Syngene

A Biocon company

Syngene Laboratory Animal Research (SLAR)

aaalac INTERNATIONAL

BfR

Syngene Laboratory Animal Research - Facility

Syngene

41,000 sft. in area / 16,500 sft GLP area

- CPCSEA approved (Govt .of India)
- AAALAC - accredited
- German & Indian GLP certified

Conformation to national and international guidelines

- Controlled environment with automated building monitoring system
- Automated lighting control and sound attenuation
- IACUC (IAEC & IBSC) approval for all protocols

Activities

- Regulatory/ Exploratory Toxicology
- Pharmacokinetics
- Animal Models (*in vivo* Pharmacology)

Syngene Laboratory Animal Research - Utilities

Syngene

Automated cage washer

Walk in Autoclave

Individual ventilated caging (IVCs) systems

Clean and Segregated Service Corridors

Syngene

A Biocon company

Toxicology

Acute, Sub-chronic and Chronic Studies

Syngene

Acute studies

- Single dose or multiple doses within 24 hr
- Dose Escalation Studies
- Tolerability Studies (MTD)

Repeated dose studies with Toxicokinetics

- 7, 14, 21 & 28 Days

Chronic studies with Toxicokinetics

- 90 Days, 180 Days

Routes:

- Oral Gavage / Parenteral (IM, SC, ID, IV, IP) / Dermal Routes

Genotox Studies

Syngene

AMES

- Salmonella typhimurium strains (TA 98, TA 100, TA 1535 and TA 1537) and Escherichia coli strain WP2uvrA pKM101

Micro Nucleus Test

- Mammalian Bone Marrow Cells (*in vivo*)

Chromosome Aberration Test

- Mammalian Bone Marrow Cells (*in vivo*)

Capability (to be standardized and validated)

- Human Lymphocyte Chromosome Aberration Test (*in vitro*)

Reproduction & Carcinogenicity Studies

Syngene

- Fertility Study – ICH S5R(2) 4.1.1
- Prenatal, Postnatal & Maternal Study – ICH S5R(2) 4.1.2
- Embryo-fetal Development study – ICH S5R(2) 4.1.3
- Multigenerational (One/ Two) Reproduction Study – ICH S5 R (2)
- 26 week study in Transgenic Mice ICH S1A & ICH S1B
- 12/18/24 Months study in Rats & Mice - OECD 451
- 24 Months Combined Chronic Toxicity & Carcinogenicity study in Rats - OECD 452

Additional Capabilities

Syngene

Safety pharmacology

- Central Nervous System – Modified Irwin's Test
- Functional Observational Battery
- Neurobehavioral Screening
- Motor Activity
- Learning And Memory
- Sensory Evaluation

Local Tolerance

- Skin Irritation
- Eye Irritation
- Mucous Membrane Irritation
- Other routes as requested

TFM, QA, TICO & Archives

Syngene

Test Facility Management (TFM)

- Appoints Qualified & Experienced Personnel
- Provides appropriate & adequate facilities
- Coordinates with Study Sponsor
- Overall Management of the GLP studies and GLP Laboratory

Quality Assurance Unit (QAU)

- Independent Unit – Reports to TFM
- Reviews, Study Plans, Reports & SOPs
- Monitors the study
- Issues Quality Statement

Test Item Control Office (TICO)

