BIONEEDS

PHARMACEUTICAL SERVICES

www.bioneeds.in

About Us - Overview

Infrastructure & Facilities

- 5 acre campus in the serene location at outskirts of Bangalore with 200,000+ sq ft built-up area
- World class Vivarium with 85 experiment rooms conforming to international standards
- 50,000 Sq.ft chemistry and biopharma facilities in Bangalore

Trusted Preclinical CRO

- 14+ years of comprehensive services for Pharma, Biopharma, Medical devices & Agrochemicals.
- Scientific Team of ~400; 80% M.Sc; M.Pharm; M.VSc; 13% PhD, 2 DABT, 3 Veterinary pathologists(board certified); 50 + experienced study directors
- Global client base of 410+ spanning from big pharma, small biotechs to research / academic institutions

Accreditations And Certifications

- Successfully audited by USFDA with no 483s (January 2017 & 2022)
- OECD GLP Certificate by National GLP Compliance Monitoring Authority (NGCMA), Dept. of Science and Technology, Government of India
- ISO 17025 Accreditation (NABL) for Biological, Chemical & Medical device Testing
- AAALAC (Association for Assessment & Accreditation of Laboratory Animal Care International) accredited laboratory for animal care
- Recognized by Department of Scientific and Industrial Research (DSIR) for in-house & Collaborative R&D
- Drug Testing License (DTL) for tests on Drugs / Cosmetics & Raw Materials used in manufacturing for marketing permission
- Ministry of Environment, Forests and Climate Change, GOI – Permission to conduct research in animals (CPCSEA)
- Approved by OLAW (Office of Laboratory Animal Welfare, US)

Management Team

Dr. S. N. Vinaya Babu | Managing Director

Dr. Nitin M. Shetty
Chief Technical Officer | Preclinical Services

Ms. Sapna Y R
Chief Business Officer

Dr. Mallikarjun N Dixit
Chief Technical Officer | Biopharma Services

Services for Pharma

- Customized to suit the product specification needs
- As per ICH guidelines
- Support ANDA submissions

Bioneeds has Successfully Delivered 300+ Impurity Qualification Package Studies!

Chemistry support

Isolation, Characterization, Identification & Synthesis of Impurities

Genetox Studies

- Ames test
- *In vitro* Chromosomal Aberration Test

***In vivo* Tox studies**

- 14 day, 28 day, 90 day, 180 day Tox studies
- TK assessment
- Method Dev & Validation

Drug Discovery: DMPK Capabilities

Absorption

Permeability
- Caco-2 (A→B and B→A);
- PAMPA; MDCK-MDR-1

Solubility
- Aqueous (various pH)
- SGF and SIF*

Pharmacokinetics
- Mice; Rats; Rabbits
- Dogs and Monkeys(Partnered)
- Dose Escalation Studies

Distribution

Protein binding
- Equilibrium dialysis (ED)
- Ultra filtration
- ED method to determine fu in plasma & brain

