	85.0	75.0

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TABLE 14 Summary of all Classified Fetal Soft Tissue Variations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Litters evaluated	n =	20	20	20	20
Fetuses evaluated	n =	119	118	127	124
live	n =	119	118	127	124
dead	n =	0	0	0	0
Unilateral dilation of renal pelvis					
fetal incidence	n =	8	5	11	6
	%	6.7	4.2	8.7	4.8
litter incidence	n =	6	5	8	5
	%	30.0	25.0	40.0	25.0
Bilateral dilation of renal pelvis					
fetal incidence	n =	16	3	10	10
	%	13.4	2.5	7.9	8.1
litter incidence	n =	8	2	8	8
	%	40.0	10.0	40.0	40.0

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TABLE 14 Summary of all Classified Fetal Soft Tissue Variations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Haemorrhages on the liver surface					
fetal incidence	n =	6	6	3	10
	%	5.0	5.1	2.4	8.1
litter incidence	n =	5	6	3	9
	%	25.0	30.0	15.0	45.0
4th cerebral ventricle enlarged					
fetal incidence	n =	10	12	13	6
	%	8.4	10.2	10.2	4.8
litter incidence	n =	8	9	9	5
	%	40.0	45.0	45.0	25.0
Unilateral hydro-ureter					
fetal incidence	n =	1	1	1	2
	%	0.8	0.8	0.8	1.6
litter incidence	n =	1	1	1	2
	%	5.0	5.0	5.0	10.0

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Di-isopropyl Naphthalene (KMC)
Examination of the Influence on the Pregnant Rat and the Fetus by Oral Administration
TABLE 14 Summary of all Classified Fetal Soft Tissue Variations

		Test Group 1 Control (5 ml sesame oil/kg b.w. p.o.)	Test Group 2 100 mg KMC/kg b.w. p.o.	Test Group 3 250 mg KMC/kg b.w. p.o.	Test Group 4 625 mg KMC/kg b.w. p.o.
Bilateral hydro-ureter					
fetal incidence	n =	0	0	1	0
	%	0.0	0.0	0.8	0.0
litter incidence	n =	0	0	1	0
	%	0.0	0.0	5.0	0.0
Slightly dislocated kidney (unilateral)					
fetal incidence	n =	2	1	0	2
	%	1.7	0.8	0.0	1.6
litter incidence	n =	2	1	0	2
	%	10.0	5.0	0.0	10.0
Epidural haematoma at cerebellum					
fetal incidence	n =	0	0	0	1
	%	0.0	0.0	0.0	0.8
litter incidence	n =	0	0	0	1
	%	0.0	0.0	0.0	5.0

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