Your partner for oral drug delivery services
Evonik Health Care
One partner – multiple benefits

More than 60 years ago, we started with the EUDRAGIT® product range. Today we are experts in coating technologies, melt extrusion, particle engineering and the development of multiple-unit dosage forms.

We tailor nearly every desired release profile specifically to your needs. We combine the functionalities of our EUDRAGIT® polymers with a smart selection of formulation technologies and deep process know-how. The result is always a customized solution that matches your demands.

To meet your requirements even better, we have created a specific range of drug delivery technologies, EUDRATEC®.

For both EUDRAGIT® and EUDRATEC® we offer tailor-made development services for commercially viable formulations. We develop and manufacture clinical trial formulations for biologics and small molecules according to your requirements, also including Highly Potent Active Pharmaceutical Ingredients (HPAPIs).
Our EUDE RATEC® technology platform

Innovative, unique and flexible oral formulations in combination with our EUDRAGIT® polymers for specific targeting of small-molecules or biologic macromolecules.

Our technologies provide you customized release profiles, besides improved properties like alcohol resistance or improved oral bioavailability. EUDRATEC® technologies are IP-protected: a perfect opportunity for you to gain a competitive edge for your product!

They utilize state-of-the-art equipment for manufacturing of oral dosage forms and are well suited to address unmet medical and regulatory needs.

<table>
<thead>
<tr>
<th>Technology</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>EUDE RATEC® PEP</td>
<td>Bioavailability enhancement and oral delivery of biologics</td>
</tr>
<tr>
<td>EUDE RATEC® ADD</td>
<td>Alcohol resistance for delayed and extended drug release formulations</td>
</tr>
<tr>
<td>EUDE RATEC® MOD</td>
<td>Controlled, time-triggered modulated release tailored to chronic diseases</td>
</tr>
<tr>
<td>EUDE RATEC® COL</td>
<td>Combined delayed and extended release for the treatment of colonic diseases</td>
</tr>
<tr>
<td>Duocoat®</td>
<td>Accelerated release in the upper small intestine</td>
</tr>
<tr>
<td>Phloral®</td>
<td>Fail-safe colon targeting with a unique dual-action concept triggered by pH and colonic bacteria</td>
</tr>
<tr>
<td>MemFis®</td>
<td>In-silico drug solubility prediction in excipient matrices for solubility enhancement</td>
</tr>
</tbody>
</table>

Concept proven in vivo
Protection up to 40% alcohol
Clinically proven
Clinically proven
Clinically proven
Clinically proven
Long track record
Your projects – our support

Do you need a new oral dosage form? We can support and guide you during the development process wherever and whenever you want. With a track record of many successful customer projects in the last 15 years, we can offer you solid expertise and far-reaching competence.

Our service offering is very flexible and always close to you. You want to collaborate on feasibility studies, development, optimization, scale-up or clinical manufacturing? Don’t hesitate to contact us at any phase of your project!

WE OFFER YOU

- Solubility enhancement
- Bioavailability enhancement
- Alcohol resistance
- Extended release
- Delayed release
- Taste masking
- Moisture protection

Comparative dissolution profile of metoprolol succinate pellets formulated with EUDRATEC® ADD technology

Drug dissolved [%] vs. Time [h]

- non-alcoholic media
- 40% v/v alcoholic media
We are an international team of highly qualified scientists with industry experience in NCE development and generic formulations.

Our formulation developments are based on Quality by Design (QbD) ICH recommendations. In combination with our long experience and state-of-the-art equipment, we are eager to be your partner for your new development. We formulate small molecules and biologics, including Highly Potent actives. In doing so we always follow the latest international safety and quality guidelines.

CASE STUDY: SWEET SPOT PLOT
Design of Experiment (DoE) enables to focus the formulation development in the right way.

Overlay of the two contour plots combined with the criteria:
1. Acid Uptake < 4.5 %
2. Disintegration time in buffer pH 6.8 35 < t < 45 [min]

Subcoat = 9.4 mg/cm²

Amount EUDRAGIT® L30D-55 [% w/w]

Quality cannot be tested into products, quality should be built in by design.
Innovative Drug Delivery Systems

Our particle formulation laboratory offers innovative formulation development for nano- and microparticles, solid dispersions and SMEDDS among others.

Evonik offers you the application of these cutting-edge technologies in combination with defined excipients to support you in solubility and bioavailability issues of a wide range of drugs.

We are the world leading experts in functional coating.

Our EUDRAGIT® polymers allow you to introduce and fulfill important features of your new oral dosage form. Pediatric use, patient compliance or storage stability can be guaranteed.
In-house analytical services

We offer a broad range of analytical tools and profound experience in characterizing formulations and APIs.

SCANNING ELECTRON MICROSCOPY (SEM)

SPECTROSCOPY
- FTIR, UV/Vis
- Fluorescence

MOLECULAR WEIGHT DETERMINATION
- Size exclusion
- Evaporative light scattering

PARTICLE SIZE ANALYSIS
- Laser light diffraction
- Dynamic light scattering

THERMAL PROPERTIES
- Differential scanning calorimetry
- Thermogravimetric analysis

DISSOLUTION TESTING
- USP Type I; II; IV

PROTEIN ANALYSIS
- SDS
- ELISA

CHROMATOGRAPHY
- HPLC, UPLC
- LC-MS
- GC (headspace & direct)
- GPC (RI)
- TLC

TITRATION
- Karl Fischer coulometric or volumetric
- Potentiometric

SOLUTION PROPERTIES
- Rheology

VISCOSITY
- Inherent viscosity (manual and automated)

SURFACE CHARGE
- Zeta potential

CELL BIOLOGY
- Cell viability assays
- Cell transport studies
- (Immunofluorescence) studies
- Mucus permeation assay

Specific analytical services extending beyond those we offer in-house, can be offered through our well established collaboration network. We will plan and execute your formulation endeavours.
Oral formulation development services. Your global partner.