Metabolism

Metabolic stability
- Liver microsomes; S-9
- Fractions and Hepatocytes

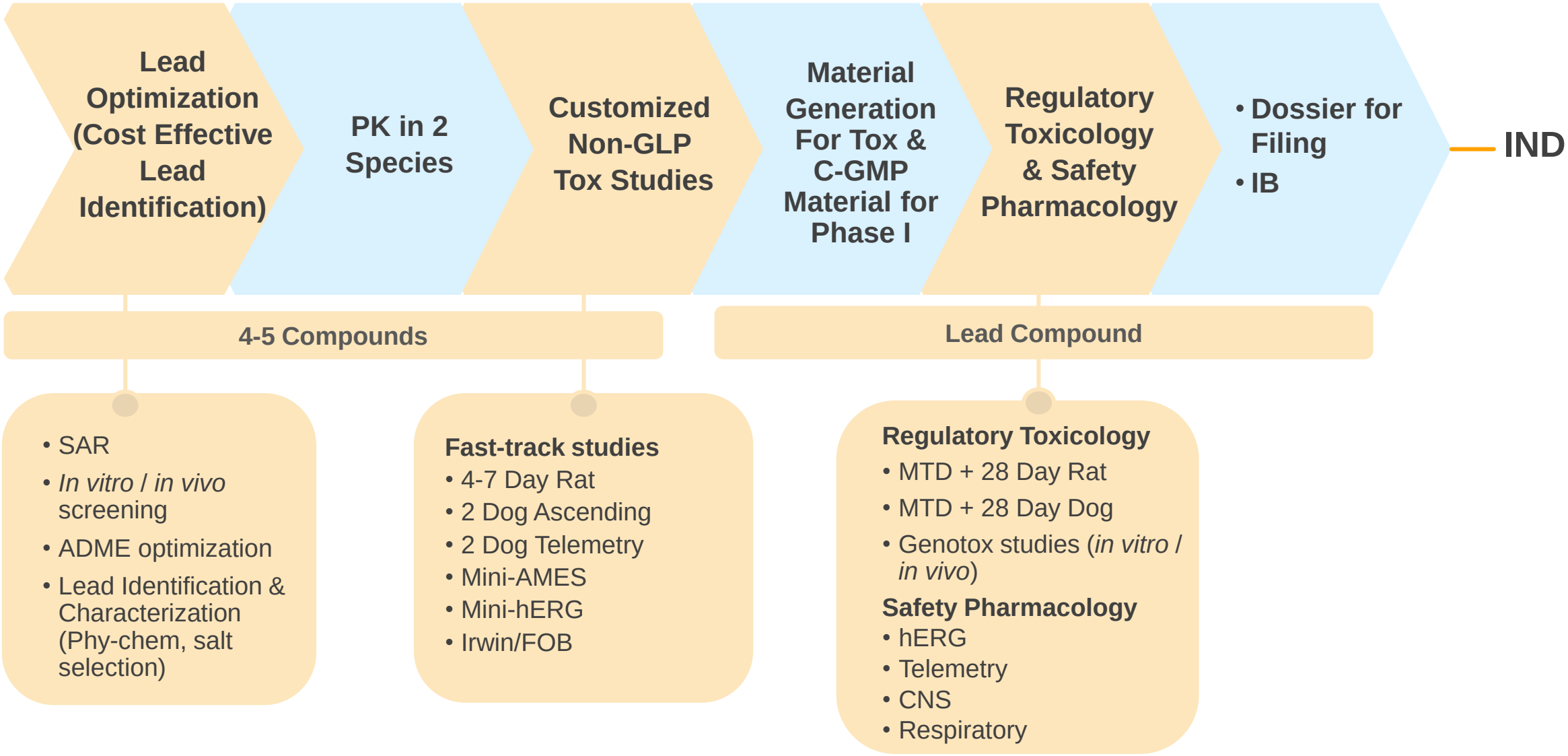
CYP and FMO profiling
- CYP inhibition

Metabolite ID
- *in vitro* using liver microsomes, hepatocytes
- *in vivo* from plasma, bile, urine and feces
- Glutathione trapping
- Blood/plasma partitioning
- Time dependent inhibition
- Plasma and Chemical stability

X-Functional Activities
- PK-PD

Excretion
- Mass balance (metabolic cages)
- Biliary & Urinary Excretion

Services for Pharma – IND Enabling Package



Services for Biopharma

Product Characterization

HPLC (ProA, RP, SE,CE), LC-MS (ORBITRAP)- Intact mass, subunit analysis, peptide mapping, Disulfide bond locations, glycan analysis
Cell/ELISA based assays, BIACORE based assays

Product Release Testing-IP, EP/BP, JP, USP compliant methods

- Pre-clinical Toxicology
- Bioassays (*in vitro* / *in vivo*)
- PK / TK Analysis
- Immunogenicity Testing
  - Screening ELISA
  - Confirmatory ELISA
  - NAb Assay
- Cell based potency & functional assays
- HCP(Host cell protein) Screening ELISA
  - Product specific PAb generation
  - Cascade Immunization
  - HCP coverage through 2D gel Electrophoresis
  - Highly sensitive ELISA method development, validation & transfer
- HCD (Host Cell DNA)
  - qPCR based method
- Polyclonal & Monoclonal Antibody Development & purification

Toxicity Studies

Acute Toxicity Studies

- Acute oral toxicity study – OECD 420/423/425
- Acute dermal toxicity study – OECD 402
- Acute inhalation toxicity study – OECD 403/433/436
- Skin irritation study – OECD 404
- Eye irritation study – OECD 405
- Skin sensitization study – OECD 406

