SEQENS
CDMO

Catalog & Custom offer for

Drug Delivery & Medical Material

CONTINUUM OF PROGRESS

SEQENS CDMO, a global Contract Development and Manufacturing Organization

With 25 years of experience in process development, scale-up and ongoing cGMP manufacturing of small molecule APIs, we support emerging, specialty and large pharmaceutical customers for their drug substance or drug delivery needs.

Continuum in the API life cycle

- Early phase development
- Late phase to commercial
- Second generation process
- Generic APIs

Continuum in the API value chain

- cGMP and non-cGMP intermediates
- RSMs
- API manufacturing
- Excipients for drug delivery
- Controlled substances

Continuum in technological capabilities

- From batch to flow chemistry
- Solid state characterization and optimization
- Hydrogenation and high pressure
- Large volume potent capabilities (0.1 µ/m³)
- Biocatalysis

SEQENS
CDMO

CONTINUUM OF PROGRESS

Continuum in production capabilities

- cGMP and non-cGMP kilo Labs
- cGMP and non-cGMP pilots units
- 2 Pre GMP production sites
- 6 cGMP / FDA inspected API production sites

Continuum in human regulatory

- Chemistry, Manufacturing and Controls
- Complementary chemistry and chemical engineering expertise for process industrialization
- Process safety
- SEQENS'LAB, a unique Center of Excellence and dynamic multidisciplinary ecosystem dedicated to innovation and development

Continuum in geographical coverage

- R&D centers in EU and US
- Manufacturing sites accross 3 continents
- Global network of sales offices
- Solutions for dual sourcing

Foster growth with Seqens

Three custom development and manufacturing organizations – PCAS S.A. in France and Finland, Chemie Uetikon in Germany and PCI Synthesis in the United States – have joined forces as Seqens CDMO to offer world-class drug substance development and manufacturing services to the pharmaceutical industry.

SEQENS CDMO ASSETS & COMPETENCIES

6
cGMP/FDA inspected sites in EU & the US

1,000 m³
600 m³ cGMP

2
Pre-GMP sites for RSMs & Building-blocks

80+
DMFs for commercial APIs

300
scientists, experts and engineers

7
R&D Centers in EU & US

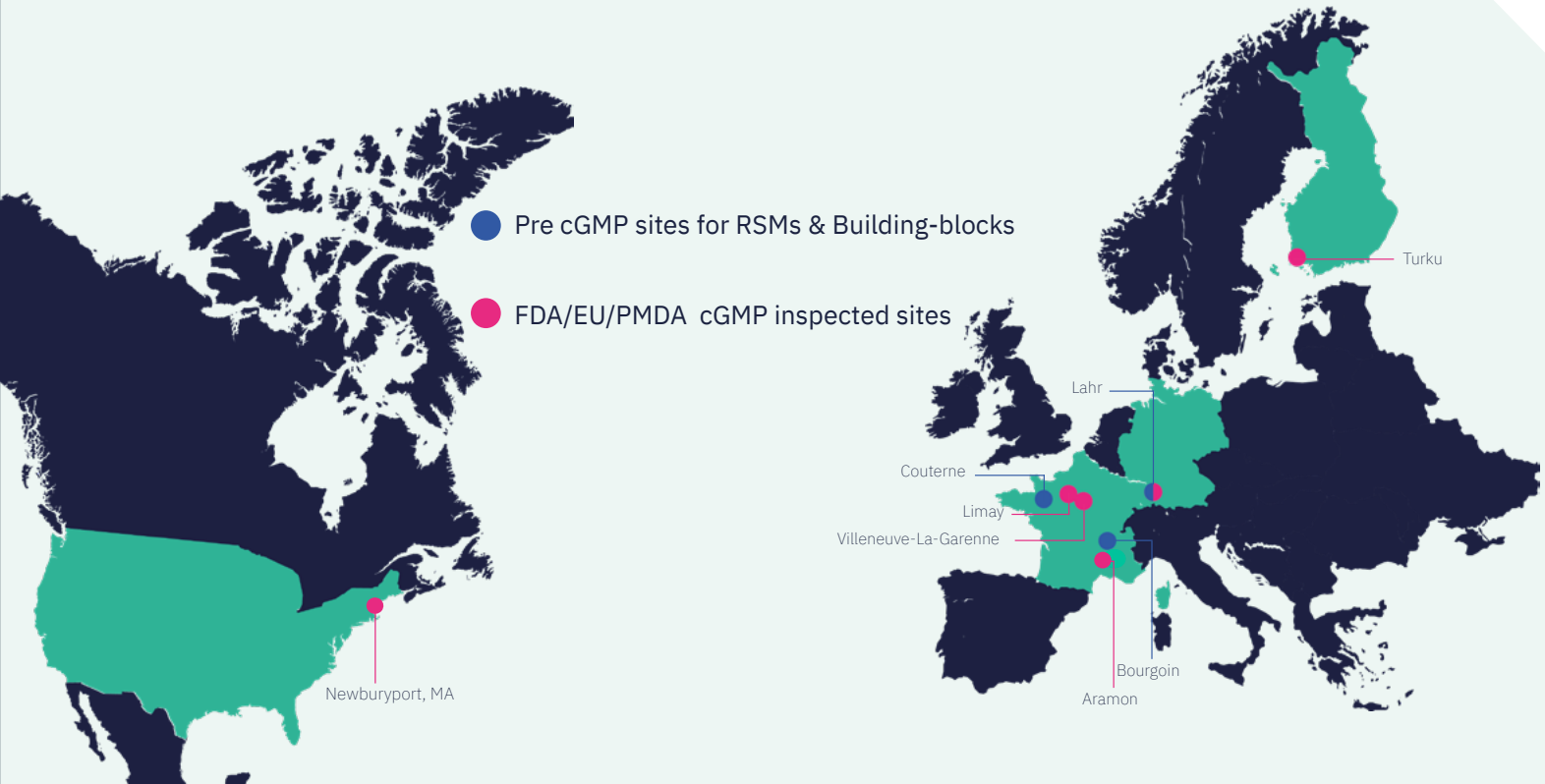
- Over 25 years of API production experience
- In-house back integration of intermediates and starting materials for safe supply
- Global sales and distribution network
- Excellent regulatory compliance track record at all GMP sites

