Chapter 2. Facilities

Specifications for the Conduct of Toxicity Studies by the Division of Translational Toxicology at the National Institute of Environmental Health Sciences

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2. Facilities

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Facilities to which these specifications apply include those of both the prime contractors and the subcontractors who perform major aspects of the activities required by the contract statement of work.

2.1. Animal Facility Requirements

All facilities for the testing program must be approved by NIEHS and will be evaluated with respect to criteria outlined by the following documents and organizations:

- Guide for the Care and Use of Laboratory Animals[1] (National Research Council) and any other additions and exceptions thereof
- Guidelines for Personal Protective Equipment in Animal Facilities[2] (NIH Office of Animal Care and Use)
- Public Health Service Policy on Humane Care and Use of Laboratory Animals[3] (NIH Office of Laboratory Animal Welfare)

A Public Health Service assurance statement and accreditation of the animal facility by AAALAC International are required in order for a laboratory to conduct in vivo studies.

2.1.1. Entry Requirements

The testing laboratory is responsible for establishing policy and procedures to address entry of approved staff and visitors into the animal facility. However, the following conditions/criteria shall be met:

- Entry shall be prohibited to those individuals who have been in another animal facility within the last 48 hours regardless of the disease status of that facility.
- The animal facilities shall be designed and managed to prevent contamination of animals with pathogenic organisms, contamination of personnel and the environment with test articles, and cross-contamination of animals with other test articles.
- A two-corridor system with intervening animal rooms is the preferred way to fulfill this requirement, assuming that (a) all materials coming in contact with animals are sanitized to a clean state suitable for introduction to the supply (clean) corridor and the animal rooms; (b) after use, these materials are removed from animal rooms by a return (dirty) corridor for disposal, destruction, or reprocessing; (c) the air pressure is

[1]https://grants.nih.gov/grants/olaw/Guide-for-the-Care-and-Use-of-Laboratory-Animals.pdf
[2]https://oacu.oir.nih.gov/system/files/media/file/2022-12/d2-Personal_Protective_Equipment.pdf
[3]https://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf

adjusted so that the animal rooms are positive to the return corridor and negative to the clean one. In cases for which animals must be moved from one room to another, such as in multigeneration studies, whole-body inhalation studies, or studies that include neurobehavioral evaluations, precautions must be followed so that the barrier system is not compromised. Animal rooms shall be compatible with direct entry of data into an electronic data capture system.

- If a two-corridor system is not available, detailed measures need to be taken to ensure the health and safety of staff and animals, and these measures shall be reviewed and approved by the contracting officer's representative prior to implementation.

2.1.2. Animal Husbandry

Facilities for sanitization of equipment, including but not limited to cages, racks, inhalation chambers, water bottles, feeders, and environmental enrichment devices, must be available and properly located in relation to the study rooms. Clean, well-ventilated, vermin-free storage space must be provided for clean supplies and equipment, cage filters, and feed/bedding awaiting use. The ability to autoclave feed and bedding is desirable.

2.1.3. Chemistry

Secured, controlled-access storage facilities shall be available for retention/storage of test articles at refrigerated (5°C ± 3°C) or ambient temperature as specified by the protocol. Cold storage at −20°C ± 5°C and −70°C or below must be available for analytical reference standards or biological/biochemical specimens, respectively. Suitable V-blenders with intensifier bars shall be used for diet mixing. The testing laboratory shall contain space and equipment for the performance of selected analytical chemistry activities, including identity and purity evaluations and analysis of dose/exposure formulations or exposure atmospheres. The specific types of equipment required will depend on the test article(s), which can be organic or inorganic. Many evaluations include gas or liquid chromatography, infrared spectrophotometry, UV-visible spectrophotometry, mass spectrometry, nuclear magnetic resonance, and similar procedures.

