Syngene

Putting Science to Work

Syngene Formulation Development Center (FDC)

Oral Small-Molecule Drug Product Development & Manufacturing

Putting Science to Work

Syngene's FDC provides an integrated, end-to-end pathway for oral small-molecule drug products—from discovery pharmaceutics and physical-form selection to phase-appropriate GMP manufacturing, analytical life-cycle management, and late-phase scale-up up to commercial manufacturing. Our co-located Drug Substance (DS), Drug Product (DP) and Analytical teams, backed by digital Quality systems and a strong global inspection history, help de-risk development and accelerate first-in-human (FIH) and pivotal milestones.

Development & Manufacturing Overview

Formulation Technologies established at Syngene

Topicals ●
- Wound care spray film technology platform
- Gels
- Creams

Denture care technology ●
- Novel transparent gel as denture adhesive

Paediatric/age appropriate formulations ●
- Delayed release sprinkles
- ODT

Liquids (Oral) ●
- Oral liquids
- Taste masked oral suspension

Injectable/ Otic/ Ophthalmic ●
- Solution/ Gel
- Micro/Nano suspensions
- Lyophillization
- In-Situ depot
- Nano-emulsions
- Liposomes

Expertise in a diverse product range for complex technologies

Enabling formulations ●
- (Pre Clinical and Late Phase)
- Spray drying
- HME
- Nanosuspension
- Liquid in Capsule

Modified release oral solids ●
- Tablets, Capsules, Pellets, minitablets
- Pulsed release
- Zero order release
- Extended release
- Enteric Coating

FIH Quick to Clinic ●
- DiB/DiC
- Formulated Tablets/Capsules with Platform Approach
- Liquid in Capsule

Nasal Formulations ●
- Spray
- Solution for nebulization

● Client dedicated facility ● Development only ● Development + GMP

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- **Dosage-form focus:** Oral solids (immediate- and modified-release tablets/capsules) with enabling delivery platforms for poorly soluble molecules. We complement this with experience across liquids and semisolids when programs require bridging
- **Enabling technologies:** Spray-dried dispersions (SDD), hot-melt extrusion (HME), nanosuspensions, micro/nano-emulsions and liquid-in-capsule
- **GMP oral solids facility:** Phase-appropriate batch sizes from 1–120 kg (Phase 1–3) with an expansion pathway to 200–400 kg within the same building footprint; OEL ≥ 1 µg/m^3 (non-cytotoxic). Primary packaging in HDPE bottles and blisters (cold/thermo-form). Immediate- and modified-release presentations supported
- **Track record:** First U.S. commercial batch manufactured in March 2021. In the last 3 years, Syngene supported multiple registrations including ~15 ANDAs/NDAs, with one product commercialized and additional launches planned

Facilities & Operations

- 16,000 sq ft multi-product oral solids GMP area; capable of running up to three products in parallel
- Granulation: top-spray fluid-bed and high-shear; roller compaction for dry granulation; pellet coating via Wurster columns
- Compression/Coating: mini-tablets (~2 mm) to large formats (up to ~14 mm); film/enteric coatings; capsule filling (gelatin/cellulose; sizes 5–000), including blinding studies
- Primary packaging: HDPE bottles and blister packs; clinical pack/label as per protocol

Quality Systems & Digitization

Our Quality Management System encompasses change control, deviations/CAPA, OOS and complaint handling (TrackWise), with in-process QA oversight during manufacturing and final batch disposition by QA. Materials are controlled through SAP with QR-enabled warehousing for traceability and segregation. Facilities, utilities and equipment are qualified and maintained with calibration, preventive maintenance and pest control programs.

Digitized labs use LabWare LIMS integrated with Electronic Lab Notebook (ELN) for method, instrument and sample management; EDMS and LMS streamline document control, training, issuance and review—enabling paper-lite operations and strong data integrity.

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Regulatory & Certifications (Function/Site-specific)

Multiple successful inspections/assessments by US FDA (CDER/Office of Compliance) and Health Canada.

