SONEAS

Chemistry for a better life

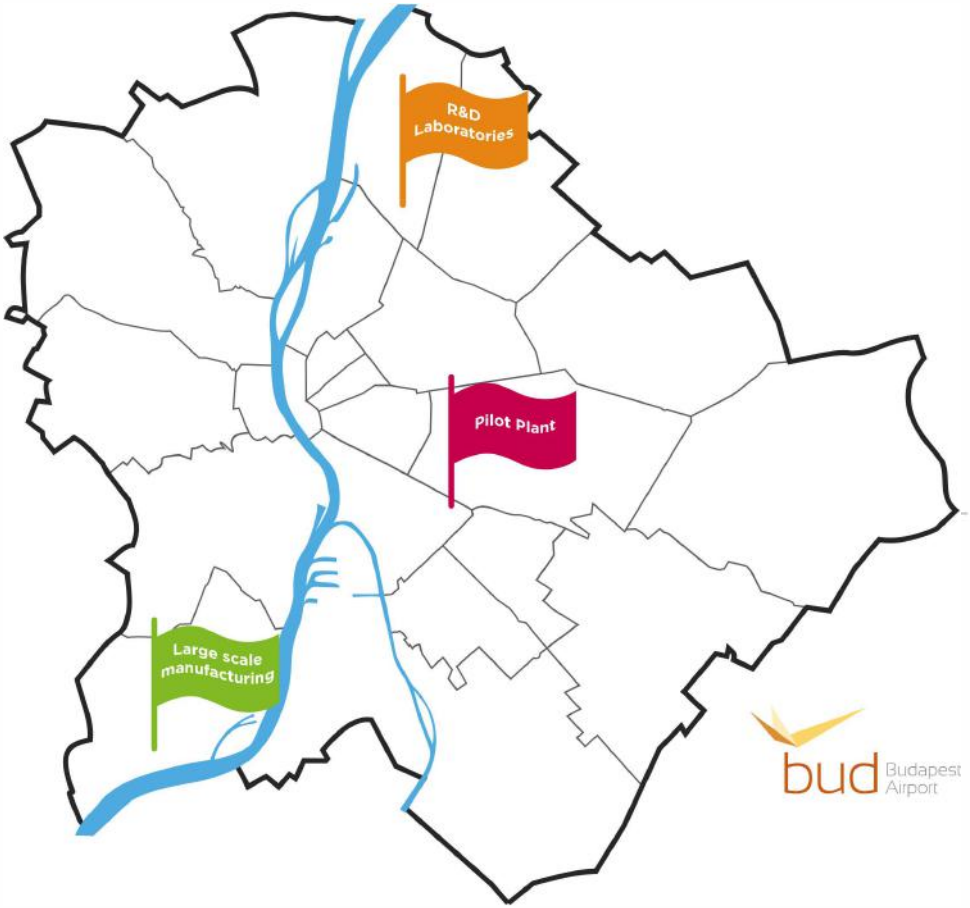
ABOUT US

SONEAS Chemicals Ltd., (Uquifa Group member) is a chemical service provider with a pragmatic approach to innovation. We are leading European CRO/CDMO with a track record of ensuring that we understand our customer needs in order to satisfy their expectation.

At SONEAS Chemicals Ltd., (Uquifa Group member) we provide a comprehensive range of chemistry services (Discovery chemistry, Lead optimization, Route scouting, Process Research and Development, Analytical method development and validation, Scale up, cGMP manufacturing of APIs, Technology transfer, Process validation) to support your preclinical and clinical trials development (Phase 1 to 3) under Pilot and cGMP conditions, manufacture of intermediates and regulated starting materials, specialty chemicals for pharma and non-pharma application under ISO 9001 standard on tonnage scale.

SONEAS Chemicals Ltd., (Uquifa Group member) with Headquarters in Illatos út 33, H-1097 Budapest, operates at three sites in Budapest, Hungary:

Berlini Site R&D Laboratories	**Illatos Site** Pilot, GMP Plant	**Bányalég Site** Large Scale Manufacturing
• Lead Optimization • Route scouting • Process Research and Development • Analytical method development and validation	• Lead Optimization • Route scouting • Process Research and Development • Analytical method development and validation • Scale up and cGMP manufacturing • Technology transfer • Manufacturing of intermediates, APIs, starting materials in small and large scale	• Route scouting • Process Research and Development • Analytical method development • Scale up • Technology transfer • Manufacture of intermediates and starting materials, specialty chemicals for pharma and non-pharma application according to ISO 9001 standard on tonnage scale



HISTORICAL MILESTONES

OUR 3 P's

PEOPLE

Are the backbone of the organization: Every task, idea and ounce of e ort contributes to our collective progress leading us to success. We genuinely value people's contributions, expertise, and enthusiasm.

