

Supplemental Digital Content 1

Table 1. Behavior Observation during Vehicle Application

Observation	Vehicle group							
Day	0	2	4	6	8	10	12	14
Weight	4	4	4	4	4	4	4	4
Neurobehavioral observation „Viewing Jar“								
External appearance	4	4	4	4	4 (6)	4	4	4
Body position	4	4	4	4	4 (6)	4	4	4
Spontaneous locomotor activity	4	4	4	4	4 (2)	4	4	4
Respiration rate	4	4	4	4	4	4	4	4
Twitching	4	4	4	4	4	4	4	4
Unusual behavior	4	4	4	4	4	4	4	4
Defecation	4	4	4	4	4	4 (6)	4	4
Observation of behavior in a novel environment „Arena“								
Transfer behavior	4	4	4	4	4	4	4	4
Locomotor activity	4	4	4	4	4	4	4	4
Palpebral closure	4	4	4	4	4	4	4	4
Piloerection	4	4	4	4	4 (6)	4	4	4
Startle response	4	4	4	4	4	4	4	4
Motion	4	4	4	4	4	4	4	4
Pelvic elevation	4	4	4	4	4	4	4	4
Tail position	4	4	4	4	4	4	4	4
Touch escape	4	4	4	4	4	4	4	4
Tail pinch	4	4	4	4	4	4	4	4
Reaction to handling	4	4	4	4	4	4	4	4
Physical examination								
Trunk curl	4	4	4	4	4	4	4	4
Reaching reflex	4	4	4	4	4	4	4	4
Body tone	4	4	4	4	4	4	4	4
Pinna reflex	4	4	4	4	4	4	4	4
Corneal reflex	4	4	4	4	4	4	4	4
Toe pinch	4	4	4	4	4	4	4	4
Body length	4	4 (2)	4 (2)	4 (2)	4 (2)	4	4 (2)	4 (2)
Skin color	4	4	4	4	4	4	4	4
Heart rate	4	4	4	4	4	4	4	4
Limb tone	4	4	4	4	4	4	4	4
Abdominal tone	4	4	4	4	4	4	4	4
Lachrymation	4	4	4	4	4	4	4	4
Pupillary reflex	4	4	4	4	4	4	4	4
Salivation	4	4	4	4	4	4	4	4
Provoked biting	4	4	4	4	4	4	4	4
Further Parameters								
Righting reflex	4	4	4	4	4	4	4	4
Tunnel test	4	4	4	4	4	4	4	4
Wire hang	4	4	4	4	4	4	4	4

Behavior scores of vehicle group in a modified Irwin test. Physiological status was graded with a score of 4. Variations from a normal score were observed with a score ranging from 0-3 or 5-8.

