

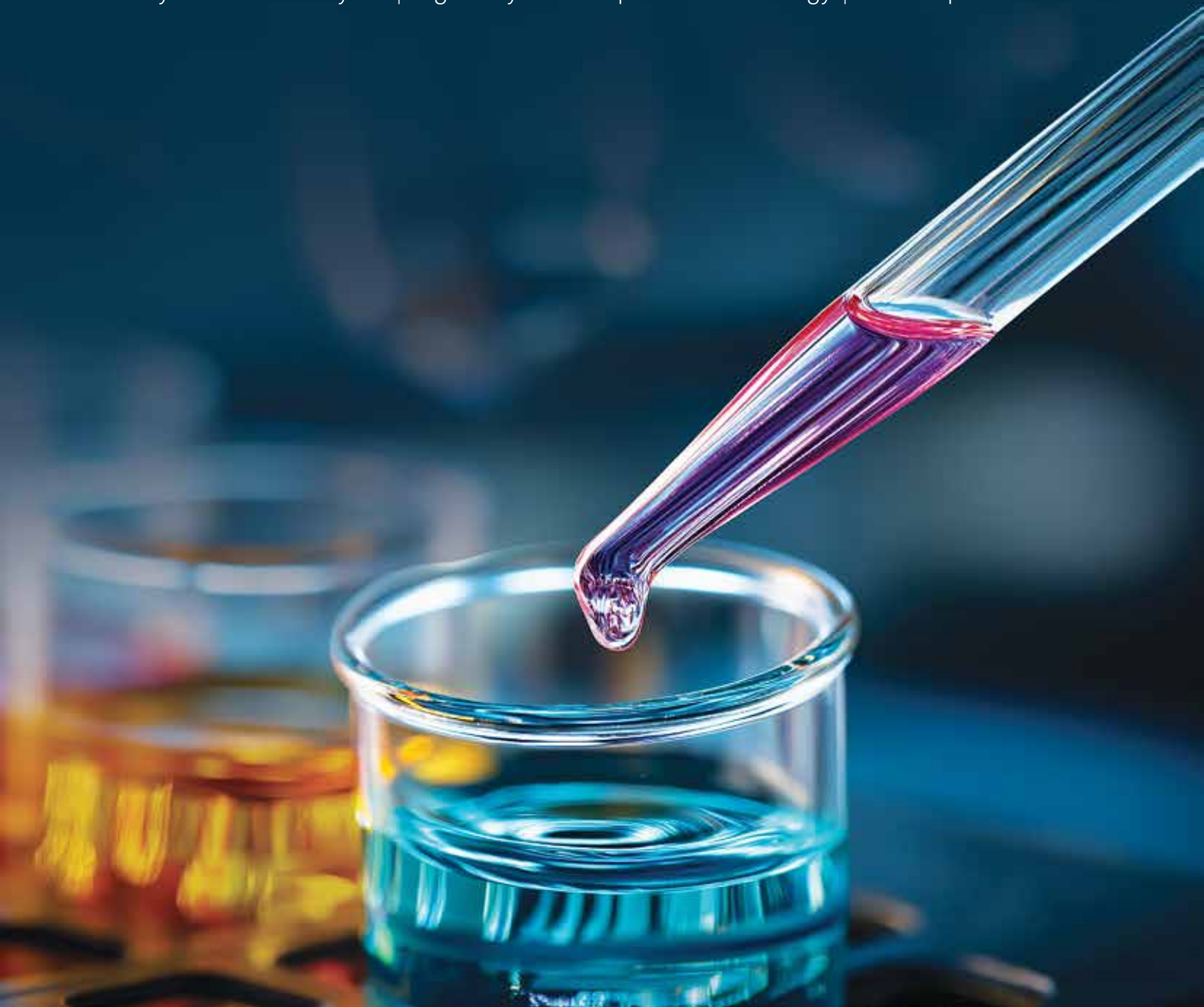
Syngene

Putting Science to Work

The Full Range of Toxicology Studies.

One Integrated Partner.

Exploratory and GLP-Regulated toxicology | Genetic and *In Vitro* toxicology |
General toxicology | Safety pharmacology | DART | Carcinogenicity | Pathology |
Analytical and Bioanalytical | Regulatory and Computational toxicology | SEND capabilities



The Comprehensive Safety Tox Package

Your program may begin with one study. Our integrated toxicology and safety assessment expertise is built to support the entire development journey

From a single exploratory study to a complete regulatory package, Syngene brings the full range of toxicology studies together under one platform.

