Complex Parenterals

A CDMO leader for advanced drug delivery with the excipients, technologies and services to deliver the outcomes you value most

EVONIK
POWER TO CREATE

Make Evonik your competitive advantage

Evonik is one of the world's leading specialty chemical companies. We hold market leading positions in 80 % of our businesses, with our team of 32,000 employees active across more than 100 countries and 180 sites.

Our Health Care business line is a global strategic partner to many of the world's largest and most innovative pharmaceutical and biotechnology companies. For oral and parenteral dosage forms, we combine versatile excipient platforms with proven drug delivery technologies and integrated CDMO services for formulation development and drug product manufacturing.

Pharmaceutical companies worldwide leverage these distinctive products and value-adding services to enhance drug performance, reduce project complexity, increase speed to market and strengthen supply security.

A GLOBAL CDMO LEADER AND PREFERRED PARTNER

90 % Of the world's top 50 pharma companies are served by us	**No. 1** The leading brand of standard and custom bioresorbable polymers	**> 20** Ready-to-ship excipients with endless customization options
> 30 Years of leadership for excipient design and supply	**> 40** Years of leadership for polymeric-based drug delivery	**> 30** Years of leadership for LNP-based drug delivery
> 6 Parenteral drug delivery technologies in our portfolio	**≈ 50 %** Of all commercial LNP-based products received our support	**≤ 50 mL** Aseptic vial filling of powders, liquids or suspensions

An integrated portfolio of excipients and cdmo services

Our portfolio of excipients, delivery technologies and CDMO services uniquely positions us to serve as a long-term partner to help transform your APIs into high-performance parenteral medicines.

RESOMER® PORTFOLIO OF PARENTERAL EXCIPIENTS

Our standard and custom PLA, PLG and PEG copolymers have more than 30 years of biocompatibility, safety, performance and supply security.

FORMULATION AND PROCESS DEVELOPMENT SERVICES

Our drug delivery experts provide integrated formulation, process and analytical support from feasibility to the scale-up of the commercial drug product.

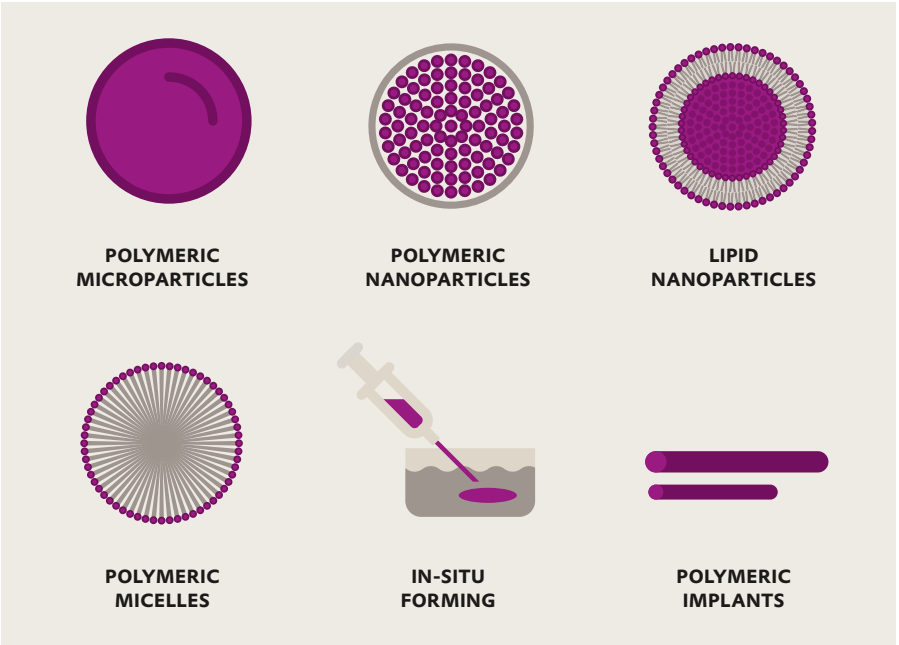
DRUG MANUFACTURING AND ASEPTIC FILLING

In addition to the cGMP clinical and commercial production of drug products, our semi- and automated aseptic lines fill powders, liquids and suspensions.

A polymeric and lipid-based drug delivery leader

Our market-leading expertise across complex formulation technologies has helped countless customers transform their small molecules, peptides, proteins, nucleic acids (e.g. mRNA), synthetic vaccines and other drug substances into high-performance medicines.

In addition to the development of formulations for systemic delivery, we specialize in the targeted and localized delivery of drugs to sites such as the eye, joints, brain, tumors and spine, as well as the targeting of specific genes or disease sites.