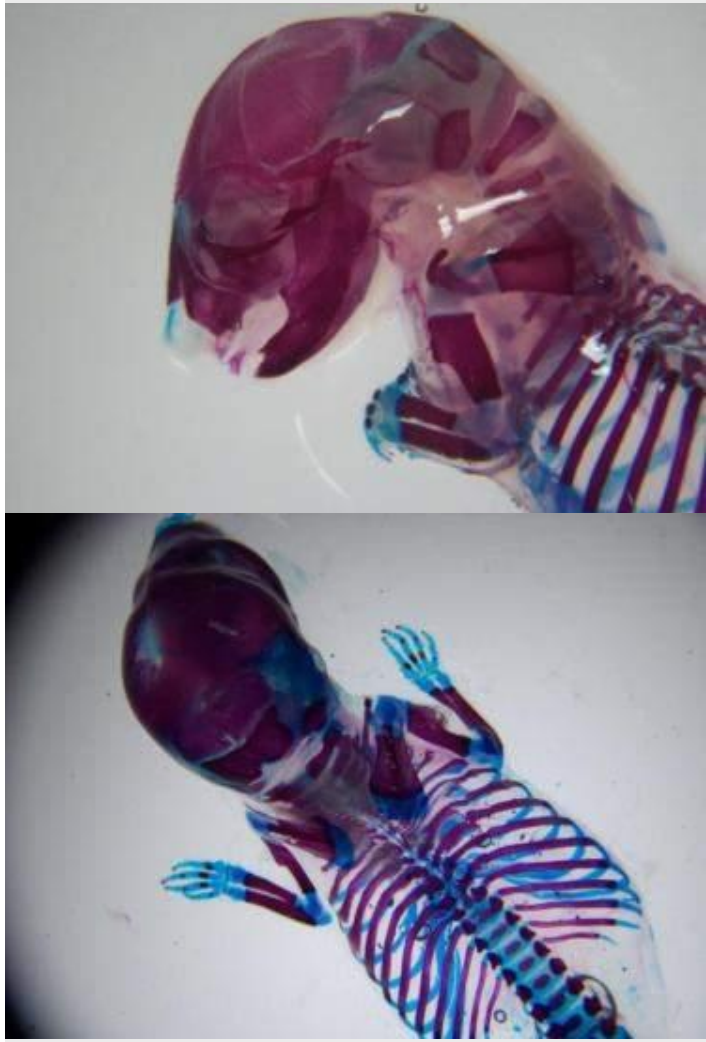
Sub-chronic & Chronic Toxicity

- 28/90/180 days repeat dose tox – OECD 407 to 411
- Carcinogenicity studies – OECD 451
- Chronic toxicity studies – OECD 452
- Combined chronic tox / carcinogenicity – OECD 453
- Neurotoxicity studies – OECD 424
- Juvenile toxicity

Toxicity Studies

Reproduction & Developmental Toxicity (DART)

- Prenatal developmental toxicity – OECD 414
- One / Two generation reproduction toxicity – OECD 415/416
- Reproduction / Developmental toxicity screening test – OECD 421
- Combined repeated dose toxicity study with reproduction / developmental toxicity screening test – OECD 422
- Segment I, II & III studies
- Extended one-generation reproductive toxicity study - OECD 443 with all Cohorts selections (1A, 1B, 2A, 2B & complete study)



Toxicity Studies

Genotoxicity Studies

- Bacterial Reverse Mutation Test (AMES) – OECD 471
- In vitro Mammalian Chromosome Aberration Test – OECD 473
- Mammalian Erythrocyte Micronucleus Test – OECD 474
- *In vivo* Chromosomal Aberration Assay in Bone Marrow Cells – OECD 475
- *In vitro* Mammalian Cell Gene Mutation test using the Hprt and Xprt locus – OECD 476
- *In vitro* Mammalian Cell Micronucleus Test – OECD 487
- Comet Assay – OECD 489
- Mouse Lymphoma Assay – OECD 490

Inhalation Toxicity

Chamber Type: Nose-only Directed-Flow Rodent Inhalation Exposure Unit

GLP Inhalation Studies

- Acute Inhalation Toxicity Study for Pharmaceuticals (Schedule Y)
- Repeated Dose (28/90 days) Inhalation Toxicity Studies for Pharmaceuticals (Schedule Y)

Liquid: *LC (Liquid Concentrate), EC (Emulsifiable Concentrate), SC (Suspension Concentrate), Technical grade*

Dust: *WG/WSG (Water Dispersible Granule),SG (Soluble Granule), WP (Wettable powder), Technical Grade*