Early-Phase Development

Our early-phase framework aligns discovery pharmaceutics, solid-state science and phase-appropriate formulation to establish a robust foundation for IND/IMPD. We have expertise in small-scale, information-rich experiments to rapidly determine developable form, dosing vehicle and analytical strategy.

Developability & Pre-formulation

- **Solution-state:** pKa, logD, aqueous solubility, pH–solubility profile, oxidative/light stability in solution
- **Solid-state:** melting point/Tg, hygroscopicity (DVS), moisture sorption–desorption, PSD, microscopy, PXRD; stress stability under temperature/RH/light
- **Amorphous API as SDD:** glass transition (Tg), physical/chemical stability, dissolution/precipitation behavior in biorelevant media for biopharmaceutics risk assessment

Salt & Polymorph Screening

We tailor screening depth to phase and material availability: in-situ salt screens to rank counter-ions by solubility/propensity; mg-scale salt synthesis with g-scale confirmation; and comprehensive polymorph screens using cooling/anti-solvent crystallization, slurry conversion, hydrate/solvate generation and humidity/thermal stress. Characterization typically includes DSC/TGA, PXRD, microscopy, solution pH/solubility, ion chromatography and impurity profiling, culminating in a recommended form for development.

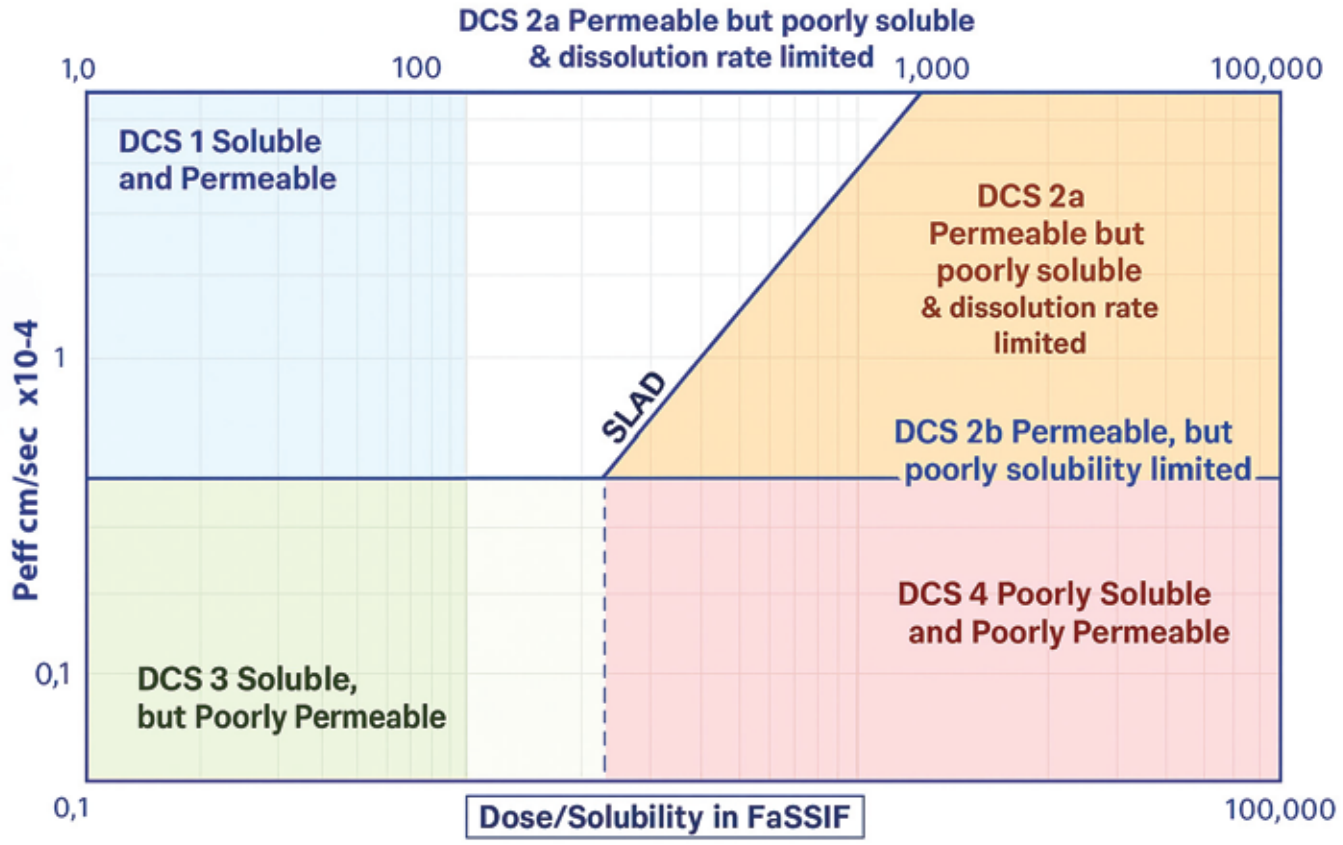
- We have a state-of-the-art solid state characterization lab which houses miniature equipment which can generate data in Pre-formulation studies with minimal material generated in Discovery stages (as low as 100 mg)

