**Supporting Information 4: Therapeutics and Pharmacology Case Report Form**

Date that this CRF was filled out:

Name of Laboratory/PI:

Name of person filling out CRF:

Project name/Identifier:

Animal ID or Study ID (as applicable):

**Type of model system:**

* Mammalian systems (e.g., rodents, other mammals): \_\_\_\_\_\_
* Non-mammalian systems (e.g., *Drosophila*, zebrafish): \_\_\_\_\_\_

**Type of study:**

* Anesthetized: \_\_\_\_\_\_
* Non-anesthetized: \_\_\_\_\_\_

**Endpoint of study:**

* Pre-defined time point: \_\_\_\_\_\_
* Seizure-induced sudden death: \_\_\_\_\_\_
* Other \_\_\_\_\_\_

|  |  |
| --- | --- |
| **CDE** | **Data Collected** |
| Type of therapeutic administered (anti-seizure medication) | ☐ Small molecule  ☐ Biologic  ☐ Anti-sense oligonucleotides  ☐ Dietary therapies / metabolic therapy  ☐ Neurostimulation  ☐ Non-traditional medication  ☐ Other \_\_\_\_\_\_ |
| Name of therapy administered; insert details on:   * Name (brand/chemical) * Lot number * Batch number * Supplier Catalog information |  |
| Dose |  |
| Frequency of administration |  |
| Method of administration | ☐ Intraperitoneal (IP)  ☐ Oral gavage  ☐ In food or water  ☐ Intramuscular (IM)  ☐ Intravenous (IV)  ☐ Subcutaneous (SC)  ☐ Intrathecal  ☐ Bath immersion  ☐ Other \_\_\_\_\_\_ |
| Timeline: when in relation to seizure onset or induction is drug administered |  |
| Name of vehicle or control, if applicable |  |
| Mechanism of action |  |
| How was mechanism of action confirmed, i.e. antagonist administration |  |
| Type of dietary therapy | ☐ Classic Ketogenic diet  ☐ Low glycemic index therapy  ☐ Modified Atkins  ☐ Other \_\_\_\_\_\_ |
| Parameters of dietary therapy |  |
| Types of Neurostimulation   1. Site of stimulation 2. General parameters 3. Duration of stimulation 4. Strength 5. Time |  |
| Overall health   1. Weight 2. Appearance (add in standardized terms) | ☐ Appeared overall healthy  ☐ Weak/sluggish  ☐ Moribund |
| Onset of therapeutic effect (time after drug administration) |  |
| Offset of therapeutic effect |  |
| Behavioral seizures | ☐ Reduction; ☐ Cessation; ☐ No effect; ☐ Other \_\_\_\_\_\_ |
| Electrographic seizures | ☐ Reduction; ☐ Cessation; ☐ No effect; ☐ Other \_\_\_\_\_\_ |
| What seizure features were affected? | ☐ Frequency; ☐ Duration; ☐ Other \_\_\_\_\_\_ |
| Prevention of respiratory arrest | ☐ Yes; ☐ No; ☐ Unknown |
| Prevention of respiratory abnormalities | ☐ Yes; ☐ No; ☐ Unknown |
| Prevention of cardiac abnormalities | ☐ Yes; ☐ No; ☐ Unknown |
| Extension of survival? | ☐ Yes; ☐ No; ☐ Unknown |
| **Comments:** | |
| **Additional/Adverse Effects** | |
| Known toxicology? | ☐ Yes; ☐ No; ☐ Unknown |
| Motor Effects | |
| Anesthesia (total loss of feeling or sensation, unresponsive to tail pinch and tapping of the eye) | ☐ Yes; ☐ No; ☐ Unknown |
| Ataxia (lack of voluntary coordination of muscle movements, can include wobbly gait) | ☐ Yes; ☐ No; ☐ Unknown |
| Loss of righting reflex (unable to turn over when placed in a dorsal recumbent position) | ☐ Yes; ☐ No; ☐ Unknown |
| Unable to grasp rotarod (inability to hold on to rotarod in order to begin test) | ☐ Yes; ☐ No; ☐ Unknown |
| Minimal motor impairment | ☐ Yes; ☐ No; ☐ Unknown |
| Loss of muscle tone (soft, with low muscle tone) | ☐ Yes; ☐ No; ☐ Unknown |
| Sedation (very calm or appear to be sleeping, but will respond to external stimuli) | ☐ Yes; ☐ No; ☐ Unknown |
| Altered startle response | ☐ Yes; ☐ No; ☐ Unknown |
| Seizure Effects | |
| Continuous seizure activity | ☐ Yes; ☐ No; ☐ Unknown |