PRODUCTS

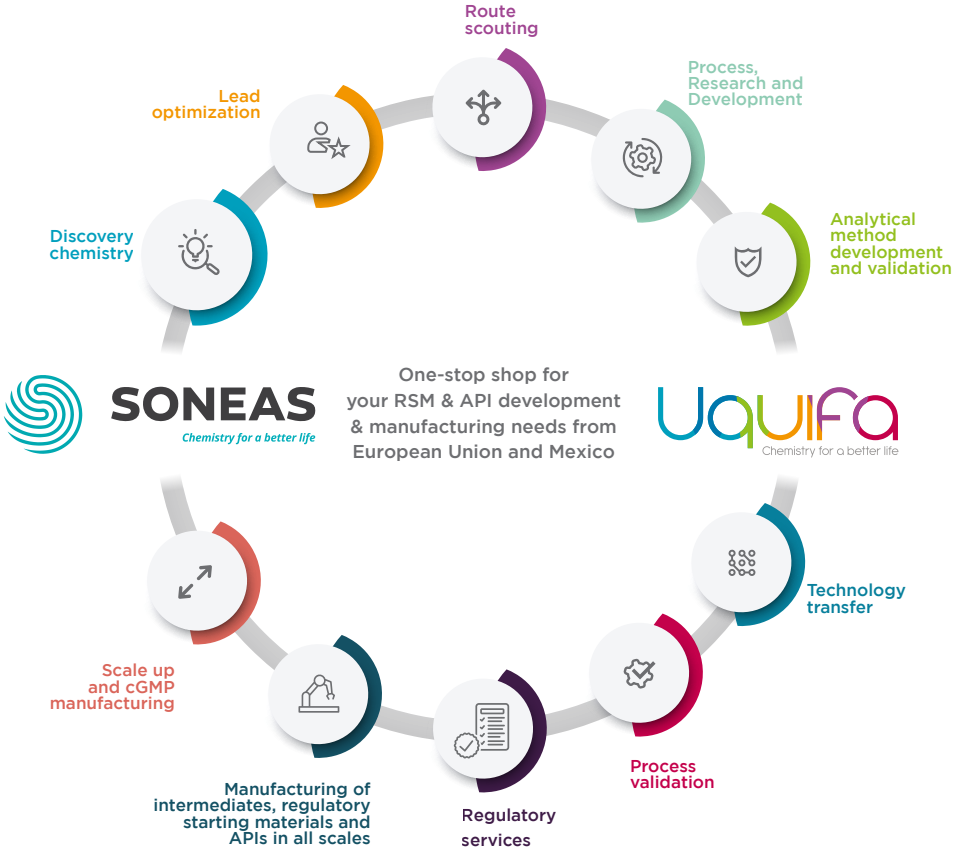
Are the lifeblood of our business and the result of our collective e orts. We work hard for consistently delivering a high-quality product reinforcing the UQUIFA Group as a reliable and trustworthy supplier.

PLANTS

Our number one priority is to ensure a safe working environment: With the right infrastructure, machinery, and technology in place, we can optimize workflow and maximize productivity allowing us to meet customer demands e ectively and delivering a high-quality product on time. Investing back in our Plants through CAPEX programs is a consistent aspiration for us.

WE PROVIDE

A comprehensive range of chemistry services from discovery stage through pilot to commercial scale. We develop and produce APIs, starting materials, intermediates, fine and specialty chemicals for pharma and non-pharma applications. Our services include full analytical provision for regulatory filing purposes.



Our pragmatic approaches ensure the rapid supply of substances to meet tight project deadlines, as required. Regular, detailed, written updates and teleconferences along with timely delivery of the material guarantee that your project remains on track.

CHEMISTRY

Some of the chemistry used on a daily base at Soneas R&D Laboratories, Pilot, GMP Plant and Large Scale Manufacturing sites:

