

Centre for Toxicology & Developmental Research



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Test Facility Management

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- **SRU is the First Medical University in India having Animal facility (CEFT) certified for GLP compliance.** 23,000 sq.ft spaces provides state-of-the art facilities for toxicology, genetic toxicology, pharmacology, behavioral, clinical & anatomic pathology evaluation.
- Access control by Biometric access system
- Double corridor systems falls under the Animal Bio Safety level II (ABSL II) category with 55:45 % air recycle ratio filtered through a 5 micron HEPA filter and 12 - 15 air exchanges per hour.
- Uninterrupted electric supply is ensured with two 1000 KVA generators.
- Environmental conditions (Temperature, Humidity, Pressure, Illumination and Noise levels) are centrally controlled, continuously monitored and recorded.
- Periodical third party analysis of feed, water and bedding material
- Exhaustive disaster management program to ensure the safety of the records, animals, and staff.
- Standard Pest control program, waste disposal and Fire safety regulations
- Separate rooms for quarantine, holding different species such as rabbits, guinea pigs, rats, mice and with individual rooms to conduct experiments.
- Individually ventilated caging system (IVC) for SPF and immune-compromised animals.
- Dedicated Non-GLP area for discovery and exploratory studies including Surgery suite and Behavioral procedures
- Small Animal Surgical Theatre
 - The suite is fitted with a ceiling mounted shadow less Operation theatre lamp with 70,000 lux capacity.
 - Homoeothermic rodent operation board mounted on a hydraulic operation table.
 - A dedicated inhalant anesthetic system.
 - Head mounted operating cope, ICU, ECG and suction unit with all micro-surgicals.
 - Stereotaxic apparatus for ICV injection

The Centre offers following services:

Test system

Rats	-	Wistar, Sprague Dawley
Mice	-	Swiss albino, Balb/C, C-57, Athymic
Rabbits	-	New Zealand White
Guinea pigs	-	Dunkin Hartley
Fish	-	Zebrafish
Bacterial strains	-	Salmonella typhimurium

Route of administration

Oral, dermal and Parental routes (iv, im, sc, ip...etc)

Test item categories

- Pharmaceuticals

- Agrochemicals / Pesticides
- Nutraceuticals
- Cosmetics
- Herbal based / Alternative medicines
- Medical devices

Toxicology services

- Acute / Single Dose Toxicity
- Maximum Tolerable dose and Dose range Findings
- Local Toxicity studies- Skin / Eye / mucus membrane,
- Skin sensitization- Guinea pig (GPMT)
- Sub-Acute / Sub-Chronic toxicity - Repeat Dose 7/14/28/90 day
- Chronic Toxicity - Repeat Dose 180 day/ one year
- Carcinogenicity
- Reproduction & developmental toxicity studies - fertility, teratology, multi-generation

Genetic Toxicity services (In-vitro and in-vivo)

- Ames reverse-mutation assay
- Micronucleus study in rodents
- Chromosomal aberration test
- Mouse lymphoma assay
- Comet assay

Biocompatibility Testing (Medical device)

- **In Vitro Cytotoxicity** (ISO 10993-5)
 - Quantitative (Colony Forming Assay)
 - Qualitative methods (Elution Test, Agar Diffusion Test)
- **Skin Sensitization, Maximization Method or Closed Patch Test** (ISO 10993-10):
- **Intracutaneous Reactivity Test** (USP <88>/ISO 10993-10)
- **Primary Skin Irritation** (ISO 10993-10)
- **Acute Ocular Irritation**
- **In Vivo Biocompatibility** - 21-Day Study
- **Mucosal Irritation Testing:** (ISO 10993-10)
- **Systemic Injection Test** (USP <88>/ISO 10993-11)
- **Implantation Test** – 1, 4, 12, 26, 52 Weeks (USP <88>/ISO 10993-6)
- **Hemocompatibility Testing**
 - ASTM Hemolysis – Direct contact and extract method
 - Complement Activation – C3a & SC5b-9 Assays
- **Genotoxicity Testing** (ISO 10993-3)
 - ISO in-vitro mouse Lymphoma with extended treatment (2 extracts)
 - ISO in-vivo mouse Micronucleus Assay (2 extracts)
 - ISO bacterial mutagenicity – Ames Assay (5 salmonella strains & 1 e. coli strain – 2 extracts)
- **Compendial Testing**
 - Abnormal Toxicity- European Pharmacopeia standard for assessment of biological.
 - Pyrogen Test (USP <151>)
 - Bacterial Endotoxin (LAL) Test (USP<85>)
 - Bacterial Endotoxin (BET)Test Validation (USP <85>)

- Biological Reactivity Tests, *in vitro* (USP<87>)
- Safety Test, General (USP <88>)- transfusion and infusion assembly extracts.
- Safety Test, Biologics (USP <88>) Test battery required by the FDA Regulations for lot validation of licensed biological products.
- Systemic Injection Test (USP <88>/ISO 10993-11)
- Biological Reactivity Tests, *in vivo* (USP<88>) {Class Plastics Testing} - to evaluate the biological response to plastics for use in medical devices, implants, containers, and base materials.

