Table 2-27

Detailed clinical signs in female rats: home cage observations (Recovery group, Week 6 of administration)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Posture			
Normal		5	5
Convulsion None		5	5
Abnormal be	havior	5	5
None		5	5

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2.3.4,4'-Tetrahydroxybenzophenone

Detailed clinical signs in female rats: home cage observations (Recovery group, Week 1 of recovery)

	Dose (mg/kg)	0	1000			
Parameter	No. of animals	5	5			
Posture Normal		5	5			
Convulsion None		5	5			
		3	ş			
Abnormal be None	ehavior	5	5			
					•	

Table 2-29

Detailed clinical signs in female rats: home cage observations (Recovery group, Week 2 of recovery)

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Posture			
Normal		5	5
Convulsion None		5	5
bnormal bel	navior	_	_
None		5	5

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Table 2-30

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

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

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Easy	noval from cage istance/avoidance	12 0	12 0	11 1	11
Fur conditi Normal	ion	12	12	12	12
Skin Normal		12	12	12	12
Secretions- Absent	Eye, Nose	12	12	12	12
Exophthalmo Absent	os	12	12	12	12
Palpebral o	closure	12	12	12	12
Mucosal men Normal	branes	12	12	12	12
Lacrimatior Normal	1	12	12	12	12
Piloerectic Absent	on ·	12	12	12	12
Pupil size Normal		12	12	12	12
Salivation None		12	12	12	12
Abnormal re Absent	espiration	12	12	12	12
Vocalizatio None Soft Moderate	מס	11 1 0 .	9 2 1	9 3 0	10 1 1
Reactivity Easy Slightly	to handling awkward	10 2	11 1	12 0	10 2

Table 2-31

Detailed clinical signs in male rats: in-the-hand observations (Main group. Week 2 of administration)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Sase of rem Easy	noval from cage	12	12	12	12
Fur conditi Normal	ion	12	12	12	12
Skin Normal		12	12	12	12
Secretions- Absent	-Eye, Nose	12	12	12	12
Exophthalmo Absent	os ·	12	12	12	12
Palpebral o	closure	12	12	12	12
Mucosal men Normal	nbranes	12	12	12	12
Lacrimation Normal	n	12	12	12	12
Piloerectio Absent	on	12	12	12	12
Pupil size Normal		12	12	12	12
Salivation None		12	12	12	12
Abnormal re	espiration	12	12	12	12
Vocalizatio None Soft	nc	12 0	9 3	11	9 3
Reactivity Easy	to handling	12	12	12	12

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Table 2-32

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

Detailed clinical signs in male rats:  $i_{\rm B}$ -the-hand observations (Main group, Week 3 of administration)

	Dose (mg/kg)	0	100	300	1000	
Parameter	No. of animals	12	12	12	12	
Easy	oval from cage stance/avoidance	12 0	11 1	11 1	12 0	
Fur conditi Normal	on	12	12	12	12	
Skin Normal		12	12	12	12	
Secretions~ Absent	Eye, Nose	12	12	12	12	
Exophthalmo Absent	s	12	12	12	12	
Palpebral c Normal	losure	12	12	12	12	
Mucosal mem Normal	branes	12	12	12	12	
Lacrimation Normal		12	12	12	12	
Piloerectio Absent	n	12	12	12	12	
Pupil size Normal		12	12	12	12	
Salivation None		12	12	12	12	
Abnormal re Absent	spiration	12	12	12	12	
Vocalizatio None Soft	n	10 2	G 6	10 2	10 2	
Reactivity Easy Slightly	to handling awkward	. 12	12 0	11 1	12 0	

Table 2-33

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

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Ease of rem Easy Some resi	oval from cage stance/avoidance	12 0	8 4	11	12 0
Fur conditi Normal	on	12	12	12	12
Skin Normal		12	12	12	12
Secretions- Absent	Eye, Nose	12	12	12	12
Exophthalmo Absent	s	12	12	12	12
Palpebral c Normal	losure	12	12	12	12
Mucosal mem Normal	branes	12	12	12	12
Lacrimation Normal		12	12	12	12
Piloerectio Absent	n	12	12	12	12
Pupil size Normal		12	12	12	12
Salivation None		12	12	12	12
Abnormal re Absent	spiration	12	12	12	12
Vocalizatio None Soft Moderate	n	10 2 0	8 4 2	7 4 1	10 1 1
Reactivity Easy Slightly	to handling awkward	11 1	10 2	10 2	1 <u>1</u>

