Planning document for CounterACT experiments (version 1.04a)

Preamble: This document is intended to provide a brief, structured means for assessing the goals of an experiment and whether the study design, study variables, sample size, planned statistical analysis, randomization scheme and study timeline are well-aligned with the goals. It should be completed by the Core C statistical consultant in collaboration with Project personnel. Example entries are shown in italicized font.

Research Question(s) *(in PICO format (https://guides.nyu.edu/c.php?g=276561&p=1847897))* or Milestone Being Addressed *(quote milestone text):*

In the TETS/SE model, is perampenal more effective than midazolam in reducing the duration of seizures or the associated mortality?

In the TETS/SE model, is perampenal more effective than diazepam in reducing the duration of seizures or the associated mortality?

Experimental model: *TETS/SE mouse model*

Outcome Table:

Construct	Operationalization / reliability evidence level / blinded assessors	Timing	Distribu-tion type	Anticipated model	Priority
Seizure duration/mortality	*Animals instrumented for EEG & videotaped. Dorota scores for presence of [detail particular seizure feature(s) of interest]. Composite indicator for seizure/death is made for each minute. /Low evidence for reliability /Not blinded*	*Minute-by-minute, up to 180 minutes post-intoxication, with treatment typically administered at 10 or 40 minutes*	*Binary*	*Composite outcomes formed by partitioning follow-up time into three periods ([0, 45), [45, 90), and 90+ minutes) and summing the minute-to-minute counts for the period Mixed-effects Poisson*	*Primary*
Convulsions/mortality	*"*	*"*	*"*	*"*	*Secondary*

Notes: Reliability evidence level should be scored as follows:
High: Operationalization is (i) purely objective measurements from laboratory instruments not prone to significant operator or batch effects or (ii) involves a subjective component where relevant evidence for reliability is available from studies in multiple labs

Medium: Operationalization is (i) purely objective measurements from laboratory instruments prone to operator or batch effects or (ii) involves a subjective component where relevant evidence for reliability is available from single-lab studies
Low: Operationalization involves a subjective component and no formal evidence for reliability is available. (Formal evidence could include reliability studies undertake in our own lab that aim to estimate the between-rater reliability of the measurement process.)

Concurrent comparison groups (including relevant dosing information) and sample size

Vehicle control for Perampenal (x.xx dose, 40 minutes) (n = XX)

Vehicle control for Midazolam (x.xx dose, 40 minutes) (n = XX)

Midazolam (x.xx dose, 40 minutes) (n = XX)

Perampenal (x.xx dose, 40 minutes) (n = XX)

Historical comparison groups (including relevant dosing information), sample size

(Source files for historical controls: DZP_MDZ_cleaned_102915V5ExtraSurvivalData.csv & forStat DZP_MDZ_cleaned_102915V5.csv *from folder* H:\CounterAct\Project1\Seizure\Data\forStat)

Vehicle control for Diazepam (x.xx dose, 40 minutes) (n = XX)

Diazepam (x.xx dose, 40 minutes) (n = XX)

Vehicle control for Midazolam (x.xx dose, 40 minutes) (n = XX)

Midazolam (x.xx dose, 40 minutes) (n = XX)

Sample Size justification: *Using results from previous studies, we applied the exemplary dataset method to determine that the given sample sizes would provide 80% power (two-sided alpha=5%) to detect incidence rate ratios of 0.50 or greater.*

Randomization plan (brief mention of scheme and personnel who will ensure valid randomization):

Anticipated date when final study data will become available to Core C for analysis: *mid-May, 2016*

Anticipated turn-around time for Core C analysis (this would typically be at 4 to 6 weeks, given the three major analysis tasks [plan, implement, and review] and the many other commitments of Core C personnel): *4 weeks*

Date experiment plan was initiated:

List (with dates) of all major changes, including changes to experimental design, choice of comparators, sample size, or study endpoints

Date of last revision: