

SEQENS

OUR SCIENCE FOR YOUR FUTURE

Drug Delivery Solutions

Custom Lipids & Polymers

Smart Excipients & Polymers Catalog



Seqens overview

Seqens is a worldwide leader in the development and production of active ingredients, pharmaceutical intermediates, specialty ingredients and cosmetics & personal care leveraging 24 manufacturing sites, 10 R&D centers and 3,200 employees in 10 countries.

As an integrated player across the value chain - from raw materials to active ingredients and from research and development to industrialization - Seqens offers a broad portfolio of active ingredients, pharmaceutical intermediates and specialty ingredients, develops and industrializes the most demanding molecules, and relies on its ability to innovate, develop and implement the best available technologies.

Driven not only by a culture of excellence and a strong entrepreneurial spirit, but also strong values such as unity, agility, and reactivity, our employees are committed to providing the highest level of service and quality to more than 1000 customers around the world while acting ethically in accordance to our strong Environmental, Social, and Governance program.



3200
people



300
scientists, experts
and engineers



10
R&D centers



1000
clients in more
than 80 countries



24
manufacturing
sites

Seqens is a major vertically integrated pharma solutions actor offering a wide range of products and services from Solvents to Custom APIs

Pharmaceutical Solutions

Custom APIs

Intermediates

Drug Delivery solutions
Lipids and Polymers

Generics

Consumer Healthcare

Life Science Inputs

Specialty Ingredients

Electronics

Cosmetics & Personal Care

Custom & Specialties

Lubricant Additives

Upstream Platform

Upstream assets to support the growth of small molecules, specialty ingredients and Life Science Inputs activities as a vertical integration platform

Seqens Pharmaceutical Solutions, leader in catalog and custom drug substances

With 25 years of experience in process development, scale-up and ongoing cGMP manufacturing of drug substances, 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



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 drug substances 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 across 3 continents
- Global network of sales offices
- Solutions for dual sourcing

SEQENS

OUR SCIENCE FOR YOUR FUTURE

Foster growth with Seqens

Four companies – PCAS in France and Finland, Chemie Uetikon in Germany, PCI Synthesis in the United States and Wavelength in Israel & India – have joined forces as Seqens Pharmaceutical Solutions to offer world-class drug substance development and manufacturing services to the pharmaceutical industry.

Assets & Competencies

8
cGMP/FDA inspected sites WW

1,000 m³
600 m³ cGMP

3
Pre-GMP sites for RSMs & Building-blocks

200+
DMFs for commercial drug substances

250
scientists, experts and engineers

7
R&D Centers worldwide

Over 35 years of drug substances production experience

In-house back integration of intermediates and starting materials for safe supply