IN VIVO TOXICOLOGY

Exploratory & Discovery

- MTD and dose-escalation studies
- 7–28 days repeat-dose toxicity
- Target organ and biomarker assessment
- Route and formulation feasibility

General Toxicology - Acute to Chronic

- Acute, single-dose and local tolerance
- 7, 14, 21 and 28-day repeat-dose
- 90-day sub-chronic toxicity
- 6-month and longer chronic studies

DART

- Fertility and early embryonic (Segment I)
- Embryo-fetal development (Segment II)
- Pre- and post-natal development (Segment III)
- Developmental neurotoxicity and juvenile studies

Carcinogenicity Assessment

- 6-month transgenic mouse studies
- 2-year rat carcinogenicity studies
- In-house pathology and peer review

GENETIC, IN VITRO & SPECIALIST STUDIES

Genetic Toxicology

- Ames - regular, mini and enhanced
- *In Vitro* and *in vivo* micronucleus
- Chromosomal aberration, *in vitro* and *in vivo*
- HPRT, TK6 and mouse lymphoma assays

In Vitro Toxicology

- Cytotoxicity (NRU, XTT, MTT, CFU)
- Skin irritation, corrosion and absorption
- Eye irritation (RhCE)
- Phototoxicity and skin sensitisation
- Hemolysis Assay

Safety Pharmacology

- CNS - FOB / modified Irwin test
- Respiratory - Whole-body Plethysmography
- Cardiovascular telemetry and ECG
- hERG assay for QT prolongation risk

Computational Toxicology

- DEREK Nexus® and CASE Ultra
- ICH M7 dual (Q)SAR assessment
- Mutagenicity and carcinogenicity prediction
- Skin and respiratory sensitisation prediction

SCIENCES THAT SUPPORT EVERY STUDY

Pathology

- Clinical pathology and histopathology
- Digital pathology and remote peer review
- Specialised sectioning, histochemistry and IHC
- Standalone histopathology support for externally conducted studies

Analytical & Bioanalytical

- Dose formulation analysis
- LC-MS/MS bioanalysis
- Method development and matrix validation
- Immunogenicity and biomarker assays

Risk Assessment & Impurities

- PDE, OEL and OEB derivation
- Nitrosamine risk assessment and CPCA
- ICH Q3A / Q3B and M7 qualification
- CTD Modules 2.4 and 2.6 writing
- Safety Data Sheets (CLP, OSHA, SWA & HSNO compliant)

SEND Data Services

- Datasets for in-house and external studies
- Legacy data conversion
- Define.xml and nSDRG

In Vivo Toxicology: Every Duration, Every Route

From a first tolerability read to six months of continuous exposure.



SINGLE DOSE



7-28 DAYS



90 DAYS



6 MONTHS+

Exploratory & Discovery Toxicology

Rapid-turnaround non-GLP and exploratory GLP studies characterising initial toxicity profiles, pharmacokinetics and target organ effects in relevant preclinical models.

Core Testing Capabilities

- Maximum tolerated dose (MTD) studies
- Short-term and repeat-dose toxicity (7-28 days and beyond)
- Target organ toxicity evaluation
- Route and formulation feasibility

Toxicokinetics & Exposure

- Toxicokinetic profiling alongside the in-life phase
- Dose-proportionality and accumulation assessment
- Biomarker-driven toxicity assessment

Integrated Bioanalytical Support

- Rapid discovery-phase method development
- High-sensitivity plasma, serum and tissue analysis
- Early immunogenicity and biomarker panels

General Toxicology - Acute to Chronic

Definitive characterisation of systemic and local toxicity across every exposure duration dose-response, target organs, NOAEL and reversibility under ICH, EMA and OECD guidelines.

ACUTE

Single-Dose Toxicity

- Single-dose oral, dermal and inhalation
- Local tolerance studies
- Skin, ocular and mucous membrane irritation studies
- Guinea pig maximisation and LLNA

SUB-ACUTE TO SUB-CHRONIC

7 to 90-Day Repeat Dose

- 7, 14, 21, 28, and 90-day repeat-dose studies
- Target organ identification
- Toxicokinetic correlation
- Recovery groups for reversibility
- Exposure margins for clinical risk assessment

CHRONIC

6 Months and Beyond

- 6-month and longer repeat-dose studies
- Target organ toxicity and reversibility
- Support for chronic dosing regimens
- Exposure margins for clinical risk assessment

Routes of Administration

- Oral gavage and dietary; dermal application
- Intravenous bolus and infusion; IM, SC, IP, intrathecal
- Inhalation - single dose

Species Coverage

- Species Coverage
- In-house: Rats, Mice, Guinea pigs, Hamsters and Rabbits
- Through partner sites: Dog, Minipig and Non-human primates with Bioanalysis, toxicokinetics and histopathology at Syngene

Specialised Studies. Deeper Safety Insight.