Preclinical Formulation for Pharmacokinetics/Dose Response Finding/GLP Toxicology studies

Species- and route-appropriate vehicles (oral/IV) are designed from solubility, stability and permeability data. Solubilization hierarchies include pH modulation, co-solvency, surfactants, cyclodextrins or combinations. Where needed, enabling systems (nanosuspension, ASD, lipidic supersaturating systems) are deployed. Prototype selection and readiness for study dosing can often be achieved in ~3–4 weeks.

Enabling Technologies & Manufacturing

We match formulation approach to absorption risks using the Developability Classification System (DCS) and solubility-limited absorbable dose concepts. DCS IIa programmes leverage micronization/co-micronization to address dissolution-rate limits; DCS IIb programmes favor amorphous solid dispersions (SDD/HME), lipid-based or self-emulsifying systems to elevate apparent solubility and, where relevant, leverage lymphatic uptake; DCS III/IV programmes may combine permeability enhancers and efflux-modulating excipients with solubilization strategies.

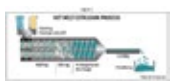


Calculating the solubility limited absorbable dose (SLAD) proposed as part of the DCS, may help to determine whether it is reasonable to attempt to use a crystalline presentation of the drug candidate in early clinical trials.

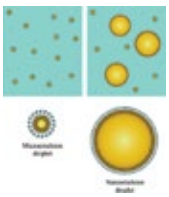
Platforms & Toolkits

- **Amorphous Solid Dispersion (Spray Dried Dispersion/Hot Melt Extrusion):** Polymer screening (e.g., HPMCAS, HPMC-P55, Eudragits, HPMC, PVP/VA-64, PEG 8000, Soluplus, Poloxamers). Process development via spray-drying or hot-melt extrusion with downstream conversion to tablets/capsules.
- **Nanosuspensions/Nano-emulsions:** Bead-milling/microfluidization; control of PSD, zeta potential and physical stability; conversion to solid dose via top-spray or high-shear granulation, or spray-drying.
- **Milling/Micronization:** Air-jet (dry), ball-mill and high-shear homogenization (wet) to increase surface area and wettability.
- **Spray Drying:** Lab and GMP units from the same make for smooth scale-up;; broad solvent handleability

Development approach

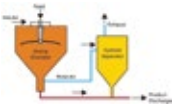


Hot melt extrusion



Nano-emulsion

Nano-suspension by bead milling



Spray Drier

Strategies

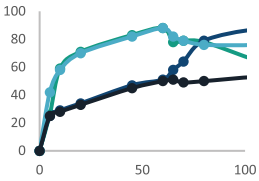
Animal screening

Screening of fatty acid, polymer surfactant or stabilizer in rodent model

Selection of 3 different stabilizers and surfactants for further evaluation

Formulation Development

Chemical Stability



Dissolution

Polymers screened for solid dispersion

HPMCAS
HPMC-P55
Eudragit®
HPMC
PVP
Co-povidone (Kollidon VA-64®)
PEG 8000
Soluplus®
Poloxamers®

