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.

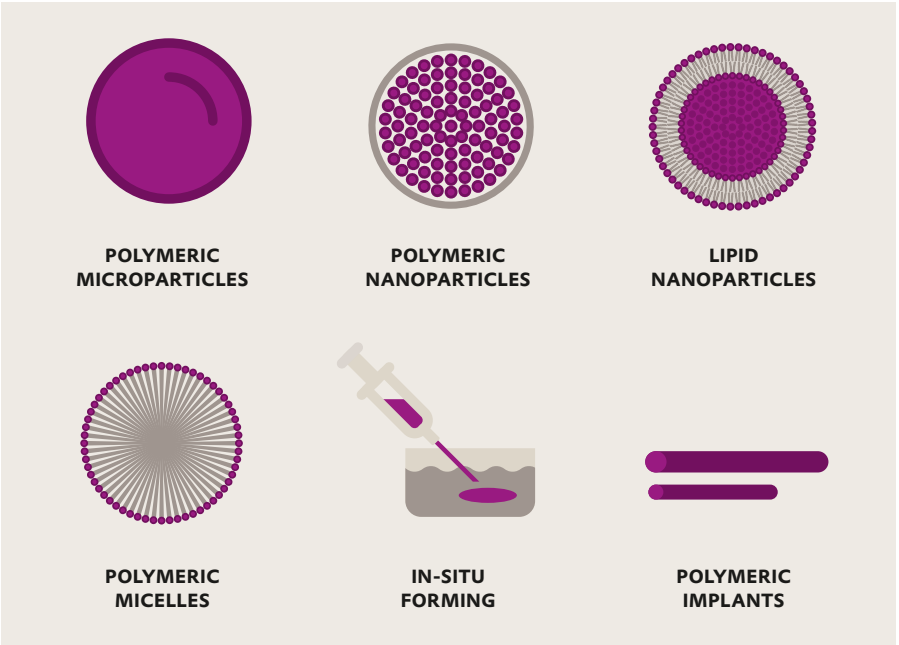
DRUG MANUFACTURING AND ASEPTIC FILLING

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

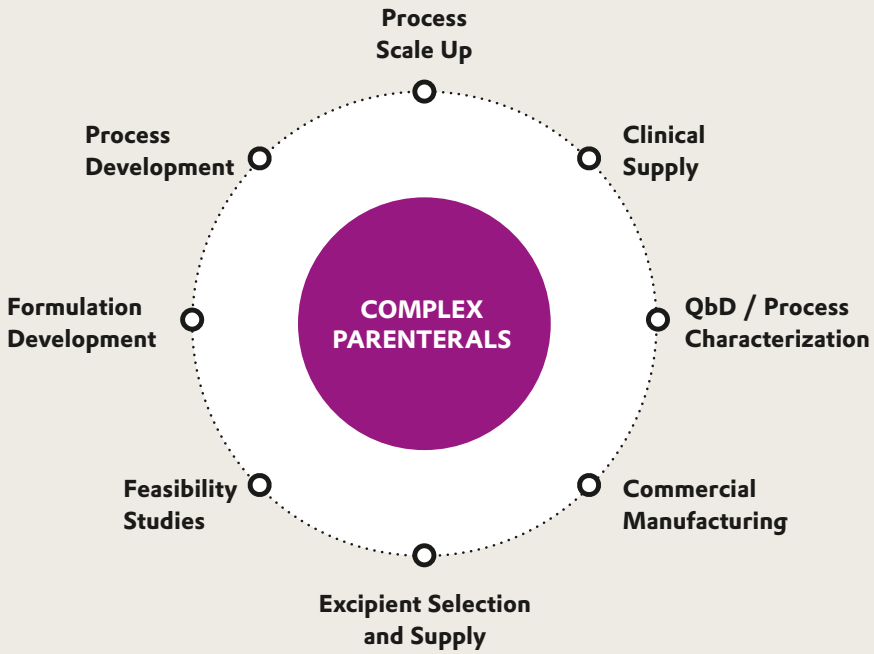
EVONIK DRUG DELIVERY LABORATORIES

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:

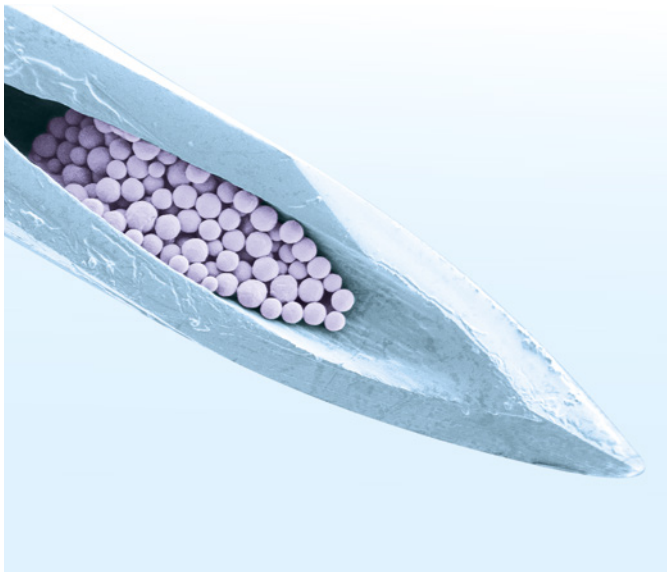
- Formulation feasibility to design prototype formulations for in vivo screening
- Analytical characterization
- Developmental stability studies
- Selection of a lead formulation candidate for non-clinical studies
- Preparation of test articles for IND-enabling toxicology studies

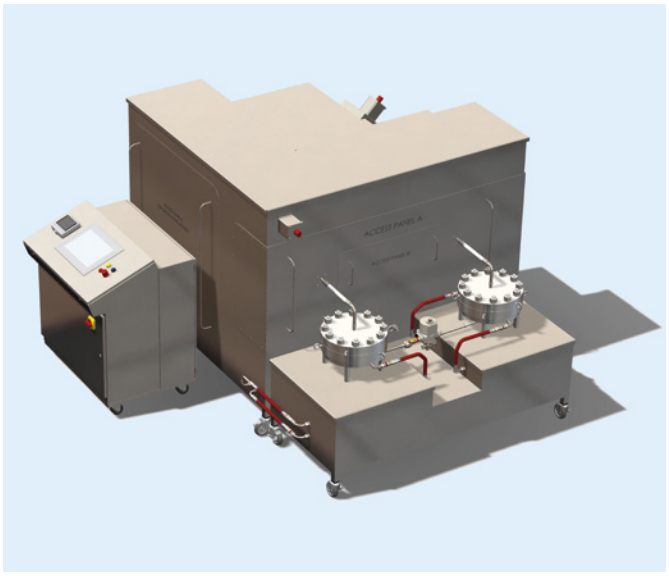
WE HAVE DECADES OF EXPERIENCE IN OBTAINING THE FORMULATION OUTCOMES YOU REQUIRE INCLUDING

- 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
POWER TO CREATE

EVONIK NUTRITION & CARE GmbH
Health Care Business Line
Pharma Polymers & Services

healthcare@evonik.com
healthcare.evonik.com

Oral Drug Delivery Solutions

An integrated portfolio of functional polymers, delivery technologies and services to release the true value of your oral solid dosage forms

EVONIK
POWER TO CREATE

Make Evonik Your Competitive Advantage

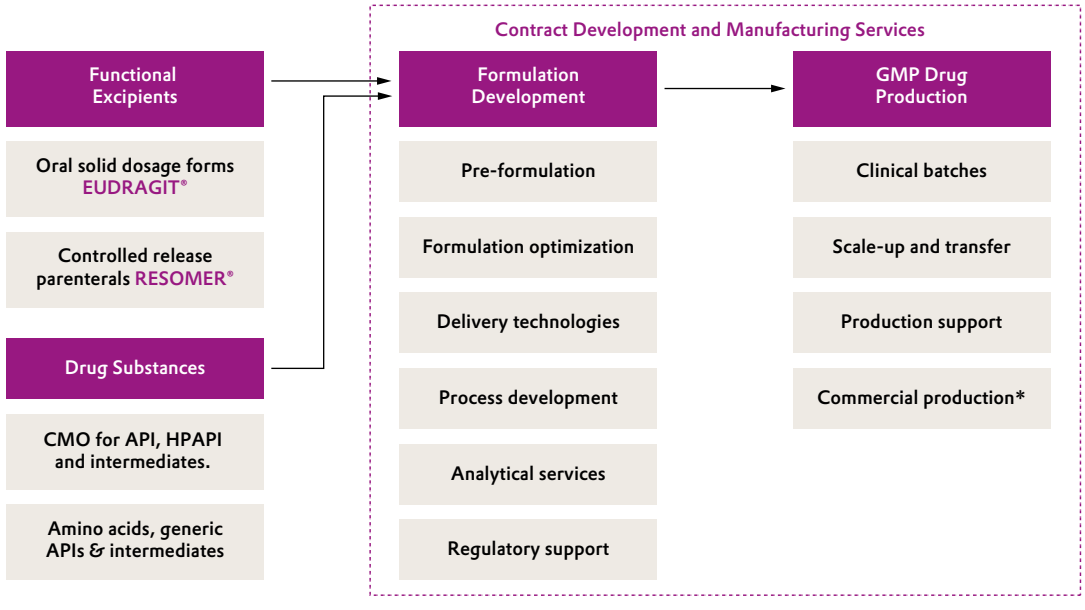
Evonik is one of the world's leading specialty chemical companies. In 2017, our more than 36,000 employees produced sales of €14.4 billion and an operating result (EBITDA) of €2.36 billion. We hold market leading positions in 80 % of our businesses, and are active across more than 100 countries and 175 sites globally.

