Vimta

Driven by Quality. Inspired by Science.

One Stop Solution to Accelerate Integrated Drug Discovery & Development

- Pharmacokinetics & ADME
- Safety Pharmacology
- *In vitro* Toxicology
- *In vivo* Toxicology
- Blowaiver Studies
- Medical Devices

60,000 sq ft State of the Art Vivarium

10,000 sq ft Specialized Laboratories

20+ Successful IND Packages

500+ Experience of handling Small & Large molecules (Biosimilars & Vaccines)

WHY VIMTA?

A proficient preclinical partner, facilitating research with dedicated multi-disciplinary teams in Pharmacology, DMPK, Safety Pharmacology, Toxicology, Pathology, Analytical, Bio-analysis and Ecotoxicology makes Vimta a **One Stop Center** for Integrated Drug Discovery & Development coupled with regulatory testing services.

Bench marking and redefining quality through a modern GLP certified, AAALAC accredited and FDA audited facility for leveraging global data acceptability. Vimta adds value through reliability, quality, time management and cost-effectiveness.

Test Facility

- OECD GLP certified, AAALAC accredited and FDA audited test facility
- 60,000 sq ft vivarium+ 10,000 sq ft specialized laboratories
- Modular facility with analytical, bioanalytical & pathology labs
- Barrier controlled rodent facility with +ve & -ve pressurised containment.
- Dedicated facilities for Beagle dogs & Mini pigs

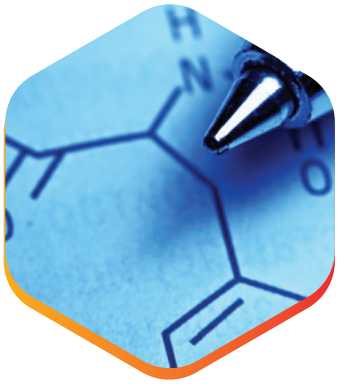
Experience

- Fast track discovery services for lead identification/optimization
- IND & NDA enabling studies in rodents & non-rodents
- Post IND/NDA enabling services in rodents & non-rodents
- 505 (b) (2) - Drug repurposing program
- Impurity qualification (DS/DP/Leachable) & biocompatibility
- Biowaiver studies to support post approval changes
- Complemented over 20 successful IND packages
- Alternate to Animal testing platform

Drug Discovery Services

- 20+ years of experience in safety evaluation
- Supported more than 500 drug molecules, 40 biosimilars & vaccines
- Efficacy & kinetic studies on new formulations and new molecule entity
- Impurity qualification through genetic and general tox studies
- Screening of NCEs and NBEs
- *In vitro* systems to facilitate lead optimization and identification
- *In vivo* models in rodents, rabbits, beagle dogs through different routes

Early Drug Development



Lead Optimization

- Maximum tolerated dose determination with toxicokinetics in rodents & non rodents
- 7-14 days in DRF in rodent & non rodent
- Ames test, comet assay, mammalian cell gene mutation test (mouse lymphoma L5178YTK+/-cells, HPRT assay)
- *In vitro* chromosome aberration in CHO/TK6 HL cell lines
- *In vitro* micronucleus
- Target organ toxicity (nephrotox, neurotox, hepatotox, bone marrow suppression) Cytotoxicity using target specific/battery of cell lines

Pharmacokinetic & Immunogenicity Studies

Pharmacokinetics /Toxicokinetics & Immunogenicity Studies in Rodents, Rabbits, Dogs & Mini Pigs

Standard/flexible Study Designs

- Single dose
- Multiple dose
- Cross over
- Cassette dose

Multiple Routes

- Oral
- Parenteral
- Dermal
- Occular
- Inhalation

Pharmacokinetics Study in Disease Models

Bioanalytical & Immunogenicity

- Matrix stability studies
- Bioanalytical method development/method transfer & validation
- Metabolite identification, profiling & structure elucidation
- Matrices: serum, plasma, tissue & milk
- ELISA assay for quantification of large molecule and antibodies

Instruments

- Mass spectrometers- single quadruple, triple quadruple, ion trap
- LC-MS/MS, MALDI/TOF/TOF, GC-MS/TOF, HRGCMS, ICP-MS
- HPLCs with UV, PDA and fluorescence detectors ELISA

Early Drug Development

Analytical Development Support

- Physicochemical characterization
- Purity assessment
- Stability studies
- Proprietary method development/method transfer & validation
- Impurity identification, profiling & structure elucidation

Instruments

- HPLC (UV and electrochemical detection)
- UV/VIS spectrophotometer
- ICP - MS
- UPLC
- LCMS/MS
- Gas chromatograph (FID, FPD, ECD)
- RT - PCR