Dog PK study
Selection of lead and back up formulation

Manufacturing Process optimization and chemical stability

Clinical supplies

Delivery Experience

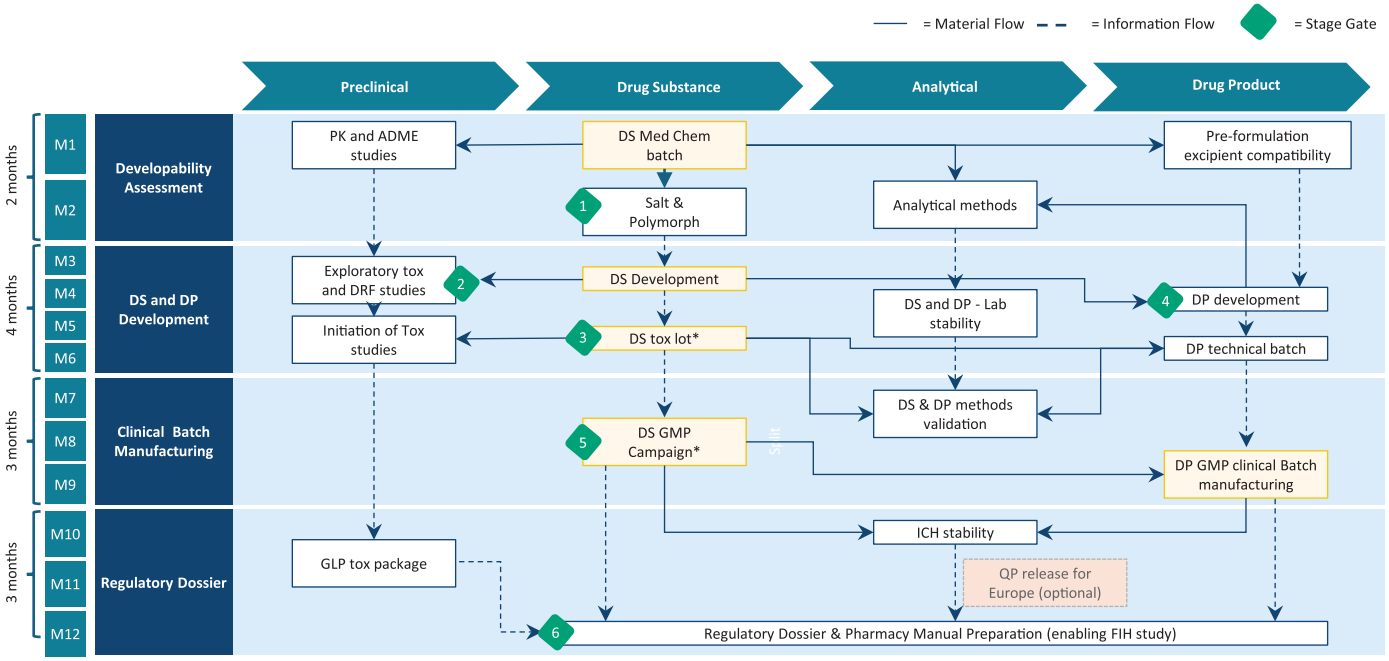
Syngene has advanced multiple NCE and complex generic/505(b)(2) programs through clinical phases using enabling formulations (SDD/HME, nanosuspensions, lipidic systems and liquid-in-capsule delivery platforms.

Integrated CMC Approach

Our early-phase framework aligns discovery pharmaceutics, solid-state science and phase-appropriate formulation to establish a robust foundation for IND/IMPD. We have expertise in small-scale, information-rich experiments to rapidly determine developable form, dosing vehicle and analytical strategy.