Global sales and distribution network

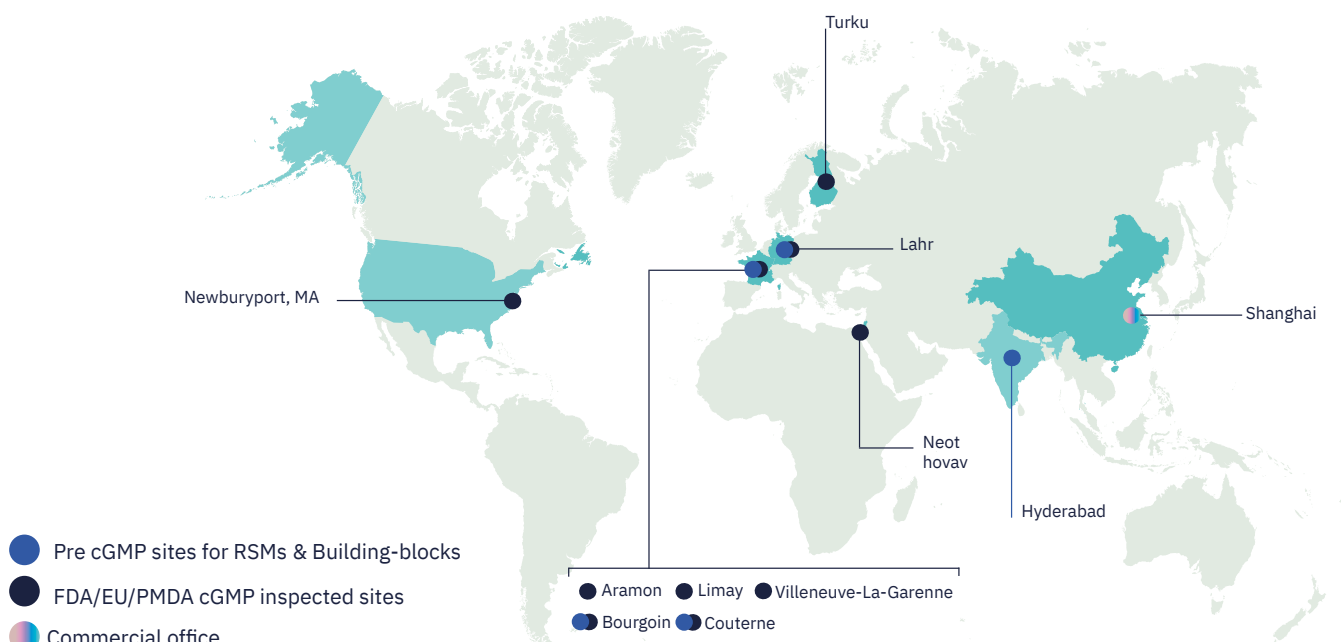
Excellent regulatory compliance track record at all GMP sites

A wide range of technologies

- High Pressure Reaction
- Low temperature technology
- Enzymatic Chemistry
- Potent API capabilities: OEL < 100 ng/m³
- API for injectable and ophthalmic FDF
- Controlled Substances
- Flow Chemistry
- Micronisation & spray drying services
- Lipids & Polymer Synthesis

An international network

Benefit from a manufacturing network of **7 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**



Drug Delivery Solutions for Bioavailability and Material for Medical Devices

SEQENS provides key expertise and capabilities in Drug Delivery Solutions for:

- RNA/DNA vectorization for the vaccines, oncology, etc.
- Materials for medical devices
- Bioavailability improvement (controlled-release, solubility enhancer, liposome)

Our Drug Delivery Solutions offer

CUSTOM LIPIDS

Custom Synthesis of Lipids as Drug delivery system for RNA/DNA vaccines, gene therapy, or liposome vectorization of APIs

CUSTOM POLYMERS

Custom synthesis of GMP polymers: bioresorbable (PLA/PLGA, PCL) and hydrosoluble polymers like PEG, PEI, etc.

SMART EXCIPIENTS & CATALOG POLYMERS

- **Expansorb®** - PLGA, PCL bioresorbable polymers
 - **IMPEKK®** Thermoplastic Polymer for 3D-printed implants
- **Vitamin E-TPGS** - solubility enhancer

A Unique Offer based on 3 Expert R&D Centers for Lipids and Polymers

BOSTON'LAB

Small molecules Lipids & polymers



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

ARAMON'LAB

Drug Delivery Polymers



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

SEQENS'Lab

Small molecules Lipids & polymers



- 4 kilo-labs
- 2 cGMP pilot plants with 11 multipurpose reactors (total capacity of 12 m³)
- 110 Scientists with > 50% PhD

- More than 25-Years Track-record in organic, polymers and lipids chemistry
- Double-sourcing offer with lipid and polymer workshops in EU and US
- In-house development and GMP scale-up capacities for lipids and polymers from kilo lab to big industrial scales
- Full regulatory support (IMPD, DMF Filing)

Our commitment is to support our customers in reaching the highest requirements in terms of ingredients performances, selectivity and quality. Our services allow to **accelerate** the development projects, **deliver** the products at all stages of the product life cycle, **fine-tune** the chemical structure, and create opportunities for **IP generation**.