Pharmacokinetics and Toxicokinetics

- Single bolus - Oral and intravenous route of administration

Bio-analytical Assays (Large Molecule)

- Method development, validation and sample analysis as per EMA/FDA guidelines

Critical reagent production

- Regular and Cascade immunization against Proteins, Peptides, Mixture of proteins, Fab fragments, Characterization by ELISA, Western, IHC, IF and Purification: Protein A/G, Affinity in Rat/Mouse, Rabbit, Guinea Pig, Goats
- *In vivo* bioidentity testing of proteins and Peptides
- Anti-sera (polyclonal/monoclonal) - Rat, Mice, Rabbit

Alternative to animal models

- Skin corrosion - *in vitro* model (study specific)
- Ocular irritation - *in vitro* model (study specific)
- Oral irritation - *in vitro* model (study specific)

Pharmacological services

CEFT have well-established and validated *in vivo* disease / screening models:

- Anxiety models (elevated plus maze, hole board, 2. Stress induced Hyperthermia)
- Cerebral stroke (middle cerebral artery occlusion, 4 vessel occlusion)
- Depression (Chemical, behavioural CUMS, Stress induced LTD in Rat Hippocampus)
- Epilepsy (pentylentetrazole, picrotoxin, strychnine, Bicuculline, Beta- Carbolines, Guanidine etc)
- Parkinsonism (MPTP model, 6-OHDA Unilateral Intrastratial Lesion Model)
- Huntington's disease (3-nitropropionic acid)
- Alzheimer's disease (Scopolamine-induced amnesia, A β peptides infusion)
- Gastric ulcer (Shay model, acetic acid/ ethanol induced, drugs induced)
- Hepatic diseases (Paracetamol, anti-TB drugs, CCl₄, Thioacetamide, Galactosamine, Azathioprine, concanavillin, Alcoholic / Non-Alcoholic Steatohepatitis)
- Diabetes (alloxan, streptozotocin, high calorie / diet model, Dithizone, G-thioglucose genetic models)
- Hyperlipidemia and obesity (triton WR 1339, high fat diet model)
- Hypertension (2K/1C - renovascular, DOCA salt induced, Goldblatt, Angiotensin-II etc)
- Cardiac toxicity (Doxorubicin, Anthramycin & Surgical models)
- Myocardial infarction (isoproterenol model)
- Immunology (Cell mediated and humoral mediated)

- Inflammatory models (carrageenan, cotton pellet granuloma etc)
- Rheumatoid arthritis (FCA model)
- Tendonitis (Collagenase & Carrageenan)
- Nootropics (radial arm maze, passive avoidance, transfer latency)
- Pain models (formalin and acetic acid, vincristine, cisplatin, oxaliplatin, paclitaxel etc)
- Stress induced LTD (Long Term Depression) in Hippocampus in rat
- Post Surgical Pain model of mechanical hyperalgesia and allodynia in rat
- Cancer Xenograft model

Serum /plasma

- Blood will be collected from untreated rats under suitable anesthesia. Details of anesthesia will be mentioned on dispatch document.
- CEFT scientists will do the procedures till plasma separation following all standard practices. Plasma/ serum will be stored in -20⁰C till samples shall be collected by sponsor from CEFT

Biochemical and Molecular techniques

- Estimation of tissue / plasma anti-*oxidant*, membrane markers, mitochondrial enzymes, Inflammatory biomarkers and apoptotic markers, Hormones etc
- Isolation and protein / Gene mRNA Expression of proteins markers.
- Single target protein or co-expression of multiple proteins cytokines expression, oxidative stress markers expression, TUNNEL assay, double immunofluorescence etc
- Cytotoxicity using Human / Animal Cell Lines and evaluation of target protein(s)

Pathology and Immunohistochemistry

- Necropsy, Fixing, trimming, embedding, sectioning and staining tissues.
- Special staining or immunohistochemistry, immunocytochemistry, protein co-localisation

Histopathology Slide reading by Veterinary Pathologists trained for toxicologic / experimental Pathology