Evonik Health Care is a global strategic partner for advanced drug delivery solutions. We combine highly versatile platforms of functional excipients for oral and parenteral dosage forms, with innovative technologies and best-in-class formulation development, manufacturing and regulatory services.

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

By helping to transform your APIs into high-performance medicines, we can become Your Competitive Advantage.

YOUR GLOBAL PARTNER FOR ADVANCED DRUG DELIVERY



*Parenteral drug products

RELEASE THE TRUE VALUE OF YOUR ORAL SOLID DOSAGE FORMS

1

EUDRAGIT® functional polymers

The versatility and reliability to protect the API, boost drug performance and reduce formulation risk

2

Delivery Technologies

Differentiated solutions for modified release to enhance drug efficacy and generate superior targeting outcomes

3

Formulation Services

Best-in-class services to reduce project complexity from concept to the final dosage form to increase speed to market

4

Clinical Supply and Transfer

High-quality GMP clinical production, robust scale-up and transfer processes, and production support and trouble-shooting

5

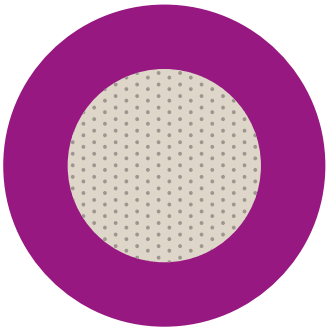
Regulatory Support

Leverage the worldwide monograph status of our excipients and local market expertise for regulatory 'peace-of-mind'

UNRIVALLED VERSATILITY TO UNLOCK THE POTENTIAL OF YOUR API

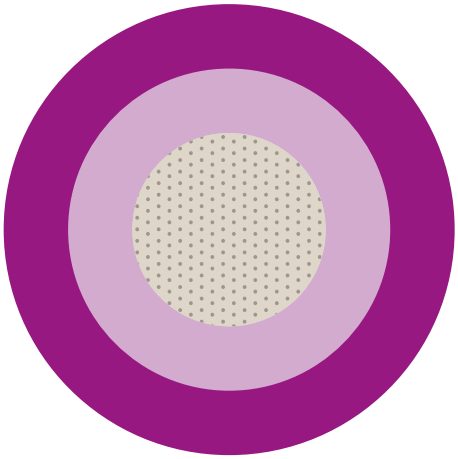
Our platform of polymers can be used individually or in combination to match virtually any target release profile

Single layers

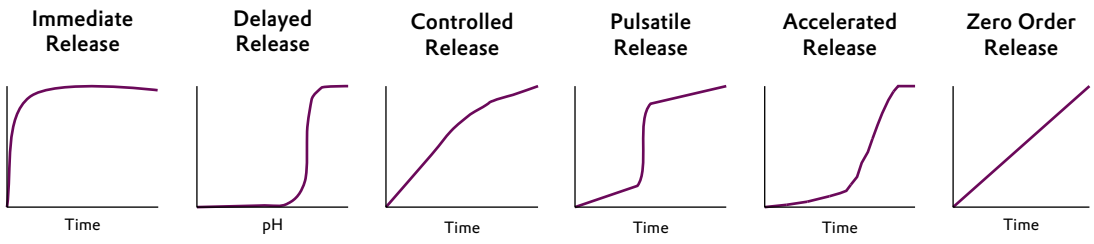


- Single EUDRAGIT® polymer
- Combination of EUDRAGIT® polymers
- Combination of EUDRAGIT® polymers and other excipients or substances

Multiple layers



- Single EUDRAGIT® polymer per layer
- Combination of EUDRAGIT® polymers and other excipients or substances
- Inert core with combination of EUDRAGIT® polymers and API layer



THE FLEXIBILITY TO ADDRESS SPECIFIC FUNCTIONALITY REQUIREMENTS

THE EUDRAGIT® ADVANTAGE

- A proven record for safety and performance spanning more than 60 years
- Ideal for all oral solid dosage forms including multiparticulates and matrix tablets
- Easy to handle and compatible with all relevant process technologies
- Consistent quality and global supply security at any clinical or commercial scale
- Unparalleled expertise across coatings, formulations and finished dosage forms

IMMEDIATE RELEASE

Protect the Drug. Boost Patient Compliance.

- Neutral in taste and smell to mask API bitterness or unpleasant odours
- Smooth, glossy surfaces as thin as 10–20 µm to improve swallowability
- Reliable protection and stability for APIs sensitive to light, moisture or oxygen
- Insoluble in saliva and readily soluble in the stomach for improved absorption
- Custom-made, easy-to-mix powder blends for rapid suspension preparation

DELAYED RELEASE

Protect the API. Avoid Discomfort. Improve Absorption.

- A broad, easy-to-combine enteric platform to achieve a specific dissolution pH
- Highly effective and stable polymers for precise targeting and rapid dissolution
- Well-defined solutions to protect the gastric mucosa from aggressive actives
- Strong expertise in safeguarding the transit of APIs sensitive to gastric fluid
- Options to improve coating productivity and reduce process and cleaning time

SUSTAINED RELEASE

Optimize Drug Effectiveness. Improve Patient Compliance.

- Sustained, modulated or custom release profiles controlled by diffusion barriers
- Multiple combination options to precisely control passage through the GIT
- Proficient in daily dosage forms including multiparticulates and matrix tablets
- Insoluble with pH-independent swelling and options for high or low permeability
- Options to improve coating productivity and reduce process and cleaning time

SOLUBILITY ENHANCEMENT

Increase bioavailability. Address poor solubility.

- Highly specialized in solid dispersions, API and silica technologies
- Well-defined, flexible processes for hot melt extrusion and spray drying
- Robust thermoplastic properties, high thermostability and miscibility
- Predictive systems to select the best carrier excipient and process parameters
- Various downstreaming options to improve dosage forms and speed to market

Innovative, highly flexible technologies to enhance the oral delivery of small molecules and biologics

- Addressing specific unmet medical and regulatory needs for advanced formulations
- Patent protected and available for narrow licensing to generate powerful brand differentiation
- Readily combined with EUDRAGIT® polymers for specific targeting of small molecules or biologics
- Commercially viable with in vitro and in vivo studies and robust, scalable specifications
- Designed for seamless integration with standard equipment and process technologies

OPTIMIZE DRUG EFFICACY WITH SUPERIOR TARGETING OUTCOMES

Alcohol Resistance

EUDRATEC® ADD

A robust, dual-layer coating technology providing protection for multiparticulates and tablets with up to 40 % alcohol

Oral Delivery of Biologics and Peptides

EUDRATEC® PEP

A modular toolbox for multiparticulates with specific functionalities in each microparticle for oral bioavailability and dose convenience

Accelerated Release in the Upper Small Intestine

DUOCOAT®

A dual-coating of enteric polymers with an inner layer customized for rapid dissolution in the upper small intestine

Time-controlled Release

EUDRATEC® MOD

A diffusion controlled, time-triggered system for multiparticulates to achieve pulsatile and other customized release profiles

High-Precision Colon Delivery

PHLORAL®

A single film coating with a dual action mechanism that combines a pH triggered polymer with a polysaccharide

DUOCOAT®

A dual-layer coating of enteric polymers with an inner layer customized for rapid dissolution in the ileocolonic region

EUDRATEC® COL

A dual-layer of pH triggered and time-controlled polymers for multiparticulates to boost bioavailability & reduce daily intake

Phoral® and Duocoat® are proprietary technologies from Intract Pharma Ltd.