Custom Lipids

With a recognized **10 years-experience** in **Custom Lipids development and manufacturing**, Seqens has the ability to serve customers with **cationic/ionizable lipids, PEG-lipids, phospholipids and derivatives**.

Our Custom Lipids offer

CUSTOM LIPID INTERMEDIATES

Leveraging Seqens world-wide non-GMP Assets

Up to **multi-tons scale**

CUSTOM LIPIDS cGMP

Synthesis and Purification Capabilities (Chromatography, Salt Screening) **in the US and EU**

Supply from **grams to hundreds of kilograms** to support from **preclinical to commercial phases**

TOLLING CAPABILITIES

For **commercial-scale** cGMP Lipid synthesis

Up to **multi-tons scale**

To serve our customer markets

Seqens answers customers' needs for **Custom Lipids**, which are typically used in **drug delivery systems** to improve the **bioavailability** of drugs:

- Lipid Nanoparticles for mRNA/siRNA/DNA
- Transfection Vectors for Gene Therapies
- Immunotherapies (CAR-T-Cells)
- Lipid prodrugs
- Liposome Vectorization for Oncology, Pain,...
- Lipid-Polymer Hybrid Nanoparticles
- Cosmetic Lipids

Best-in-class analytical tools

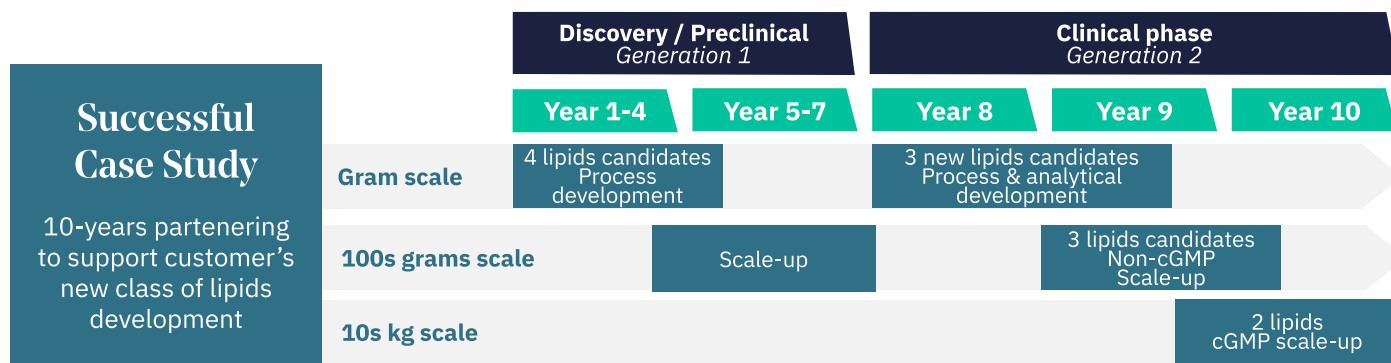
Analytical methods development and GMP validation

Stability studies, Process safety studies

Full range of Solid State Analytical tools, incl. XRPD characterization, morphological analysis

Impurities characterization and Genotoxicity Assessment (AMES, in vitro micronucleus test)

Track record and successes



Custom Polymers

Our custom development and manufacturing offer of cGMP polymers to serve our customers' markets

Biodegradable Polymers for Controlled-release	APIs vectorization and Nanocarriers	Vaccine Formulation (RNA Delivery)	Solubility / Bioavailability Enhancer
Therapeutic Polymers & Pro-drugs	Polymers Functionalization & small molecules PEG-ylation	Chromatographic Resins Synthesis & Functionalization	Materials for medical devices and Biomedical Implants

Seqens has a High-End Pharma Polymer Expertise Center Covering a Complete Range of Polymerization Technology.