| Clonic seizures (muscle convulsions of the forelimbs and/or hindlimbs) | ☐ Yes; ☐ No; ☐ Unknown |
| Neurological Manifestations | |
| Intense, repeated jumping straight up | ☐ Yes; ☐ No; ☐ Unknown |
| Myoclonic jerks (non-rhythmic muscle twitch, jerk, shake or spasm) | ☐ Yes; ☐ No; ☐ Unknown |
| Wild running (frantic running) | ☐ Yes; ☐ No; ☐ Unknown |
| Writhing (a stretch, tension to one side, extension of hind legs, contraction of the abdomen, or twisting of the trunk) | ☐ Yes; ☐ No; ☐ Unknown |
| Hyperactivity (increased velocity of movement, faster motion than typical) | ☐ Yes; ☐ No; ☐ Unknown |
| Severe tremors (strong rhythmic muscle contraction, shaking movements in the limbs or body leading to complete or near incapacitation) | ☐ Yes; ☐ No; ☐ Unknown |
| Exophthalmos (eye bulging) | ☐ Yes; ☐ No; ☐ Unknown |
| Tremors (rhythmic muscle contraction, shaking movements in the limbs or body) | ☐ Yes; ☐ No; ☐ Unknown |
| Muscle spasms (continuous or intermittent muscle contraction or rigidity) | ☐ Yes; ☐ No; ☐ Unknown |
| Wet dog shakes (a brief, ~1 second shaking of entire body. not restricted to single body part) | ☐ Yes; ☐ No; ☐ Unknown |
| Stretching and rolling (extension/elongation of the body; rolling onto one side with or without completely exposing the ventral body surface) | ☐ Yes; ☐ No; ☐ Unknown |
| Retropulsion (backward locomotion or backward circling) | ☐ Yes; ☐ No; ☐ Unknown |
| Arching (arching of the back) | ☐ Yes; ☐ No; ☐ Unknown |
| Hypoactivity (decreased velocity, slower-than-typical motion) | ☐ Yes; ☐ No; ☐ Unknown |
| Physiological Manifestations | |
| Diarrhea (loose, watery stool) | ☐ Yes; ☐ No; ☐ Unknown |
| Salivation (noticeable saliva outside the mouth) | ☐ Yes; ☐ No; ☐ Unknown |
| Piloerection (hairs become erect and bristle due to hair follicle contraction i.e., goose bumps) | ☐ Yes; ☐ No; ☐ Unknown |
| Hyperesthesia (increase in sensitivity for all senses, i.e., jumping at noises, running or jumping when touched) | ☐ Yes; ☐ No; ☐ Unknown |
| Vocalizations (noises audible to humans) | ☐ Yes; ☐ No; ☐ Unknown |
| Excessive grooming (intense, excessive or disproportionate body cleaning; may be restricted to specific body parts, with or without visible signs of tissue damage) | ☐ Yes; ☐ No; ☐ Unknown |
| Urinary staining (pigmented urine) | ☐ Yes; ☐ No; ☐ Unknown |
| Bloody urine (bright red urine) | ☐ Yes; ☐ No; ☐ Unknown |
| Cold tail (tail feels cold when touched) | ☐ Yes; ☐ No; ☐ Unknown |
| Cold to the touch (animal’s body feels colder than typical - more severe than cold tail, above) | ☐ Yes; ☐ No; ☐ Unknown |
| Changes in heart rate | ☐ Yes; ☐ No; ☐ Unknown |
| Other toxic effect |  |
| **Comments:** | |

Abbreviations: CRF: Case Report Form; PI: Principal investigator.

Instructions: Please check boxes where applicable. If none of the predetermined options is appropriate, use the default space to specify your answer. This form is to be filled in for one individual animal, unless otherwise specified.

Please refer to more extensive CRF where suitable, as developed by the ILAE/AES Joint Translational Task Force:

Report on preclinical Core CDEs

<https://onlinelibrary.wiley.com/doi/10.1002/epi4.12234>

Report on preclinical neurobehavioral CDEs

<https://onlinelibrary.wiley.com/doi/10.1002/epi4.12236>

Report on preclinical physiology CDEs

<https://onlinelibrary.wiley.com/doi/10.1002/epi4.12261>

Report on preclinical pharmacology model CDEs

<https://onlinelibrary.wiley.com/doi/10.1002/epi4.12254>

Report on preclinical EEG CDEs

<https://onlinelibrary.wiley.com/doi/10.1002/epi4.12260>