A wide range of technologies

- High Pressure Reaction
- Low temperature technology
- Flow chemistry
- Potent API capabilities OEL : 100pg/m3 to 0,1µg/m3
- Mass Polymerisation without solvent
- Ethylene Oxide under GMP

SEQENS CDMO, AN INTERNATIONAL NETWORK

Benefit from a manufacturing network of **6 cGMP** plants located in Europe and the United States with a strong **regulatory track record** with international health authorities and the best **workshop & expertise in specialized technologies**

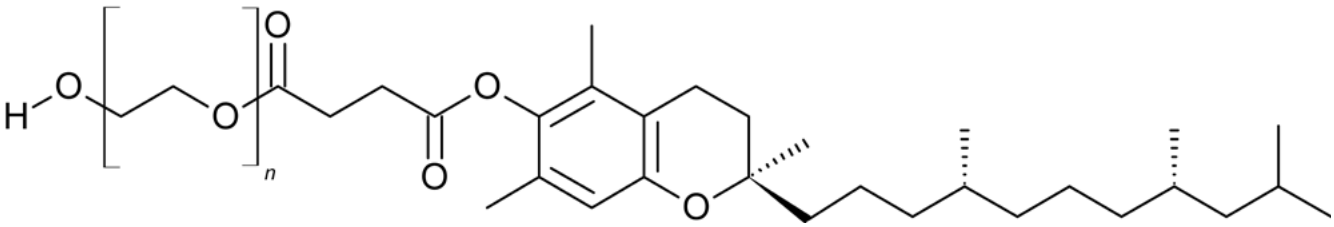


VITAMIN E TPGS

VITAMIN E TPGS comes from the esterification of Vitamin E succinate with PEG 1000.
It's a multirole excipient for drug delivery formulations.

CHEMICAL STRUCTURE

Chemical Name: D-α tocopheryl polyethylene glycol 1000 succinate
Synonym/acronym : TPGS, Tocophersolan, Tocofersolan



PROPERTIES OF VITAMIN E TPGS

Oral delivery Applications

- Improves Drug Bioavailability
- Surfactant, enhances solubilization of poorly water soluble drug
- Enhances solubilization of poorly permeable drugs that are water soluble
- Enhances drug permeability by P-glycoprotein efflux inhibition
- Vitamin E bioavailability enhancer
- Controlled delivery application

Non oral Applications

- Nasal/pulmonary application
- Ophthalmic
- Parenteral
- Dermal (carrier for wound care treatment, reducing drug sensitivity on skin or tissues

- *Functional ingredient in self-emulsifying formulations*
- *Thermal binder in granulation/extrusion processing*

OTHER REGULATORY STATEMENTS AVAILABLE

- GMO, BSE, TSE and other certificates available upon request
- BSE / TSE
- Others certificates available upon request (Residual solvents, elemental impurities ...)