RESOMER® excipients for parenteral controlled release

RESOMER® delivers unrivaled reliability and versatility for the controlled release of complex parenteral drug products. With a long history of safety and biocompatibility, these well-characterized polymers are highly trusted for use with small molecules, peptides, proteins and other substances.

The broad range of catalog and custom compositions in high and low molecular weights ensure our polymer properties are precisely tuned to match your target release profile. We can leverage our extensive expertise across a range of application areas to address specific requirements for systemic or local drug delivery.

In addition to RESOMER®, we also provide custom polymer synthesis services for the supply of your own excipients.

Essential polymer characteristics

- 100 % bioresorbable and completely metabolized
- Suitable for terminal sterilization
- Shelf life exceeds five years
- Customizable for products with narrow specifications
- Simple to process with conventional equipment

Quality and regulatory excellence

- IPEC-GMP Guide for Pharmaceutical Excipients 2014
- Master files and technical dossiers maintained
- ISO 9001 and 13485 certifications
- Full range of inventory maintained, safety stocks

cGMP MANUFACTURING IN THE U.S. AND EUROPE FOR QUALITY AND SUPPLY SECURITY

Manufacturing occurs in IPEC-GMP cleanrooms with specially engineered equipment at modern U. S. and German sites. Multiple reactor sizes are available to support lab scale, clinical and commercial batch volumes. Production strategies can be aligned to your global supply security and market requirements.

Evonik Birmingham Laboratories, Alabama, USA

RESOMER® Science Center, Darmstadt, Germany

RESOMER® standard catalog

An extensive range of high and low molecular weight polymers are available ready-for shipment to meet your lab, clinical and commercial requirements. Acid and ester end group chemistries are available. In addition to GMP manufacturing, all standard products are available in custom RESOMER® Select, RESOMER® Sterile and RESOMER® Zero configurations.

RESOMER® R
Poly (D,L-lactide)

- Degradation time from weeks up to 12 months
- Inherent viscosity (IV) from 0.15 to 0.75 dL/g

RESOMER® RG
Poly (D,L-lactide-co-glycolide)

- 50:50, 65:35, 75:25, 85:15 mole ratio
- Degradation time up to 18 months
- IV from 0.09 to 1.7 dL/g

RESOMER® CONDENSATES
Poly (D,L-lactate-co-glycolide)

- 50:50 mole ratio
- M_n 800 and 2,300 daltons
- Short degradation time of less than 3 months

RESOMER® SELECT

The leading brand of custom-made polymers

- Tailored to meet your specific formulation needs:
  - Monomer selection
  - Polymer composition and microstructure
  - Milled to target particle size distributions
  - Acid and ester end groups
  - Molecular weight and inherent viscosities
- Di-block copolymers of polylactide and mPEG
- Batch sizes from lab to production scale
- All catalog polymers available as RESOMER® Select
- Process technologies to meet extremely tight product specification requirements

RESOMER® ZERO

Ultra-low tin content (≤1 ppm) to address specific processing and application requirements

RESOMER® STERILE

The world's first sterile, extended release PLG excipient to support aseptic production

CDMO SERVICES

Full project support from feasibility through to the scale-up and supply of the commercial drug product

Evonik is one of the world's leading CDMOs for complex parenteral drug products.

For polymer-based and lipid-based drug delivery, we bring together market-leading expertise in the formulation development, process development, analysis, scale-up and production of complex parenteral drug products.

Our expertise focuses on parenteral drug products that deliver small molecules, peptides, proteins, and nucleic acids (e. g. mRNA) for new treatment modalities across a wide range of therapy areas.

Our Western-based network of audited, cGMP manufacturing sites and formulation and analytical labs, backed by dozens of customer support offices worldwide, ensure you have the right project teams for reliable, responsive support.

EVONIK VANCOUVER LABORATORIES

Vancouver, Canada

- Competence center for liposomes and nanoparticles

	R&D	Pre-clinical	Phase I
Development and cGMP Manufacturing Services	Formulation feasibility	Formulation development	
	Process identification	Process development	
	Developmental stability	Test article supply IND-enabling stability	
	Lead candidate identification		
Analytical Services	Method development		
	Analytical characterization support		
Process Equipment	Extruders < 100 mL	Extruders < 800 mL	

EVONIK BIRMINGHAM LABORATORIES

Birmingham, AL, USA

- Competence center for polymeric microparticles, nanoparticles and implants
- Excipient design and production