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Table 2-34

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

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

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Ease of rem Easy Some res	noval from cage istance/avoidance	12 0	11	11	12 0
Fur conditi Normal	ion	12	12	12	12
Skin Normal		12	12	12	12
Secretions- Absent	-Eye, Nose	12	12	12	12
Exophthalmo Absent	os	12	12	12	12
Palpebral o	closure	12	12	12	12
Mucosal men Normal	mbranes	12	12	12	12
Lacrimation Normal	n	12	12	12	12
Piloerectic Absent	on	12	12	12	12
Pupil size Normal		12	12	12	12
Salivation None		12	12	12	12
Abnormal re Absent	espiration	12	12	12	12
Vocalizatio None Soft	on	9 3	9 -	10 2	1 <u>1</u>
Reactivity Easy	to handling	12	12	12	12

Table 2-35

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

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
FACT	moval from cage istance/avoidance	12 0	1 <u>1</u>	12 0	12 0
Fur condit Normal	ion	12	12	12	12
Skin Normal		12	12	12	12
Secretions Absent	-Eye, Nose	12	12	12	12
Exophthalm Absent	os	12	12	12	12
Palpebral Normal	closure	. 12	12	12	12
Mucosal me Normal	mbranes	12	12	12	12
Lacrimatio Normal	n	12	12	12	12
Piloerecti Absent	on	12	12	12	12
Pupil size Normal		12	12	12	12
Salivation None		12	12	12	12
Abnormal r Absent	espiration	12	12	12	12
Vocalizati None Soft Moderate		10 2 0	8 3 1	10 2 0	1 1 1 0
Reactivity Easy	to handling	12	12	12	12

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Table 2-36

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 (Main group, Week 1 of administration)

Dose (n	g/kg)	0	100	300	1000		
Parameter No. of	animals	12	12	12	12	 	
Ease of removal from Easy Some resistance/av	ı cage roidance	12	11 1	12 0	12 0		
Fur condition Normal		12	12	12	12		
Skin Normal		12	12	12	12		•
Secretions-Eye. Nose Absent	:	12	12	12	12		
Exophthalmos Absent		12	12	12	12		
alpebral closure Normal		12	12	12	12		
Nucosal membranes Normal		12	12	12	12		
acrimation Normal		12	12	12	12	,	,
Piloerection Absent		12	12	12	12	,	
Pupil size Normal		12	12	12	12		
alivation None		12	12	12	12		
bnormal respiration Absent	ı	12	12	12	12		
ocalization None Soft		10 2	11	10 2	9 3		•
Reactivity to handli Easy Slightly awkward	ng	10 2	10 2	10 2	11		

Table 2-37

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

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	12
Easy	oval from cage stance/avoidance	12 0	11 1	12 0	12 0
Fur conditi Normal	on	12	12	12	12
Skin Normal		12	12	12	12
Secretions- Absent	Eye, Nose	12	1,2	12	12
Exophthalmo Absent	s	12	12	12	12
Palpebral c Normal	losure	12	12	12	12
Mucosal mem Normal	branes	12	12	12	12
Lacrimation Normal		12	12	12	12
Piloerectio Absent	n	12	12	12	12
Pupil size Normal		12	12	12	12
Salivation None		12	12	12	12 .
Abnormal re Absent	spiration	12	12	12	12
Vocalizatio None Soft	n	12 0	11	12 0	11
Reactivity Easy Slightly	to handling awkward	12 0	11	12 0	12