PHYSICAL AND CHEMICAL PROPERTIES

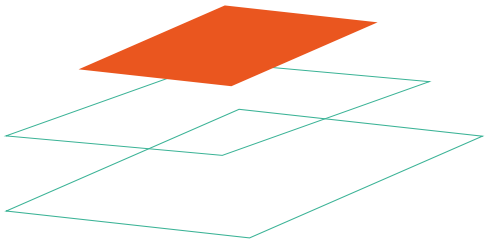
Chemical Abstract Index Name

Poly(oxy-1,2-ethanediyl), α-[4-[[(2R)-3,4-dihydro-2,5,7,8-tetramethyl-2-[(4R,8R)-4,8,12-trimethyltridecyl]-2H-1-benzopyran-6-yl]oxy]-1,4-dioxobutyl]-ω-hydroxy-

Empirical Formula: $C_{33}O_5H_{54}(CH_2CH_{20}O)n$
CAS : 9002-96-4
Molecular weight: ~1.5 kDa
Melting Point: 36-42 °C
Physical form: waxy solid with low melting point
Color: white to light tan
Vitamin E content (D-α-tocopherol): 25 % minimum weight basis; standard range 25-30 %

SEQENS UNIQUE OFFER

Active DMFs i.e. US type IV (Excipients)
Produced in Europe (Lahr, Germany)
GMP compliant (EU, USFDA)
NF compliant (USP)



MORE ABOUT VITAMIN E TPGS

Application & Properties References

Water soluble cannabinoids. *PCT Int. Appl.* (2021), WO 2021026456 A1 20210211. B. Antharavally, A.R. Oroskar, P. Sharma, A.A. Oroskar

A novel vitamin E TPGS- based formulation enhances chlorhexidine bioavailability in corneal layers. *Pharmaceutics* (2020), 12(7), 642. C. Caruso, A. Porta, A. Tosco, D. Eletto, L. Pacente, S. Bartollino, C. Costagliola

Nanocarriers based on vitamin E- TPGS: Design principle and molecular insights into improving the efficacy of anti-cancer drugs. *International Journal of Pharmaceutics,* (2021), 592, 120045. S. Rathod, P. Bahadur, S. Tiwari

Development and optimization of vitamin E TPGS based PLGA nanoparticles for improved and safe ocular delivery of ketorolac. *Journal of Drug Delivery Science and Technology*, (2021), 61, 102121. M. Warsi

Safety Studies References

Final Report on the Safety Assessment of Tocopherol, Tocopheryl Acetate, Tocopheryl Linoleate, Tocopheryl Linoleate/ Oleate, Tocopheryl Nicotinate, Tocopheryl Succinate, Dioleyl Tocopheryl Methylsilanol, Potassium Ascorbyl Tocopheryl Phosphate, and Tocophersolan. *International Journal of Toxicology*, (2002), 21(Suppl. 3), 51-116. M. Zondlo Fumie

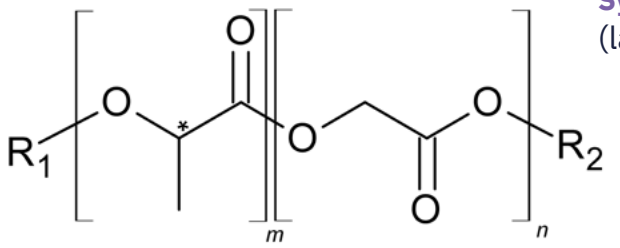
One-Year Chronic Oral (Intubation) Study In Dogs and Rats, *National Cancer Institute*, (1994) National Institute of health, Bethesda M.D.

EXPANSORB®

EXPANSORB® GMP PLA & PLGA copolymers are obtained by copolymerization of the corresponding cyclic dimers lactide and glycolide. PLGAs are among the best-in-class functionnal excipients for controlled-release of injectable drugs, included in multiple commercial formulations, and commonly used material for resorbable medical devices.