3 Inhalation Chambers

Non-rodent Studies

Beagle Dogs

- Upgraded 76 pen world class facility

Studies offered

- PK, MTD & DRF, Regulatory toxicology studies
- Safety Pharmacology

Minipigs (Göttingen Minipigs)

- Non-clinical testing for topical drugs
- Pharmacokinetics & safety studies through our associate partner

Analytical / Bioanalytical Services

Formulation analysis

Method Development, Method Validation & Dose formulation analysis (HPLC, LC-MS/MS, GC-MS/MS, ICP-MS/MS)

Bioanalysis

Method Development, Method Validation, sample analysis in various matrices – Pharmacokinetics, Toxicokinetics

Test Systems & ROA

Test System	Species
• Rats	Wistar, Sprague Dawley
• Mice	Swiss albino, Balb/C, C-57, CBA/J
• Rabbits	New Zealand White
• Guinea pigs	Dunkin Hartley
• Dogs	Beagle Dogs (limited approval)
• Mini Pigs	Göttingen minipigs (With collaborative partner)
• Test Systems for Eco-toxicity	Fish, Honeybee, Earthworm, Daphnia, Alga, Pigeon, Fowl, Japanese Quail

Routes of Administration(ROA):
Oral (Dietary / Gavage), SC, IM, IV, IP, Inhalation, Infusion, Intranasal, Intravitreal, Ocular