Safety pharmacology, DART and carcinogenicity studies designed to characterise risks across critical safety endpoints.

Safety Pharmacology

Standalone or combined with repeat-dose toxicology as per ICH S7A and S7B the data behind first-in-human dose selection, with fewer animals used when designs are integrated.

Central Nervous System

- Functional Observational Battery / modified Irwin test
- Behaviour, posture, locomotor and neurological function
- Neurobehavioral profiling

Cardiovascular System

- *In Vivo* telemetry assessment
- ECG, heart rate and blood pressure monitoring
- hERG assay for QT prolongation risk, via partner laboratories

Respiratory System

- Whole-body plethysmography
- Tidal volume and minute volume evaluation
- Respiratory rate

Developmental & Reproductive Toxicology (DART) and Juvenile Toxicity

Fertility, embryonic development and post-natal outcomes in rodent and non-rodent models.

SEGMENT I

Reproductive Toxicity

- Fertility and early embryonic development
- Estrous cyclicity, mating performance, sperm analysis

SEGMENT II

Developmental Toxicity

- Embryo-foetal development in rodents and rabbits
- External, visceral and skeletal foetal examinations

SEGMENT III

Pre & Post-Natal

- Lactation, maternal care and offspring survival
- Neurobehavioral and developmental milestones

SPECIALISED

Juvenile Toxicity

- FOB, learning, memory and behavioural assessment
- Juvenile studies for paediatric indications

Carcinogenicity Assessment

ACCELERATED MODEL

6-Month Transgenic Mouse Studies

- Well-characterised transgenic models
- Mechanism-relevant carcinogenic potential
- Histopathology assessment with peer review

GOLD STANDARD

2-Year Rat Carcinogenicity Studies

- Full lifetime exposure design
- Tumour incidence and survival analysis
- Histopathology assessment with peer review



Genetic & In Vitro Toxicology

Complete genetic and in vitro toxicology batteries, from individual assays to integrated testing programmes.

Genetic Toxicology - Screening to IND

Rapid-turnaround non-GLP and exploratory GLP studies characterising initial toxicity profiles, pharmacokinetics and target organ effects in relevant preclinical models.

GENETIC TOXICOLOGY TEST

Bacterial Reverse Mutation Test (Ames)

In Vitro Chromosomal Aberration Test

In Vitro Micronucleus Test

Mammalian Erythrocyte Micronucleus Test

Mammalian Bone Marrow Chromosome Aberration Test

HPRT Cell Gene Mutation Test

Mouse Lymphoma Assay

In Vivo Mammalian Alkaline Comet Assay (non-GLP)



Enhanced Ames Test

- 30-minute pre-incubation method
- 30% rat and 30% hamster S9 for broader metabolic coverage
- Nitrosamine and NDSRI-specific positive controls

Mini Ames

- 5 or 2-strain designs as required
- Five times less test item than a regular Ames (500 mg)
- 2–3 week timeline

In Vitro Toxicology

Validated OECD test-guideline methods across the standard endpoint set. Cytotoxicity and phototoxicity read out in 3–4 weeks, RHE skin irritation in around 10 days, and skin corrosion and eye irritation in around 15 days.



IN VITRO TEST

Cytotoxicity Test (NRU, XTT, MTT, CFU)

In Vitro 3T3 NRU Cytotoxicity Test

In Vitro 3T3 NRU Phototoxicity Test

In Vitro Skin Irritation Test

In Vitro Skin Corrosion Test

In Vitro Eye Irritation / Serious Eye Damage

In Vitro Skin Absorption

In Vitro Skin Sensitisation

The Sciences Behind Every Toxicology Study

The full range is supported by complementary scientific capabilities on the same platform



**TOXICOLOGY
STUDY**



Pathology

Analytical &
Bioanalytical

Computational
Toxicology

Risk
Assessment

SEND

Pathology Services

Our Pathology Bench

- 7 veterinary pathologists, 4 board-certified (DIBTP), plus a senior US-based consultant
- 18 histotechnicians and 4 clinical pathology specialists
- In-house peer review, or review by your own pathologist

Anatomic & Digital

- 10-station necropsy suite; trimming to slide preparation
- 7-level brain, 4-level nasal and rabbit ocular sectioningAperio GT450 whole-slide scanning for remote peer review

Clinical Pathology & Flexible Model

- Haematology, coagulation, clinical chemistry, urinalysis
- Specialised panels; in vitro haemolysis testing
- Standalone processing, evaluation, peer review or slide scanning for studies conducted at external sites