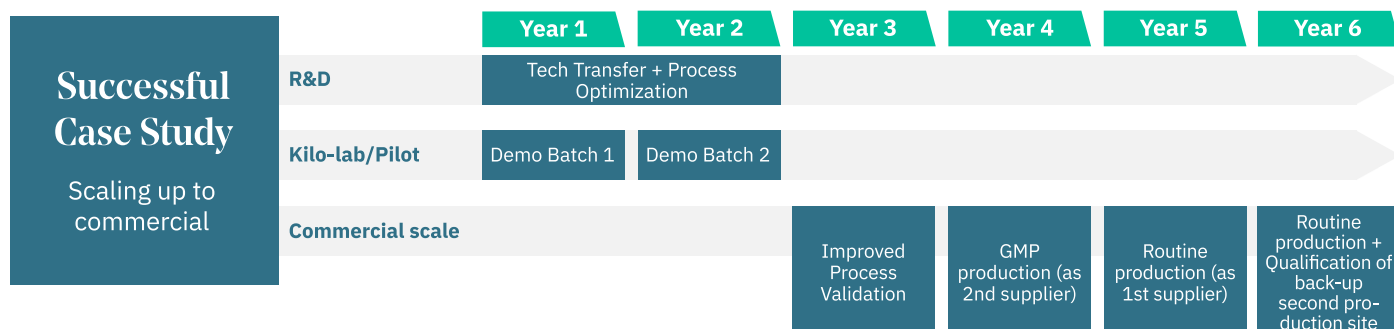
POLYMERS SYNTHESIS

- **Ring Opening Polymerizations:** PLA/PLGA, PEG/PPG, Polycaprolactone, Glycofurool
- **Radical Polymerizations** (controlled and uncontrolled)
- **Polycondensation:** Polyethylenimine, Polyamino acids, Polyfumarate co-polymers, Polyurea/urethane, Polyacrylic acid, EVA/PVA, Hydrogels
- **Block copolymer synthesis**
- **Sol-Gel Processes**
- **Lipids, Linkers and APIs PEGylation**

POLYMERS MODIFICATION

- **Graft Polymerization:** Polyvinylpyridine, Polysaccharide, Polysiloxane
- **GMP Filtration / Purification**
- **GMP Lyophilization**

Track record and successes

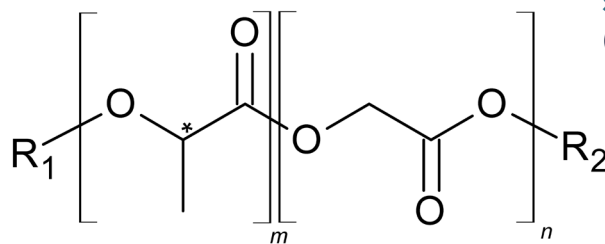


EXPANSORB®

EXPANSORB® GMP PLA & PLGA copolymers are obtained by copolymerization of the corresponding cyclic dimers lactide and glycolide. PLGAs are among the best-in-class functional 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