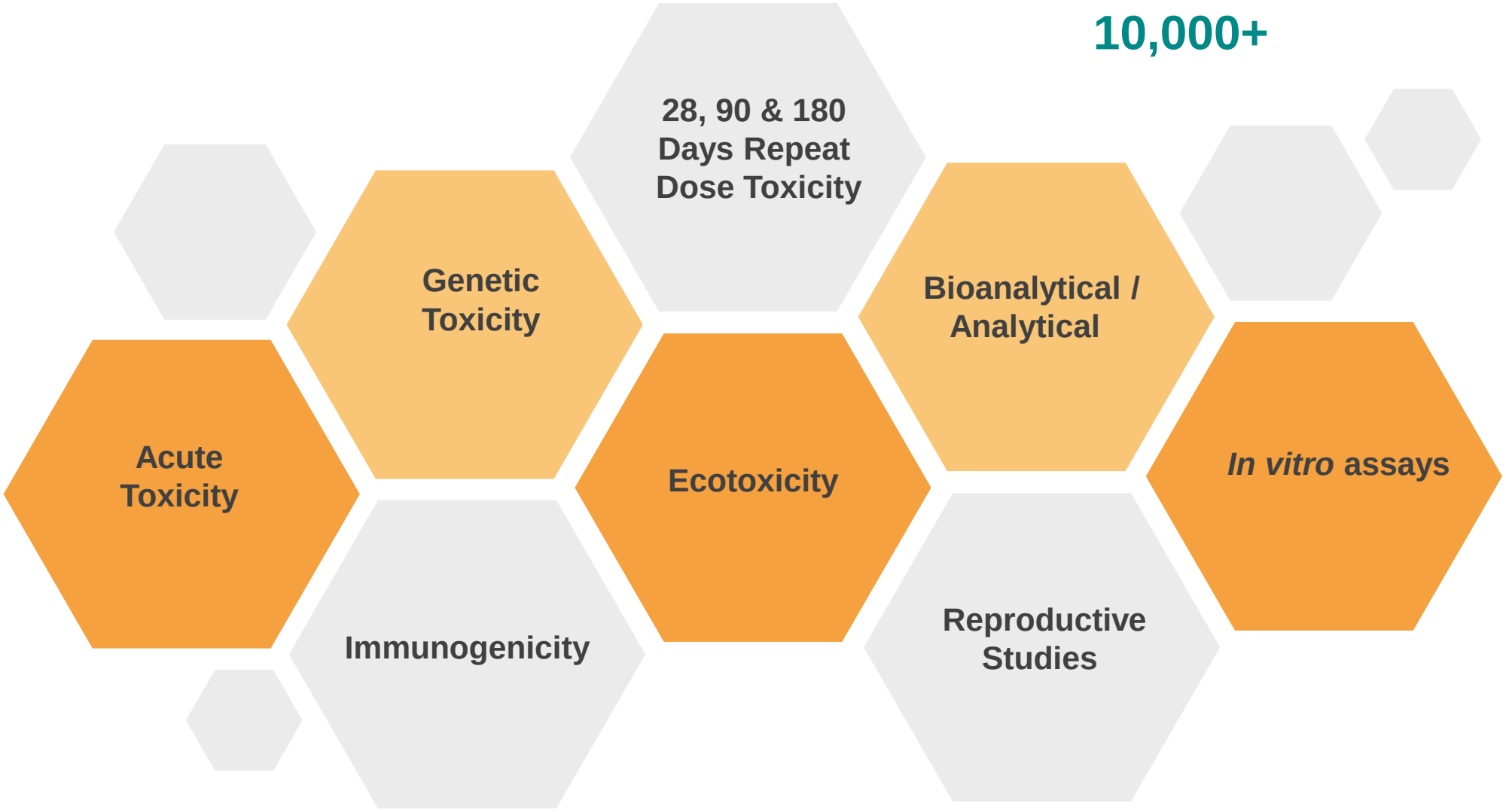
Alternative to Animal Studies

Alternate Studies	Animal Studies
• Bovine corneal opacity & permeability test (BCOP) - OECD 437	Eye irritation studies
• Isolated chicken eye test - OECD 438	Eye irritation studies
• *In Vitro* ocular irritation test (EpiOcular™) - OECD 492	Eye irritation studies
• Direct peptide reactivity assay (DPRA) - OECD 442C	Sensitization studies/ GPMT
• *In Vitro* skin irritation test (Episkin™ / Epiderm™) - OECD 439	Skin irritation
• *In Vitro* dermal absorption (Episkin™ / Epiderm™) / Human cadaver skin / porcine skin / cornea - OECD 428	Dermal absorption
• *In Vitro* 3T3 NRU phototoxicity - OECD 432	*In vivo* acute phototox. Studies
• Local Lymph Node Assay (LLNA): BrdU-ELISA * - OECD 442B	Sensitization studies/ GPMT
• *In vitro* skin corrosion: reconstructed human epidermis (RHE) test method - OECD 431	Skin corrosion studies
• Luciferase assay - OECD 442D	Skin sensitization studies
• *In vitro* skin sensitization study (hCLAT method) - OECD 442E	Skin sensitization studies

*** *In vivo* Assay - Reduction of animals**

Our Experience – GLP studies

GLP Studies
10,000+



Chemistry Services

Discovery Chemistry

- Design & synthesis of novel scaffolds, building blocks & NCEs (Hit to Lead & LO)
- Design & Synthesis of novel focused libraries (15-20 compounds)
- Synthesis of novel metabolites & impurities for initial studies

Custom Synthesis

- Synthesis & Supply of Advanced Intermediates, NCEs, Reference Standards, Impurities & Metabolites
- Chemistries handled (Representative): Heterocyclic, Solution phase peptide (up to 4 AA), Carbohydrate, Transition Metal Coupling etc.
- Qty: mg to 10 Kg, non-GMP

Process R&D & Scale up

- Route Scouting, Process R&D, Process Optimization, Process Validation & Demonstration (Lab Scale)
- Process Improvement & Novel Process Development
- Scale-up of intermediates and final compounds (Kilo Lab & Pilot Plant Scale)
- Analytical support (MD/MV, Impurity Profiling etc.)

Case Study 1 – IND (Investigational New Drug Enabling Studies)

Background: To facilitate IND application for NCE developed to control Vitiligo.

Project Scope: Support IP, Novel synthetic route, NCE synthesis with GLP characterization for GLP studies, CMC dossier, IND enabling studies, summary document for IND application with detailed reports & Topical cream formulations development for clinical trials.

- Animal dermal PK in rats & rabbits
- Single dose dermal studies in 2 species
- Local tolerance studies (Skin sensitization study)
- 90-day dermal tox studies with TK in 2 species
- *In vitro* & *in vivo* genetic tox studies
- Local tolerance in formulation (cream)
- absorption studies
- *In vitro* irritation studies

All studies completed within 10 months. IND dossier completed. IND application in process.