Analytical, Bioanalytical & Data

Analytical & Bioanalytical Sciences

- LC-MS/MS bioanalysis of plasma, serum and tissue
- Dose formulation analysis concentration, homogeneity, stability
- Method development and validation across diverse matrices
- Custom ELISA for immunogenicity and safety biomarkers

SEND Data Services

- Datasets for in-house and external studies, plus legacy conversion
- 60+ studies since 2017, including 22+ standalone conversions from other CROs
- Define.xml, nSDRG and Pinnacle 21 validation

Computational Toxicology & Risk Assessment

In Silico Prediction

- DEREK Nexus® and CASE Ultra - dual (Q)SAR meeting ICH M7
- Carcinogenicity, mutagenicity, genotoxicity, sensitisation

Health-Based Risk Assessment

- PDE, OEL and OEB derivation
- Nitrosamine risk assessment and CPCA with AI limits
- Read across and Category justification

Impurity Qualification & Dossiers

- ICH Q3A / Q3B qualification studies; ICH M7 classification
- CTD Modules 2.4 and 2.6 nonclinical writing
- Safety Data Sheets (CLP, OSHA, SWA & HSNO compliant)

*The same GLP-certified platform also supports agrochemical and food-ingredient safety programmes.

The Full Range, Delivered on Schedule

Breadth counts for nothing if the data lands late. Lead times, in-life execution and reporting cadence are built to hold a timeline whether you book one study or a dozen running in parallel.

12 WEEKS - GLP 28-day toxicity study, consignment to draft report

Lead time of 2-3 weeks from study request to start of in-life for non-GLP and GLP rodent studies; pathology results within 28 days of necropsy for a 5-week study.

PRE-STUDY ACTIVITIES

DAY 1-5*

- Consignment arrival
- SEZ clearance initiated
- GLP-TICO
- Document verification (CoA, TRIDS)
- Coding of test item and study allotment

DAY 6-48**

- DAY 6-48**
- Bioanalytical method development and validation

DAY 1-12

- Animal arrival
- Quarantine
- Acclimatization

28-DAY TOX STUDY TIMELINE

DAY 1-28

- In-life / dosing phase
- 40 tissues per animal (n=10/sex/main tox group)

DAY 29 & DAY 43

- Clinical pathology
- Necropsy
- In-life results

DAY 30-48

- Trimming
- Processing
- Embedding and sectioning
- Staining of slide

DAY 45-62

- Slide evaluation

DAY 63-75

- Peer review
- Target organ evaluation
- Pathology results

DAY 76-84

- Draft pathology report

TICO: Test Item Control Office | TRIDS: Test or Reference Item Datasheet. *Cold shipment handled on priority.

**Timeline varies upon method transfer & validation or method development & validation.



14 STUDIES RUNNING IN PARALLEL - A TYPICAL 26-WEEK TOXICOLOGY & SAFETY PHARMACOLOGY PROGRAMME

SL	NonGLP and GLP Safety Tox Studies	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
1	nonGLP MTD/DRF Rat and Dog Tox Studies																										
2	HPLC analytical method development & validation for <i>in vivo</i> dose confirmation analysis																										
3	LCMS/MS bioanalytical method validation - rat plasma																										
4	LCMS/MS bioanalytical method validation - non-rodent plasma																										
5	28-day repeat dose tox study with TK & 14-day recovery - rats																										
6	<i>In Vivo</i> micronucleus test in rat																										
7	HPLC analytical method development and validation - <i>in vitro</i> studies																										
8	<i>In Vitro</i> Ames test																										
9	<i>In Vitro</i> chromosomal aberration test																										
10	28-day repeat dose tox study with TK & 14-day recovery - Dog																										
11	CNS safety pharmacology - rat																										
12	Respiratory safety pharmacology - rat																										
13	Cardiovascular telemetry study - dog																										
14	<i>In Vitro</i> hERG assay																										
15	eCTD summary table and SEND Data Sets																										

Notes

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Visit our website:



About Syngene

Syngene International Ltd. (BSE: 539268, NSE: SYNGENE, ISIN: INE398R01022) is an integrated research, development, and manufacturing services company serving the global pharmaceutical, biotechnology, nutrition, animal health, consumer goods, and specialty chemical sectors. Syngene's 5000+ scientists offer both skills and the capacity to deliver great science, robust data security, and quality manufacturing, at speed, to improve time-to-market and lower the cost of innovation. With a combination of dedicated research facilities for Baxter, and Bristol-Myers Squibb, as well as 2.2 million sq. ft of specialist discovery, development and manufacturing facilities, Syngene works with biotech companies pursuing leading-edge science as well as multinationals, including GSK, Zoetis, and Merck KGaA.

For more details, visit www.syngeneintl.com or write to us at bdc@syngeneintl.com