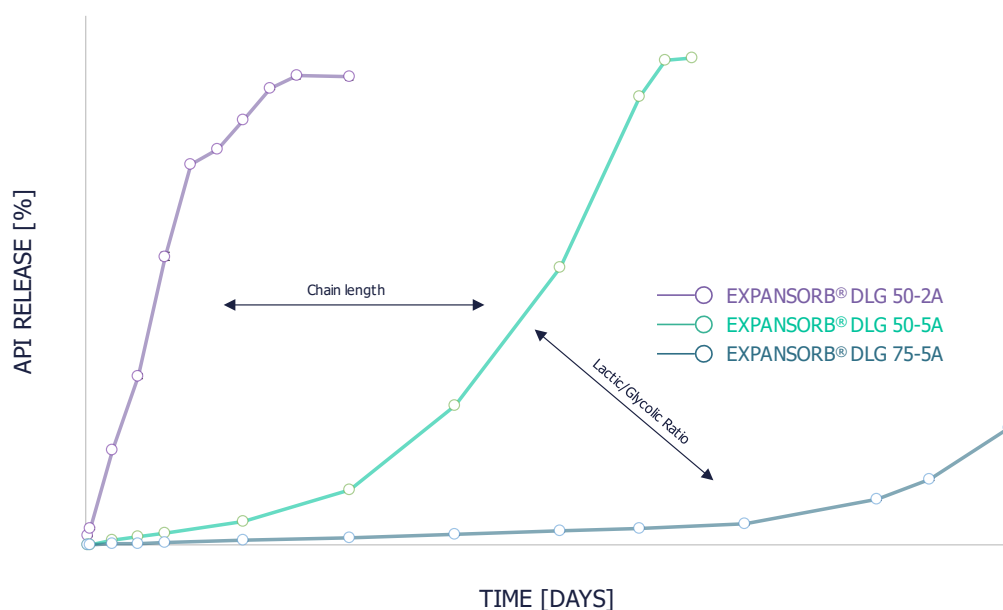
Properties

- 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 medicine surgery
- Matrix for tissue engineering

Take the control of your drug release!



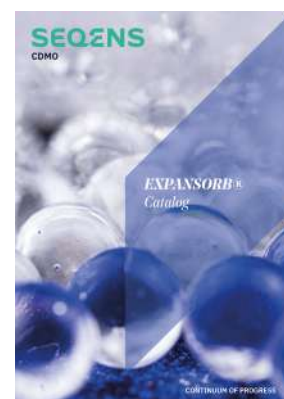


Seqens Unique Offer

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 ultra-pure **Low Monomer and Powder** grades available

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



**Ask for our
EXPANSORB® catalog**

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. *Journal of Drug Delivery Science and Technology*, 2021 (61), 102239. L. de Souza, R. Eckenstaler, F. Syrowatka, M. Beck-Broichsitter, R. Benndorf, K. Mäder

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. Mäder

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

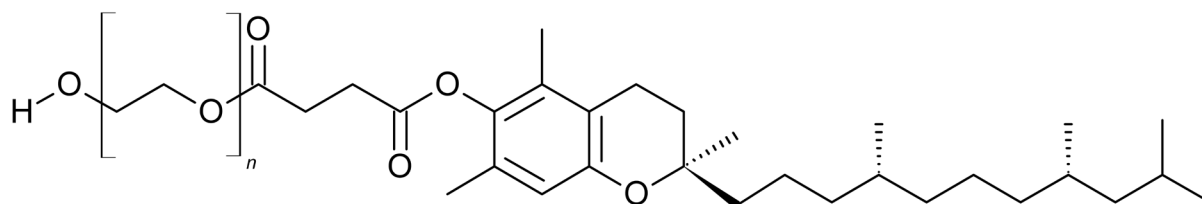
Vitamin E TPGS

Application field of Vitamin E-TPGS: Pharmaceutical, Nutraceutical, Food and beverage, Cosmetic and Personal Care, Animal nutrition.

Chemical structure

Chemical Name: D- α tocopheryl polyethylene glycol 1000 succinate

Synonym/acronym: TPGS, Tocophersolan, Tocofersolan



Properties of Vitamin E TPGS

Vitamin E TPGS, a non-ionic surfactant, water soluble derivative of natural Vitamin E, is a multi-role excipient for pharmaceutical drug delivery innovation.

Improving bioavailability

- Absorption enhancer
- P-gp inhibitor

Surfactant properties

- Drug solubilizer
- Emulsifier
- Vehicle for lipid based formulation (SEDDS* and SMEDDS**)
- Plasticizer for hot Melt Extrusion
- Stabilizer for Amorphous solid
- Dispersion