Our Integrated approach to early phase CMC Development

Developability assessment to Regulatory Dossier preparation possible in 12 months

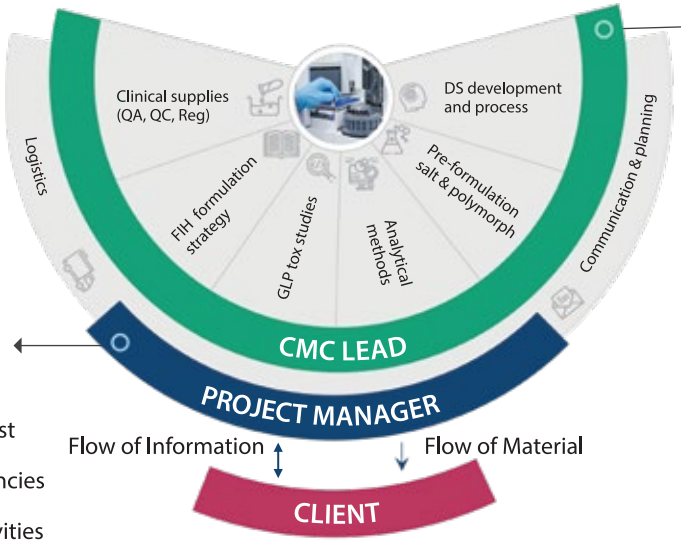


*Split lot/single lot strategy can be used – for tox. and FIH GMP campaign of DS

A single, program-level timeline coordinates DS, DP and Analytical workstreams from developability assessment through dossier authoring, enabling FIH in approximately 12 months in suitable scenarios. Dedicated project management, stage-gate governance and risk registers are reinforced by cross-functional focus groups (chemical/physical form, biopharmaceutics risk, genotoxicity, lab-to-tox-to-GMP bridging, TPP/TMP, specification templates and overall quality/regulatory risk).

We have dedicated teams for CMC projects fortified by strong Project Management

- SPOC for all communications
- Project planning and Risk assessment
- Re-aligning with change request
- Introducing operational efficiencies
- Managing sub-contracted activities



- CMC development strategy
- Development of robust, scalable, cost-effective process
- Phase appropriate analytical methods
- Quality & regulatory compliance
- Authoring regulatory dossier

Analytical Development Capabilities

A 200+-scientist analytical organization across ~72,000 sq ft provides end-to-end support: assay/related substances/dissolution method development; forced degradation and excipient/packaging compatibility; release and ICH stability under cGMP; reference standard qualification; and method validation/transfer (GMP ↔GMP) with risk-based protocols and statistical comparability.

Knowledge transfer: Development to Validation

Method development

Develop method and perform pre-validation

Method Criticality assessment

Assess the critical parameters & document in the method of analysis

Knowledge transfer

Team discussion between the development and validation team and discussion on the each steps and criticality

Document transfer

Take feedback from the validation team and incorporate the changes in the final method of analysis

Analytical method transfer (GMP to GMP)

Pre-transfer phase

- Alignment of instrument similarity between Syngene and our partner
- Analytical methods validation
- Cleaning method validation
- Risk Assessment and mitigation strategies for individual analytical method

Technical Documents and knowledge transfer

- Analytical Methods Development Report
- Risk Assessment Report
- Analytical Methods Transfer Protocol with predefined acceptance criteria and detailed checklist
- Specifications: RM, PM, In-process and Finished Product
- Review of analytical transfer results

Analytical Methods Transfer

- Sample concentration & LOQ determination
- Sample preparation optimization – solvent selection,
- Sample extraction procedure – crushing/grinding, centrifuge, sonication, shaking

Oral Dosage Testing & Characterization

- **Tablets/Capsules:** assay & content uniformity, related substances, residual solvents, water, dissolution (single/multi-media; biorelevant), disintegration, PSD, PXRD
- **Solutions/Suspensions/Lipidic Systems:** pH/viscosity, assay/CU, degradation, preservative/antioxidant assays, PSD, dissolution/release testing
- **Solid-state & Structural Tools:** optical microscopy, PXRD, DSC/TGA, DVS, particle sizing; LC–MS/GC–MS/HRMS, IC, qNMR, prep/semi-prep HPLC and SFC

