INITIAL BRIEFING PACKAGE OUTLINE
FOR ANIMAL MODEL QUALIFICATION SUBMISSION
Updated: 11/01/13

Provide the Initial Briefing Package (IBP) details requested below. The Qualification Review Team (QRT) may request additional information.

1. Administrative Information

a. Submitters should refer to resources and information at the following link: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm284078.htm
b. Provide submitter name and contact information including Principal Investigator(s), Consortium Group Member(s), associated institutions, regulatory consultants and government agencies.

2. Questions for FDA

3. Animal Model Development Plan

Describe the overall animal model development plan (i.e., complete list of in vitro and in vivo studies planned, rationale for each study, protocols [both experimental and IACUC], and proposed timeline of studies). The plan should allow for modification or refinement as data are gathered and analyzed, and projections or expectations change.

4. Overview of the Proposed Animal Model

The information requested below should provide a comprehensive overview of the human disease or condition and the characteristics of the proposed animal model. This section should include an overview as presented in the Letter of Intent (LOI) and more in-depth discussions of each topic, including any new information since the submission of the LOI.

a. Introduction – This section should be written in abstract form, similar to the introduction provided in the LOI. It should include brief summaries of the human disease or condition including the identification of key features, the corresponding proposed animal model, justification of why this animal model is needed, and its intended future use in drug[1] development[2] under the Animal Rule.

b. Human disease or condition – This section should provide a detailed description of the human disease or condition. Include the information provided in the corresponding section of the LOI (e.g., route of exposure, disease time course) and the following, if available:
    i. Pathophysiological mechanisms

[1] As used in this outline, all references to *drugs* include human drugs, therapeutic biological products, cellular and gene therapies, and vaccines.
[2] Qualified animal models are to be used for product development; therefore, the submitter should include one or more of the following possible therapeutic indications with regard to the disease or condition (pre-, post-exposure prophylaxis or treatment).

ii. Methods of diagnosis (e.g., laboratory tests, characteristic clinical signs/symptoms)

c. Proposed animal model – This section should provide a detailed description of the proposed animal model. Include the information provided in the corresponding section of the LOI (e.g., route of exposure, disease time course) and the following, if available:
   i. Pathophysiological mechanisms of the disease or condition
   ii. Critical diagnostic findings (e.g., results from microbiology, hematology, blood chemistries, immunological assays)

d. Include a point-by-point comparison between the features of the human and animal disease or condition caused by the etiologic and challenge agent[3], respectively. If there are features for the human disease or condition that are substantially different from those in the animal model, they should be listed and discussed. A tabular format is suggested for this comparison.

5. Proposed Context of Use (COU)

The information provided in the proposed COU should reflect current scientific understanding. Depending on the degree of model development, the amount of data available at the time of the IBP submission may limit your ability to provide all the details requested in the proposed COU. The COU should specify how the animal model is to be used in drug development under the Animal Rule, and should include details necessary to replicate the model as well as measures of quality control and assurance. The development of the COU is an iterative process between the QRT and the submitter as the model is refined.

Characteristics of the animal should include information such as species, strains and substrains, breeds (where applicable), age, sex, weight, origin of the animals (to the extent known), and animal vendors. Additional information such as microbial specifications, tests necessary to rule out prior exposure to substances or biological organisms that may affect the study, necessary screening assays, and exclusion criteria should also be included. Characteristics of the challenge agent should include information such as name, source, method of preparation, method of delivery, route of exposure, and means by which it was verified that the challenge agent was given at the specified dose. Depending on the type of challenge agent, additional information may be included.

Data necessary to support the proposed COU should be submitted. If FDA identifies any inconsistencies between the proposed COU and the data submitted, the Agency may request additional data or restatement of the COU.

[3] The term *etiologic agent* in this outline, refers to a substance causing disease in humans. The term *challenge agent* refers to a substance used in the animal studies to model the human disease.

6. Knowledge Gaps

The submitter should consider and describe the limitations of the existing information and identify critical gaps in knowledge related to qualifying the animal model.

7. Data Quality and Integrity

It is the submitter's responsibility to provide complete and accurate submissions. Since qualification is a regulatory conclusion,[4] FDA recommends the use of Good Laboratory Practices[5] (GLP) to the extent practicable, for the model-defining natural history studies[6] submitted to support the qualification of an animal model, to facilitate study conduct in a manner that ensures data quality and integrity. Indicate which studies, if any, will be or have been done in accordance with GLP regulations. A plan to ensure data integrity should be included for studies not performed in accordance with GLP regulations. Discuss any issues encountered during the conduct of completed studies, or anticipated issues related to planned studies, that may affect the quality and interpretation of the data; include how these issues have affected or will affect the conclusions from the studies.

8. Methods and Results

This section should provide a summary of the completed studies, including individual study synopses and an integrated analysis of the animal model qualification study results. Include final study protocols and amendments, statistical plans, final IACUC approved protocols including amendments, summary data tabulations of dependent variables for each experimental group, animal medical records, and inclusion/exclusion criteria for animal subjects.

The detailed methodology for measuring the primary and any secondary endpoints, including information regarding the validation of these measurements should be provided. If telemetry data are included, a description of how the data were collected and presented should be discussed.

9. Appendix

Include a list of references and electronic copies of those that are most relevant for FDA review.

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[4] Woodcock, J, S Buckman, F Goodsaid, MK Walton, I Zineh, 2011, Qualifying Biomarkers for Use in Drug Development: A US Food and Drug Administration Overview, Expert Opin Med Diagn, 5(5):369-374.
[5] See 21 CFR 58.
[6] In the context of animal model qualification, the *model-defining natural history studies* are the animal studies that establish the ranges of values of key parameters of the disease or condition that will be specified in the context of use for the qualified model and that will be used as measures of quality control and quality assurance when the model is replicated.