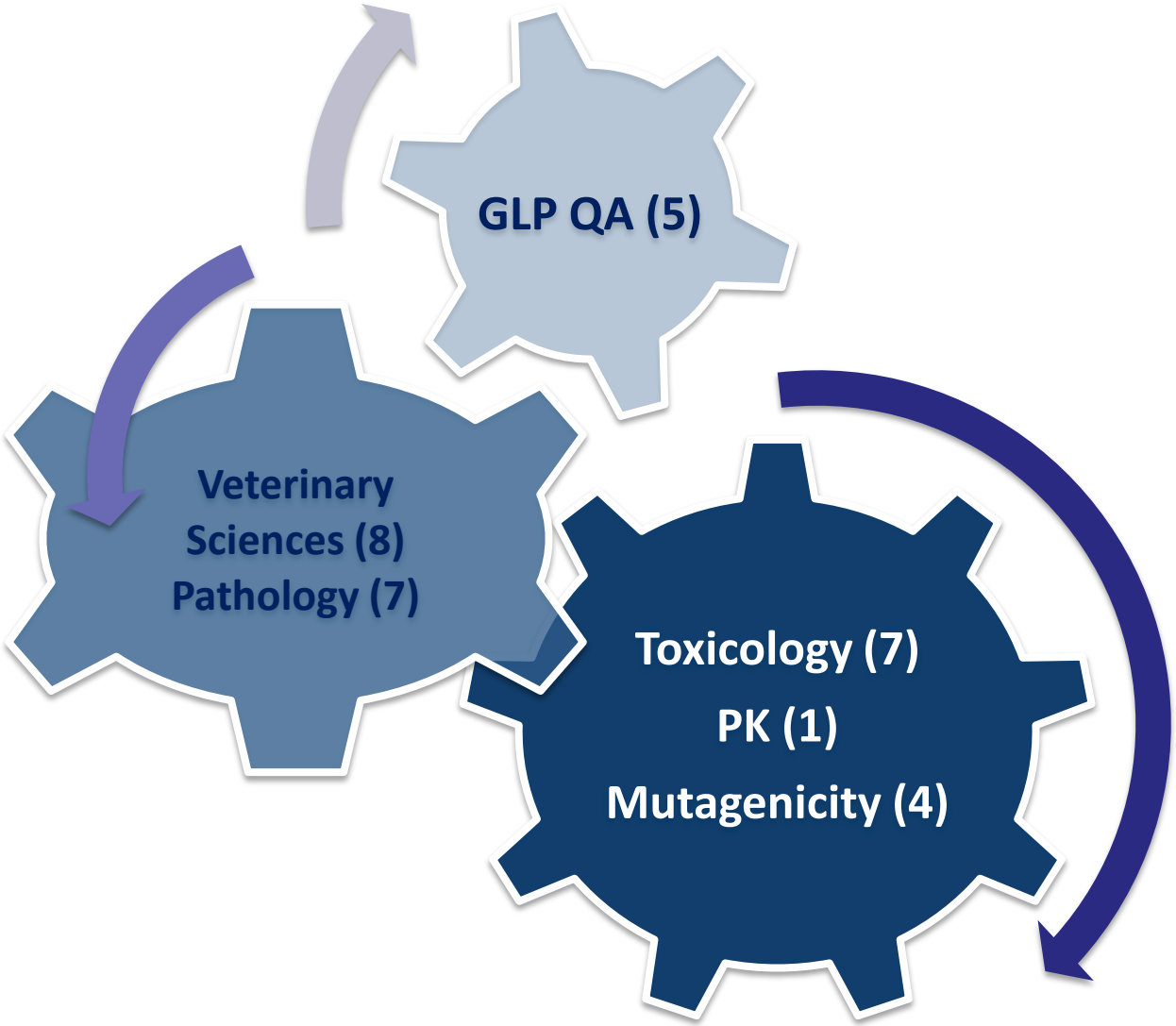
- Test / reference Article receipt, storage and dispensing
- Dedicated TICO Officer

Archives

- Dry & Wet Archives

Key Teams for Toxicology

Syngene



Syngene

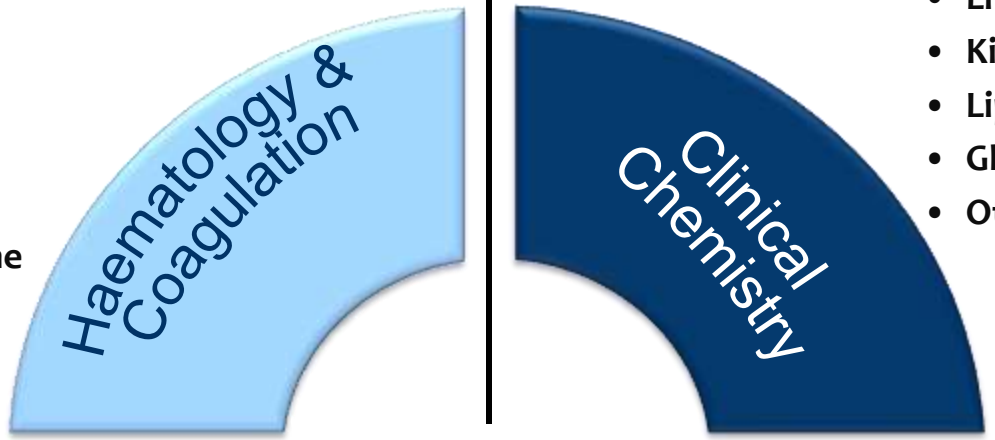
A Biocon company

Pathology

PATHOLOGY SUPPORT - TOXICOLOGY

Syngene

- Haemotocrit
- Total RBC, WBC
- Haemoglobin , Platelets
- DLC and
- Reticulocyte Count
- Prothrombin time
- Activated Prothrombin time
- Fibrinogen



- Liver function test
- Kidney function test
- Lipid profile
- Glucose
- Other parameters

- Appearance, Volume,
- Specific Gravity
- pH
- Protein
- Glucose
- Blood Cells
- Microscopy

- Necropsy
- Organ Weights & Ratios
- Gross Pathology
- Histopathology
- Peer review

Pathology Infrastructure

Syngene

- Automated clinical chemistry analyzer
- Automated hematology analyzer
- Semi-automated Coagulation analyzer
- Electrolyte analyzer

Pathology Infrastructure

Syngene

- Six prosectors accommodation- necropsy
- Automated vacuum tissue processor
- Embedding centre
- Semi automated microtome.
- Automated stainer
- Nikon 50i & 80i microscope.