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Table 2-38

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 (Main group, Day 1 of gestation)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	11
			<del></del>	<del>-</del>	
Easy	loval from cage	12	ıį	12	9 2
	stance/avoidance	0	1	U	Z
Fur conditi Normal	.on	12	12	12	11
Skin Normal		12	12	12	11
Secretions-	Eye. Nose				
Absent	-	12	12	12	11
Exophthalmo Absent	s	12	12	12	11
Palpebral c	losure	12	12	12	11
Mucosal mem	hranes	12		12	11
Normal	ior anco	12	12	12	11
Lacrimation Normal	l	12	12	12	11
Piloerectio	n				
Absent		12	12	12	11
Pupil size Normal		12	12	12	11
Salivation None		12	12	12	11
	on i wat i on	12	12	12	11
Abnormal re Absent	spiration	12	12	12	11
Vocalizatio None	n	11	11	12	10
Soft		11	11	-õ	ĭ
Reactivity Easy	to handling	10 2	11	12	9 2
Easy Slightly	awkward	2	1	0	2

Table 2-39

Detailed clinical signs in female rats: in-the-hand observations (Main group, Day 7 of gestation)

	Dose (mg/kg)	0	100	300	1000	
Parameter	No. of animals	12	12	12	11	
Ease of rem Easy	oval from cage	12	12	12	11	
Fur conditi	on .	12	12	12	11	
Skin Normal		12	12	12	11	
ecretions- Absent	Eye, Nose	12	12	12	11	
Exophthalmo Absent	s	12	12	12	11	
Palpebral c. Normal	losure	12	12	12	11	
Mucosal mem	branes	12	12	12	11	
Lacrimation Normal		12	12	12	11	
Piloerection Absent	n	12	12	12	11	
Pupil size Normal		12	12	12	. 11	
Salivation None		12	12	12	11	
Abnormal re Absent	spiration	12	12	12	11	
Vocalizatio None Soft	n	12 0	11	11	110	
Reactlvity Easy Slightly	to handling awkward	11 1	12 0	12 0	110	

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Table 2-40

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 (Main group, Day 14 of gestation)

	Dose (mg/kg)	0	100	300	1000	
Parameter	No. of animals	12	12	12	11	
Ease of rem Easy	noval from cage	12	12	12	11	
Fur conditi Normal	on	12	12	12	11	
Skin Normal		12	12	12	11	
Secretions- Absent		12	12	12	11	
Exophthalmo Absent	s	12	12	12	11	
Palpebral o	losure	12	12	12	11	
Mucosal mem Normal	branes	12	12	. 12	11	
Lacrimation Normal		12	12	12	11	
Piloerectic Absent	n	12	12	12	11	
Pupil size Normal		12	12	12	11	
Salivation None		12	12	12	11	
Abnormal re	espiration	12	12	12	11	
Vocalizatio None Soft	n	12 0	10	11	11	
Reactivity Easy Slightly	to handling awkward	12	11	12 0	11 0	

Table 2-41

Detailed clinical signs in female rats: in-the-hand observations (Main group, Day 20 of gestation)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	11
Easy	noval from cage istance/avoidance	12 0	10 2	12 0	11 0
Fur conditi Normal	ion	12	12	12	11
Skin Normal		1,2	12	12	11
Secretions- Absent	Eye, Nose	12	12	12	11
Exophthalmo Absent	os	12	12	12	11
Palpebral c Normal	losure	12	12	12	11
Mucosal mem Normal	branes	12	12	12	11
Lacrimation Normal	ı	12	12	12	11
Piloerectio Absent	on	12	12	12	11
Pupil size Normal		12	12	12	11
Salivation None		12	12	12	11
Abnormal re Absent	espiration	12	12	12	11
Vocalizatio None Moderate	on	12 0	11 1	12 0	11
Reactivity Easy Slightly	to handling awkward	12	10 2	12	10 1

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Table 2-42

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 (Main group, Day 4 of lactation)

	Dose (mg/kg)	0	100	300	1000
Parameter	No. of animals	12	12	12	10
Easy	noval from cage Istance/avoidance	11	12	1 <u>1</u>	9 1
Fur conditi Normal	ion	12	12	12	10
Skin Normal		12	12	12	10
Secretions- Absent	-Eye, Nose	12	12	12	10
Exophthalmo Absent	os	12	12	12	10
Palpebral o Normal	closure	12	12	12	10
Mucosal men Normal	branes	12	12	12	10
Lacrimation Normal	n	12	12	12	10
Piloerection Absent	on	12	12	12	10
Pupil size Normal		12	12	12	10
Salivation None		12	12	12	10
Abnormal re	espiration	12	12	12	10
Vocalizatio None Soft	on .	12 0	11	12 0	10
Reactivity Easy Slightly	to handling awkward	12	11	11 1	9 1