Late-Phase Development & Scale-Up

We apply Quality by Design as standard—defining QTPP and CQAs, mapping risks via FMEA, and using DoE (Design-Expert®, Minitab®) to understand factor interactions, optimize formulation/process and establish design spaces or proven acceptable ranges. Scale-up leverages geometric/kinematic/dynamic similarity; where not possible, CPP-centric customization ensures product CQAs are maintained at target scale for first-time-right outcomes

Why Syngene

- One-campus integration: DS–DP–Analytical under one roof minimizes handoffs and accelerates decisions, with single-platform knowledge transfer and program management
- Speed with rigor: Early sharing of physicochemical/biopharmaceutics risks informs phase-appropriate formulation choices to unlock exposure and dose feasibility
- On time delivery track record of above 95% for the past 3 years, ensuring ontime clinical study start for various complex programs for our clients across different geographies
- Digital quality backbone: EDMS, TrackWise, LMS and LabWare LIMS–ELN ensure traceability and data integrity backed with excellent track record with regulatory agencies
- Proven execution: Multiple programs delivered across geographies, including ~15 ANDAs/NDAs supported in the last 3 years, one product commercialized and additional launches planned
- End-to-end accountability: From salt/polymorph selection and preclinical enablement to GMP clinical supplies, late-phase QbD and commercial manufacturing

Animal Heathcare Drug Product Development & Manufacturing

Overview of Capabilities

Protein Formulation Development

DP Development (Aqu/Non-aqu/Lyo)
Fill & Finish (Engineering & GMP batches) Commercialization

Monoclonal Antibody Development

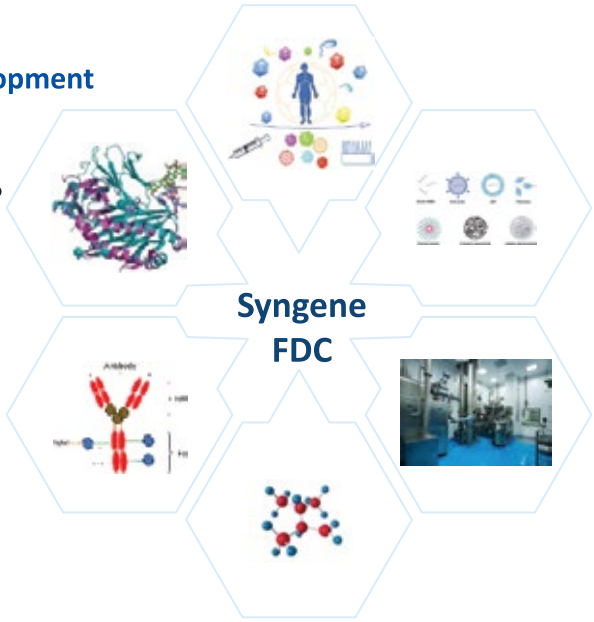
DP Development (Aqueous/Lyophilized)
Fill & Finish (Engineering & GMP batches)
Commercialization

Biosimilar (mAb & Protein)

DP Development (Aqueous/Lyophilized)
Fill & Finish (Engineering & GMP batches) Commercialization

ICH Stability Study

DP Stability study
40/75, 25/60, 2-8°C, -20°C



Vaccine Formulation

DP Development (Aqueous/Lyophilized)
Nasal Device Performance Testing
Fill & Finish (Engineering & GMP batches)
Commercialization

LNP Oligonucleotide

DP Development (Aqueous/Lyophilized)
Fill & Finish (Engineering & GMP batches)
Commercialization

Antibody Drug Conjugates

DP Development (Solution & Lyo)

Dossier filing

Pre-IND Meeting
IND & NDA filing
Regulatory Query Response

- Syngene aims to be a strategic partner for animal healthcare product development, offering end-to-end solutions from discovery to clinical and commercial manufacturing
- Expertise spans **large molecules** (biologics), **small molecules,** and **chemical development** for APIs (excluding antibodies and steroids)

