

Table 2-27 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 6 of administration)

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

Table 2-28 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)

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

Table 2-29

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 2 of recovery)

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

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)

Parameter	Dose (mg/kg) No. of animals	0	100	300	1000
		12	12	12	12
Ease of removal from cage					
Easy		12	12	11	11
Some resistance/avoidance		0	0	1	1
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
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		11	9	9	10
Soft		1	2	3	1
Moderate		0	1	0	1
Reactivity to handling					
Easy		10	11	12	10
Slightly awkward		2	1	0	2

Table 2-31 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 2 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	12	12	12
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
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	9	11	9
Soft		0	3	1	3
Reactivity to handling					
Easy		12	12	12	12

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: in-the-hand observations (Main group, Week 3 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	11	11	12
Some resistance/avoidance		0	1	1	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
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		10	6	10	10
Soft		2	6	2	2
Reactivity to handling					
Easy		12	12	11	12
Slightly awkward		0	0	1	0

Table 2-33

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 4 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	8	11	12
Some resistance/avoidance		0	4	1	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
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		10	6	7	10
Soft		2	4	4	1
Moderate		0	2	1	1
Reactivity to handling					
Easy		11	10	10	11
Slightly awkward		1	2	2	1

R-944

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)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	11	11	12
Some resistance/avoidance		0	1	1	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
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		9	9	10	11
Soft		3	3	2	1
Reactivity to handling					
Easy		12	12	12	12

Table 2-35

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 6 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	11	12	12
Some resistance/avoidance		0	1	0	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
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		10	8	10	11
Soft		2	3	2	1
Moderate		0	1	0	0
Reactivity to handling					
Easy		12	12	12	12

R-944

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)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	11	12	12
Some resistance/avoidance		0	1	0	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
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		10	11	10	9
Soft		2	1	2	3
Reactivity to handling					
Easy		10	10	10	11
Slightly awkward		2	2	2	1

Table 2-37

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 2 of administration)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	12
Ease of removal from cage					
Easy		12	11	12	12
Some resistance/avoidance		0	1	0	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
Palpebral closure					
Normal		12	12	12	12
Mucosal membranes					
Normal		12	12	12	12
Lacrimation					
Normal		12	12	12	12
Piloerection					
Absent		12	12	12	12
Pupil size					
Normal		12	12	12	12
Salivation					
None		12	12	12	12
Abnormal respiration					
Absent		12	12	12	12
Vocalization					
None		12	11	12	11
Soft		0	1	0	1
Reactivity to handling					
Easy		12	11	12	12
Slightly awkward		0	1	0	0

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)

Parameter	Dose (mg/kg)	0	100	300	1000
	No. of animals	12	12	12	11
Ease of removal from cage					
Easy		12	11	12	9
Some resistance/avoidance		0	1	0	2
Fur condition					
Normal		12	12	12	11
Skin					
Normal		12	12	12	11
Secretions-Eye, Nose					
Absent		12	12	12	11
Exophthalmos					
Absent		12	12	12	11
Palpebral closure					
Normal		12	12	12	11
Mucosal membranes					
Normal		12	12	12	11
Lacrimation					
Normal		12	12	12	11
Piloerection					
Absent		12	12	12	11
Pupil size					
Normal		12	12	12	11
Salivation					
None		12	12	12	11
Abnormal respiration					
Absent		12	12	12	11
Vocalization					
None		11	11	12	10
Soft		1	1	0	1
Reactivity to handling					
Easy		10	11	12	9
Slightly awkward		2	1	0	2

Table 2-39

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 7 of gestation)

Parameter	Dose (mg/kg)		0	100	300	1000
	No. of animals					
Ease of removal from cage			12	12	12	11
Easy			12	12	12	11
Fur condition			12	12	12	11
Normal			12	12	12	11
Skin			12	12	12	11
Normal			12	12	12	11
Secretions-Eye, Nose			12	12	12	11
Absent			12	12	12	11
Exophthalmos			12	12	12	11
Absent			12	12	12	11
Palpebral closure			12	12	12	11
Normal			12	12	12	11
Mucosal membranes			12	12	12	11
Normal			12	12	12	11
Lacrimation			12	12	12	11
Normal			12	12	12	11
Piloerection			12	12	12	11
Absent			12	12	12	11
Pupil size			12	12	12	11
Normal			12	12	12	11
Salivation			12	12	12	11
None			12	12	12	11
Abnormal respiration			12	12	12	11
Absent			12	12	12	11
Vocalization			12	11	11	11
None			0	1	1	0
Soft			12	11	11	11
Reactivity to handling			11	12	12	11
Easy			1	0	0	0
Slightly awkward			12	12	12	11