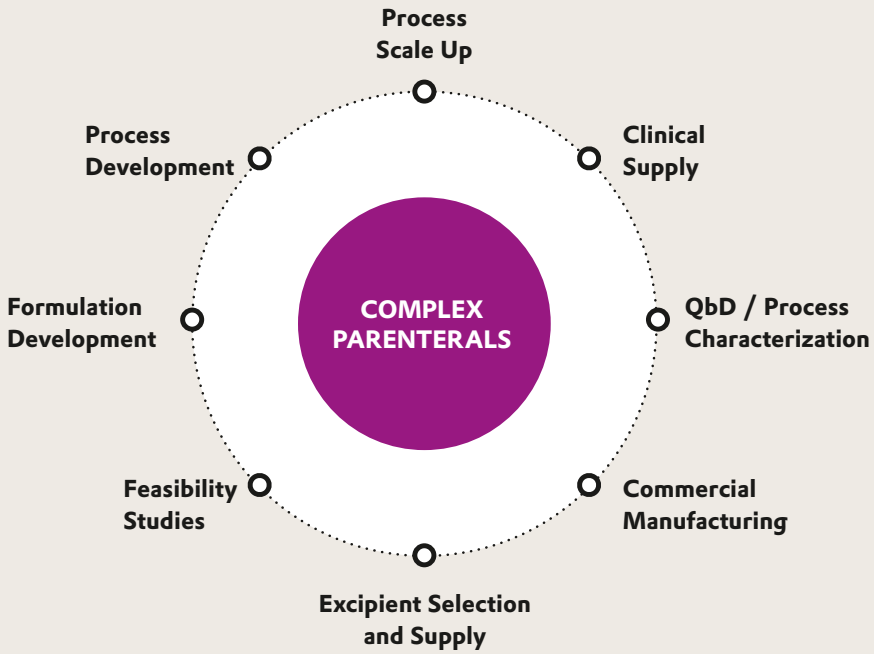
EVONIK DRUG DELIVERY LABORATORIES

Darmstadt, Germany

- Excipient design and production
- Formulation development and services

Phase II	Phase III	Commercial
Formulation optimization		Lifecycle management
Process optimization, scale up, QbD	Process performance qualification (PPQ)	
Clinical cGMP production and aseptic filling		Commercial cGMP production and aseptic filling
Technology transfer and scale-up		
Phase-specific method transfer, qualification and validation to ICH guidelines		
Drug product release testing and stability studies		
Client-owned and dedicated extrusion equipment		Custom extruders
Microfluidics and micro-mixing devices		

Formulation and Process Development



We leverage our formulation and process development expertise to develop complex parenteral drug products that are safe, efficacious, reproducible and efficient for clinical scale-up and commercial use. Our teams have a strong track record in helping companies develop human and animal drug products, including those with highly potent APIs and controlled substances (III-V). These services have helped enhance and differentiate drug products across a range of therapeutic areas including oncology, rare diseases, ophthalmology, CNS, and orthopedics.

Starting with your API, we apply our drug delivery and product-by-process technologies to design drug products that match the target product profile and route of administration requirements. Development-stage appropriate Quality by Design (QbD) and process characterization principles are used to identify and control critical process parameters throughout the development, scale-up and optimization of the drug product manufacturing process for clinical production and commercial supply.

OUR DEVELOPMENT SERVICES INCLUDE:

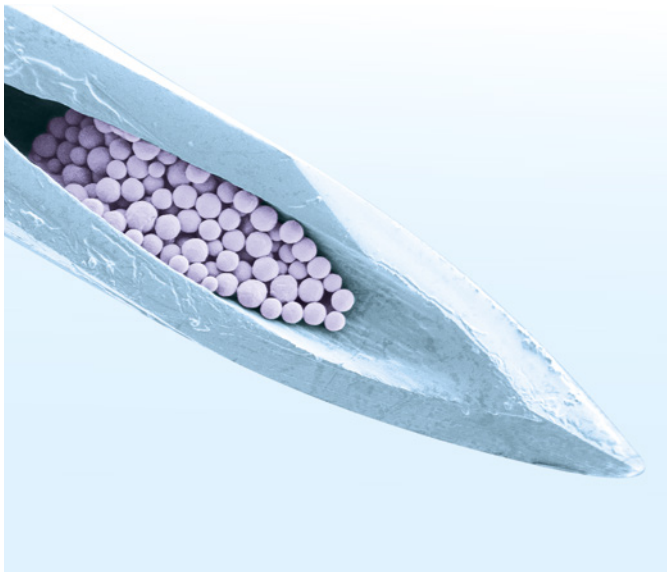
- Formulation feasibility to design prototype formulations for in vivo screening
- Analytical characterization
- Developmental stability studies
- Selection of a lead formulation candidate for non-clinical studies
- Preparation of test articles for IND-enabling toxicology studies

