Table 2-51

Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 1 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Ease of rem Easy	oval from cage	5	5
Fur conditi Normal	on	5	5
Skin Normal		5	5
Secretions- Absent	Eye, Nose	5	5
Exophthalmo: Absent	s	5	5
Palpebral c Normal	losure	5	5
Mucosal mem Normal	branes	5	5
Lacrimation Normal		5	5
Piloerectio Absent	n	5	5
Pupil size Normal		5	5
Salivation None		5	5
Abnormal re Absent	spiration	5	5
Vocalizatio None	n	5	5
Reactivity Easy Slightly		5 0	4 1

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Table 2-52

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2.3.4.4'-Tetrahydroxybenzophenone

Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 2 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Ease of rem Easy	noval from cage	5	5
Fur conditi Normal	on	5	5
Skin Normal		5	5
Secretions- Absent	Eye, Nose	5	5
Exophthalmo Absent	s	5	5
Palpebral c Normal	losure	5	5
Mucosal mem Normal	branes	5 .	5
Lacrimation Normal	ı	5	5
Piloerectio Absent	n	5	5
Pupil size Normal		5	5
Salivation None		. 5	5
Abnormal re	spiration	5	5
Vocalizatio None	on	5	5
	to handling	5	5

Table 2-53

Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 3 of administration)

	Dose (mg/kg)	0	1000		
arameter	No. of animals	5	5		
ase of rem	oval from cage	5	5		
ur conditi Normal	on	5	5		
Skin Normal		5	5		
Secretions- Absent	Eye, Nose	5	5		
Exophthalmo Absent	s	5	5		
alpebral c Normal	losure	5	5		
ucosal mem Normal	branes	5	5	•	
acrimation Normal		5	5		
Piloerectio Absent	n	5	5		
Pupil size Normal		5	5		
Salivation None		5	5		
Abnormal re Absent	spiration	5	5		
Vocalizatio None	n	5	5		
Reactivity Easy	to handling	5	5		

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Table 2-54

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2.3.4.4 -Tetrahydroxybenzophenone

Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 4 of administration)

Dose (mg/kg)	0	1000
Parameter No. of animals	5	5
Ease of removal from cage Easy	5	5
Fur condition Normal	5	5
Skin Normal	5	5
Secretions-Eye, Nose Absent	5	5
Exophthalmos Absent	. 5	5
Palpebral closure Normal	5	5
Mucosal membranes Normal	5	5
Lacrimation Normal	5	5
Piloerection Absent	5	5
Pupil size Normal	5	5
Salivation None	5	5
Abnormal respiration Absent	5	5
Vocalization None	5	5
Reactivity to handling Easy	5	5

Table 2-55

Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 5 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Ease of rem Easy	oval from cage	5	5
Fur conditi Normal	on	5	. 2
Skin Normal		5	5
Secretions- Absent	Eye, Nose	5	5
Exophthalmo Absent	s	5	5
Palpebral c Normal	losure	5	5
Mucosal mem Normal	branes	5	5
Lacrimation Normal		5	5
Piloerectio Absent	n	5	5
Pupil size Normal	<b>x</b>	5	5
Salivation None		5	5
Abnormal re Absent	spiration	5	5
Vocalizatio None	n	5	5
Reactivity Easy	to handling	5	5

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Table 2-56

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2.3,4,4'-Tetrahydroxybenzophenone

Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 6 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Ease of rem Easy	oval from cage	5	5
Fur conditi Normal	on	5	5
Skin Normal		5	5
Secretions- Absent	Bye, Nose	5	5
Exophthalmo Absent	s	5	5
Palpebral c Normal	losure	5	5
Mucosal mem Normal	oranes	5	5
Lacrimation Normal		5	5
Piloerectio Absent	n	5	5
Pupil size Normal		5	5.
Salivation None		5	5
Abnormal re Absent	spiration	5	5
Vocalizatio None	n	5	5
Reactivity Easy	to handling	5	5