Microbiology /Analytical / IT/ EHS Support

Syngene

Microbiology	• Microbiological monitoring of the animal room environment • Microbial analysis -diet, water, bedding, & animal cages, water bottles • Fecal examination for Parasite Ova / pathogen test
Bio - analytical	• Bio analytical assay method development • Validation and analysis of study samples
Analytical	• Method Development/Method Transfer • Stability studies • Dose confirmation analysis (A.I. and Homogeneity)
IT	• Access control in place for computer • Users defined access levels and privileges • Data back-up system • Computer validation as per GLP Guidelines
EHS	• Pest Control • Fire Alarm System • Disaster Management Plan • Periodic Medical Check – up /Special Vaccination for staff

Ongoing/completed Projects

Syngene

Client # 01	• Acute studies (OECD) • Repeat Dose 28 day Toxicity studies (OECD) • Repeat Dose 90 day Toxicity studies (OECD)
Client # 02	• Male fertility (ICH) –US FDA • Developmental Toxicity (ICH) – US FDA • Pre and Post natal study (ICH) – US FDA
Client # 03	• Developmental Toxicity – Dose range finding study in Rabbits • Developmental Toxicity – Main study in Rabbits (ICH) - US FDA

GLP Certificate - German

Syngene

Bundesinstitut für Risikobewertung /
Federal Institute for Risk Assessment

BfR

GUTE LABORPRAXIS / GOOD LABORATORY PRACTICE

(gemäß / according to § 19b Abs.2 Nr.3 Chemikaliengesetz / Chemical Act)

Eine GLP-Inspektion wurde durchgeführt in / A GLP inspection was carried out at

Prüfeinrichtung / Test facility

Syngene International Ltd.
Biocon Park, Plot no. 2 & 3 – Bommasandra IV Phase
Jigani Link Road
Bangalore – 560 099, INDIA

Prüfkategorien / Area of Expertise

- Prüfungen zur Bestimmung der physikalisch-chemischen Eigenschaften und Gehaltsbestimmungen / Physical-chemical testing
- Prüfungen zur Bestimmung der toxikologischen Eigenschaften / Toxicity studies
- Prüfungen zur Bestimmung der erbgutverändernden Eigenschaften (*in vitro, in vivo*) / Mutagenicity studies
- Analytische Prüfungen an biologischen Materialien / Analytical and clinical chemistry testing

Datum der Inspektion / Date of Inspection

July 13 - 16, 2009

Auf der Grundlage des Inspektionsberichtes und der Besprechung über zu erfolgende Maßnahmen wird hiermit bestätigt, dass in dieser Prüfeinrichtung die oben genannten Prüfungen unter Einhaltung der GLP-Grundsätze durchgeführt werden können. /
Based on the inspection report and the discussion of follow up activities it can be confirmed, that the test facility is able to conduct the aforementioned studies in compliance with the Principles of GLP.

Eine Überprüfung dieser GLP-Bestätigung ist spätestens zwei Jahre nach der o. g. Inspektion zu beantragen. Ohne diesen Antrag wird nach Ablauf der Frist die Prüfeinrichtung aus dem deutschen GLP-Überwachungsprogramm genommen und diese GLP-Bestätigung verliert ihre Gültigkeit. /
Verification of this GLP Certificate has to be applied two years after the above mentioned inspection at the latest. Elapsing this term, the test facility will be taken out of the German GLP Monitoring Programme and this GLP Certificate becomes invalid.

December 21, 2009
Im Auftrag / For the Director

Dr. H.W. Hembeck
GLP-Bundesstelle / GLP Federal Bureau

Bundesinstitut für Risikobewertung / Federal Institute for Risk Assessment
Thielallee 88-92
14195 Berlin, GERMANY

GLP Certificate - Indian

Syngene

NATIONAL GLP COMPLIANCE MONITORING AUTHORITY

GLP CERTIFICATE

GLP Inspection was carried out at **GLP Test Facility, Syngene International Limited, (A Biocon Company), Biocon Park, Plot no. 2 & 3, Bommasandra IV Phase, Jigani Link Road, Bangalore - 560 099, Karnataka, India** in the following areas of expertise:

- **Physical-chemical testing**
- **Toxicity studies**
- **Mutagenicity studies**
- **Analytical and clinical chemistry testing**

Based on the Inspection Report and the follow-up actions taken by the test facility, it is confirmed that the test facility is capable of conducting the above-mentioned tests in compliance with **OECD Principles of Good Laboratory Practice (GLP) and Norms, as** adopted by the National GLP Compliance Monitoring Authority.

This GLP Certificate is valid for a period of **three years** from October 25, 2010, subject to the condition that the test facility complies with the **Terms & Conditions of the National GLP Compliance Monitoring Authority's Document Number GLP-101**.

Certificate No.: GLP/C-0030

Issue Date: 25-10-2010

(DR. VINITA SHARMA)
Head
National GLP Compliance Monitoring Authority
Department of Science & Technology
Technology Bhavan New Delhi-110016

Syngene

A Biocon company

Thank You