HARNESS THE VALUE OF OUR BEST-IN-CLASS PROJECT SERVICES

1 COMPREHENSIVE SUPPORT

Extensive polymer and formulation support from the first sample to the final dosage form

2 DECADES OF TECHNICAL EXPERTISE

Projects led by scientists and pharmacists with indepth technical and scientific knowledge

3 GLOBAL LABORATORY NETWORK

Access to a dozen formulation and application labs worldwide including local onsite support

4 PROCESS TECHNOLOGY EXPERTISE

Strong capabilities across all relevant process technologies and equipment

5 SUPPORTING SCALE-UP AND LAUNCH

Broad knowledge of physiological aspects, clinical requirements and GMP scale-up

6 STRONG RECORD OF ACHIEVEMENT

Decades of commercial project success for small molecules or biologics

7 ANY ORAL SOLID DOSAGE FORM

Deep expertise across complex dosage forms including monolithics and multiparticulates customized dose forms

8 LOCAL MARKET EXPERTISE

Highly familiar with local regulatory processes and requirements

9 QUALITY BY DESIGN APPROACH

QbD principles guide each process step to reduce risk and improve speed to market

10 HPAPI AND CONTROLLED SUBSTANCES

HPAPI handling down to 1 µg/m^3 OEL with a U.S. license to handle controlled substances

CREATING EXCEPTIONAL VALUE FROM FEASIBILITY TO FINAL DOSAGE FORM

PRE-FORMULATION SERVICES	▪ Fast-track feasibility studies ▪ Rapid evaluation of polymer options ▪ Evaluation of formulation technologies (small to intermediate scale)	
FORMULATION DEVELOPMENT	▪ Technology matching to target release profile ▪ Quality by Design approach ▪ Formulation and reformulation projects	▪ Method development and validation ▪ Prototypes for stability or PK studies ▪ GMP clinical batches for PI to IIA
ANALYTICAL SERVICES	▪ Advanced analytical development methods ▪ Compendial methods and specifications ▪ Dissolution testing	▪ Assay and purity evaluation ▪ Particle size analysis ▪ Molecular weight determination ▪ Characterization technologies
PRODUCTION AND TRANSFER SUPPORT	▪ Process technology expertise GMP and non-GMP scale ▪ On-site production support and troubleshooting	▪ CMO review and recommendation for clinical and commercial scale-up ▪ Transfer to production site

OUR HIGHLY SPECIALIZED CAPABILITIES ENABLE US TO EFFICIENTLY MANAGE COMPLEX PROJECTS FOR:

- Drug types including small molecules, peptides, enzymes, nucleic acids, high potent APIs and controlled substances
- Specialized formulation areas including personalized medicine and 3D printing, pediatric and geriatric medicine, continuous manufacturing, microbiome delivery and the oral delivery of biologics
- Regulatory and lifecycle management strategies including expedited approval pathways such as 505(b)(2)

4 Clinical Supply and Transfer

FAST, FLEXIBLE AND RELIABLE CLINICAL DRUG SUPPLY

- Support for clinical phases from I to IIA at our established facility in Darmstadt, Germany
  - 135 m^2 clean room area
  - Four classified manufacturing suites
- Manufacturing operations of human investigational medicinal products for clinical trials" issued by German authorities
  - GMP system complies with EU guidelines
  - DIN EN 9001 and DIN EN ISO 14001
- Handling of HPAPI and controlled substances

Equipment	GMP Scale
Fluid bed coating	0.8 – 10 kg
Automatic capsule filling	< 3,000 capsules / hour
High-shear granulation	0.2 – 4.0 kg
Extrusion – spheronization	< 25 kg / hour
Drug layering	0.8 – 10 kg
Tablet compression	< 3,600 tablets / hour
Tablet, capsule and particle coating	0.5 – 3.5 kg
Melt extrusion	0.06 – 3 kg / hour

5 Regulatory Support

WORLDWIDE MONOGRAPH ACCEPTANCE. LOCAL MARKET EXPERTISE.

PHARMACOPOEIAL MONOGRAPHS AND DMFS

- Global acceptance of monographs for EUDRAGIT® series across key regions including U.S., EU, Japan and China
- EUDRAGIT® types detailed in Type IV U.S. DMFs
- EXCiPACT™ certificate system for audit efficiency

EXTENSIVE DOCUMENTATION SUPPORT

- Global quality systems (IPEC-GMP)
- Robust documentation to support NDAs and marketing authorizations including
  - Safety and Toxicology Packages
  - Polymer specifications
  - Letters of Authorization for DMFs
  - Detailed statements for special purposes

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EVONIK
POWER TO CREATE

EVONIK NUTRITION & CARE GMBH
Health Care Business Line
Pharma Polymers & Services

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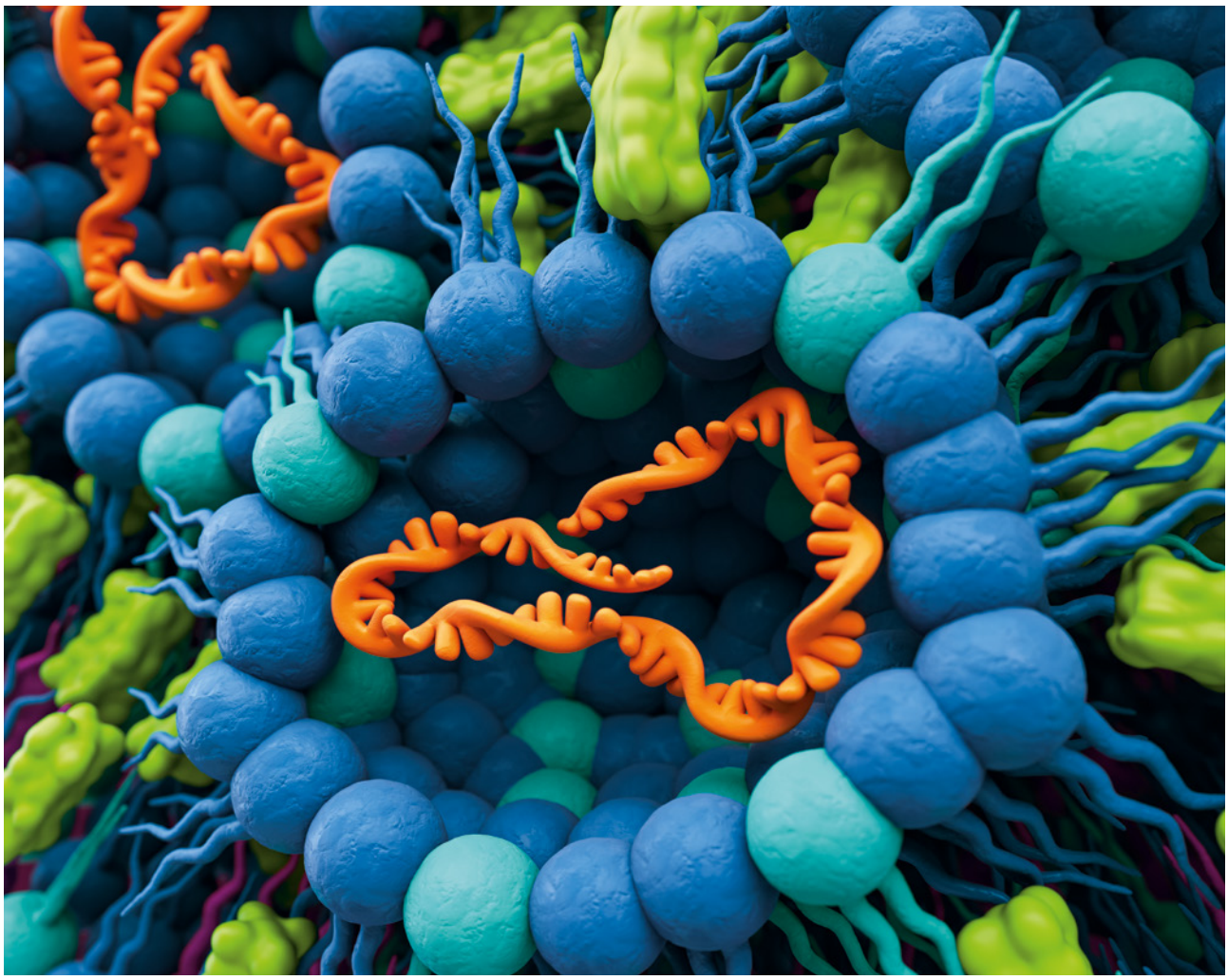
Lipid-based delivery of nucleic acids