Genetic Toxicology

- Bacterial reverse mutation test (*Salmonella typhimurium, Escherichiacoli*)
- Mammalian cell gene mutation test (mouse lymphoma L5178Y tk +/- cells and HPRT)
- Mammalian chromosome aberration test (*In vitro/In vivo*)
- Micronucleus test (*In vitro/In vivo*)
- Comet assay (*In vitro/In vivo*)

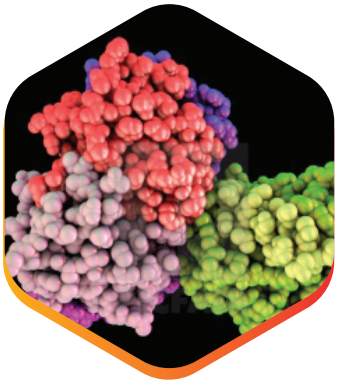
Safety Pharmacology

- HERG assay (*In vitro*)
- Cardio Vascular Safety (CVS)
- Central nervous system (CNS)
- Gastrointestinal Safety
- Respiratory safety

Supplementary Tests

- Analgesic assessments
- Sleeping time
- Tail flick
- Physiological temperature
- Convulsant activity
- Motor in-coordination
- Bleeding time
- Functional observation battery

Early Drug Development

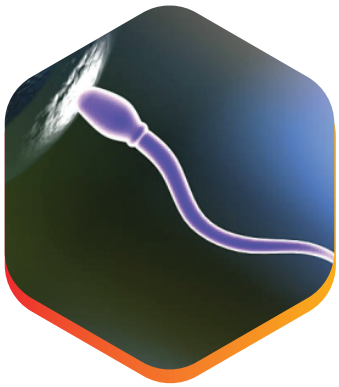


General Toxicology

- Single dose toxicity studies, dermal irritation/ corrosion, eye irritation/ corrosion
- and skin sensitization tests
- Maximum tolerable/dose range finding studies
- Sub-acute/sub-chronic toxicity studies
- Chronic toxicity studies
- Combined chronic toxicity and carcinogenicity studies
- Carcinogenicity studies in rats & mice

Development & Reproductive Toxicology (DART)

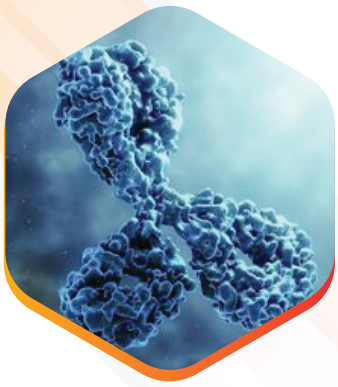
- Extended one-generation reproductive toxicity studies (All 5 Cohorts)
- Combined repeated dose with reproduction/developmental toxicity
- screening studies
- Reproduction/developmental toxicity screening studies
  Teratology studies/developmental toxicity studies
- Multi generation reproduction toxicity studies
- Developmental neurotoxicity studies
- Endocrine disruptor studies
- Neonatal/Juvenile toxicity studies



Special Studies

- Tissue distribution
- Metabolism
- Ocular toxicity
- Local tolerance
- Pharmacology screening
- Development of *In vivo* model for pharmacology response
- Immunotoxicology
- Neurotoxicology
- Phototoxicology
- Dermal toxicology
- Target organ toxicity using cell line, zebra fish etc

Special Services



Biosimilar & Vaccine Development

- Characterization
- Immunogenicity studies
- Pharmacokinetic studies in healthy and disease model
- Proof of Concept (POC) studies [effective dose range; route of administration and dose schedule; putative MOA and biological outcome]
- Toxicology studies (mimic proposed clinical trial, dose route, dosing schedule, delivery system)
  - Single /repeated dose toxicity
  - Maximum tolerable/dose range studies finding studies
  - Local tolerance
  - Reproductive toxicity
- Bridging study for change in manufacturing/formulation of product/dosing regimen/schedule, delivery system
- Adjuvant and excipient testing

Alternatives to Animal Studies

Genetic Toxicity Studies

- Bacterial reverse mutation test
- Chromosomal aberration test
- Micronucleus Test
- Comet Assay

Irritation Study

- *In vitro* dermal irritation study using reconstructed human epidermal skin (rHES)
- *In vitro* ocular irritation study with reconstructed human cornea-like epithelium (RhCE)

Phototoxicity

- 3T3 NRU phototoxicity study

Sensitizaation Study

- Direct peptide reactivity assay (DPRA)