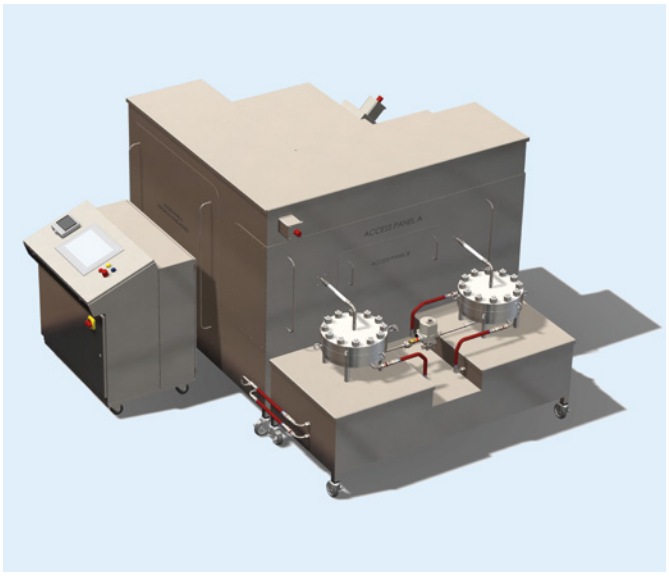
WE HAVE DECADES OF EXPERIENCE IN OBTAINING THE FORMULATION OUTCOMES YOU REQUIRE INCLUDING

- Extended release for systemic delivery
- Improved drug uptake at target site
- Increased efficacy
- Solubility and bioavailability enhancement
- Extended release for local delivery
- Targeted drug delivery and drug distribution
- Smaller needles and reduced injection volumes
- Reduced side effects for improved safety

Process Technologies

Based upon your API and drug product requirements, we will identify and develop the most effective and scalable manufacturing process. Based upon our comprehensive understanding of the critical process parameters that impact performance, as well as our strong manufacturing record, we help to reduce scale-up and regulatory risk.





POLYMERIC-BASED DRUG PRODUCTS

Continuous microencapsulation
We have more than 40 years of microencapsulation expertise in making polymeric nanoparticles and microparticles via continuous solvent extraction. The emulsion-based process is reproducible, scalable to commercial batches, and can produce a range of drug particle sizes for extended release from weeks to months of duration. Additional outcomes can include reductions in needle size and lower injection volumes.

Precise Hot Melt Extrusion
We specialize in the development of injectable implants with precise shape and diameter control for the extended release of small molecules and peptides over periods of up to a year. Proprietary post-extrusion processing methods can be used to control burst and tune drug release for specific applications including ocular delivery.

LIPID-BASED DRUG PRODUCTS

LIPEX® extruders
Evonik's platform of LIPEX® extruders have set the industry standard for liposomal drug product manufacturing for more than 20 years. Our extruders create homogeneous populations of liposomes and are available in lab, pilot, intermediate and commercial-scale (pictured above). A one-step process forces aqueous suspensions of lipids through filters with a defined pore size for optimal size reduction and trapping efficiency.

Microfluidics and Micro-mixing
Evonik and our partners have developed strong competencies for this fast-growing process segment, whereby micromixers create homogeneous populations of liposomes via the controlled channeling of lipids dissolved in solvent and an aqueous buffer.

CDMO SERVICES

cGMP Manufacturing and Aseptic Filling

Regardless of your benchtop, clinical or commercial batch requirements for microparticles, nanoparticles, liposomes and drug-loaded implants, our cGMP manufacturing facilities provide quality and supply security.

We can also support sterile product manufacturing and handling for high-potency APIs and controlled substances. Automated, semi-automated and manual systems are available for the aseptic filling of parenteral drug products in powder, suspension or liquid forms into vials. All aseptic filling and lyophilization is conducted in ISO 5 (Grade A) isolators.

To support the filling of highly specialized drug products such as personalized medicines and orphan drugs, we have established a fully-integrated line with SKAN isolators and GEA lyophilization technology that can aseptically fill powders, liquids and suspensions into vials up to 50 mL in size.

CDMO SERVICES

Analysis and Testing

Our laboratories in North America and Europe provide a comprehensive range of analytical development and quality control services to support projects from feasibility to clinical and commercial supply.

These services include:

- Analytical support of development activities
- Polymer and lipids excipient testing
- Raw material and drug product release testing
- Method development, transfer, and validation according to ICH guidelines
- Stability storage and testing (–80 °C to 40 °C)
- Microbiology testing

ANALYTICAL TESTING CAPABILITIES AVAILABLE FOR USE INCLUDE:

- Assay/impurities
- Drug content
- Content uniformity
- In vitro release
- Particle size
- Surface charge
- Residual solvents
- Water content
- Encapsulation efficiency
- Thermal properties
- Inherent viscosity
- Polymer molecular weight
- Lipid content/impurities
- Reconstitution
- Solution properties
- Elemental analysis
- Particulates – subvisible
- Bioburden
- Endotoxin
- Sterility

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EVONIK
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EVONIK NUTRITION & CARE GmbH
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Pharma Polymers & Services

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