Table 2-43

Detailed clinical signs in male 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	no	5	5
Skin Normal		5	5
Secretions-: Absent	Eye, Nose	5	5
Exophthalmo: Absent	5	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 Soft	<u>.</u>	2 3	5 0
Reactivity Easy Slightly	to handling awkward	4	5 0

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Table 2-44

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

Detailed clinical signs in male 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	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	losure	5	5
Mucosal mem Normal	branes	5	, 5
Lacrimation Normal	ı	5	5
Piloerectio Absent	on .	5	5
Pupil size Normal		5	5
Salivation None		5	5
Abnormal re	espiration	5	5
Vocalizatio None Soft		4 ' 1	5 0
Reactivity Easy	to handling	5	5

Table 2-45

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

Dose (mg/kg)	0	1000	•
Parameter No. of animals	5	5	
Ease of removal from cage Easy Some resistance/avoidance	4 1	5 0	
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 Soft Moderate	3 1 1	4 1 0	
Reactivity to handling	5	5	

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Table 2-46

A combined repeated-dose/reproductive-developmental toxicity study in rats treated orally with 2,3.4.4 Tetrahydroxybenzophenone

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

	Dose (mg/kg)	0	1000	
Parameter_	No. of animals	5	5	
Ease of rem	oval from cage	5	5	
Fur conditi Normal	on	5	5	
Skin Normal		, 5	5	
Secretions- Absent		5	5	
Exophthalmo Absent	s	5	5	
Palpebral c	losure	5	5	
Mucosal men Normal	branes	5	5	
Lacrimation Normal	ı	5	5	
Piloerectic Absent	on	5	5	
Pupil size Normal		5	5	
Salivation None		5	5	
Abnormal re Absent	espiration	5	5	
Vocalizatio None Soft	on	4	4	
Reactivity Easy	to handling	5	5	

Table 2-47

Detailed clinical signs in male 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	5
Skin Normal		5	5
Secretions- Absent	Eye, Nose	5	5
Exophthaimo 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
Vocalizatlo None	n	5	5
Reactivity Easy	to handling	5	5 ·

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Table 2-48

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

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

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Easv	oval from cage stance/avoidance	4 1	5 0
Fur conditi Normal	on	5	5
Skin Normal		5	5
Secretions-	Eye, Nose	5	5
Exophthalmo Absent	s	5	5
Palpebral c Normal	losure	5	5
Mucosal mem Normal		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 Soft	on	2 3	4 1
Reactivity Easy	to handling	5	5

Table 2-49

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

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Ease of rem Easy Some resi	noval from cage stance/avoidance	3 2	5 0
Fur conditi Normal	on	5	5
Skin Normal		5	5
Secretions- Absent	Eye. Nose	5	5
Exophthalmo Absent	es	5	5
Palpebral c Normal	losure	5	5
Mucosal mem Normal		5	5
Lacrimation Normal	ı	5	5
Piloerectio Absent	on	5	5
Pupil size Normal		5	5
Salivation None		5	5
Abnormal re Absent	espiration	5	5
Vocalizatio None Soft Moderate	ασ	3 0 2	4 1 0
Reactivity Easy	to handling	5	5

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Table 2-50

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

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

	Dose (mg/kg)	0	1000
Parameter	No. of animals	5	5
Easv	oval from cage stance/avoidance	3 2	5 0
Fur condition	on	5	5
Skin Normal		5	5
Secretions-I Absent	Eye, Nose	5	5
Exophthalmos Absent	s	5	5
Palpebral c. Normal	losure	5	5
Mucosal memi	branes	5	5
Lacrimation Normal		5	5
Piloerection Absent	n	5	5
Pupil size Normal		5	5
Salivation None	•	5	5
Abnormal re	spiration	5	5
Vocalization None Soft Moderate	n	3 1 1	3 2 0
Reactivity Easy Slightly		5 0	4 1