CHEMICAL STRUCTURE

(PLA : n=0)



PLGA

Chemical Name: poly (lactic acid) / poly (lactic-co-glycolic) acid
Synonym/acronym : PLGA, PLAGA, poly (lactide-co-glycolide)

PROPERTIES & APPLICATIONS OF GMP-grade PLGA

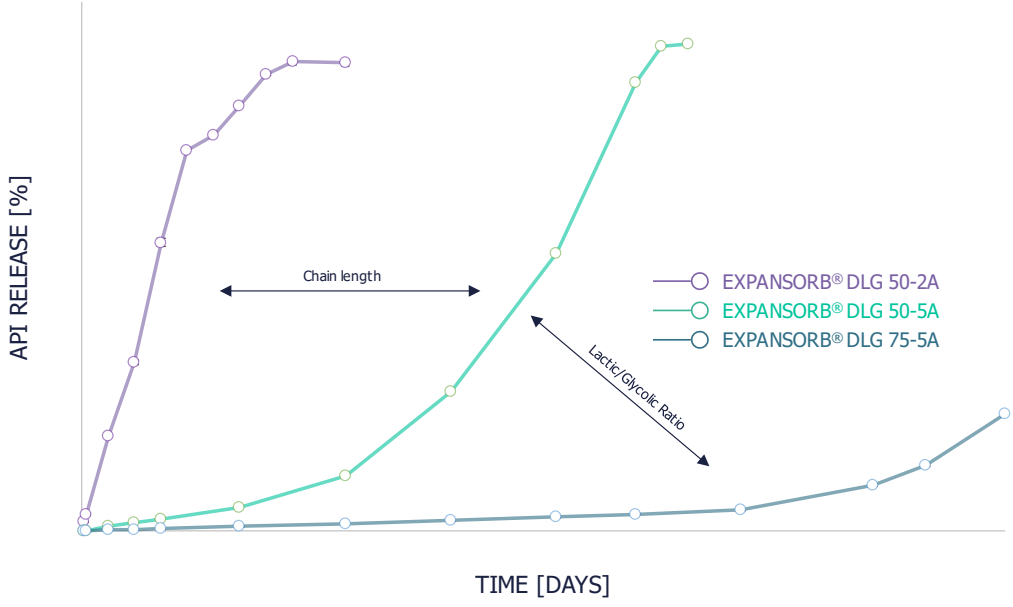
Properties

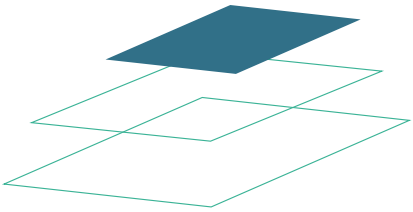
- Excellent biocompatibility, controllable biodegradability / bioresorbability
- Highly tunable properties :
  - LA/GA ratio
  - Lactide enantiomer ratio (D,L)
  - Chain length
  - End-chain
  - Copolymerization...