Your global CDMO for advanced drug delivery



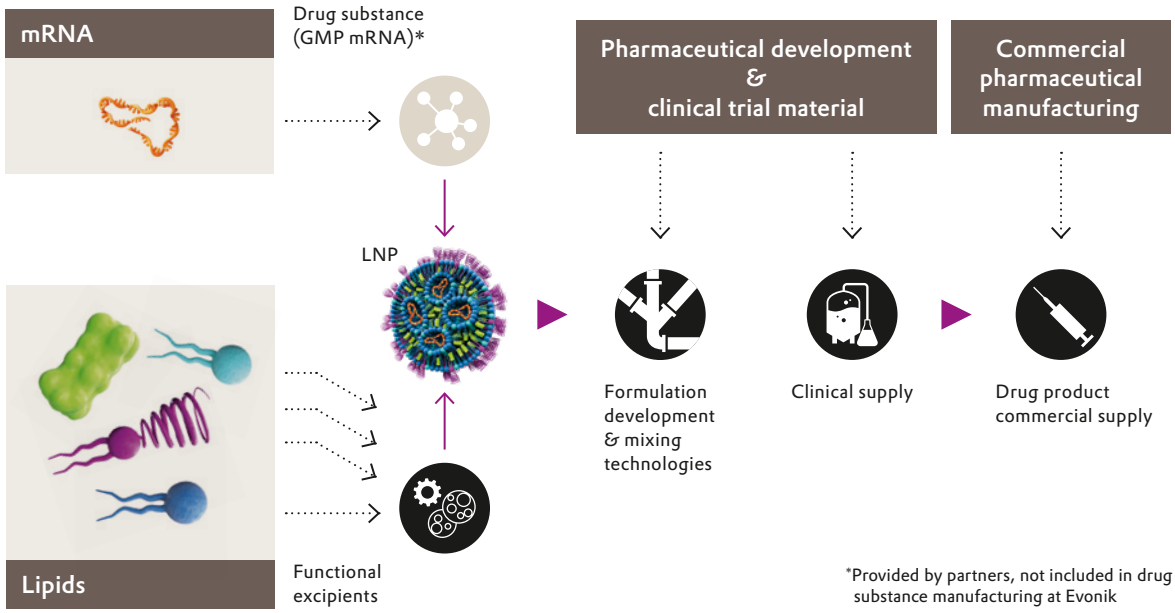
EVONIK
Leading Beyond Chemistry

Your preferred partner for advancing gene delivery and mRNA technologies

Genetic technologies are rapidly evolving and have great potential to treat a range of acquired and hereditary diseases, from cancer and metabolic disorders to infectious diseases. As a partner to many of the world's largest and most innovative pharmaceutical and biotechnology companies, Evonik's Health Care business line is ideally placed to help you realize the potential of gene therapies.

We are a fully integrated solutions provider for advanced drug delivery and can support any stage of the drug development process, from the manufacturing of pharmaceutical excipients to the development of innovative formulations, as well as the production of clinical and commercial drug products.

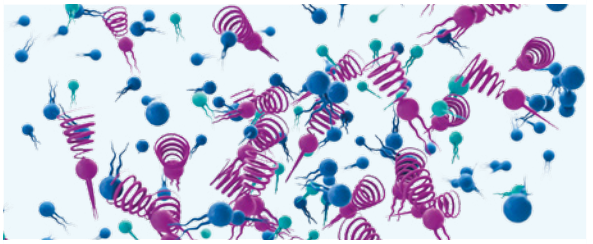
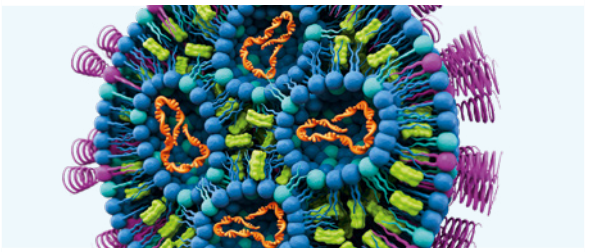
How Evonik contributes to the value chain of mRNA-LNP therapeutics



Fueling the growth of advanced biopharmaceuticals

- Nucleic acid-based therapeutics
- Anticancer agents
- Synthetic vaccines: peptide and protein-based
- Ligand-targeted formulations
- Drug combinations

We support customers with end-to-end CDMO services for nucleic acid therapeutics

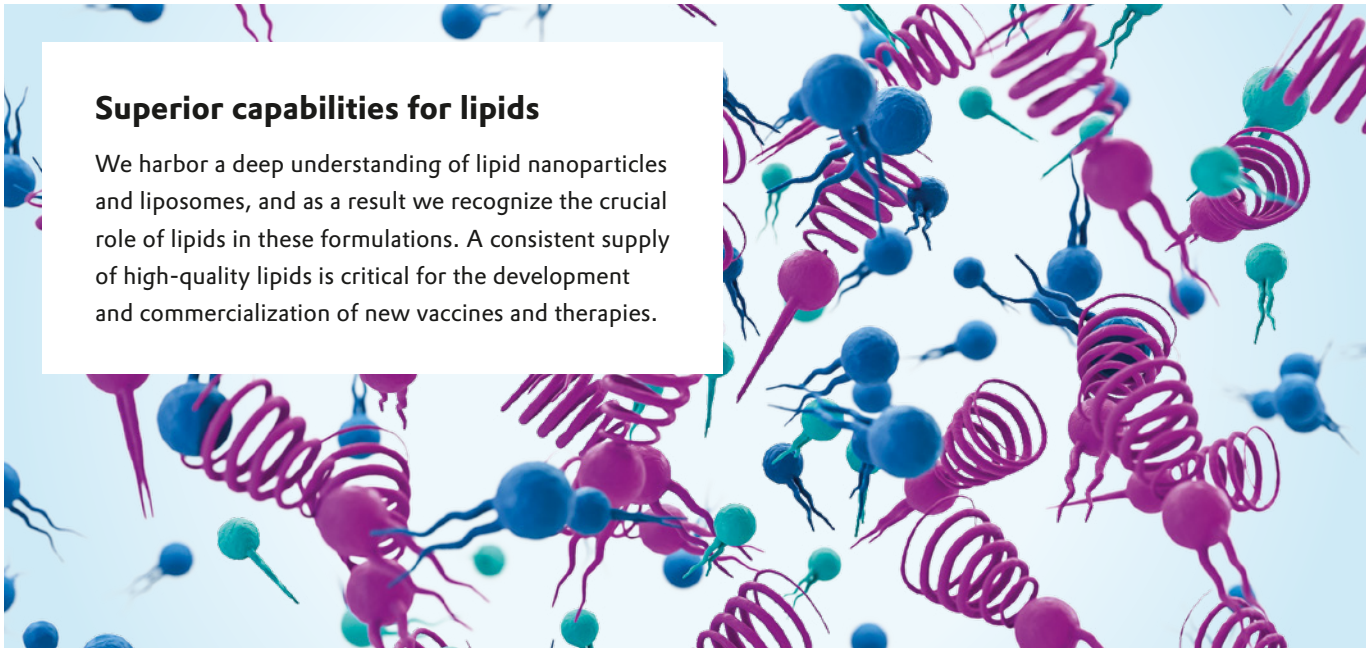
Excipients and biomaterials		**PLG excipients, plant-derived cholesterol, recombinant collagen**
Drug delivery technologies		**A delivery leader for liposomes, nano-and microparticles and drug-loaded implants**
Formulation and process development		**Seamless support from concept to commercial, including extrusion and micromixing**
cGMP drug manufacturing		**High-quality clinical and commercial production at North American sites**
Aseptic filling		**Semi- and automated vial filling of powders, liquids and suspensions**

We build on our expertise in parenteral excipients, formulation, and contract manufacturing

- Integrated CDMO for gene therapies
- Specialized in complex parenterals
- Involved in many mRNA projects including multiple COVID-19 vaccines

CONTACT US
healthcare@evonik.com

An experienced provider of novel and established functional excipients



Superior capabilities for lipids

We harbor a deep understanding of lipid nanoparticles and liposomes, and as a result we recognize the crucial role of lipids in these formulations. A consistent supply of high-quality lipids is critical for the development and commercialization of new vaccines and therapies.

