C(D)MO by Egis Pharma Services

From 2023, Egis offers a wide range of small molecule drug substance and intermediate development and manufacturing services to pharmaceutical partners.

At Egis, the roots of active pharmaceutical ingredient development and manufacturing date back to the 1920s, and our experts have special experience in this field. We make it sure that the knowledge gathered over the decades is passed on and the high level of competence of our specialists, complemented by state-of-the-art technological equipment, ensures innovative and efficient solutions while meeting the highest quality standards.

CDMO

We have established the cutting-edge infrastructure required for the development of both traditional and so-called highly potent (HP) drug substances. As for HP drug substances, our colleagues work completely separated from the substances and use special gloves to manipulate the instruments and equipment — which is placed in transparent, closed isolators. The modern isolator setup ensures a convenient and safe working environment, while we protect our environment with a closed system of waste collection and elimination.

Our manufacturing processes and activities fully comply with cGMP principles.

Our facilities have successfully undergone comprehensive audits and received accreditation from key regulatory authorities, including FDA (USA, first in 1976), PMDA (Japan), EDQM (EU) and Hungarian authority.

OUR SERVICES

Chemical Research

- Route scouting & selection
- Synthesis development – batch & flow platform
- Process optimization: reaction conditions, solvent, catalyst optimization
- Impurity determination & standard supply
- Polymorph and salt selection
- Support of in-house and partner's drug product projects

Chemical Process Development

- Scale-up to maximum 20 L volume
- Process optimization: quality, yield, cost, safety, scalability
- Risk evaluation – ICH Q11
- Production of intermediates and drug substances (100 g – 2 kg)

HP Drug Substance Development

- 1 µg/m³ < OEL < 10 µg/m³ (OEB4)
- Synthesis development and scale-up to maximum 15 L volume
- Polymorph and salt selection
- Process optimization: quality, yield, cost, safety, scalability
- Risk evaluation – ICH Q11
- HP API production for formulation experiments, clinical trials and commercial purposes
- Manufacturing under cGMP – ICH Q7

Chemical Process Engineering Laboratory

- Process development of physico-chemical unit operations: crystallization, filtration, drying, milling
- Reaction calorimetry
- Process transformation from batch to flow platform

Drug Substance Pilot Plant

- Quick and flexible process development from kilolab up to plant scale
- Production of materials for
  - toxicity testing
  - formulation experiments
  - safety and stability studies
  - clinical trials
  - commercial batches
- Production of APIs under cGMP regulations
- Non-HP: 5-50 kg batch size, HP: 5-20 kg batch size
- Highly Potent Drug Substance GMP production line
  - 1 µg/m³ < OEL < 10 µg/m³ (OEB4)
  - annual capacity: ca. 600 kg drug substance
  - handling solid HP substance in isolators
  - isolated production areas by airlocks
  - disposed effluent gases
  - dedicated sewer & waste handling

Drug Substance Analytical Development

- Analytical development and quality control (QC) in non-GMP and GMP environment
- Liquid- and solid-state NMR measurements
- Structure determination by single crystal XRD
- Analytical method development (purity and assay testing, impurity identification, reaction kinetics, in-process tests, etc.)
- Analytical support of drug substance technology development
- QbD/Design space support (analytical data support to statistical models)
- Validation of analytical methods – ICH Q2(R1)
- Stress tests and forced degradation studies
- Stability studies – ICH Q1A(R2)
- Determination of quality requirements
- Genotoxic impurities – ICH M7
- Elemental impurities – ICH Q3D
- Elaboration of CTD 3.2.S modules – ICH M4
- Batch release of BE and registration batches
- Drug substance and intermediate storage testing
- **HP Analytical Laboratory**
  - **dedicated infrastructure for HP intermediates and drug substances**

Intellectual property (IP) support

CMO

In Budapest, at the main production site in Keresztúri Street, we produce intermediates and active pharmaceutical ingredients with organic chemical synthesis on large-scale production lines and in several production halls.

Our manufacturing processes and activities fully comply with cGMP principles.

Our facility has successfully undergone comprehensive audits and received accreditation from key regulatory authorities, including FDA (USA) (first in 1976), EDQM (EU), PMDA (Japan), KFDA (South Korea), ANVISA (Brazil).

Thanks to its technology upgrading investments, ***Egis is able to produce faster, more efficiently and at lower costs, even in small batches, and can safely produce a wide range of active pharmaceutical ingredients.***

Recipe-controlled production lines with fully automated process control systems enable safe operation, with lower energy consumption and lower CO_2 emissions. From an operational point of view, one of the most significant advantages is that our production lines are multifunctional, i.e. they are capable of producing several types of active pharmaceutical ingredients, and they can be switched from one product to another flexibly and in a very short time.

