STUDY DESIGN GUIDE

Process Overview

The following represents principal features of nonclinical studies relating to the design and conduct of your program. Our scientists, veterinarians, pathologists, and other CBSET staff are happy to discuss and review these features in greater detail to formulate a study design specific to your technology/therapy. Once we have settled on specifics for your study, we will issue a "Letter of Payment Authorization" (LOPA) summarizing the scope of work and cost estimates. Upon receipt of the signed LOPA, our operations team will schedule dates to commence work on your study and coordinate related logistics.

1) **Aims & Objectives:** Simple proof of concept, performance evaluations or safety & efficacy.

2) **GLP/Non-GLP:** Studies can be carried out in compliance with US FDA regulations for Good Laboratory Practice (GLP). GLP studies necessarily entail more detailed assessments of animal health, internal quality assurance auditing and extensive reporting. All studies relating to safety assessments or related claims should be run per GLP regulations.

3) **In-life Phase:**

   i) Is there an established animal model or will a new model need to be developed?

   ii) Does CBSET have an approved Institutional Animal Care and Use Committee (IACUC) protocol for the model or will a new protocol need to be approved?

   iii) Total number of animals required

   iv) Age/weight/sex requested

4) **Procedural Requirements:** Description of operating procedures such as laparoscopy, endoscopy, heart surgery, interventional procedure, etc., including who will perform the procedures (e.g., sponsor-provided physician or CBSET staff).

5) **Medical Imaging Modalities:** Radiography, CT scan, angiography, fluoroscopy, echocardiography or specialized/third-party equipment.

6) **Treatment Description:** Devices, biologics, control or comparator regimens.

   i) Are any pre-treatment procedures required (e.g., special diets, co-therapies, etc.)?

   ii) Are there any post-treatment requirements (e.g., daily administration of medication)?

ABOUT CBSET

CBSET is a state-of-the-art translational research institute located in the greater Boston area of MA.

Our mission is to advance biomedical research, through innovative, high-quality services. We combine top-tier research with operational expertise. Since our inception, CBSET has continued to develop technical and scientific acumen through collaborative projects in the medical device, pharmaceutical and academic communities.

Our 40,000 square foot, GLP-compliant, AAALAC- accredited facility includes vivaria, procedure rooms, catheterization / imaging labs, surgical and necropsy suites, histopathology, SEM, and a range of other technologies.

Why CBSET?

- **Credibility.** We are recognized as unbiased experts, bringing independent credibility to your regulatory filings.
- **Culture.** Our culture is based in science; we value new models and creative collaboration.
- **Mission.** Our motivation is to enable your success; your product is our mission.
- **Integrated resource.** Our multidisciplinary team includes board-certified veterinary, quality, biological and quantitative sciences expertise, as well as board-certified pathologists – all in one facility.

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INTEGRATING SCIENCE
IMPROVING LIVES

7) **In-life Sample Collection and Endpoints:** Blood collections, clinical observations, photographs, imaging, body weights, and clinical pathology.

8) **Necropsy:**

   i) Acute (i.e., non-recovery) or chronic? What are the necropsy time point(s) for chronic studies (groups may be sacrificed at varying intervals)?

   ii) Biopsies to be obtained/organs to be harvested

9) **Histology:**

   i) Are there solid metal or non-metallic devices to be sectioned?

   ii) Number of tissue types

   iii) Staining (primary and immunostaining per tissue type)

   iv) Assay development. CBSET can develop novel assays.

10) **Pathology:** Is a pathologist's assessment required?

   i) Scoring (quantitative or semi-quantitative scoring paradigm)

   ii) Morphometry

   iii) Micro-imaging

11) **Report Type:** Report generation and requested image panels.

   i) Data-only (i.e., PowerPoint, Excel files)

   ii) Summary (brief summarization of results and methods)

   iii) GLP/Non-GLP report (comprehensive report including all elements recommended per regulatory guidelines).

   iv) Pathology narrative (brief discussion of macro observations/slide review, without summarizing data in tables/graphs)

   v) Image panels