Our capabilities – your benefit

We are certified according to:
- DIN EN 9001
- DIN EN ISO 14001

We hold a “Manufacturing Authorization – Manufacturing Operations of Human Investigational Medicinal Products for Clinical Trials” issued by the German authorities.

Our GMP system complies with EU GMP guidelines and is prepared to meet FDA requirements on a short-term basis.

High Potent API
- Laminar flow work station system, negative pressure environment and separate filter system.
- HPAPI GMP facility for oral dosage forms in Darmstadt (OEB 3, 1 - 10\(\mu\)g/m\(^3\) OEL*)
- HPAPI handling in particle formulation laboratory for lab scale feasibility trials (OEB 4, 0.1 - 1\(\mu\)g/m\(^3\))
- Controlled Substances

OEL* = Occupational Exposure Level
### Technology capabilities and scale

<table>
<thead>
<tr>
<th>Equipment</th>
<th>Non-GMP</th>
<th>1–10µg/m³</th>
<th>&gt;10µg/m³</th>
<th>1–10µg/m³</th>
<th>&gt;10µg/m³</th>
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</thead>
<tbody>
<tr>
<td>OEL Value</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Fluid bed coating</td>
<td>&lt;7kg</td>
<td>&lt;4kg</td>
<td>&gt;7kg</td>
<td>&lt;4kg</td>
<td>&gt;7kg</td>
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<tr>
<td>Tablet coating</td>
<td>&lt;45kg</td>
<td>&lt;4kg</td>
<td>&lt;4kg</td>
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<td>&lt;4kg</td>
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<tr>
<td>Fluid bed granulation</td>
<td>&lt;4kg</td>
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<td>&lt;4kg</td>
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<tr>
<td>High shear granulation</td>
<td>&lt;3kg</td>
<td>&lt;2kg</td>
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<tr>
<td>Wet extrusion &amp; spheronomiza-</td>
<td>&lt;25kg</td>
<td>–</td>
<td>&lt;25kg</td>
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<td></td>
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<tr>
<td>tion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixing</td>
<td>&lt;30kg</td>
<td>&lt;10kg</td>
<td>&lt;30kg</td>
<td>&lt;10kg</td>
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</table>

### Compression

<table>
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<tr>
<th></th>
<th>Non-GMP</th>
<th>1–10µg/m³</th>
<th>&gt;10µg/m³</th>
<th>1–10µg/m³</th>
<th>&gt;10µg/m³</th>
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<tbody>
<tr>
<td>Single punch</td>
<td>3600tab/h</td>
<td>3600tab/h</td>
<td>3600tab/h</td>
<td>3600tab/h</td>
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<tr>
<td>Rotary</td>
<td>67500tab/h</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Automatic capsule filling</td>
<td>3000caps/h</td>
<td>3000caps/h</td>
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<tr>
<td>Melt extrusion</td>
<td>5kg/h</td>
<td>5kg/h</td>
<td>0.5kg/h</td>
<td>0.5kg/h</td>
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<tr>
<td>Milling</td>
<td>300kg/h</td>
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<tr>
<td>Spray drying</td>
<td>&lt;1kg</td>
<td>–</td>
<td>–</td>
<td>–</td>
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</tr>
</tbody>
</table>

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1 **DARMSTADT, GERMANY**  
Since 1966

3 **MUMBAI, INDIA**  
Since 2003

4 **SHANGHAI, CHINA**  
Since 2003

5 **TSUKUBA, JAPAN**  
Since 2003

8 **DHAKA, BANGLADESH**  
Since 2012

10 **BANGKOK, THAILAND**  
Since 2016
Value added by Health Care

FEASIBILITY STUDIES
- Fast track feasibility studies
- Prototype supplies

FORMULATION DEVELOPMENT
- Matching desired release profiles by various process technologies
- Long-standing formulation and analytical experience

GMP SERVICES
- Fast and flexible clinical supply manufacture
- High Potent API handling

PROOF OF CONCEPT
- Added value formulations for lifecycle management and generic development
- Customized data packages

EUDRATEC® PLATFORM
- Licensing of proprietary drug delivery technologies
- Joint development of enabling technologies

Intensity of cooperation

Project management – the engine of your success

- Professional project management organization with global standard and regional presence ensures outstanding service.
- Our mission is to work closely with you and to provide expert support for your product developments with EUDRAGIT® products – from the first feasibility studies to scale-up and production.

- From the moment you start working with us until the project has been completed, you will be assigned to a specialist project manager who will be your main contact and who will coordinate all interactions with other departments.

CONTACT US
at healthcare@evonik.com
to find out more about how our service offerings can support your next project.
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 supplier 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.

Duocoat® – reg. trademark of Evonik Industries AG and its subsidiaries

EUDRAGIT® – reg. trademark of Evonik Industries AG and its subsidiaries

EUDRATEC® – reg. trademark of Evonik Industries AG and its subsidiaries

MemFis® – reg. trademark of Evonik Industries AG and its subsidiaries

Phloral® – reg. trademark of Intract Pharma Ltd.