OUR SERVICES

Chemical reactions

- Aminolysis
- Amination (with NH_3, or reduction)
- Grignard reaction
- Alkylation
- Etherification
- Nitration
- Nitrosation
- Acylation
- Esterification
- Friedel-Crafts reaction
- Mannich reaction
- Hydrolysis
- Chiral resolution
- Reduction using sodium borohydride and lithium aluminium hydride
- **Methylation with dimethyl sulfate**
- Chlorination
- Hofmann rearrangement
- Vilsmeier reaction
- **Hydrogenation**
  - Disulfide bond cleavage
  - Enantioselective hydrogenation of the C=C double bond
  - Reductive amination of a carbonyl group
  - Hydrogen addition to an imine double bond
  - Saturation of the interchain C≡C triple bond
  - Reduction of N-nitroso group to N-amine
  - Reduction of aromatic nitro group to amine
  - Condensed ring aromatization
  - Hydrogenation of a nitrile group to an amino group
  - Partial saturation of a N-heterocycle partial saturation
  - Reduction of esters
  - Reduction of a carbonyl group

- Knoevenagel condensation
- Eschweiler–Clarke reaction
- Lithiation
- Specialities
  - **Tantalum-coated reactor,** for highly acidic reactions under high pressure
  - **Short path three-stage distillation apparatus**
  - **Incineration**

Equipment

- Reactor lines from 630 to 10.000 L
- Catalytic hydrogenation capabilities
  - 2.000 L, 50 bar, 100 °C
  - 2 x 2.500 L, 2 x 1.600 L, 6 bar, 100 °C
  - 250 L, 20 bar, 100 °C
- Clean area
  - Tray dryers, vacuum dryers, fluid bed dryer, double cone dryer, paddle type dryer
  - Hammer mills, pin mills, micronizing equipment, various powder handling systems

To learn more about our Services, please contact us or visit our website:

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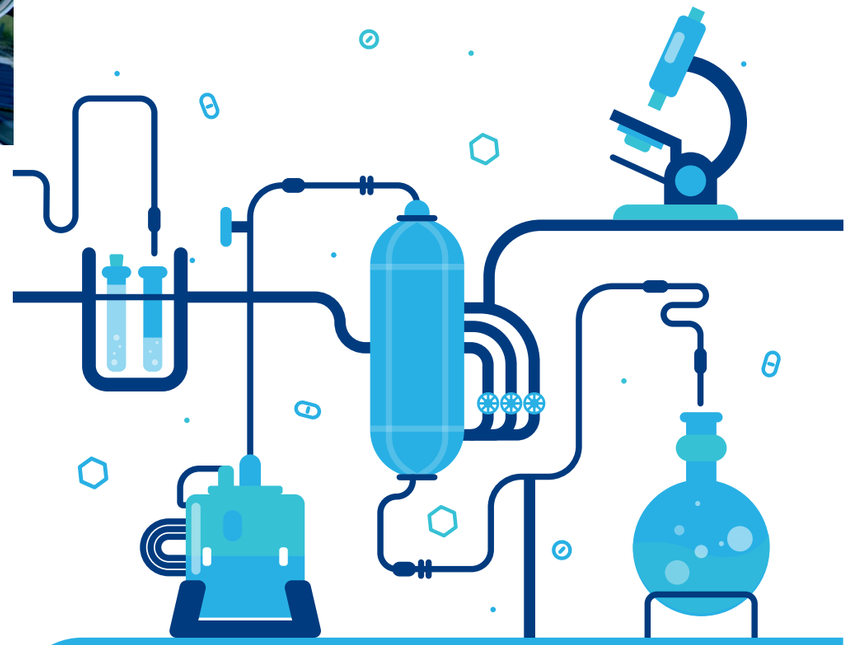
EGIS Pharma Services



Egis Pharmaceuticals PLC is a Hungarian pharmaceutical company with an impressive history, which has developed from a small factory producing nutriments in Budapest to one of the ***leading generic pharmaceutical companies in Eastern and Central Europe in more than 110 years.***

Besides Hungary, Egis sells its products under ***Egis' brand names in 17 countries.*** In total, the company's APIs and finished products are ***available in 103 countries through the network of Egis subsidiaries and representative offices or partners.***

Our activities incorporate all areas of the generic pharmaceutical value chain: ***from R&D through the production of APIs and FPs to sales and marketing.***