

Institutional Handbook of Operating Procedures
Policy 11.02.01

Section: Research	Responsible Vice President: Executive Vice President and Provost
Subject: Nonclinical Studies	Responsible Entity: Regulated Studies

I. Title

Institutional Office of Regulated Nonclinical Studies

II. Policy

The Institutional Office of Regulated Nonclinical Studies (ORNcS) is granted authority to assess/evaluate funding applications that include regulatory compliance with the Good Laboratory Practices (GLP) regulations and the New Drug and Biological Drug Products; Evidence Needed to Demonstrate Effectiveness of New Drugs When Human Efficacy Studies Are Not Ethical or Feasible (21 CFR Parts 314 and 601) regulations (a.k.a. the Animal Rule). The subsequent planning, management and regulatory oversight of GLP compliant studies or adequate and well controlled studies requiring conduct under a Quality System using GLP as the reference standard is managed through the ORNcS via a partnership with the Principal Investigator. This includes studies where GLP compliance is expected “to the extent practicable” as stated in the FDA guidance document “Product Development Under the Animal Rule Guidance for Industry.”

ORNcS is required to be involved in all studies regarding any material or mention of GLP standards. Moreover, no study conducted at UTMB shall be referenced, conducted or portrayed in any manner as a close equivalent or partially GLP-compliant study without involvement of ORNcS as mandated by the Executive Vice President, Provost.

All GLP statements are to be prepared by ORNcS. All external communications referencing GLP statements are required to be reviewed by ORNcS. Regulated nonclinical studies meeting the scope of the GLP regulations require written authorization from ORNcS.

Violation of this policy may result in disciplinary action up to and including termination for employees; a termination of employment relationship in the case of contractors or consultants; or suspension or expulsion in the case of a student. Additionally, individuals may be subject to loss of access privileges and civil and/or criminal prosecution.

III. Mission

The mission for the University of Texas Medical Branch (UTMB) Office of Regulated Nonclinical Studies (ORNcS) is to provide scientific, regulatory, and Good Laboratory Practice support to research and development programs during planning and conduct of in vitro and in vivo nonclinical studies to support licensure.

IV. Office Structure

ORNcS is structured to include:

1. Regulatory & Scientific Affairs

- a)** RSA, with mutual partnership of PI, determines what nonclinical test data are needed to show that a product is sufficiently safe and efficacious. RSA assistance

promotes product development by identifying strategies associated with regulatory needs, technical pieces and institutional support for project development and testing. RSA provides the management and oversight of the regulated study and independent analysis to the PI nonclinical test results and conclusions that sets standards for laboratories conducting nonclinical testing.

- b) The Director of RSA is authorized to effectuate primary communications related to regulated nonclinical studies between the FDA, International Regulatory Agencies and UTMB.

2. Regulatory Operations

- a) Regulatory Operations independently monitors both the quality and integrity of data used to support the approval of a regulated product. FDA GLP regulations, applicable to the end stages of product development, govern diverse topics including, but not limited to:
 - (1) equipment qualification and maintenance records;
 - (2) standard operating procedures;
 - (3) animal facility observations;
 - (4) personnel training records;
 - (5) test and control article handling documentation;
 - (6) protocol and final report.
- b) Regulatory Operations provides Records Retention Management for the storage and retrieval of records and data. All raw data, documentation, protocols, and final reports generated as a result of a nonclinical laboratory study shall be retained. Records are indexed, archived and electronically documented. Record retention requirements follow the standards set forth in 21 CFR Part 58, Subpart J, 58.195.

V. **Procedure Pre-Award**

- A. All regulated grant and contract applications must be reviewed and receive written approval from both: a) the Director, Regulatory & Scientific Affairs and/or scientific consultant as necessary; and b) the Director, Regulatory Operations.
- B. Partnership with PI is enlisted for review and determination of regulatory requirements towards plan development and implementation to protect the Institution, PI and associated vendors of study.
- C. To expedite the procedure the following is required:
 - 1. Notification from PI of intent to respond to funding opportunity at time of consideration;
 - 2. Five (5) day review period PRIOR to application deadline. A decision regarding UTMB's capacity, ability and/or willingness to perform the requested study will be provided by ORNcS in the form of a signed letter;
 - 3. Where animal research is involved, the Animal Resources Center (ARC) Director, or designated personnel, is required to confirm, review, and approve the Pre-Award animal protocol.
- D. ORNcS has the authority to grant "Pending Institutional Approval" at their discretion. The "Pending Institutional Approval" will be granted in the form of a letter signed by one or both the Director, RSA and the Director, Regulatory Operations and provided to the PI.