Cytotoxicity

- Cytotoxicity study
- Direct Contact & MEM Elusion Methods

Permeation and Release Studies

- *In vitro* permeation testing
- *In vitro* release testing

- *In vitro* corneal permeability study

Absorption/Permeability

- PAMPA/MDCK/Caco-2

In Vitro Screening

Screening Platform

Physio-chemical Properties

» Solubility, pka, log P/logD

***In vitro* Permeability Assays**

» PAMPA/MDCK/Caco2

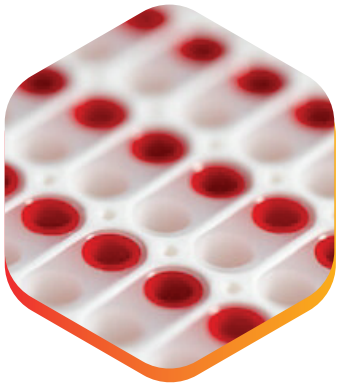
***In vitro* Drug-Drug Interaction Assays**

» CYP inhibition (reversible and time dependent)
» CYP induction & CYP phenotyping

Transporter assay

In vitro Protein Binding & Partitioning Assays

» Plasma protein binding
» Tissue protein binding assays
  » Microsomes
  » Brain homogenate
  » Liver homogenate
  » Hepatocyte
» Blood/plasma partitioning



In vitro Stability Assays

» Buffer, simulated intestinal fluid and simulated gastric fluid stability
» Hepatic phase 1/11 metabolic stability (hepatocyte, liver microsomes, liver S9 and cytosol etc.)
» Ex-hepatic metabolic stability (intestinal microsomes, lung microsomes, plasma and blood etc.)

Pharmacology Models

» Chemical induced models
» Genetic models
» Surgical models

Special Services

Topical Drug Development

In silico Models

- » Rule based approach
- » Algorithm approach

Ex vivo Models

- » Permeation testing (IVPT)
- » *Ex vivo* skin permeability

In vitro Models

- » *In vitro* release testing (IVRT)
- » Topical formulation screening
- » Dermal irritation studies
- » T3T NRU phototoxicity
- » Genetic toxicity

In vivo Models

- » Dermal pharmacokinetics
- » Dermal bio-distribution studies
- » Dermal irritation studies
- » Safety pharmacology
- » Skin sensitization
- » Dermal toxicology
  - Single-dose toxicity
  - Repeated dose toxicity
  - Tolerability testing

Ocular Drug Development

In silico Models

- » Bacterial reverse mutation test
- » Chromosomal aberration test
- » Micronucleus Test
- » Comet Assay

In vitro Models

- » *In vitro* dermal irritation study using reconstructed human epidermal skin (rHES)
- » *In vitro* ocular irritation study with reconstructed human cornea-like epithelium (RhCE)

Ex vivo Models

- » Ocular efficacy models
  - Glaucomas model (IOP): aqueous loading, surgically. induced
  - Anti-infective models
  - Models for diagnostic tools
- » Ocular Pharmacokinetics
- » Ocular bio-distribution Studies
- » Ocular irritation studies
- » Ocular toxicology
  - Single-dose ocular toxicity
  - Repeated dose ocular toxicity
  - Tolerability testing
  - Ocular sensitization

Experience:

- » BCS class molecules
- » Controlled substance handling and testing
- » Biowaver (USFDA) studies

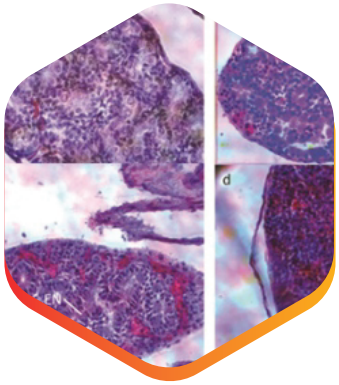
Special Services

Inhalation Testing

- Testing compliance to OECD/ICH/EMA/EPA
- Analytical support services -dose concentration verification
- Inhalation delivery in rodents
- High precision directed flow (flow-past) systems: CFR Part 11 compliant
  - Nose-only or oronasal exposure
  - Prevents re-breathing
  - Restraint designed to minimize thermal stress
  - Maintains homogeneous breathable atmosphere at all levels of the inhalation tower
- State-of-the-art technologies to generate powder, liquid, or vapor atmospheres
- Early-stage inhalation toxicology evaluation with intratracheal aerosol delivery
- Oropharyngeal aspiration