Table 2-57

Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 1 of recovery)

	Dose (mg/kg)	0	1000	•
Parameter	No. of animals	5	5	
Ease of remo	oval from cage	5	5	
Fur condition	on	5	5	
Skin Normal	•	5	5	•
Secretions-H Absent	Eye, Nose	5	5	•
Exophthalmos Absent	3	5	5	
Palpebral ci Normal	losure	5	5	
Mucosal memi Normal	oranes	5	5	
Lacrimation Normal	•	5	5	
Piloerection Absent	1	5	5	
Pupil size Normal		5	5	
Salivation None		5	5	
Abnormal re: Absent	spiration	5	5	
Vocalizatio None	1	5	5	
Reactivity Easy	to handling	5	5	

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Table 2-58

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone

Detailed clinical signs in female rats: in-the-hand observations (Recovery group, Week 2 of recovery)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Ease of rem Easy	noval from cage	5	5
Fur conditi Normal	on	5	5
Skin Normal		5	5
Secretions- Absent	-Eye, Nose	5	5
Exophthalino Absent	ns	5	5
Palpebral c Normal	losure	5	5
Mucosal mem Normal	branes	5	5
Lacrimation Normal	·	5	5
Piloerectio Absent	on	5	5
Pupil size Normal		5	5
Salivation None		5	5
Abnormal re Absent	espiration	5	5
Vocalizatio None	on .	5	5
	to handling	5	5

Table 2-59

Detailed clinical signs in male rats: open field observation (Main group, Week 1 of administration)

Dose (mg/	kg)	0	100	300	1000
Parameter No. of an	imals	12	12	12	12
Arousal Normal		12	12	12	12
Convulsion					
None		12	12	12	12
Abnormal behavior None		12	12	12	12
		12	12	12	
Stereotypy None		12	12	12	12
Gait					
No/minimal location Normal		0 12	1 11	2 10	1 11
NOTHAL		12	11	10	11
Posture Normal		12	12	12	12
Grooming None		12	12	12	12
Rearing (Mean <u>+</u> S.D.)		3 <u>+</u> 2	3 <u>+</u> 2	3 <u>+</u> 2	3 <u>*</u> 2
Defecation count (Mean	<u>+</u> s.d.)	1 <u>*</u> 1	0 <u>+</u> 0	0 <u>+</u> 0	1 <u>+</u> 2
Urination					
None Small amount		12 0	9 3	11 1	10 2

No significant difference in any treated groups from control group.

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Table 2-60

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone

Detailed clinical signs in male rats: open field observation (Main group, Week 2 of administration)

Dose (mg/kg)	O	100	300	1000
Parameter No. of animal	s 12	12	12	12
Arousal Normal	12	12	12	12
	12	12	12	12
Convulsion None	12	12	12	12
Abnormal behavior None	12	12	12	12
Stereotypy None	12	12	12	12
Gait No/minimal location	0 12	0 12	1 11	0 12
Normal	12	12	11	12
Posture Normal	12	12	12	12
Grooming None	12	12	12	12
Rearing (Mean+S.D.)	3 <u>+</u> 2	3 <u>+</u> 2	3 <u>+</u> 2	4 <u>+</u> 2
Defecation count (Mean+S.D	0.)	0 <u>∓</u> 7	0 <u>+</u> 1	0 <u>+</u> 1
Urination None Small amount	12 0	10 2	12 0	11 1

Table 2-61

Detailed clinical signs in male rats: open field observation (Main group, Week 3 of administration)