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)

Parameter	Dose (mg/kg)		0	100	300	1000
	No. of animals					
Ease of removal from cage			12	12	12	11
Easy			12	12	12	11
Fur condition			12	12	12	11
Normal			12	12	12	11
Skin			12	12	12	11
Normal			12	12	12	11
Secretions-Eye, Nose			12	12	12	11
Absent			12	12	12	11
Exophthalmos			12	12	12	11
Absent			12	12	12	11
Palpebral closure			12	12	12	11
Normal			12	12	12	11
Mucosal membranes			12	12	12	11
Normal			12	12	12	11
Lacrimation			12	12	12	11
Normal			12	12	12	11
Piloerection			12	12	12	11
Absent			12	12	12	11
Pupil size			12	12	12	11
Normal			12	12	12	11
Salivation			12	12	12	11
None			12	12	12	11
Abnormal respiration			12	12	12	11
Absent			12	12	12	11
Vocalization			12	10	11	11
None			0	2	1	0
Soft			12	10	11	11
Reactivity to handling			12	11	12	11
Easy			0	1	0	0
Slightly awkward			12	11	12	11

Table 2-41

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 20 of gestation)

Parameter	Dose (mg/kg) No. of animals	0	100	300	1000
		12	12	12	11
Ease of removal from cage					
Easy		12	10	12	11
Some resistance/avoidance		0	2	0	0
Fur condition					
Normal		12	12	12	11
Skin					
Normal		12	12	12	11
Secretions-Eye, Nose					
Absent		12	12	12	11
Exophthalmos					
Absent		12	12	12	11
Palpebral closure					
Normal		12	12	12	11
Mucosal membranes					
Normal		12	12	12	11
Lacrimation					
Normal		12	12	12	11
Piloerection					
Absent		12	12	12	11
Pupil size					
Normal		12	12	12	11
Salivation					
None		12	12	12	11
Abnormal respiration					
Absent		12	12	12	11
Vocalization					
None		12	11	12	11
Moderate		0	1	0	0
Reactivity to handling					
Easy		12	10	12	10
Slightly awkward		0	2	0	1

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)

Parameter	Dose (mg/kg) No. of animals	0	100	300	1000
		12	12	12	10
Ease of removal from cage					
Easy		11	12	11	9
Some resistance/avoidance		1	0	1	1
Fur condition					
Normal		12	12	12	10
Skin					
Normal		12	12	12	10
Secretions-Eye, Nose					
Absent		12	12	12	10
Exophthalmos					
Absent		12	12	12	10
Palpebral closure					
Normal		12	12	12	10
Mucosal membranes					
Normal		12	12	12	10
Lacrimation					
Normal		12	12	12	10
Piloerection					
Absent		12	12	12	10
Pupil size					
Normal		12	12	12	10
Salivation					
None		12	12	12	10
Abnormal respiration					
Absent		12	12	12	10
Vocalization					
None		12	11	12	10
Soft		0	1	0	0
Reactivity to handling					
Easy		12	11	11	9
Slightly awkward		0	1	1	1



Table 2-43

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 1 of administration)

Parameter	Dose (mg/kg) No. of animals	0	1000
		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		2	5
Soft		3	0
Reactivity to handling			
Easy		4	5
Slightly awkward		1	0

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)

Parameter	Dose (mg/kg) No. of animals	0	1000
		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		4	5
Soft		1	0
Reactivity to handling			
Easy		5	5

Table 2-45 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 3 of administration)

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

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)

Parameter	Dose (mg/kg) No. of animals	0	1000
		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		4	4
Soft		1	1
Reactivity to handling			
Easy		5	5

Table 2-47

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 5 of administration)

Parameter	Dose (mg/kg)	0	1000
	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 2-48

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 6 of administration)

Parameter	Dose (mg/kg)	0	1000
	No. of animals	5	5
Ease of removal from cage			
Easy		4	5
Some resistance/avoidance		1	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		2	4
Soft		3	1
Reactivity to handling			
Easy		5	5

Table 2-49

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 1 of recovery)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy		3	5
Some resistance/avoidance		2	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		3	4
Soft		0	1
Moderate		2	0
Reactivity to handling			
Easy		5	5

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)

Parameter	Dose (mg/kg) No. of animals	0	1000
		5	5
Ease of removal from cage			
Easy		3	5
Some resistance/avoidance		2	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		3	3
Soft		1	2
Moderate		1	0
Reactivity to handling			
Easy		5	4
Slightly awkward		0	1