Table 2. Behavior Observation during ALX5407 Application

Observation	ALX5407 group							
Day	0	2	4	6	8	10	12	14
Weight	4	4	4	4	4	4	4	4
Neurobehavioral observation „Viewing Jar“								
External appearance	4	4	4	4	4	4	4	4
Body position	4	4	4	4	4	4	4	4
Spontaneous locomotor activity	4	4	4	4	4	4	4	4
Respiration rate	4	4	4	4	4	4	4	4
Twitching	4	4	4	4	4	4	4	4
Unusual behavior	4	4	4	4	4	4	4	4
Defecation	4	4	4	4	4	4	4	4
Observation of behavior in a novel environment „Arena“								
Transfer behavior	4	4	4	4	4	4	4	4
Locomotor activity	4	4	4	4	4	4	4	4
Palpebral closure	4	4	4	4	4	4	4	4
Piloerection	4	4	4	4	4	4	4	4
Startle response	4	4	4	4	4	4	4	4
Motion	4	4	4	4	4	4	4	4
Pelvic elevation	4	4	4	4	4	4	4	4
Tail position	4	4	4	4	4	4	4	4
Touch escape	4	4	4	4	4	4	4	4
Tail pinch	4	4	4	4	4	4	4	4
Reaction to handling	4	4	4	4	4	4	4	4
Physical examination								
Trunk curl	4	4	4	4	4	4	4	4
Reaching reflex	4	4	4	4	4	4	4	4
Body tone	4	4	4	4	4	4	4	4
Pinna reflex	4	4	4	4	4	4	4	4
Corneal reflex	4	4	4	4	4	4	4	4
Toe pinch	4	4	4	4	4	4	4	4
Body length	4	4 (2)	4	4 (2)	4 (2)	4 (2)	4	4 (2)
Skin color	4	4	4	4	4	4	4	4
Heart rate	4	4	4	4	4	4	4	4
Limb tone	4	4	4	4	4	4	4	4
Abdominal tone	4	4	4	4	4	4	4	4
Lachrymation	4	4	4	4	4	4	4	4
Pupillary reflex	4	4	4	4	4	4	4	4
Salivation	4	4	4	4	4	4	4	4
Provoked biting	4	4	4	4	4	4	4	4
Further Parameters								
Righting reflex	4	4	4	4	4	4	4	4
Tunnel test	4	4	4	4	4	4	4	4
Wire hang	4	4	4	4	4	4	4	4

Behavior scores of ALX5407 group in a modified Irwin test. Physiological status was graded with a score of 4. Variations from a normal score were observed with a score ranging from 0-3 or 5-8.

Table 3. Behavior Observation during ALX1393 Application

Observation	ALX1393 group							
Day	0	2	4	6	8	10	12	14
Weight	4	4	4	4	4	4	4	4
Neurobehavioral observation „Viewing Jar“								
External appearance	4	4	4	4	4	4	4	4
Body position	4	4	4	4	4	4	4	4
Spontaneous locomotor activity	4	4	4	4	4	4	4	4
Respiration rate	4	4	4	4	4	4	4	4
Twitching	4	4	4	4	4	4	4	4
Unusual behavior	4	4	4	4	4	4	4	4
Defecation	4	4	4	4	4	4	4	4
Observation of behavior in a novel environment „Arena“								
Transfer behavior	4	4	4 (6)	4	4	4	4	4
Locomotor activity	4	4	4	4	4	4	4	4
Palpebral closure	4	4	4	4	4	4	4	4
Piloerection	4	4	4	4	4	4	4	4
Startle response	4	4	4	4	4	4	4	4
Motion	4	4	4	4	4	4	4	4
Pelvic elevation	4	4	4	4	4	4	4	4
Tail position	4	4	4	4	4	4	4	4
Touch escape	4	4	4	4	4	4	4	4
Tail pinch	4	4	4	4	4	4	4	4
Reaction to handling	4	4	4	4	4	4	4	4
Physical examination								
Trunk curl	4	4	4	4	4	4	4	4
Reaching reflex	4	4	4	4	4	4	4	4
Body tone	4	4	4	4	4	4	4	4
Pinna reflex	4	4	4	4	4	4	4	4
Corneal reflex	4	4	4	4	4	4	4	4
Toe pinch	4	4	4	4	4	4	4	4
Body length	4	4 (2)	4	4 (2)	4	4	4	4 (2)
Skin color	4	4	4	4	4	4	4	4
Heart rate	4	4	4	4	4	4	4	4
Limb tone	4	4	4	4	4	4	4	4
Abdominal tone	4	4	4	4	4	4	4	4
Lachrymation	4	4	4	4	4	4	4	4
Pupillary reflex	4	4	4	4	4	4	4	4
Salivation	4	4	4	4	4	4	4	4
Provoked biting	4	4	4	4	4	4	4	4
Further Parameters								
Righting reflex	4	4	4	4	4	4	4	4
Tunnel test	4	4	4	4	4	4	4	4

Behavior scores of ALX1393 group in a modified Irwin test. Physiological status was graded with a score of 4. Variations from a normal score were observed with a score ranging from 0-3 or 5-8.