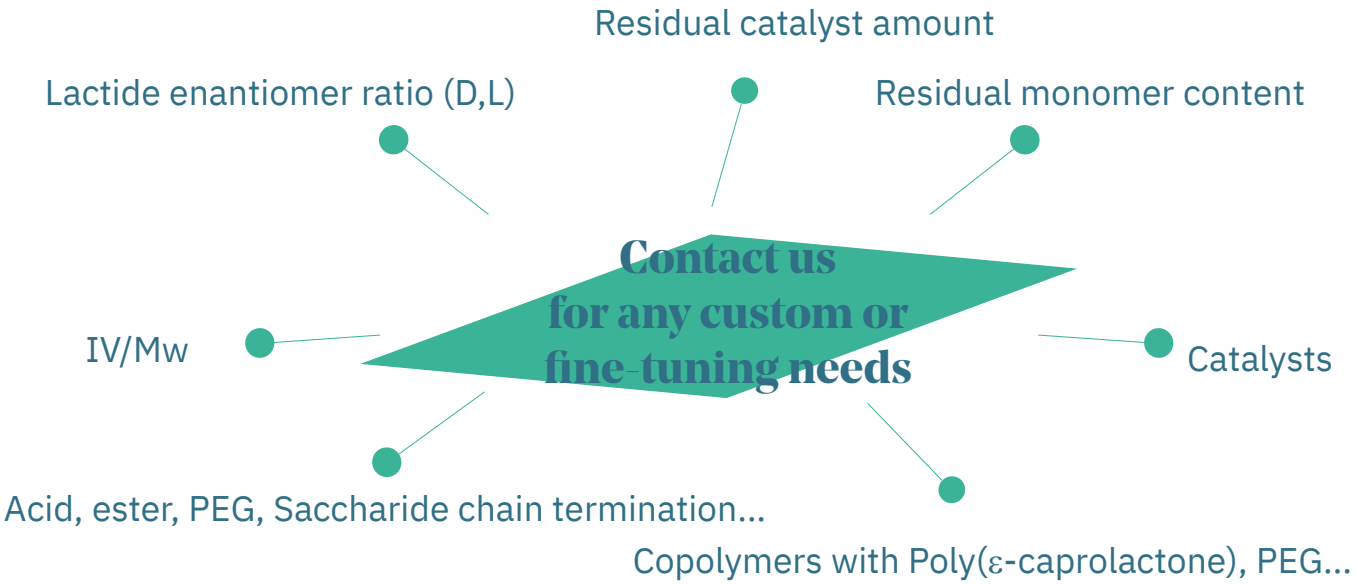
Applications

- FDA-approved excipient
- Controlled release formulations (nanoparticles, microparticles)
- Implantable systems for drug delivery
- Resorbable materials for medecine surgery
- Matrix for tissue engineering

Take the control of your drug release !





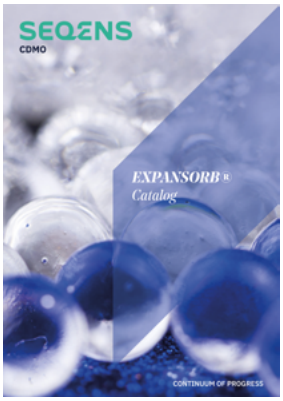


SEQENS UNIQUE OFFER

20+ years expertise on PLGA manufacturing within several on-the-market formulations

- Active DMFs i.e. US type IV (Excipients)
- Dedicated onsite R&D capabilities to any fine tuning from lab to industrial scale
- Regulatory services support : IMPD, DMF Filing
- Produced in Europe (Aramon, France)
- GMP compliant (EU, USFDA)
- Classic and ultrapure ***low-monomer and powder*** grades available.

New !
Ultrapure LMP Grade available !
With <0,5% monomer content



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References

A Scalable Manufacturing Approach to Single Dose Vaccination against HPV. *Vaccines*, 2021 (9(1):66), S. Shao, O.A. Ortega-Rivera, S. Ray, J.K. Pokorski, N.F. Steinmetz.

Has PEG-PLGA advantages for the delivery of hydrophobic drugs? Risperidone as an example. J*ournal of Drug Delivery Science and Technology,* 2021 (61), 102239. L. de Souza, R. Eckenstaler, F. Syrowatka, M. Beck-Broichsitter, R. Benndorf

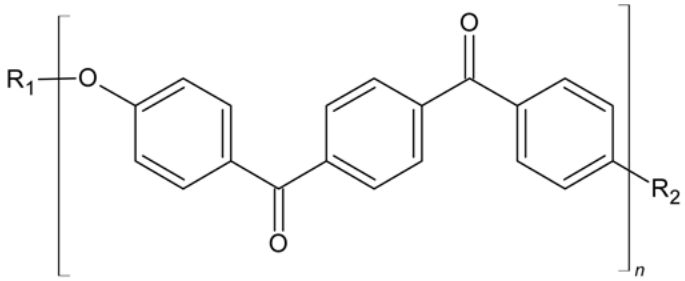
Novel biodegradable Round Window Disks for inner ear delivery of dexamethasone. *International Journal of Pharmaceutics,* 2021 (594), 120180. E. Lehner, A. Liebau, F. Syrowatka, W. Knolle, S. Plontke, K. Mader

Apigenin-Loaded PLGA-DMSA Nanoparticles: A Novel Strategy to Treat Melanoma Lung Metastasis. *Molecular Pharmaceutics,* 2021 (March), R. Sen, So. Ganguly, Sh. Ganguly, M. Debnath, S. Chakraborty, B. Mukherjee, D. Chattopadhyay