- E. All proposed studies are submitted with the explicit understanding that the request may be denied by the ORNcS and UTMB. Submission does not guarantee approval or “Pending Institutional Approval” of the grant and/or contract application. Any appeal of ORNcS’s decision should be submitted to the Associate Chief or Chief Research Officer within ten (10) days of the decision.
- F. Any study intended to support FDA licensure is required to be reviewed by ORNcS prior to be submission as a GLP or Animal Rule study.

VI. Procedure, Post-Award

- A. RSA provides management and oversight for conduct, organization, implementation and execution of the funded regulated study. All studies are planned with the PI, Study Director and Director, RSA. Execution of the study will be conducted under the direction of the Study Director in consultation with PI and Director, RSA as appropriate.
- B. Review for regulatory compliance will be conducted under the direction of the Director, Regulatory Operations.
- C. All personnel involved in the study will comply with the applicable regulations, study protocol and UTMB Standard Operating Procedures.
- D. This policy applies to:
 - 1. ALL UTMB faculty;
 - 2. Visiting Scientists regarding approval and oversight of scientific studies performed in compliance with or represented as in compliance with regulations, and;
 - 3. ALL Staff participating in a nonclinical research study to collect data that will be submitted to the FDA, EPA, or equivalent foreign agency for product approval.

VII. Repercussion of Non-Compliance

Instances of deliberate breach of Policy including, but not limited to, failure to file or knowingly filing an incomplete, erroneous, or misleading form, violations of the guidelines, or failure to comply with prescribed monitoring procedures, will be adjudicated in accordance with applicable disciplinary policies and procedures for each individual. Possible sanctions may include some or all of the following actions:

- 1. Termination of the activity;
- 2. Disciplinary action against the employee in accordance with discipline described in the policy section above.

VIII. Monitoring

A regulatory compliance monitoring plan will be developed for each GLP or Animal Rule study under the direction of Director, Regulatory Operations. Quality Assurance (QA) plans may be developed for laboratories operating under Quality Systems who voluntarily, or by contract requirement, necessitate periodic independent QA inspections or data reviews.

All inspections of regulated studies by either the sponsor or federal agency officials are managed through the Quality Assurance Unit within ORNcS.

Vendors and/or subcontractors, for regulatory nonclinical studies, may require assessment through a vendor qualification and/or subsequent quality assurance process under the direction of Director, Regulatory Operations.

IX. Definitions

Director, Regulatory & Scientific Affairs: Regulatory & Scientific Affairs (RSA) provides regulatory guidance for nonclinical studies which include infectious disease related projects to develop vaccines, therapeutics and diagnostics. The incumbent advises the university administration and principal investigators (PI) on scientific and regulatory policy involving strategy in the design and conduct of regulated and non-regulated studies to support development of products designed for the treatment and prevention of human disease for study in clinical trials and may be candidates for licensure. Involved is the design and conduct of both in vitro and in vivo GLP studies that meet scientific and regulatory requirements. The studies are designed to demonstrate vaccine potency, efficacy and safety to prevent disease, implementation of therapeutics to treat infectious disease, definition of antigens that stimulate protective immunity, diagnostic tests to improve clinical medicine, and translation of scientific discovery in the regulatory pathway to product development. Effort is focused on collaborative and programmatic research involving the cooperation of multiple scientific disciplines working together in an environment disciplined by regulatory principles and compliance. (UTMB JD A0401)

Director, Regulatory Operations: The incumbent provides strategic, regulatory, and educational support and expert advice regarding compliance with federal and state requirements related to regulated nonclinical studies at UTMB; provides oversight for regulatory operations of the Institutional Office of Regulated Nonclinical Studies including the Quality Assurance Unit and Good Laboratory Practices (GLP) archive; approves institutional policies and Standard Operating Procedures (SOPs) governing regulatory operations for nonclinical studies. (UTMB JD A0946)

Principal Investigator: An individual authorized by the institution to direct the externally funded project or activity. He or she is responsible and accountable to the institution and funding entity, such as NIH, for the proper conduct of the project or activity. (I.E., NIH Office of Extramural Research Glossary & Acronym Definitions.)