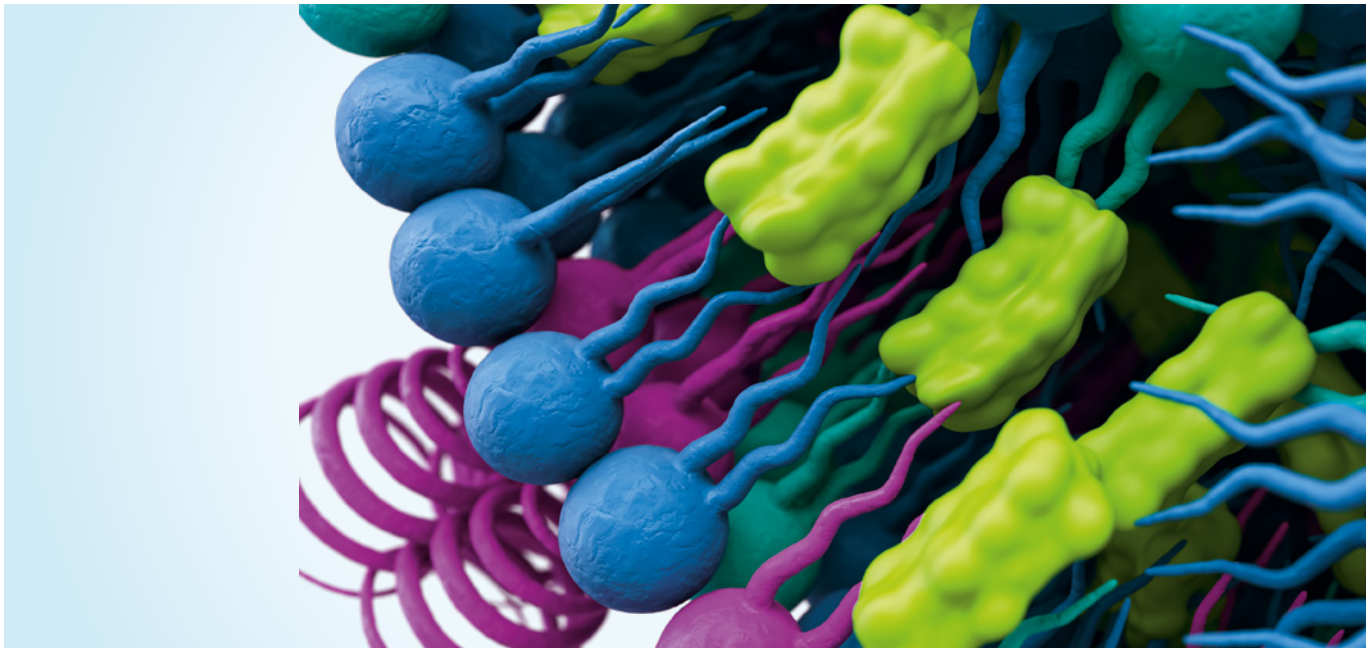
Meeting your need for custom lipids

We support our clients with custom lipid projects by combining this understanding with decades of expertise in process development, analytics, scale up, validation and GMP manufacturing. Regardless of your current scale and requirements, Evonik can support with non-GMP and GMP capabilities from small-scale through large-scale production.

As an integrated solution provider, we combine all these capabilities in one package, at any scale

- Chemical process R&D
- Flow chemistry
- PEGs (polyethylene glycol) and mPEGs (methoxy-PEG)
- Purification technology
- Particle engineering
- Analytical services

Stable supply of plant-derived synthetic cholesterol



PhytoChol® provides you with the following advantages

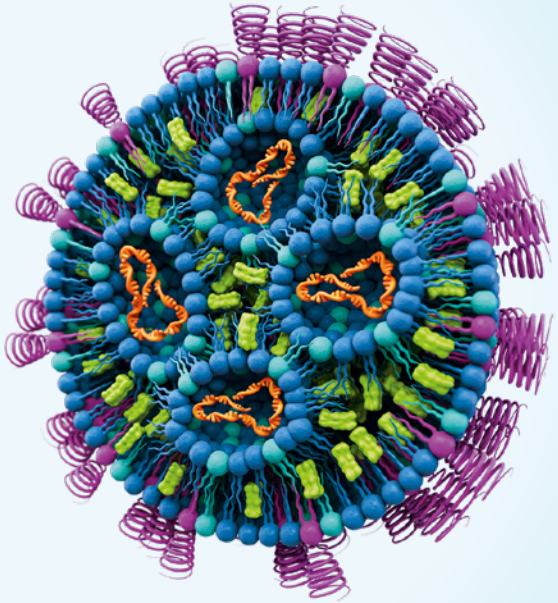
- Non-animal derived
- Secure and stable supply
- Large-scale manufacturing
- High purity
- vegetal-derived
- Ultra-low endotoxin
- USP-NF, Ph. Eur. and JP compliant

PhytoChol®

A leader in formulation technologies for nucleic acid therapeutics

Seamless support for your formulation and processing needs

As a specialist CDMO for lipid-based drug delivery systems for almost 30 years, we have an unparalleled track record in early-stage development, process development and scale up, and analytical characterization. With a broad base of pharmaceutical and biotech customers across the world, we have accumulated extensive expertise across all classes of pharmaceuticals, including nucleic acid therapies and other advanced nanomedicines.



Lipid-based particles are a versatile formulation platform

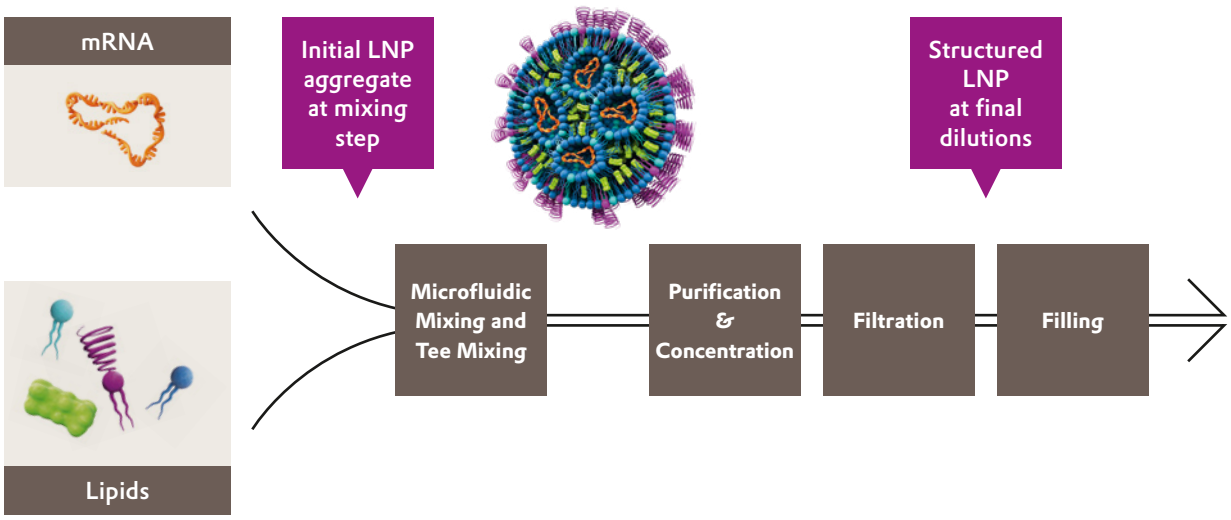
- Decreased toxicity / side effects and improved safety
- Increased efficacy
- A well-studied technology; proven in humans

Typical composition of a lipid nanoparticle
Nucleic acid payload is encapsulated in lipids

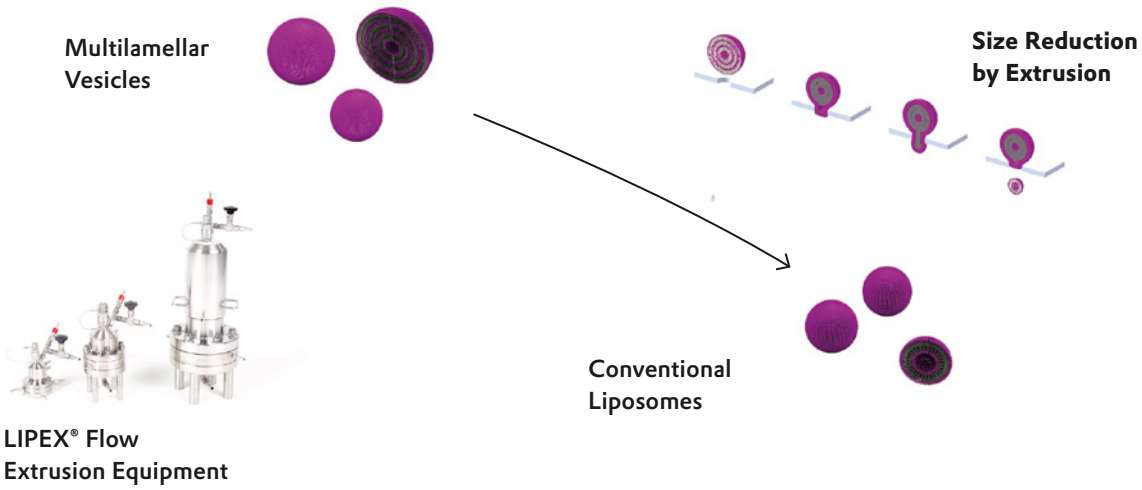
Nucleic Acid		▪ The active payload
Cholesterol		▪ ~38.5 % ▪ Improves stability of LNPs and improves overall encapsulation of payload; affects transfection efficiency
Ionizable Cationic Lipid		▪ ~50 % ▪ Complexes the nucleic acid ▪ Destabilizes the endosome
PEG Lipid		▪ ~1.5 % ▪ Stabilizes LNPs during formation and controls particle size
Structural Lipid		▪ ~10 % ▪ Examples or DSPC or DOPE ▪ Required for overall stability

We use two key processes to manufacture lipid-based drug delivery systems at a large scale

LNP formulation



Liposome formulation



Advantages of our integrated formulation services

- More than 25 years' experience developing lipid-based delivery systems
- Significant experience formulating nucleic acid-based drugs
- Enhancement of solubility and bioavailability of high potency APIs through encapsulation in a lipid carrier
- Seamless transition from scale up through clinical manufacturing
- Comprehensive analytical services to accompany R&D, toxicology, clinical and commercial manufacturing
- LIPEX® extruders ranging from benchtop to commercial production scale to support conventional liposomal formulations

Advanced cGMP manufacturing and fill-finish capabilities

Versatile and reliable filling lines and cGMP manufacturing can enable the production of highly potent drug products, as well as vaccines, gene therapy technologies and personalized medicine. As the number of drug products requiring advanced drug delivery technologies increases, the need to address manufacturing challenges becomes crucial.