Endocrine Disruptor Studies

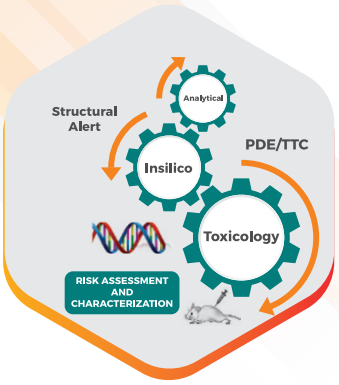
- Uterotrophic bioassay
- Hershberger assay
- Steroidogenesis
- Pubertal development and
- Thyroid function in intact
- Juvenile female rats
- Pubertal development and thyroid function in intact juvenile male rats



Data Presentation for Global Submissions

- SEND modules compilation
- Validated data files
- nSDRG template
- Safe and secure storage
- Online data recording
- Controlled terminology in line with SEND
- A complete two-step validation
- Generation of define.XML
- Validation of XML

Impurity Qualification & Medical Devices



Safety & Risk Assessment of Impurity

Classification Approach

- Bacterial reverse mutation assay/mammalian cell gene mutation test
- *In vitro* / *In vivo* mammalian chromosomal abberation test
- *In vitro* / *In vivo* micronucleus test (MEMT)
- *In vitro* / *In vivo* Comet assay

Qualification Approach

- 14–28-day toxicity studies in rodents (rats/mice) & non-rodents
- 90-day studies in rodents (rats/mice) & non-rodents
- Stand-alone / integrated TK studies

Leachables & Extractables

- Extractions as per ISO-10993
- Quantification & characterization
- High precision and wide range of Instrumentation
- Trained technical expertise
- Faster turn around time
- Risk easement using *in silico* model and read across approach

Chemical charecterization/ Biocompatibility Testing

Chemical Charecterization / Toxicological Risk Assessment

In vitro Cytotoxicity

- MEM elusion
- MTT assay
- Neutral red uptake
- Agar diffusion
- CFU assay
- Growth inhibition assay

Implantation

- Subcutaneous, muscular, bone, ocular

Systemic Toxicity

- Single and repeat dose

Genotoxicity

- Gene mutations
- Clastogenicity in mammalian cells
- Micronucleus test

Irritation Studies

- Eye, skin irritation (dermal, intracutaneous reactivity
- Mucosal irritation (oral, rectile, penile, vaginal)

Skin Sensitization

- GPMT
  Buehler's test

DART & Hemocompatibility

Biowaiver Studies

In vitro Release Testing (IVRT)

- Synthetic membrane mounted in Franz cells containing thermostatically controlled physiologically relevant solution
- Unidirectional permeability assessment of test article across appropriate synthetic membrane
- Optimization of study conditions analytical, receptor medium, membrane selection, inertness
- Qualification of the optimized assay parameters and establishment of sensitivity, selectivity and robustness
- Analytical method validation covering specificity, linearity, accuracy and precision, repeatability, stability, robustness
- *In vitro* release rate comparison with statistical evaluation

In vitro Permeation Testing (IVPT)

- Skin mounted in Franz cells thermostatically controlled at 37°C
- Unidirectional permeability assessment of test article across frozen dermatomed human cadaver skin
- Optimization of study conditions includes analytical, receiver buffer, stirring rate, time-point selection & dose amount
- Qualification of the optimized assay parameters
- Establishment of sensitivity, selectivity & robustness
- Analytical method validation and test system including recovery, mass balance & dose depletion
- Pivotal bioequivalence comparison with statistical evaluation: parallel, single dose & multiple donors

Caco-2 Permeability Assay

Caco-2 permeability assay to investigate intestinal permeability and understand suitability for oral dosing for BCS class Drugs

- Bi-directional Caco-2 transport to screen for permeability and involvement of active transport
- Evaluation of gut wall permeability and investigate drug efflux

Studying the permeability of compounds across a Caco-2 cell monolayer is an established *in vitro* model to screen for oral absorption and to evaluate the mechanism of transport. Samples derived from Caco-2 cell studies using LC-MS/MS allows rapid and accurate determination of drug transport across the Caco-2 cell monolayer

About Vimta

Founded in 1984 with headquarters in Hyderabad, India, Vimta Labs Limited., is a leading contract research and testing organization, providing bio/pharmaceutical companies an integrated scientific, technical and regulatory expertise to support all stages ofdrugdevelopment and manufacturing process.

Vimta has been supporting many national and overseas companies for more than 3 decades, for their third party testing, research and outsourcing needs. Along with the growth in pharma, food and other manufacturing sectors, we have been able to grow and also expand our services to international markets.

Accreditations & Certifications

GLP CERTIFIED · FDA INSPECTED · AAALAC ACCREDITED · DSIR RECOGNIZED · WHO PREQUALIFIED · CPCSEA REGISTERED

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