Dose (mg/kg)	0	100	300	1000
Parameter No. of animals	12	12	12	12
Arousal				
Normal	12	12	12	12
Convulsion None	12	12	12	12
Abnormal behavior				
None	12	12	. 12	12
Stereotypy None	12	12	12	12
Galt				
No/minimal location Normal	0 12	2 10	2 10	0 12
Posture Normal	12	- 12	12	12
	12	.12	12	12
Grooming None	12	12	12	12
Rearing (Mean <u>+</u> S.D.)	3 <u>+</u> 2	3 <u>+</u> 3	3 <u>+</u> 2	3 <u>+</u> 2
Defecation count (Mean+S.D.)	0 <u>+</u> 0	0 <u>+</u> 1	0± 0	0 <u>+</u> 0
Urination None	10	7	11	11
Small amount Moderate amount	10 2 0	3 2	1 0	1 0

No significant difference in any treated groups from control group.

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Table 2-62

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2.3.4.4'-Tetrahydroxybenzophenone

Detailed clinical signs in male rats: open field observation (Main group, Week 4 of administration)

Dose (mg/k	g)	0	100	300	T000
Parameter No. of ani	nals	12	12	12	12
rousal Normal		12	12	12	12
Convulsion None		12	12	12	12
Abnormal behavior None		12	12	12	75
Stereotypy None		12	12	12	12
Gait No/minimal location Normal		0 12	11	0 12	0 12
Posture Normal		12	12	12	12
Grooming None		12	12	12	12
Rearing (Mean+S.D.)		5 <u>+</u> 2	4 <u>+</u> 2	4 <u>+</u> 2	4 <u>+</u> 1
Defecation count (Mean <u>+</u>	S.D.)	0 <u>+</u> 0	0 <u>+</u> 1	0± 0	0 <u>+</u> 0
Urination None Small amount Moderate amount		10 2 0	7 4 1	11 1 0	11 1 0

Table 2-63

Detailed clinical signs in male rats: open field observation (Main group, Week 5 of administration)

Dose (mg/kg)	0	100	300	1000	
Parameter No. of animals	12	12	12	12	·
Arousal Normal	12	12	12	12	
Convulsion None	12	12	12	12	
Abnormal behavior None	12	12	12	12	
Stereotypy None	12	12	12	12	
Gait No/minimal location Normal	0 12	1 11	0 12	0 12	
Posture Normal	12	12	12	12	
Grooming None	12	12	12	12	
Rearing (Mean <u>+</u> S.D.)	4 <u>+</u> 2	4 <u>+</u> 2	5 <u>+</u> 2	4 <u>+</u> 1	
Defecation count (Mean + S.D.)	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>+</u> 0	
Urination None Small amount	11 1	7 5	11 .	12 0	

No significant difference in any treated groups from control group.

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Table 2-64

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone

Detailed clinical signs in male rats: open field observation (Main group, Week 6 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Arousal Normal		12	12	12	12
Convulsion None		12	12	12	12
bnormal be None	havior	12	12	12	12
Stereotypy None		12	12	12	12
Gait No/minima Normal	l location	0 12	0 12	0 12	1 11
Posture Normal		12	12	12	12
Grooming None		12	12	12	12
Rearing (Me	an <u>+</u> S.D.)	5 <u>+</u> 2	4 <u>+</u> 2	5 <u>+</u> 2	4 <u>+</u> 2
Defecation	count (Mean+S.D.)	0 <u>+</u> 0	0 <u>+</u> 1	0 <u>±</u> 0	0 <u>+</u> 0
Urination None Small amo Moderate		10 2 0	7 4 1	9 3 0	12 0 0

Table 2-65

Detailed clinical signs in female rats: open field observation (Main group, Week 1 of administration)

Dose (mg/kg)	0	100	300	1000
Parameter No. of animals	12	12	12	12
Arousal Normal	10	10	••	10
NOTHAL	12	12	12	12
Convulsion None	12	12	12	12
Abnormal behavior None	12	12	12	12
Stereotypy None	12	12	12	12
Gait Normal	12	12	12	12
Posture . Normal	12	12	12	12
Grooming None	12	12	12	12
Rearing (Mean+S.D.)	6 <u>+</u> 2	5 <u>+</u> 2	6 <u>+</u> 3	6 <u>+</u> 2
Defecation count (Mean+S.D.)	0 <u>+</u> 0	0 <u>±</u> 0	0 <u>+</u> 0	0 <u>+</u> 0
Urination None Small amount	12 0	12 0	11 1	12

No significant difference in any treated groups from control group.