We operate a global network of development and manufacturing sites

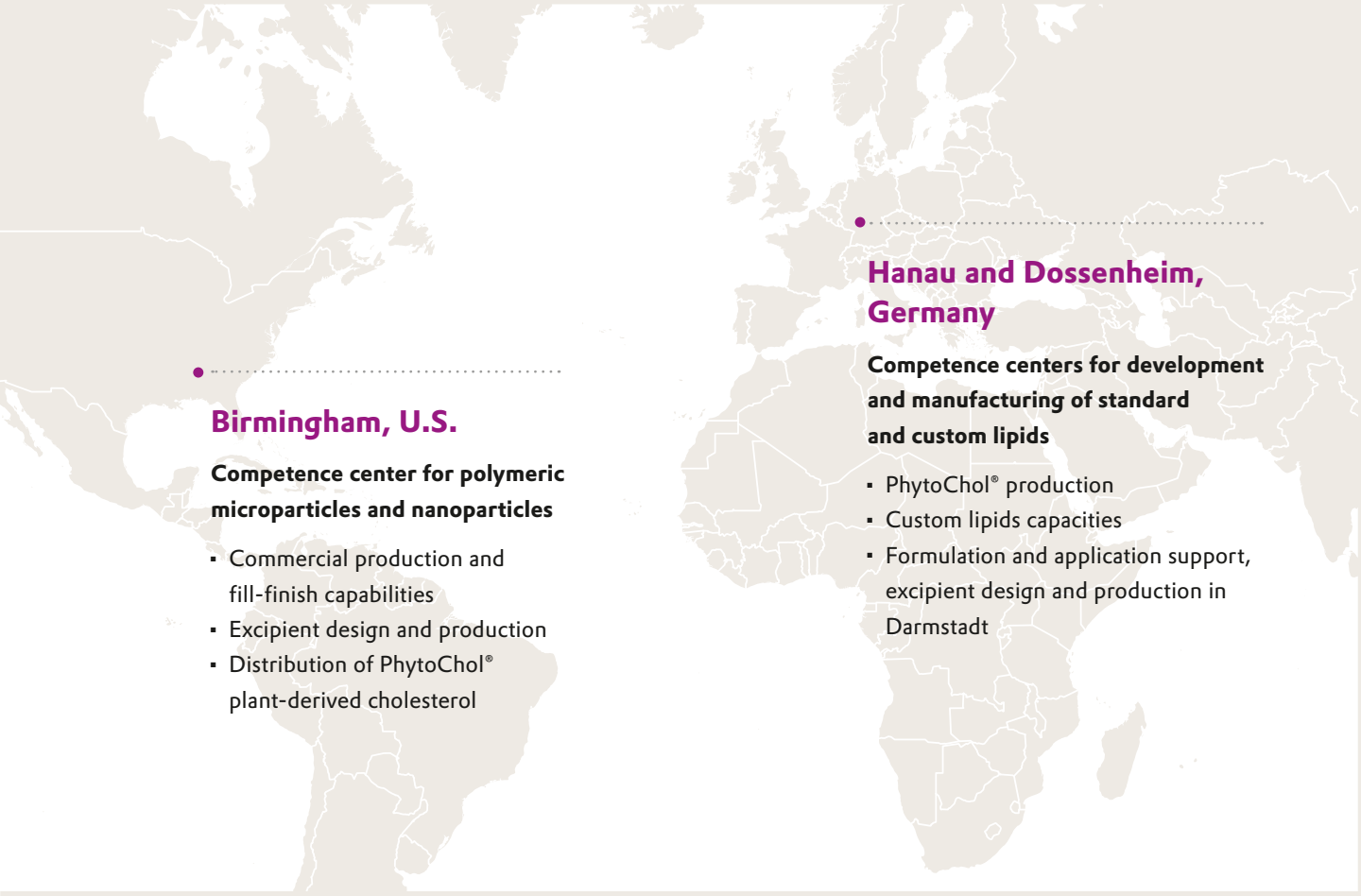
- cGMP production for clinical batches and commercial products
- Specializing in advanced parenteral dosage forms such as liposomes, lipid nanoparticles, and micelles
- Full support in process development, engineering and scale-up
- Aseptic fill/finish, performed in Grade A isolators
- Fully integrated, automated commercial filling line, and filling lines for clinical batches
- Encapsulation of small molecules, peptides, and proteins for systemic or localized drug delivery
- Scalable extrusion technologies for manufacturing of conventional liposomes
- Handling of high potency drug substances to > 0.1 µg/m^3 (OEL)

Vancouver, Canada

Competence center for liposomes and nanoparticles

- LIPEX® extruders
- Formulation and process development
- Clinical manufacturing

	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	



Birmingham, U.S.

Competence center for polymeric microparticles and nanoparticles

- Commercial production and fill-finish capabilities
- Excipient design and production
- Distribution of PhytoChol® plant-derived cholesterol

Hanau and Dossenheim, Germany

Competence centers for development and manufacturing of standard and custom lipids

- PhytoChol® production
- Custom lipids capacities
- Formulation and application support, excipient design and production in Darmstadt

	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			

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EVONIK
Leading Beyond Chemistry

Evonik Operations GmbH
Health Care Business Line

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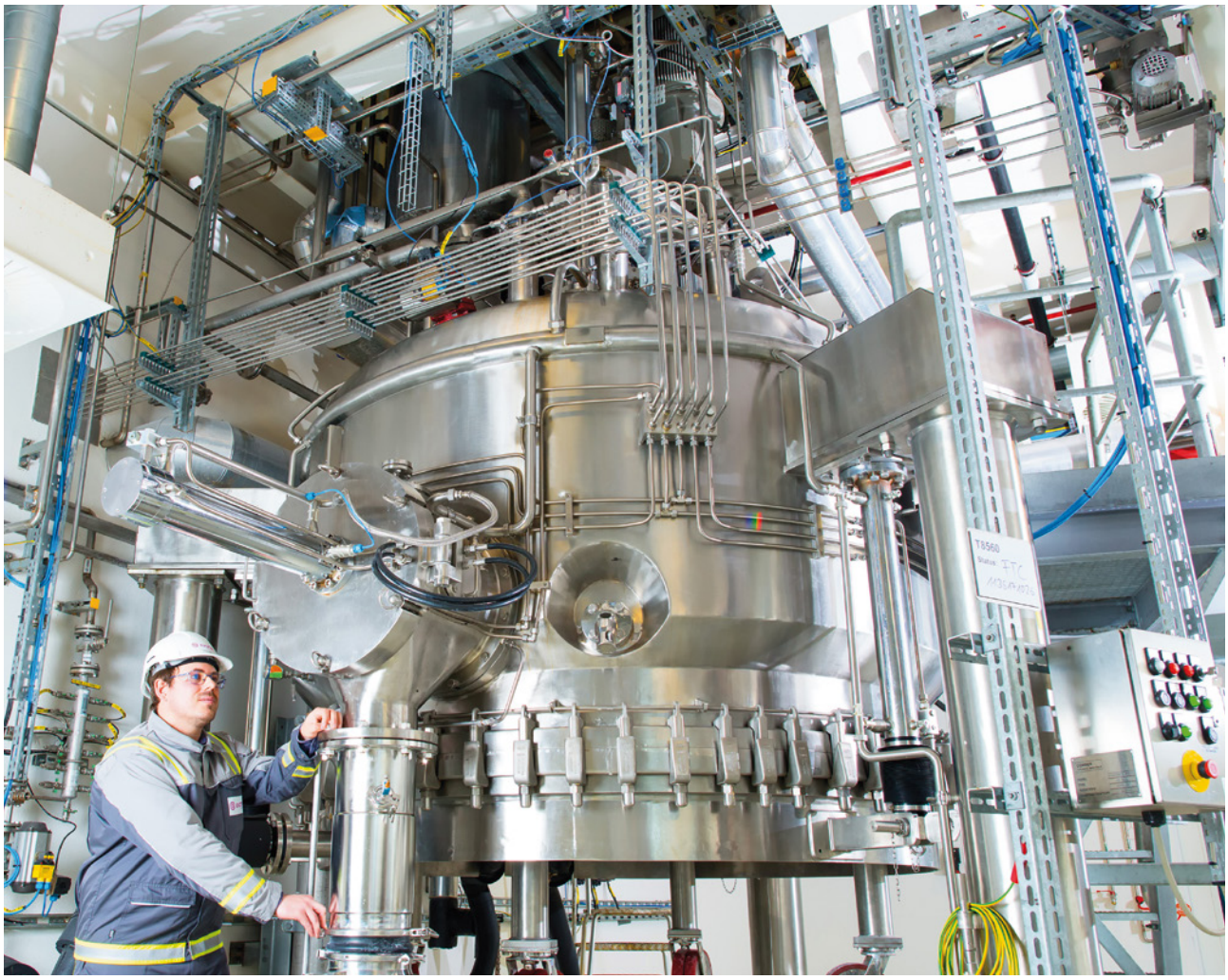
Exclusive Synthesis

A global CMO leader and preferred partner for API, HPAPI and intermediates with a broad portfolio of advanced technologies



EVONIK
POWER TO CREATE

MAKE EVONIK YOUR COMPETITIVE ADVANTAGE

Evonik is one of the world's leading specialty chemical companies. In 2018, our more than 36,000 employees produced sales of € 15.0 billion and an operating result (EBITDA) of € 2.6 billion. We hold market leading positions in 80 % of our businesses, and are active across more than 100 countries and 175 sites globally.