Post IND Plans: Reproductive toxicity studies in rats & rabbits

Case Study 2 – Impurity Qualification Studies for ANDA Submission

Background: Synthesize a novel API-Glucose adduct impurity [no CAS No.] in multi-gm scale to enable conduct of TOX studies followed by ANDA filing by world's largest US based generic company in a tight timeline 45 days

Project Scope: Synthesis, isolation, characterization & supply of 10g of the API-Glucose adduct impurity in 2 weeks. Draft report required for ANDA filing as per US-FDA format

SOLUTIONS provided…

- Successfully selected & optimized a feasible synthetic protocol after screening multiple ROS in parallel
- Developed prep HPLC method and effected isolation of the target compound
- In-house impurity standard was generated, thoroughly characterized and potency was determined
- Thus isolated impurity sample was qualified against In-house prepared impurity standard and a comprehensive report was submitted to the client as per US-FDA required format
- All Deliverables supplied well within the timelines

Case Study 3 -Vaccines

Bioneeds has been in the forefront in assessing safety & immunogenicity of various vaccines in different animal models.

Types of Vaccines handled :

Pneumococcal vaccine (23 strains), Typhoid conjugate vaccine, Hepatitis A and Hepatitis B, Rubella, Influenza, Rabies, Measles & COVID-19 vaccine

- Successfully conducted repeat dose intranasal toxicity study in rabbits for COVID 19 vaccine. (Second study under way)
- The timely submission of final study report enabled initiation of clinical trials
- Following studies are being performed for COVID-19 vaccines and multiple batches have been released with COA.
    - Specific activity assessment by ELISA
    - Specific reactivity assays
    - Specific safety assays
    - Organ distribution assays
    - RT PCR based assay

Case Study 3 – Vaccines (Contd..) – Repeat Dose Toxicity Study of 3 Manufactured Covid Vaccine Products with one Adjuvant in Rats by Intramuscular Route

Background: To assess the toxic potential of the vaccines, when administered with and without the adjuvant, by the intramuscular route to Sprague Dawley rats on different days.

Clients' partners were beginning their clinical trial and the regulatory agencies requested the Tox report be submitted with a deadline.

Project Scope:

- This study conducted to provide information on, on-set of major toxicity, compound-related target organ toxicity and No Observed Adverse Effect Level (NOAEL).
- Haptoglobin and alpha2-macroglobulin were analyzed from Elisa method.
- Serum samples collected were assessed for immunogenicity.
- Multisite study

SOLUTIONS provided…

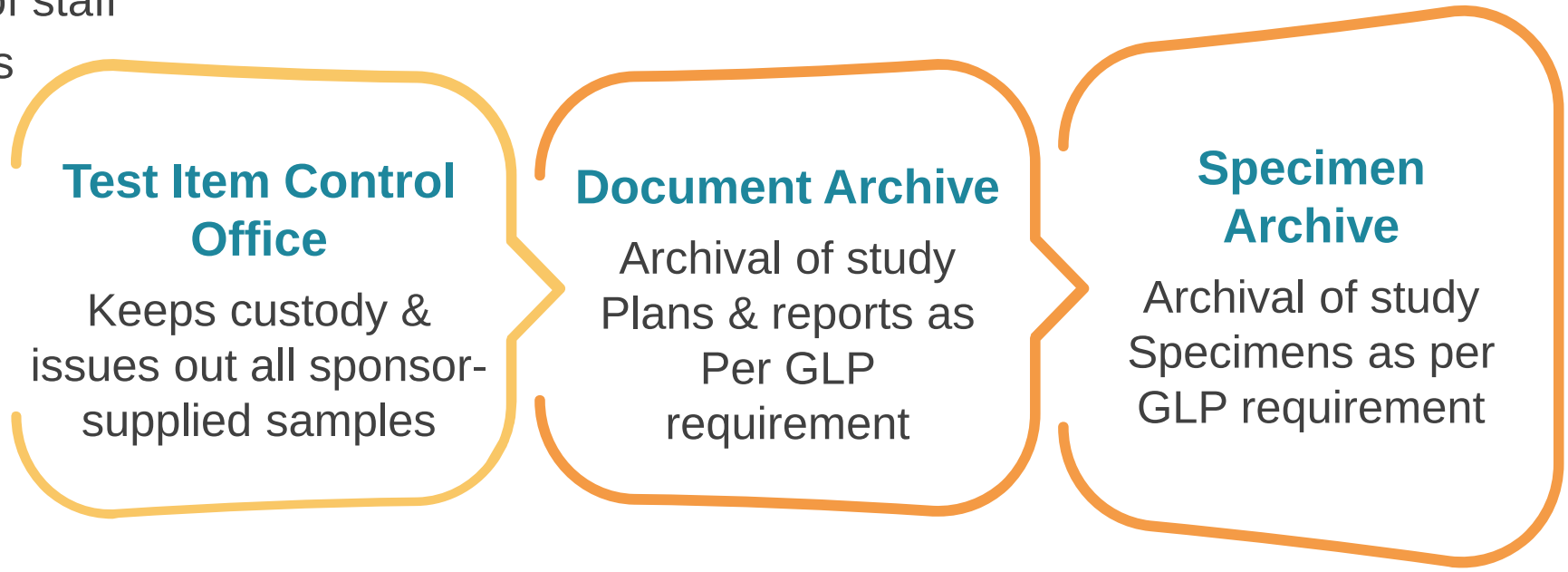
- Weekly telecons and real time communication with the study director was instrumental in increasing the efficiency with which the project was executed.
- The timely submission of final study report enabled initiation of clinical trials for three COVID vaccine candidates in three countries.
- The client's partners were very appreciative of the quality of the work and the timeliness with which it was delivered.
- Team's dedication, hard work and technical expertise has been widely recognized