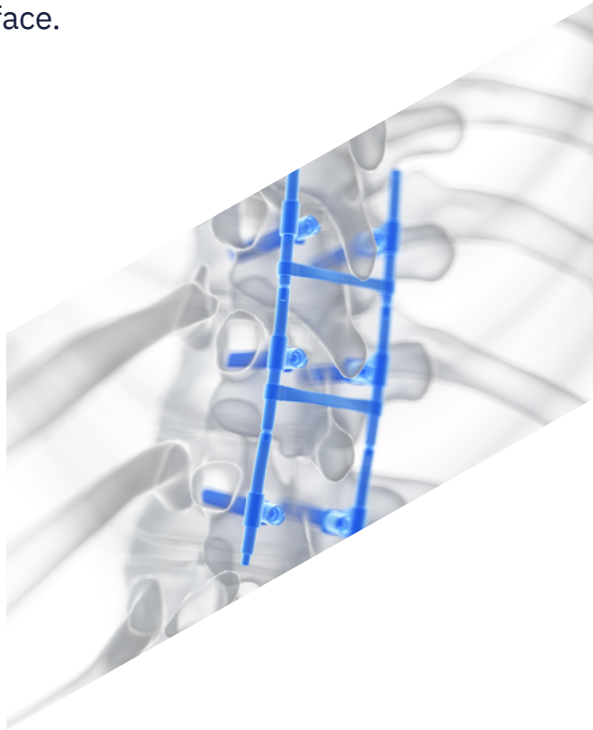
PEKK MEDICAL GRADE

PEKK Medical grade is a Thermoplastic polymer obtained by polymerisation of monomer EKKE with Isophtaloyl and Terephtaloyl chloride. Allowing various applications (dental and long term implants biomaterial) because of its higher mechanical strength and the presence of the second Ketone group, that allows more surface modification on its surface.

CHEMICAL STRUCTURE



Chemical Name: poly-ether-ketone-ketone
Synonym/acronym : PEKK



PROPERTIES & APPLICATIONS

Properties

- Shock absorbance
- Fracture resistance
- Mechanical strength
- Chemical resistance
- Thermostability

Applications

- Excellent barrier properties and the highest compressive strength among all polyarylether ketones
- Easy processing
- Suitable for sterilization
- **Excellent shaping capacity beyong it melting point, suitable for :**
  - injection molding
  - extrusion (films, plastics, tubes)
  - 3D printing (FDM, SLS)

SEQENS UNIQUE OFFER

Ultra high performance copolymer that allows for crystallization profiles that match really what you are looking for.

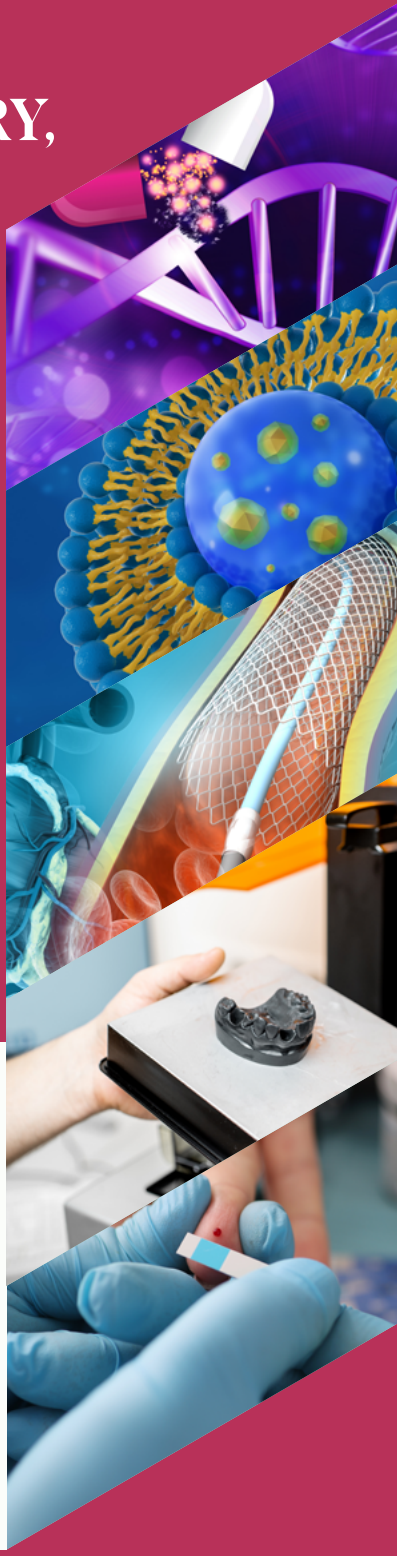
Available PEKK medical grades :

	SP	CE	C
Appearance	White to cream solid	White to cream solid	White to cream solid
Tg (°C)	155-165	160-170	160-170
Crystallization point (°C)	NA	280-300	285-315
% Terephtaloyl / Isophtaloyl*	60/40	80/20	80/20
Equivalence with industrial series	6002	8001	8002

* The ratio of isophthaloyl and terephthaloyl chlorides allows the crystallinity of the polymer to be modified and therefore influences the viscosity and crystallization temperatures.