Study Director (associated with GLP study): The individual responsible for the overall conduct of a nonclinical laboratory study. The study director has overall responsibility for the technical conduct of the study, as well as for the interpretation, analysis, documentation and reporting of results, and represents the single point of study control. (21 CFR Part 58 Subpart A58.3(m) and Subpart B58.33) The ORNcS Study Director provides support for both regulated and non-regulated scientific studies regarding regulatory oversight, summaries and protocols. The ORNcS Study Director will work with the PI, Director RSA and technical staff associated with given study.

21CFR Part 58: U.S. Food & Drug Administration (FDA) Code of Regulations for Good Laboratory Practice (GLP) for Nonclinical Laboratory Studies.

21CFR Parts 314 and 601: U.S. Food & Drug Administration (FDA) Code of Regulations for New Drug and Biological Drug Products; Evidence Needed to Demonstrate Effectiveness of New Drugs When Human Efficacy Studies Are Not Ethical or Feasible.

Animal Rule Studies: Studies outlined in the U.S. Food & Drug Administration Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) Product Development Under the Animal Rule Guidance for Industry (October 2015), to include:

- Adequate and well-controlled animal efficacy studies
- PK and/or PD studies in animals used to select a dose and regimen in humans
- Model-defining natural history studies

Adequate and Well Controlled Study: An adequate and well-controlled study (21CFR Part 314, Sec. 126) has the following characteristics:

(1) There is a clear statement of the objectives of the investigation and a summary of the proposed or actual methods of analysis in the protocol for the study and in the report of its results. In addition, the protocol should contain a description of the proposed methods of analysis, and the study report should contain a description of the methods of analysis ultimately used. If the protocol does not contain a description of the proposed methods of analysis, the study report should describe how the methods used were selected.

(2) The study uses a design that permits a valid comparison with a control to provide a quantitative assessment of drug effect. The protocol for the study and report of results should describe the study design precisely; for example, duration of treatment periods, whether treatments are parallel, sequential, or crossover, and whether the sample size is predetermined or based upon some interim analysis.

Good Laboratory Practices (GLP): As stated in 21 CFR Part 58 Subpart A58.1(a), Nonclinical laboratory studies that support or are intended to support applications for research or marketing permits for products regulated by the FDA, including food and color additives, animal food additives, human and animal drugs, medical devices for human use, biological products, and electronic products. Compliance with this part is intended to assure the quality and integrity of the safety data filed. Procedures for regulated studies follow GLP guidelines.

Quality Assurance Unit (QAU): Any person or organizational element, except the Study Director, designated by testing facility management to perform the duties relating to quality assurance of nonclinical laboratory studies. The QAU shall be responsible for monitoring each study to assure management that the facilities, equipment, personnel, methods, practices, records, and controls are in conformance with regulations in this part. For any given study, the QAU shall be entirely separate from and independent of the personnel engaged in the direction and conduct of that study. (21 CFR Part 58 Subpart A58.3(l) and Subpart B58.35)

Testing Facility Management: Testing Facility Management associated with the Institution include Associate Chief and Chief Research Officer, Director, RSA and the Principal Investigator of the grant/contract.

Study Protocol: For GLP studies, each study shall have an approved written protocol that clearly indicates the objectives and all methods for the conduct of the study. (21 CFR Part 58 Subpart G 58.120) A Regulated Study Protocol is written by the Study Director under the guidelines provided by the PI and Director, RSA and approved by same.

Regulatory Science: The science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products. (www.fda.gov)

X. Relevant Federal and State Statutes

[21 CFR Part 58](#), Good Laboratory Practice for Nonclinical Laboratory Studies.

[40 CFR Part 160](#), Good Laboratory Practice Standards for Federal Insecticide, Fungicide and Rodenticide Act (FIFRA).

[40 CFR part 792](#) Good Laboratory Practice Standards for Toxic Substances Control Act (TSCA).

21CFR Parts 314 and 601: U.S. Food & Drug Administration (FDA) Code of Regulations for New Drug and Biological Drug Products; Evidence Needed to Demonstrate Effectiveness of New Drugs When Human Efficacy Studies Are Not Ethical or Feasible.

XI. Additional References

[Organization for Economic Cooperation and Development \(OECD\), Principles on Good Laboratory Practice](#)

U.S. Food & Drug Administration Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) Product Development Under the Animal Rule Guidance for Industry. October 2015.

XII. Dates Approved or Amended

<i>Originated:</i> 10/06/2011	
<i>Reviewed with Changes</i>	<i>Reviewed without Changes</i>
	10/18/2016
11/08/2023	

XIII. Contact Information

Research Services
(409) 266-9400