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Table 2-66

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone

Detailed clinical signs in female rats: open field observation (Main group, Week  $\dot{z}$  of administration)

bose (mg/kg)	0	100	300	1000	•
Parameter No. of animals	12	12	12	12	
Arousal Normal	12	12	12	12	
Convulsion None	12	12	12	12	
Abnormal behavior None	12	12	12	12	
Stereotypy None	12	12	12	12	
Gait Normal	12	12	12	12	
Posture Normal	12	12	12	12	
Grooming None	12	12	12	12	
Rearing (Mean <u>+</u> S.D.)	8 <u>+</u> 3	7 <u>+</u> 2	7 <u>+</u> 2	7 <u>+</u> 2	
Defecation count (Mean <u>+</u> S.D.)	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>+</u> 0	
Urination None	12	12	12	12	

Table 2-67

Detailed clinical signs in female rats: open field observation (Main group, Day 1 of gestation)

	Dose (mg/kg)	0	100	300	1000
Paramete <i>r</i>	No. of animals	12	12	12	11
Arousal Normal		12	12	12	11
		12	**	12	,11
Convulsion None		12	12	12	11
Abnormal be None	havior	12	12	12	11 .
Stereotypy None		12	12	12	11
Gait Normal		12	12	12	11
Posture Normal		12	12	12	11
Grooming None		12	12	12	11
Rearing (Me	an <u>+</u> S.D.)	7 <u>+</u> 2	6 <u>+</u> 1	7 <u>+</u> 2	7 <u>+</u> 3
Defecation	count (Mean_S.D.)	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>+</u> 0
Urination None		12	12	12	11

No significant difference in any treated groups from control group.

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Table 2-68

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3,4,4'-Tetrahydroxybenzophenone

Detailed clinical signs in female rats: open field observation (Main group, Day 7 of gestation)

Dose (mg/kg)	0	100	300	1000		
Parameter No. of animals	12	12	12	11		
Arousal Normal	12	12	12	11		
Convulsion None	12	12	12	11		
ibnormal behavior None	12	12	12	11	•	
tereotypy None	12	12	12	11		
ait Normal	12	12	12	11		
osture Normal	12	12	12	11		
cooming None	12	12	12	11		
Rearing (Mean <u>+</u> S.D.)	G <u>+</u> 2	7 <u>+</u> 2	8 <u>+</u> 2	6 <u>+</u> 2		
efecation count (Mean+S.D.)	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>+</u> 0		
Trination None Small amount	12 0	12 0	12 0	10 1		

Table 2-69

Detailed clinical signs in female rats: open field observation (Main group, Day 14 of gestation)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	11
Arousal Normal		12	12	12	11
		12	12	12	**
Convulsion None		12	12	12	11
Abnormal be None	ehavior	12	12	12	11
Stereotypy None		12	12	12	. 11
Gait Normal		12	12	12	11
Posture Normal		12	12	12	11
Grooming None		12	12	12	11
Rearing (Me	ean <u>+</u> S.D.)	5 <u>*</u> 1	6 <u>+</u> 2	5 <u>+</u> 2	4 <u>+</u> 1
Defecation	count (Mean+S.D.)	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>+</u> 0
Urination None		12	12	12	11

No significant difference in any treated groups from control group.