CUSTOM MATERIAL FOR DRUG DELIVERY, MEDICAL MATERIALS & BIOMEDICAL APPLICATIONS

Seqens can offer a full range of services to develop and produce materials for medical applications.



SEQENS UNIQUE OFFER

- Excellence in organic and polymers chemistry since 1962
- Materials involved on several commercially available formulations or medical devices
- Dedicated polymer workshops units in Europe and US
- Full project management with regular reporting under strict confidentiality
- In-house development and scale-up capacities from kilolab to big industrial scales
- Full regulatory support : IMPD, DMF Filing
- Analytical resources and manufacturing units operating according to ICHQ7 and GMP guidelines on QA authorities (european, FDA...) inspected sites

SOME EXAMPLES OF OUR EXPERTISE ON CUSTOM MATERIALS

- Molecules for glycemia measurement in diabete medical devices
- Resin for injectable formulation
- Filter aid for peptids
- Hydrophilic coating solution for catheters

FOCUS ON 4 OF SEQENS' EXPERT DD&MM R&D CENTERS

BOSTON'LAB

Small molecules & polymers

- 1,000 M² lab-floor
- 5 Kilo Labs
- 30 Scientists with > 50% PhD

ARAMON'LAB

Drug Delivery Polymers

- DD&MM Polymers dedicated R&D team
- 2 kilolab suites (1 dedicated for melt polymerisation)
- 7 scientists with >50% PhD

LAHR'LAB

Accelerated R&D

- Industrialization center
- Lab Surface : 700sqm
- 3 Kilo-lab Suites

SEQENS 'Lab

Small molecules & Polymers

- 4 kilo-labs
- 2 cGMP pilot plants with 11 multipurpose reactors (total capacity of 12 m³)
- Temperature range: -15/+150°C (hastelloy reactor: -80/+200°C)
- 110 Scientists with > 50% PhD

About Seqens

Seqens is an integrated global leader in pharmaceutical solutions and specialty ingredients, delivering outstanding performance, unrivalled market responsiveness and custom-made solutions to its customers.
In the pharmaceutical industry, Seqens supports its customers in developing, scaling up and manufacturing drug substances from the pre-clinical phase to the commercial phase. Seqens also offers a large portfolio of APIs and proprietary products.

SEQENS

#Pharma Solution

- SEQENS CDMO
- SEQENS ESSENTIAL DRUG SUBSTANCES
- SEQENS IN VITRO DIAGNOSTIC

#Specialty ingredients

- SEQENS ADVANCED SPECIALTIES
- SEQENS CUSTOM SPECIALTIES
- SEQENS COSMETICS
- SEQENS ACID & DERIVATIVES
- SEQENS SOLVENTS & PHENOL SPECIALTIES
- SEQENS MINERAL SPECIALTIES

SEQENS R&D SERVICES

- proteus *Biocatalysis*
- SEQENS 'Lab *Small molecules & polymers*
- BOSTON *Early phase projects*
- LAHR *Accelerated R&D*
- ARAMON *Drug delivery polymers*
- MONTREAL *Electronics*
- MIDDLESBROUGH *Cosmetics & fine chem*

3200 people

300 scientists, experts and engineers

7 R&D centers

1000 clients in more than 80 countries

24 manufacturing sites

DISCOVER SEQENS PHARMA SOLUTIONS PRODUCTS & SERVICES OFFER

Custom manufactuting

SCAN ME

Early stage manufacturing

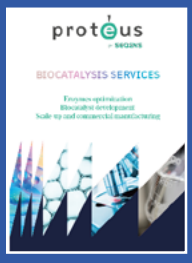
SCAN ME

Intermediates

SCAN ME

API

SCAN ME



Biocatalysis services

SCAN ME

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