Source of Vitamin E

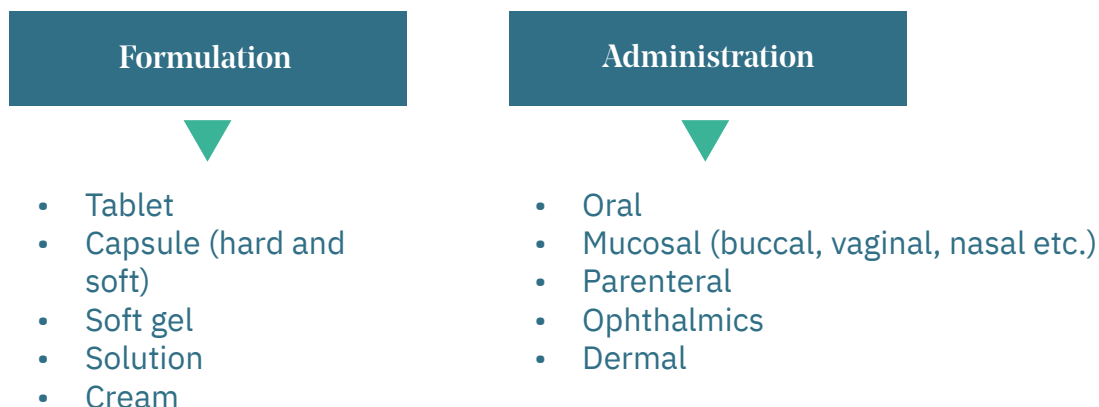
- API for Vitamin E (water soluble source of vitamin E)
- Antioxydant

* SEDDS: Self-Emulsifying Drug Delivery

** SMEDDS: Self-MicroEmulsifying Drug Delivery System



Type of formulation and administration pathway



Regulatory Status



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

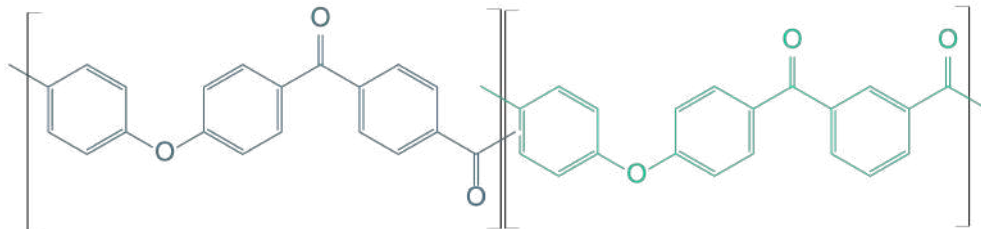
Color: white to light tan

Vitamin E content (D- α -tocopherol): 25 % minimum weight basis; standard range 25-30 %

IMPEKK®

PEKK produced by Seqens "IMPEKK® polymer" is a high performance thermoplastic designed for permanent surgical implants such as spinal, cranial, orthopedics and dental implants. Its tailored crystallization speed enables IMPEKK® polymer to be perfectly suited for Additive Manufacturing.

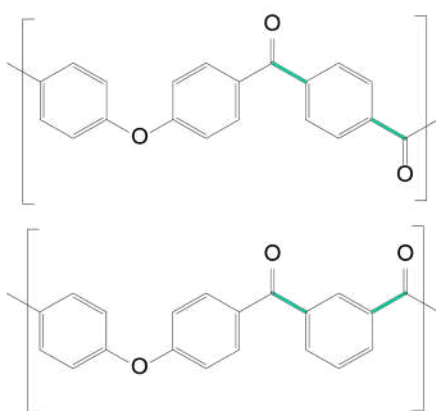
Chemical structure of Poly-Ether-Ketone-Ketone (PEKK)