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Table 2-70

A combined repeated-dose/reproductive-developmental toxicity study in rats treated or ally with 2,3,4,4'-Tetrahydroxybenzophenone

Detailed clinical signs in female rats: open field observation (Main group, Day 20 of gestation)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	11
Arousal	4				
Normal		12	12	12	11
Convulsion None		12	12	12	11
Abnormal be None	havior	12	12	12	11
Stereotypy None		. 12	12	12	11
Gait Normal		12	12	12	11
Posture Normal		12	12	12	. 11
Grooming None		12	12	12	11
Rearing (Me	ean <u>+</u> S.D.)	6 <u>+</u> 2	5 <u>+</u> 2	5 <u>±</u> 1	4: 2*D
Defecation	count (Mean <u>+</u> S.D.)	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>+</u> 0
Urination None		12	12	12	11

<sup>• :</sup> p<0.05 (Significant difference from control group)
D : Dunnett's test

Table 2-71

Detailed clinical signs in female rats: open field observation (Main group, Day 4 of lactation)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	10
Arousal Normal		12	12	12	10
	*			~-	~~
Convulsion None		12	12	12	10
Abnormal be None	ehavior	12	12	12	10
Stereotypy None		12	12	12	10
Gait Normal		12	12	12	10
Poșture Normal		12	. 12	12	10
Grooming None		12	12	12	10
Rearing (Me	ean <u>+</u> S.D.)	7 <u>+</u> 2	7 <u>±</u> 1	6 <u>*</u> 2	5 <u>+</u> 2
Defecation	count (Mean+S.D.)	0 <u>+</u> 0	0 <u>+</u> 0	0 <u>±</u> 0	0 <u>±</u> 0
Urination None		12	12	12	10

No significant difference in any treated groups from control group.

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Table 2-72

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2.3.4.4'-Tetrahydroxybenzophenone

Detailed clinical signs in male rats: open field observation (Recovery group, Week 1 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Arousal		_	5
Normal		5	5
Convulsion None		5	5
Abnormal bel None	havior	5	ક
Stereotypy None		5	5
Gait			
No/minima: Normal	l location	0 5	2 3
		5	•
Posture Normal		5	5
Grooming None		5	5
Rearing (Me	an <u>+</u> S.D.)	3 <u>+</u> 1	2 <u>+</u> 2
Defecation	count (Mean <u>+</u> S.D.)	0 <u>+</u> 0	0± 0
Urination		_	
None Small amor	unt	5 0	4

No significant difference between treated group and control group.

Table 2-73

Detailed clinical signs in male rats: open field observation (Recovery group, Week 2 of administration)

Dose (mg/kg)	0	1000		
Parameter No. of animals	5	5		
Arousal	-	_		
Normal	5	Ę		
Convulsion None	5	5	•	
Abnormal behavior None	5	5		
Stereotypy				
None	5	5		
Gait				
Normal	5	5		
Posture	_	_		
Normal	5	5		
Grooming None	5	. 5		
Rearing (Mean <u>+</u> S.D.)	5 <u>+</u> 2	3 <u>+</u> 2		
Defecation count (Mean+S.D.)	0 <u>+</u> 0	0 <u>+</u> 0	•	
Urination			•	
None Small amount	5 0	4 1		

No significant difference between treated group and control group.

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Table 2-74

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2.3,4.4'-Tetrahydroxybenzophenone

Detailed clinical signs in male rats: open field observation (Recovery group, Week 3 of administration)

	Dose (mg/kg)	0	1000		
Parameter	No. of animals	5	5	_	
Arousal Normal		5	. 5		
		ð	ъ		
Convulsion None		5	5		
Abnormal be	havior	5	5		
Stereotypy None		5	5		
		·	Ğ		
Gait Normal		5	5		
Posture Normal		5	5		
Grooming					
None		5	5		
Rearing (Me	an <u>+</u> S.D.)	3 <u>+</u> 1	3 <u>+</u> 2		
Defecation	count (Mean <u>+</u> S.D.)	0 <u>+</u> 0	0 <u>+</u> 1		
Urination None		5	5		

No significant difference between treated group and control group.