Case Study 4 - Tissue Distribution Studies

Test Item	Iron Based Nanoparticle	Liposomal Products-Doxorubicin, Tacrolimus and Amphotericin
Guideline	EMA reflection paper (EMA/CHMP/SWP/620008/2012)	Guideline on bioanalytical method validation, 21 July 2011 EMEA/CHMP/EWP/192217/2009 Rev. 1 Corr. 2
Outline	**Pre-Study**- 11 time points **Main Study**- Single dose with 11 time points	**Pre-Study**- 5 time points **Main Study-** Single / Repeat dose with 5 time points
Organs & Matrix	Liver, Spleen, Heart, Lungs, Kidneys, Urine, Faeces, Blood & Plasma	Brain, Liver, Lung, Kidney, Spleen & Plasma
Instrumentation	ICP MS	LC MS
Studies Conducted:	• Analytical method development • Method validation - Total iron & transferrin bound iron • Biodistribution study of colloidal injectable product in Rats by IV route	• Bioanalytical method development • Method validation • Tissue distribution study in SD Rats
Conclusion	Analysis of both total iron & transferrin bound iron.	Analysis of both bound and unbound compounds. Report successfully submitted to EMEA and USFDA
TAT	5 months	6 months

Quality Assurance, TICO & Archives

- Planning of QA activities
- Review of study plans, study reports and SOPs
- Conducts study based, process based and facility based inspections
- Reporting of inspection findings to Management & respective personnel
- Issue of QA statement in the final report
- Archiving of QA & facility documents
- Regular GLP Training of staff
- Vendor / Supplier audits



Systems - Project Management

Project Net : Project Management Platform

A dedicated Project Manager for each project responsible for

- Resource allocation
- Logistics, shipment receipts
- Reports, communication management
- Timeline projection

Technical teams interface directly with sponsor

Value Proposition

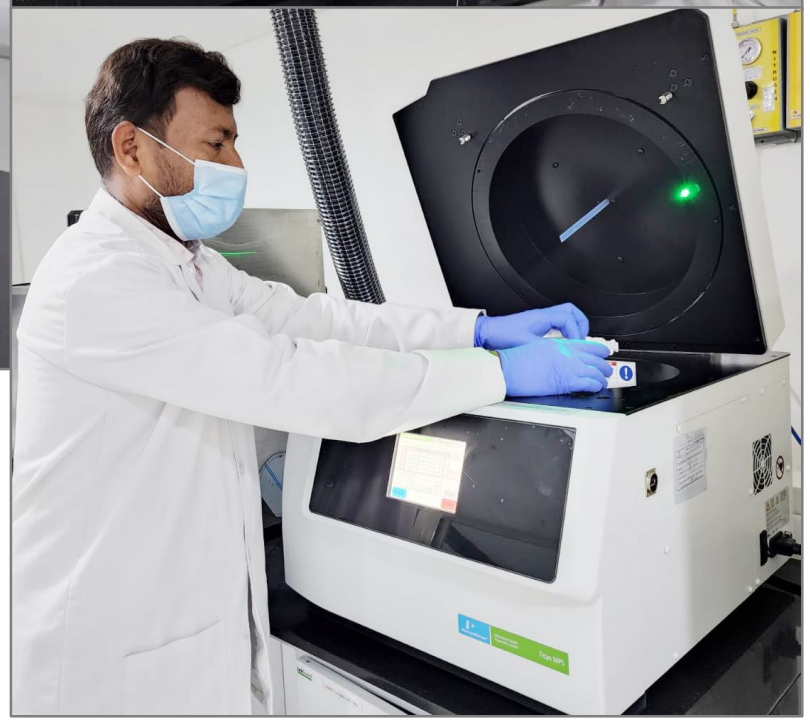
- Integrated drug discovery & preclinical solutions
- Established track record of successful regulatory preclinical studies for 14+ years
- Reproducible & high quality data generation acceptable to global regulatory agencies
- Multidisciplinary scientific professionals with rich industry experience
- Adherence to stringent quality & compliance
- Customer oriented & collaborative approach with internationally accepted business models