Key properties

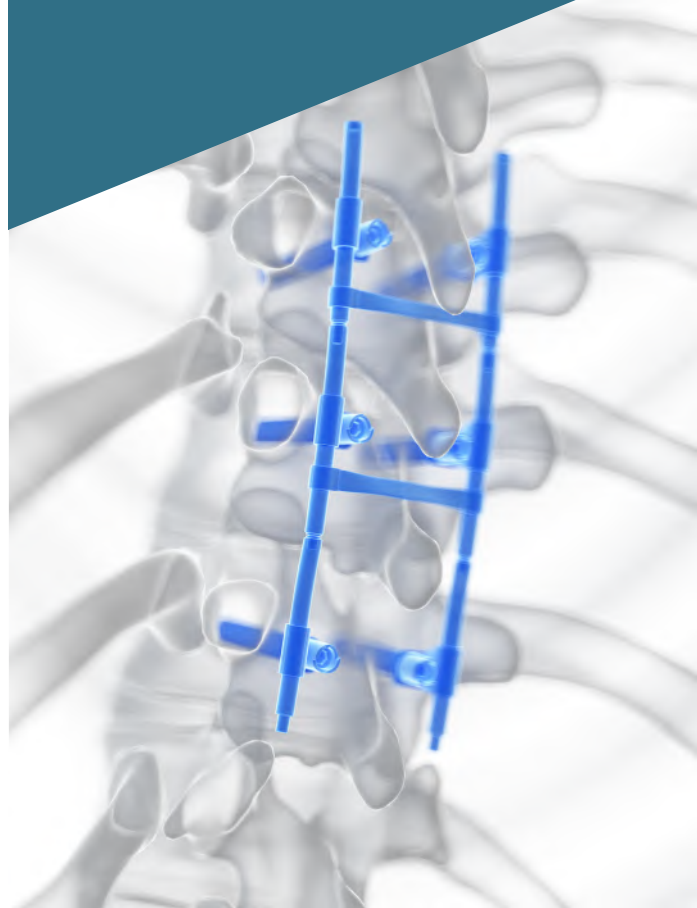
The presence of 2 ketone groups compared to other PAEK polymers (Poly-Aryl-Ether-Ketone) gives IMPEKK® polymer **greater polarity** and allows for better acceptance of functional fillers, providing a wide range of formulation choices for implantable medical device manufacturers. IMPEKK® polymer is composed of ether (flexibilizing) and ketone (rigidifying) groups. The more ketone groups there are, the higher the Tg (Glass Transition temperature) and the better the mechanical properties. IMPEKK® is a **copolymer** that includes terephthaloyl and isophthaloyl units. This **modularity** allows fine tuning of crystallization rate and Melting point temperature (Tm).

- Elastic modulus close to cortical bone
- X-ray translucency
- Chemical inertness
- Outstanding compressive strength
- High Tg
- Excellent tribological properties
- Excellent barrier properties
- Toughness
- Sterilizable



Terephthaloyl *Para linkage*

Isophthaloyl *Meta linkage*



Applications

Amenable to all polymers processing techniques (Injection Molding/Extrusion): **IMPEKK® 1G-T** (granules for Testing and Development)

	Norm	IMPEKK® 1G-T
Appearance	/	Golden Yellow or White to cream solid
Polymer type	/	Semi-crystalline
Melting range/point (°C)	DSC DIN EN ISO 11357	345-375/358
Glass Transition (°C)	DSC DIN EN ISO 11357	160-170
Tensile test at Break (MPa)	DIN EN ISO 527-1	115
Tensile Modulus (GPa)	DIN EN ISO 527-1	3,7
Impact Strength	DIN EN ISO 179-1eU	180 kJ/m ²
Impact Strength (notched)	DIN EN ISO 179-1eA	5,7 kJ/m ²
Density	DIN EN ISO 1183	1,30 g/cm ³
% Tere/Iso	/	80/20
Crystallization speed	/	Very fast
Processing temperature (°C)	/	385°C
Availability	/	Q3/22

Particularly suited for Additive Manufacturing: **IMPEKK® 3D-F-T** (filaments for Testing and Development)

IMPEKK® 3D can be printed both amorphous and semi-crystalline.

	IMPEKK® 3D-F-T
Appearance	Golden Yellow or White to cream solid
Polymer type	Pseudo-amorphous
Diameter	1,75 mm
Packaging	500 g spool
Availability	Available



PEKK-based Cranial Implant
printed by Kumovis



PEKK-based Spinal Cage Implants
printed by Kumovis



IMPEKK® 3D-F-T Filament

If you are interested in our IMPEKK® for implantable medical application, please contact us for more information: alexandra.ngawazenang@Seqens.com

Contact us:
dds@seqens.com

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- Biocatalysis services

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