APPENDIX B

DEFINITION OF TERMS AND LEXICON OF CLINICAL OBSERVATIONS IN NONCLINICAL (ANIMAL) STUDIES

Movement

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tr>
<td>Anesthetized</td>
<td>The absence of or reduced response to external stimuli, accompanied with a loss of righting reflex.</td>
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<tr>
<td>Ataxia</td>
<td>Incoordination of muscular action involving locomotion, including loss of coordination and unsteady gait.</td>
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<td>Hyperactivity</td>
<td>An abnormally high level of motor activity.</td>
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<td>Hypersensitivity</td>
<td>An abnormally strong reaction to external stimuli such as noise or touch.</td>
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<td>Lethargy</td>
<td>A state of deep and prolonged depression stupor from which it is possible to be aroused, followed by an immediate relapse.</td>
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<td>Low carriage</td>
<td>The animal’s torso is carried very close to the ground during movement.</td>
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<td>Prostrate</td>
<td>Animal assumes a recumbent position due to loss of strength or exhaustion and may show intermittent uncoordinated movements.</td>
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<tr>
<td>Righting reflex</td>
<td>The ability of an animal, when placed on its back, to regain a position on all fours.</td>
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<tr>
<td>Unsteady gait</td>
<td>An erratic manner or style of walking.</td>
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Catalepsy A condition characterized by a waxy rigidity of the muscles such that the animal tends to remain in any position in which it is placed.

Paralysis Inhibition or loss of motor function; may be characterized by affected portion of the body.

**Respiration**

Audible respiration An abnormal respiratory sound heard while listening to the breathing of the animal (e.g., wheezing and rales).

Bradypnea An abnormal slowness of the respiration rate.

Dyspnea "Shortness of breath"; difficult or labored breathing.

Gasping Spasmodic breathing with the mouth open, or laborious respiration with the breath caught convulsively.

Hyperpnea Deep and rapid breathing.

Cheyne–Stokes respiration Breathing characterized by rhythmic waning and waxing of the depth of respiration, with regularly recurring periods of apnea: seen especially in coma resulting from affection of the nervous centers.

Hypopnea Shallow and slow breathing.

Irregular respiration No definite cycle or rate of breathing.

Labored respiration Forced or difficult, usually irregular breathing.

Tachypnea An excessive rapidity of the respiration rate.

**Condition of Skin and Fur**

Alopecia Deficiency of hair (baldness).

Cyanosis Visible skin and/or mucous membranes turn dusky blue due to lack of oxygenation of the blood.

Necrosis Actual tissue destruction, masses of dead/destroyed tissue.

**Urogenital Region**

Anuria An absence of or sharp decline in urine excretion.

Diarrhea An abnormal frequency and liquidity of fecal discharge.

Polyuria An abnormally sharp increase in the amount of urine excretion.

**Convulsions and Tremors**

Convulsions Transient, self-sustaining electrical dysrhythmias which have a tendency to recur. Convulsions are generally associated with a finite period of unconsciousness and have a muscular involvement manifested as disorganized limb movements.

Clonic This is often seen as a “paddling” motion of the forelegs of the animal.
Tonic  Muscular contraction, keeping limbs in a fixed position, generally extended to the rear.
Torsion  Postural incoordination or rolling. This is generally associated with the vestibular (ear canal) system.
Fasciculation  Rapid, often continuous contraction of a bundle of skeletal muscle fibers which does not produce a purposeful movement (twitching).
Tremor  Fine oscillating muscular movements which may or may not be rhythmic.

**Condition of Eyes**

Blepharospasm  A twitching or spasmodic contraction of the orbicularis oculi muscle.
Chemosis  Edema of conjunctiva(e). The conjunctival tissue responds to noxious stimuli by swelling.
Chromodacryorrhea  The response of reddish conjunctival exudate; no blood cells present in exudate (i.e., not true “bloody tears”).
Conjunctivitis  Inflammation of conjunctiva (mucous membrane which lines the eyelids and is reflected into the eyeball).
Exophthalmos  An abnormal protrusion of the eyeball from the orbit.
Lacrimation  The secretion of tears.
Miosis  Constriction of the pupil.
Mydriasis  Dilation of the pupil.
Nystagmus  An abnormal involuntary movement of the eyes. It may be rotational or horizontal or vertical plane.
Ocular exudate  Secretion (usually transparent and yellow) directly from the eye.
Opacity  A loss of transparency of the eyeball.
Pinpoint pupils  Ultimate state of miosis.
Ptosis  Refers to a dropping of the upper eyelid, thought to be due to impaired conduction in the third cranial nerve.

**Miscellaneous**

Analgesia  The absence of (or reduced response to) painful stimuli.
Hunched posture  The drawing-in of both ends of the body and extremities with a sharp arching of the back.
Kyphosis  Humpback—an abnormal curvature and dorsal prominence of the vertebrae column.
Nasal discharge  Fluid secretion from the nostrils.
Piloerection  Body hair stands on end; dilation of the pupils usually accompanies piloerection.
Salivation  Excessive secretion of saliva from the mouth.
Straub tail  Condition, especially in mice, in which the animal carries its tail in an erect (vertical or nearly vertical) position. This
sign is commonly associated with chemicals (e.g., morphine) that bind to opiate receptors.

**Reflexes**

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<tr>
<th>Reflex Type</th>
<th>Description</th>
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<tr>
<td>Corneal reflex</td>
<td>Closure of the eyelids in response to a corneal touch (e.g., with a soft brush bristle).</td>
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<td>Grip strength (or Screen Grip)</td>
<td>Measure of the grip strength of the forelimbs or hindlimbs; may be evaluated quantitatively or by subjective estimate or impairment (rodents only).</td>
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<td>Pinna reflex</td>
<td>Twitch of the outer ear in response to a gentle touch.</td>
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<td>Preyer's reflex (auditory startle response)</td>
<td>Involuntary movement of the outer ears produced by an auditory stimulus (especially in rats).</td>
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<tr>
<td>Pupillary reflex</td>
<td>Contraction of the pupil in response to light stimulation of the retina.</td>
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<tr>
<td>Righting Reflex</td>
<td>The ability to land on (when dropped) or regain normal stance on all four limbs.</td>
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<tr>
<td>Startle reflex</td>
<td>Response to sharp sound, touch, or other startling stimulus; response may range from “absent,” to “normal,” to “hyperreactive,” including exaggerated jerking, jumping, frantic attempts to escape, and even convulsion.</td>
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