Assessing safety of telemetric devices in preclinical studies of primates – data aggregation step

Yulia Skovpen[1], Sonal Thakar[1], Oleg Stroganov[1], Fedor Novikov[1], Tania Khasanova[1], Dale Stevens[2], Noel Dybdal[2], Julie Bryant[1]

[1] Rancho BioSciences, LLC, USA. [2] Genentech, Inc., South San Francisco, USA

Conventional monitoring of clinical and physiological measurements during experimentation can be intrusive, adding disruptive variables to study endpoints. In addition, there are growing societal concerns regarding the welfare, ethics and value of using large numbers of animals for medical research. The latter has encouraged focused development and application of the principles of replacement, reduction and refinement (3R's) in the use of animals in medical research. Advances in telemetry signal acquisition provide the opportunity for both improved animal study data collection and applications of 3R's. Improved animal welfare results from the opportunity to integrate general toxicology and safety pharmacology studies into a single study providing reduction in animal use and Bluetooth telemetry signal acquisition supports animal social housing providing an important refinement in study design. Here, we evaluated if implanted telemetry instrumentation acquired data parallel conventional methods for quantifying physiological measurements. In addition, we compared clinical and pathology data for telemetry instrumented vs non-instrumented animals to assess for potential off target effects. Data was collected, aggregated, harmonized and evaluated for any potential effects the implantation of the telemetry instrumentation may have on measurements.

Thirty integrated general toxicology plus cardiovascular safety pharmacology preclinical studies carried out in Cynomolgus monkeys were selected for the aggregated datasets. The studies were standardized into a uniform format where test parameters, assessments and evaluations have the same structure, layout, parameter gradation system, and units. Tedious, but necessary, work was done to collect and bring to a uniform format all telemetric values and timepoints to allow researchers to evaluate prior dosing, dosing and post-dosing time intervals in the consolidated dataset. For individual clinical signs, clinical observations, neurological exam, ophthalmological exam and histopathology datasets, dictionaries were created to standardize terminology. The consolidated dataset can now be used for statistical analysis and help researchers answer many questions, for example:

1) Are telemetry measurements from integrated studies more, less, or similarly accurate compared to conventional non-telemetric (restrained and/or sedated, external leads) measurements?
2) In animals for which physiological data were recorded using both telemetric and non-telemetric methods, were the measurements comparable?
3) Does surgical telemetry instrumentation impact clinical or physiological measurements over time as compared with non-instrumented?
4) Are there any unforeseen adverse effects related to inclusion of surgically instrumented animals in a general toxicology study (i.e. ability to interpret or negative impact on general toxicology outcomes or safety pharmacology outcomes)?