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Manufacturing Facilities & Infrastructure

- **Oral solids development and manufacturing:** Granulation suites, tablet compression (up to 14mm), campaign-based manufacturing, and robust waste management
- **Sterile fill-finish facility:** Robotic filling for vials and pre-filled syringes, lyophilization, and batch sizes up to 25,000 vials
- **Stability Chambers:** Walk-in and reach-in chambers catering to ICH requirements for various temperature and humidity zones

Analytical Development and Validation

- Extensive analytical instrumentation (HPLC, UPLC, MS, NMR, GC-MS, dissolution apparatus, etc.) for drug product and method development
- Proven technology transfer protocols for both drug product and analytical methods, including risk assessment, cleaning validation, and regulatory support

Veterinary Formulation Experience & Innovation

- Experience with a wide range of veterinary dosage forms: hard/soft chew tablets, liquids, injectables, microspheres, and depot formulations
- Dedicated facilities for animal health products, including large-size tablets (up to 6g) and impurity characterization
- Successful collaborations with top 5 global animal healthcare companies.

Case Studies & Success Stories

- Integrated drug development for complex combination products, including scale-up, technology transfer, and stability studies.
- Development of analytical methodologies (e.g., texture analyzer for soft tablets) to differentiate and characterize products

Differentiators & Strategic Advantages

- Syngene offers comprehensive, integrated solutions for animal health product development, leveraging its experience in human health to drive innovation in veterinary formulations
- The company's infrastructure, regulatory compliance, and technology transfer capabilities position it as a preferred strategic partner for global animal health organizations

Parenteral Dosage form Development & Manufacturing

Syngene offers integrated parenteral drug product (DP) development through commercial supply: end-to-end services from preformulation and analytical characterization to clinical and commercial sterile fill finish, stability, regulatory support and technology transfer. Their capability set covers small molecules, potent compounds and biologics (including LNPs, ADCs, oligonucleotides and mRNA-based vaccines).

Drug Product – Capabilities to support early stage to late stage development and manufacturing

Integrated development

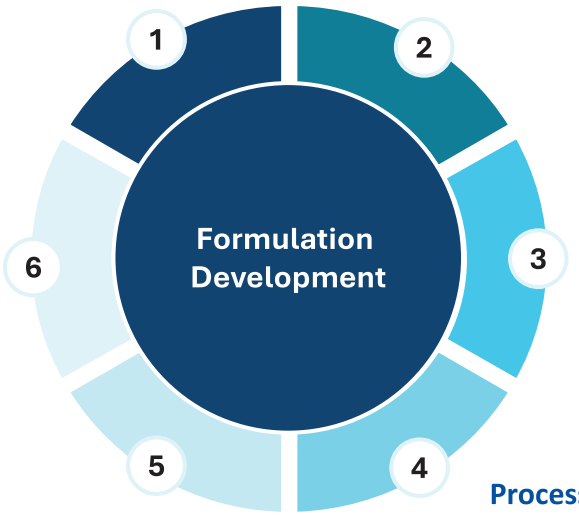
Tox formulation and supplies

Integrated CMC development – DS, DP, Regulatory

Preformulation

Physicochemical Characterization studies

Compatibility studies



Clinical supplies

cGMP Pilot facility for solid orals

VICH Batches Mfg

Injectables

Formulation development

Solid orals (Tablets/Capsules/Granules), Parenteral, spot on, Liquids, Pediatrics formulation, Semisolids