GALLERY

Clean Services Corridor

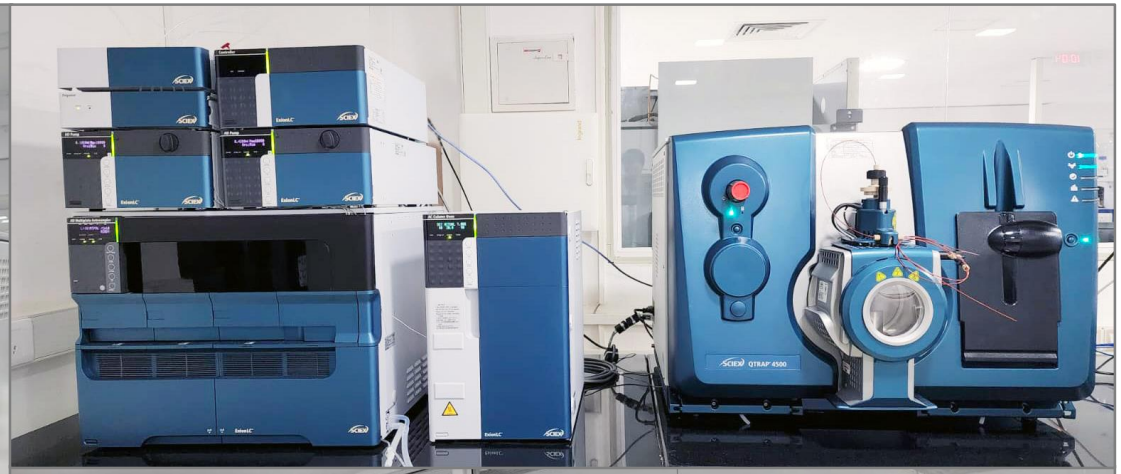
Laboratory Corridor

Analytical Lab



Analytical Lab

Analytical Lab



Bioanalytical Lab

Bioanalytical Lab

Clinical Pathology

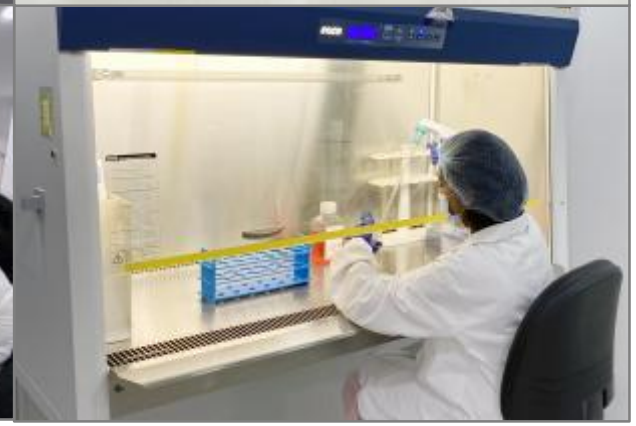
Histopathology

Microbiology

Mutagenicity Lab

Test Item Control Office

Archives – Documents & Specimens



Biopharma R&D Facility

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Synthetic Chemistry Labs

Thank You

BIONEEDS INDIA PVT. LTD.,

GLP Accredited Preclinical Development Center

Devarahosahally, Sompura Hobli, Nelamangala Tq,
Bengaluru Rural District-562111, Karnataka, INDIA
Tel: +91 816-2214400 | Contact No.: +91 9844457677
Email: bioneeds@bioneeds.in | Website: www.bioneeds.in

Chemistry & Biopharma R&D Facility

P-3, Peenya Industrial Area, 1st Main Road,
Peenya 1st Stage, Bengaluru-560058,
Karnataka, INDIA
Tel: +91 80-22658400