2.1.4. Pathology

The necropsy facility should be in close proximity to the pathologist(s) office(s). The necropsy facility must be equipped with adequate working surfaces, dissection boards, running water with drains, adequate lighting, ventilation, and exhaust hoods. Necropsy and microscopic photography capabilities are required. Refrigeration shall be available for holding dead animals until necropsy. Dead animals shall not be frozen before necropsy. The histology laboratory should be separated from the necropsy area and equipped with automatic tissue processor(s), microtomes, embedding and staining equipment, and with supplies and appropriate ventilation adequate for the expected volume. Acceptable storage space must be available for storage of residual archival and histological materials that will be retained by the testing laboratory before shipment to the sponsor-designated recipient. These areas must have secured, limited access. Facilities shall be compatible with the direct entry of data into an electronic data capture system.

2.2. Emergency Facility Support

Facilities shall be equipped with a tested back-up power source with automatic change-over equipment that is sufficient to preserve the integrity of the testing experiment. Emergency power must be able to handle those areas critical to the study, including but not limited to animal rooms, inhalation chambers, HVAC, storage freezers/refrigerators, and waste storage. Essential mechanical equipment must be guarded or alarmed. Provisions for prompt maintenance response must be provided. Alternative air handling systems for inhalation studies are required.

2.3. Facility Floor Plans

Floor plans shall document locations where all required study activities will be conducted. Floor plans shall be submitted in an electronic form before the initiation of pre-study and study activities under a contract, every time there are physical changes to the facilities, or if requested by the sponsor.

2.3.1. Types of Floor Plans

Three separate floor plans shall be provided:

(1) The locations of showers, changing areas, and restrooms; quarantine rooms; animal rooms; general storage areas and those for feed and bedding storage; cage and rack washers; and emergency power sources and those areas in which emergency power operates. This floor plan is to indicate traffic flow for personnel, animals, test articles, feed/bedding, supplies, and equipment through the facility.

(2) Room airflow directionality and the location of all safety equipment, including, but not limited to, eyewash stations, safety showers, and fire control equipment.

(3) Ventilation equipment and ductwork, including interior and exterior exhausts. The location of each of the building(s) general air intakes and exhausts and the location of the exhaust for each hood or vented enclosure shall be provided.

2.3.2. Areas to Identify in Floor Plans

- Chemistry: space for test article storage and laboratory space for dose/exposure formulation preparation, test article identity, purity evaluations, analysis of dose/exposure formulations and biological samples analysis, supporting equipment, and exhaust hoods
- Inhalation: laboratory space for the generation and control of vapor and liquid and particulate aerosol atmospheres exposure room(s) for exposure via nose-only and whole-body inhalation
- Clinical pathology: laboratory space for the performance of terminal bleeds and preparation, analysis, and storage of specimens
- Fetal examinations: laboratory space for specimen preparation and storage and the performance of external, visceral, and skeletal exams
- Anatomic pathology: laboratory space for necropsy/gross examinations, histology, and storage of specimens

- Neurobehavioral evaluations: laboratory space for the performance of neurobehavioral tests, including motor activity, motor function, motor-sensory function, and learning and memory
- Additional laboratory spaces: laboratory space for the performance of additional study-related activities, including biochemical, molecular, and in vitro evaluations
- Waste storage: spaces for the storage of hazardous and nonhazardous waste before disposal
- Study data and quality assurance records: secure, limited-access space for the performance of quality assurance audits and storage of quality assurance records, and storage/archival of study data for which Food and Drug Administration Good Laboratory Practices shall be cited

2.4. Peer Review

The Division of Translational Toxicology (DTT) conducted a peer review of chapters 1, 2, 3, 4, 11, and 12 within the draft *Specifications for the Conduct of Toxicity Studies by the Division of Translational Toxicology at the National Institute of Environmental Health Sciences* by letter in February 2022 by the expert listed below. Reviewer selection and document review followed established DTT practices. The reviewer was charged to:

1. Peer review the following chapters within the draft Specifications for the Conduct of Toxicity Studies by the Division of Translational Toxicology at the National Institute of Environmental Health Sciences.
    - Chapter 1: General Personnel Requirements
    - Chapter 2: Facilities
    - Chapter 3: Health and Safety
    - Chapter 4: Quality Program
    - Chapter 11: Data Collection and Submission
    - Chapter 12: Report Formats and Guidance
2. Comment on the completeness of each chapter.

DTT carefully considered reviewer comments in finalizing this document.

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