The Evonik business line Health Care serves more than 1,000 pharmaceutical, medical device and nutraceutical customers, including 90 % of the world's top 50 life science companies.

For the exclusive synthesis of API, HPAPI and intermediates, we bring together unique core competencies across chemistry, biotechnology and engineering. Combined with a proud record of performance for quality and supply, and a broad portfolio of advanced technologies, we can address the specific needs of even the largest or most complex projects.

OUR CREDENTIALS TO SERVE AS YOUR CMO PARTNER

The global scale, technical expertise and flexibility to serve your long-term needs

3 One of the world's top 3 CMOs for API, and intermediates	**170 m³** The world's largest HPAPI process developer and manufacturer	**0.05 µg/m³** OEL for HPAPI	**6** FDA-inspected sites in the U.S., EU and Asia
– 80 °C Cryogenic reactions	**> 200 m³** The world's largest cGMP capacity for cryogenic reactions	**> 4,000 m³** Total fermentation capacity	**> 20** Different enzymes applied in commercial scale
> 25 Lab groups for chemical CMO development	**> 800** In-house engineers and chemists for investment projects	**5** Consecutive years as an EcoVadis gold medal recipient for sustainability	**> 50** Years of continuous processing expertise

BEST-IN-CLASS INDUSTRY CAPABILITIES

API AND INTERMEDIATES

- API (bulk, controlled) at any clinical or commercial scale
- From grams to thousands of tons per year
- Western-centered network of FDA-inspected production sites
- Germany, USA, France, Slovakia and China
- Extensive particle design and API conjugation expertise

HIGH POTENCY AND ANTI-CANCER API

- The world's largest HPAPI CMO capacity from grams to tons
- 170 m^3 total capacity, OEL down to 0.1 µg/m^3 (large-scale)
- cGMP high potent lab down to 0.05 µg/m^3
- Support from process development to large-scale production
- A broad range of reaction types covered
- The ability to produce up to 7 different API steps in parallel

CHEMISTRY AND BIOTECHNOLOGY

- The world's largest cryogenic capacity (–80 °C, 200 m^3)
- Backward integration in catalysts
- Large portfolio of homogeneous and heterogeneous catalysts
- Total fermentation capacity of more than 4,000 m^3
- More than 20 different enzyme types already used in production

PROCESS ENGINEERING

- A proven track record of execution for major investment projects
- An in-house process engineering unit with more than 800 staff
- Flexible project teams can be formed on demand
- A complete set of competencies such as particle technologies, fluid processing, bioprocess technology, supply chain management, CAPE and automation and reaction technology

A BROAD, FLEXIBLE PORTFOLIO OF ADVANCED TECH

HPAPI

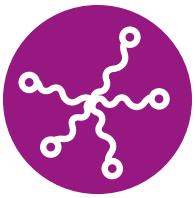
THE WORLD's LARGEST HPAPI CAPACITY FROM GRAMS TO TONS

- A total capacity of 170 m^3 across two different sites in the U.S. and Europe
- Main site Tippecanoe Laboratories, Lafayette, IN, U.S.
  - From lab scale up to 8,000 l reactor volume
  - OEL down to 0.1 µg/m^3 (large-scale)
- Small-scale production unit for ultra-HPAPI with an OEL down to 0.05 µg/m^3

CONTINUOUS PROCESSING

MORE THAN 2/3 OF EVONIK's PRODUCTS MADE USING CONTINUOUS PROCESSES

- From process development to customized production, separation and work-up
- Established processes with a broad variety of reactor technologies including micro reactors, tube reactors, loop reactors, trickle-bed reactors plus CSTR and SMB
- Continuous separation and work-up technologies including distillation, extraction, crystallization and membranes
- New modular, continuous processing cGMP pilot plant (OEB 3) in Germany



PEGs AND mPEGs

CUSTOM-TAILORED PEG SPECIALTIES FOR THE HIGHEST STANDARDS

- mPEG labs and a pilot plant in Germany for highly pure synthesis at the kg scale
- Commercial-scale cGMP production sites in Germany and the U.S.
- mPEG support from synthesis through to isolation, activation and conjugation
- Polydispersity (Mw/Mn): < 1.05, Diol content (mPEG): < 0.5 %, Average molecular weight: +/– 2 %

CARBOHYDRATE CHEMISTRY

A UNIQUE PORTFOLIO WITH DECADES OF SUGAR MODIFICATION EXPERTISE

- An expert in sugar derivatization, protective groups, and bioconversions
- Broad technology range for nucleoside API
- Fermentative production of oligosaccharides from kg to multi-ton scales

POLYMER API

POLYMER CHEMISTRY EXCELLENCE APPLIED TO PHARMA APPLICATIONS

- A wide range of polymerization platforms including solution, suspension, emulsion, coordinative, radical, anionic, bulk and ring opening
- > 60 years of expertise in polymer development, optimization and scale-up
- A network of U.S. and EU sites for the flexibility to support all polymer API process steps, with both batch and continuous process options available

NOLOGIES TO ADDRESS SPECIFIC PROJECT NEEDS

A GLOBAL LEADER FROM STRAIN DEVELOPMENT TO COMMERCIAL-SCALE

- 4000 m^3 fermentation capacity across six sites in the EU, U.S. and Asia
- Flexible downstream processing pilot plant in Slovakia
- >30 years of expertise in microbial fermentation and biocatalytic technologies
- >25 commercial products based on fermentation
- Expertise across pharma, advanced food ingredients and nature-identical materials

FERMENTATION

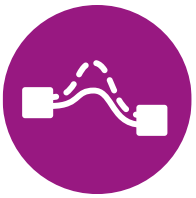
THE NUMBER ONE WHITE BIOTECH IN EUROPE

- Full service from screening to biocatalyst supply and large-scale production
- Enzymatic chemistry with >20 different enzymes applied at production scale
- A strong record in developing new enzyme platforms (bacteria, algae, fungi)
- More than 40 years of biotechnology expertise
- Development and scale-up of biocatalytic processes

BIOCATALYSIS

FULL SERVICE FROM CATALYST DEVELOPMENT TO SCALE-UP AND PRODUCTION

- Large portfolio of heterogeneous and homogeneous catalysts
- >30 years of process development expertise, with all key reactions covered
- Five global sites for catalytic reactions: Up to 25 bar; 80 °C–200 °C; 100–16.000 L; glass lined, steel or Hastelloy; with HPAPI options available



CATALYSIS

DECADES OF EXPERTISE IN ASYMMETRIC SYNTHESIS AND CHIRAL RESOLUTION

- A full portfolio from chiral pool synthesis to chemo-catalysis and biocatalysis
- Established production of >100 chiral products including various amino acids
- A technology toolbox for chiral compounds including heterogeneous and homogeneous catalysts, reductive animation, and hydrazine reduction

CHIRAL CHEMISTRY

THE WORLD's LARGEST cGMP CAPACITY FOR CRYOGENIC REACTIONS

- A total capacity of 200 m^3 across four different sites, reactions down to –80 °C
- Reactors from 500 L to 8 m^3 reactors (glass lined and Hastelloy), up to 10 bar
- >50 reactors with cryogenic capacities (batch or continuous processing)
- Organometallic reactions including Grignard available at three sites globally

CRYOGENIC CHEMISTRY

A TRUSTED GLOBAL PRODUCTION NETWORK

TIPPECANOE, LAFAYETTE, INDIANA, US

- Four cGMP plants and pilot plant: 860 m^3 capacity
- Total HPAPI capacity of 170 m^3, down to 0.1 µg/m^3 (large-scale)
- From lab scale up to 8,000 l reactor volume
- Extensive cryogenic capabilities (–80 °C)
- Large-scale fermentation capacities (2,500 m^3)

HANAU, GERMANY

- Multi-purpose cGMP site: 196 m^3 capacity
- HPAPI-capable process / analytical labs (0.05 µg/m^3)
- Catalysis: Up to 25 bar, –80 °C – 200 °C
- Dedicated PEG / mPEG kilolab
- Modular continuous processing pilot plant

DOSSENHEIM, GERMANY

- Multi-purpose cGMP site: 180 m^3 capacity
- Three plants for API and intermediates
- Equipped for controlled and organometallic substances, batch or continuous processing
- Catalysis: Up to 6 bar, –80 °C – 200 °C

FERMAS, SLOVAKIA

- Multi-purpose fermentation site
- Amino acids, API building blocks, food ingredients
- Total fermentation volume of 1,150 m^3
- DSP pilot plant including continuous sterilization

HAM, FRANCE

- Multi-purpose cGMP site: 65 m^3 capacity
- Three plants with 34 vessels (0.25 – 6 m^3)
- Large-scale ion chromatography
- Purification of amino acids and derivatives

NANNING, CHINA

- Multi-purpose site: 70 m^3 capacity
- Three cGMP sites and four amino acid plants
- 240 m^3 fermentation and biotransformation capacity
- Crystallization and ion exchange technology

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EVONIK
POWER TO CREATE

EVONIK NUTRITION & CARE GMBH
Health Care Business Line
Exclusive Synthesis

exclusive-synthesis@evonik.com
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Nutraceutical Solutions

Innovative health ingredients and functional coatings for improved delivery.