Development processes

QbD, Risk analysis (FMEA), DOE

Process Development & Scale up

DOE, CPPs, Control strategy

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End-to-end services

- **Formulation development:** Solutions, lyophilized products, suspensions, depot (LAI microspheres, in situ gels), nanoemulsions, nanosuspensions, liposomes and LNPs. Ability to handle compounds having OEL: ≥ 1 µg /m3
- **Clinical to commercial manufacturing:** Clinical batches (2–100 L) through commercial scales (200–1,300 L). GMP sterile and non sterile operations, pilot trials, and client technology transfer
- **Analytical & stability:** Method development/validation, forced degradation, impurity isolation/qualification, ICH stability programs and in house, Extractables and leachables, microbiology/photostability testing
- **Regulatory support:** Pre IND engagement support, IND/NDA/ANDA dossier preparation and responses, method remediation and lifecycle management

Facilities, scale and throughput

- **Pilot facility:** 2 L–100 L compounding; isolator with robotic arm; filling speeds ~30 vials/min, 15 PFS/min; pilot vial throughput in thousands to low millions per year
- **Commercial facility:** Stainless steel (SS) and single use (SU) lines sized 200–1,300 L; vial and PFS lines capable of high throughput (up to tens or hundreds of millions of vials/year depending on configuration). Grade A isolators, automated visual inspection, vial washing, autoclaves and nested RTU presentations for vials and PFS
- **Fill/finish modalities:** SS lines for small molecules; SU bag systems for biologics; robotic filling for reduced human intervention; terminal sterilization (autoclave) and two stage aseptic filtration options

Technical equipment and lab footprint

- **Key process equipment:** High pressure homogenizers (Panda Plus, Microfluidizer), Silverson/Ultra Turrax high speed homogenizers, spray dryer (lab/pilot), Vertis lyophilizer, microfluidizer, autoclaves including PFS capability, Instron for PFS functionality testing
- **Analytical lab scale & tools:** 200+ scientists across ~72,000 sq ft of lab/stability space; HPLC (UV/PDA/ELSD/RI), LC MS/MS, GC MS/HS, ICP OES, ion chromatography, pXRD, DSC, TGA, DVS, particle sizing (Malvern/Zeta), HIAC particulate counters, headspace, KF coulometry, microscopy and NMR capabilities. LIMS, QA, SAP, EDMS and TrackWise for data and quality management

Potent/biocontainment and specialized capabilities

- **Containment and biosafety:** Facilities designed to OEL 4 (cytostatic) and BSL 2 operations; isolators with HEPA exhaust and scrubber, controlled AHU modes and dedicated dispensing/pass box arrangments
- **Complex biologics:** DP development and fill/finish for vaccines, mAbs, ADCs, oligonucleotide LNPs and biosimilars with SU sterile lines, stability testing at multiple temperature profiles (including –20°C, –80°C), and cold chain storage/shipment capabilities
- **Analytical differentiation:** In house de formulation, impurity isolation/characterization and synthesis of reference impurities, trace analysis (elemental, nitrosamine, residual solvents), and end to end method lifecycle management to accelerate filings

Quality, compliance and operational support

- **Quality systems:** cGMP operations, CSV compliant labs, dedicated QC centers, method validation and transfer, audit ready teams, serialization & aggregation readiness for primary packaging
- **Tech transfer & commercialization:** Support for technology transfer from client to Syngene, scale up from pilot to ommercial lines, packaging, stability program execution and dossier support for global regulatory filings

Key differentiators and implications for partners

- Integrated bench to bedside offering combining formulation, analytical, clinical GMP manufacture and high throughput commercial fill finish
- Strong track record across small molecule sterile solutions/lyos, several liposome projects and nanoparticle experience
- Ability to handle small molecules and biologics under appropriate containment with robotic isolator filling to minimize contamination and human error
- Analytical depth (impurity synthesis/qualification, de formulation) that shortens timelines for troubleshooting and regulatory submission

Suggested engagement angles (practical next steps)

- Early technical assessment or gap analysis to map your molecule's required containment, analytics and fill format
- Pilot run to de risk formulation and scale up using microfluidizer/homogenizer and pilot isolator
- Integrated filing package support combining analytical, stability and GMP batch data to accelerate IND/ANDA/NDA timelines

Scan the QR code to learn how our capabilities can advance your program

Notes

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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 6000+ 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

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