EVONIK
Leading Beyond Chemistry

NEW PRODUCTS

Innovating for your nutraceutical success – we move with the market

GuardCap™

Our ready-to-fill hard capsule for **colon delivery** guarantees the protection of sensitive ingredients from gastric acid, bile acid and enzymes. GuardCap™ helps you increase your speed in development and reduce supply chain complexity.

You benefit from:

- Capsules that are **easy to open, fill** and **close**
- No additional sealing or banding needed
- Moisture protection of sensitive ingredients
- **Clean label formulation** without TiO_2 or talc, no solvents used
- **Reliable** dissolution and disintegration
- Increased viability of probiotics

IN VIVO BIOTICS™

Our most advanced synbiotic products (bulk capsules and powder) for prevention and well-being re-enable the body's self-protecting competences for inner health through the microbiome. IN VIVO BIOTICS™ are scientifically proven synergistic combinations of our proprietary microorganisms and bioactive ingredients.

You benefit from:

- Clinical evidence for **human applications**
- **Comprehensive** consumer insights
- Fast **market entry**
- A **strong partner** along the value chain

Discover:

- **IN VIVO BIOTICS™ butyrate**
  enables intrinsic butyrate production
- **IN VIVO BIOTICS™ resolvin**
  enables intrinsic SPM / resolvin production
- **IN VIVO BIOTICS™ gluten tolerance**
  enables intrinsic gluten degradation

ADVANCED FOOD INGREDIENTS

Science-based health ingredients to differentiate your nutraceutical brands

AvailOm®

Our highest load omega-3 powder ingredient is a best-in-class platform with superior bioavailability and stability. AvailOm® omega-3 powders are highly efficacious, sustainably sourced and can be leveraged to develop single, small tablets or capsules that are easy-to-swallow.

You benefit from:

- 50 % EPA/DHA concentration in powder – **highest in its class**
- 5 times more **bioavailable** than standard omega-3 softgels
- Directly **compressible** and **easily combined** with other ingredients
- Unmatched oxidation protection with **4 years stability**

Discover:

- **AvailOm® 50 High DHA Algae**
  An algal oil-based grade ideal for vegans and vegetarians.
- **AvailOm® 50 High DHA**
  A fish oil-based grade ideal for use during pregnancy and early motherhood, or to support eye and cognitive health in later stages of life.
- **AvailOm® 50 High EPA**
  A fish oil-based grade to support heart health at all life stages.

Healthberry®

Our anthocyanin powder extract derived from natural bilberries and blackcurrants is the ideal health ingredient to help enhance the value of a range of functional foods and beverages. Healthberry® can be used in effervescent tablets or capsules, small volume shots, tea capsules and as a concentrated ready-to-mix powder in the cap of sports drinks.

You benefit from:

- An **anthocyanin-rich powder** for functional food and beverages
- **Constant, stable composition** with 40 % anthocyanins on average
- **Patented process** avoids seasonal fluctuations in natural ingredients

EUDRAGUARD® FUNCTIONAL COATINGS

A toolbox of functional solutions to boost performance and consumer convenience

Enables sustained release

Increases consumer compliance

Eliminates environmental factors

Allows delayed release

Bioavailability enhancement via solubility enhancement

EUDRAGUARD® protect

- Single polymer as a powder
- Can be formulated on individual demand
- Taste and odor masking, moisture protection
- Solubility enhancement via HME or spray drying
- Also available as fully fomulated ReadyMix

EUDRAGUARD® control

- Single polymer as 30 % aq. dispersion
- Can be formulated on individual demand
- Sustained release over the whole GI tract
- Protection from gastric acid in combination with sodium alginate

EUDRAGUARD® biotic

- Single polymer as 30 % aq. dispersion
- Can be formulated on individual demand
- Colonic delivery

PRECISION FERMENTATION

Your global fermentation leader from strain development to large-scale production

We have served as a reliable fermentation partner to innovative companies for more than 30 years. Our areas of industry excellence span alternative proteins and other complex molecules to probiotics and whole cell catalysts.

Benefit from our CDMO services:

- Sustainability as the guiding business principle
- Trusted fermentation partner with proven track record for short time-to-market project realization
- From strain development to large-scale manufacturing e. g. 250 m^3 fermenter volume
- 4,000 m^3 CDMO fermentation capacity
- Comprehensive experience with all relevant host organisms
- Impressive piloting capabilities
- Worldwide presence across seven sites in the U.S., Europe, and Asia
- Significant in-house engineering expertise and capabilities for continuous improvement, plant extension or technical upgrades

To find out more about the seamless support that we can offer, visit **oncare.evonik.com** or email **healthcare@evonik.com**

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Leading Beyond Chemistry

EVONIK OPERATIONS GMBH
Health Care Business Line

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GuardCap™

Functional hard capsules for colonic delivery of dietary supplements and food supplements

GuardCap™

EVONIK
Leading Beyond Chemistry

Challenges in developing colonic-delivered nutraceuticals

Sensitivity of certain probiotic strains and health ingredients

- 60 percent of probiotic bacteria are killed in the gastric environment prior to reaching the intestine.
- Many ingredients are sensitive to moisture, heat or mechanical stress which may occur during a production process.

Delays in development

- New products are needed constantly to meet fast-changing consumer requirements and scientific developments.
- Testing different coatings, including stability studies, can be time consuming and may not match the challenging timeline.
- Need for scale-up trials of the coating process.

Complex supply chains

- Many supplement companies do not have their own coating capabilities and need to work with a contract manufacturing organization (CMO).
- Lengthy production times prolong the final supplement and increase the complexity of the supply chain.
- Some probiotics, such as spore formers, are not welcome at CMOs due to the risk of cross-contamination.

Our Solution GuardCap™

We use empty, pre-locked HPMC (hydroxypropyl methylcellulose) hard capsules that are coated with EUDRAGUARD® biotic based formulation. The coating is applied across the entire surface, including the gap between the body and the cap.

Through this technique the gap is very narrow and hence very leak-proof. The capsules are compatible with conventional capsule filling machines and can be easily opened manually as well as mechanically.

GuardCap™ is suitable for a range of fillings

Powders

Pellets

Granules

Leveraging the power of EUDRAGUARD® biotic

Our ready-to-fill functional capsules GuardCap™

- Ensure streamlined development of new dietary / food supplements
- Require no coating process – which may be harmful to sensitive health ingredients such as probiotics
- Guarantee the protection of sensitive ingredients from gastric acid, bile acid and enzymes
- Allow targeted release in the colon at a pH > 7
- Are compatible with high-speed capsule filling systems – capsules are delivered in a pre-locked status and ready to fill. They are easy to open, fill and close

Key benefits of GuardCap™

- Available in different capsule sizes
- Batch size flexibility for your final product
- Easy-to-swallow
- Reliable dissolution and disintegration
- Quality compliance with regulations for dietary / food supplements
- Storage-stable capsule
- No additional sealing or banding needed
- Free from formulation: Solvent-free, TiO_2-free, talc-free
- Increased viability of probiotics
- Moisture protection

CONTACT US and learn more about our functional ready-to-fill capsule GuardCap™

To get in touch with a member of our expert technical team, visit **oncare.evonik.com** or email **healthcare@evonik.com**

This information and all further technical advice are based on our present knowledge and experience. However, it implies no liability or other legal responsibility on our part, including with regard to existing third party intellectual property rights, especially patent rights. In particular, no warranty, whether express or implied, or guarantee of product properties in the legal sense is intended or implied. We reserve the right to make any changes according to technological progress or further developments. The customer is not released from the obligation to conduct careful inspection and testing of incoming goods. Performance of the product described herein should be verified by testing, which should be carried out only by qualified experts in the sole responsibility of a customer. Reference to trade names used by other companies is neither a recommendation, nor does it imply that similar products could not be used.

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