- Alkylation (for example with diethyl sulfate)
- Carbene additions
- Carbonylation with CO
- Cryogenic reactions (-70 °C ÷ -60 °C)
- Cyanations
- Cyclopentadiene chemistry
- Cyclopropanation
- Diazotation (for example Sandmeyer)
- Diels Alder reactions
- Friedel-Crafts reactions
- Halogen chemistry:
  - Bromination with Bromine
  - Chlorination, by using chlorinating reagents (for example NCS)
  - Fluorination, by using fluorinating reagents (for example DAST, XtalFluor)
  - Acyl chloride preparations
- Flow chemistry:
  - Nitration
  - Hydrogenation
  - Special chemistries
- High temperature reactions (150 ÷ 250 °C)
- Homogeneous catalytic coupling reactions
- Hydrazine reaction
- Hydrogenation
- Hydroxyethylation/propylation with ethylene and propylene oxide
- Isomerization
- Metathesis reactions (with Mo, W, Ru catalyst)
- Optical resolutions
- Organo peroxide chemistry
- Organometallic reagents (Grignard, Organolithium, Metal Hydrides)
- Synthesis of boron organic compounds (for example organic boronic acids)
- Triphosgene chemistry

Legend:

- R&D Laboratories, Pilot, cGMP Plant and Large Scale Manufacturing sites
- R&D Laboratories, Pilot
- R&D Laboratories, cGMP Plant and Large Scale Manufacturing sites

UNIQUE TECHNOLOGIES

Over the years Soneas chemistry team developed several unique technologies to progress the customer projects, some of it are listed below:

Metathesis application *

- Metathesis reaction with Ru, Mo andW catalysts
  - Ring closing metathesis with Ru catalyst
  - Cross metathesis with Ru catalyst
  - Z-selective catalytic ring-closing metathesis (RCM) reactions:
  - Asymmetric Ring-Closing Metathesis (RCM)
  - Enantioselective Metathesis Reaction
  - Z-selective metathesis reactions

Ethylene & propylene oxide chem **

- Hydroxyethylation/propylation

* Details on page 26
** Details on page 29

DISCOVERY SERVICES

SONEAS Chemicals Ltd., (Uquifa Group member) has a 20+ years' experience in early phase development, now strengthening capabilities to offer an end-to-end solution in API development. Our highly skilled chemist team (PhD and MSc) can deliver projects with high flexibility, extraordinary solutions in extra short timeframes.

Discovery chemistry team covers targeted library synthesis, lead optimization supported by computational chemistry through partnerships if required. Our highly qualified team has a versatile understanding of asymmetric transformation methods, organometallic chemistry, including metathesis to deliver the desired compounds in the most economical way. The chemists have large synthetic experience synthesizing building blocks and reference compounds, scaffold analoging, focused library, heterocyclic chemistry, asymmetric synthesis, natural product synthesis, impurities & metabolite synthesis, route scouting, early and late-stage PRO.

Our discovery chemistry services are backed by strong analytical chemistry support, robust IT infrastructure and ELN, as well as efficient data and compound management.

Chemical expertise

- Strong understanding in synthesis of enantiomerically pure compounds, whether by targeted stereoselective synthesis, resolution, or separation by chiral preparative HPLC methods.
- Homogenous catalytic couplings are widely applied (including Kharasch, Suzuki, Negishi, Sonogashira, Kumada, Kumada-Corriu, Buchwald-Hartwig and Stille couplings).
- Hydrogenations (under H_2 pressure or transfer hydrogenation). Asymmetric syntheses based on carbohydrate frame-molecules, natural product analogues.
- E and Z selective metathesis in glow boxes to access chemical entities which would be hard to achieve with ordinary chemical transformations.
- Synthesis of stable labelled API analogues.

Isolation techniques

We have expertise in all important isolation techniques and have the capabilities to choose the best way to deliver your target compounds (including crystallization, distillation, flash chromatography, preparative HPLC, lyophilization).

Analytical Support

Our high-quality chemistry and aggressive target timelines require high quality analytical chemistry support. Having confidence in the structural characterization of the compounds is essential. Our company makes it priority to have the analytical department up-to-date and precise as much as possible supported by heavy investments. Our wide range of analytical equipment's is ready to support the discovery needs:

- 500 MHz Bruker NMR spectrometer allowing high sensitivity data to be obtained on 1H along with other nuclei such as ^{13}C, ^{19}F, ^{31}P, ^{11}B and ^{15}N.
- A range of homonuclear and heteronuclear experiments are regularly employed for structure confirmation, structure elucidation and to make purity assessments.
- Structure conformation can also be probed
- LCMS, HPLC and UPLC equipped with PDA and CAD detection.
- Highly qualified analytical team to develop customized methods immediately if some molecule structures require.
- GC-FID and GCMS available to support GC compatible molecule analysis.
- Chiral method development on both HPLC and GC.
- Method development supports the preparative HPLC purification of the target compounds.
- FTI R, UV-VIS spectrometer, polarimeter, titrators, DSC and melting point apparatus aid in providing full characterization data.

Streamlining Lead Optimization in Neurological Disease Treatment:

A Collaborative Approach by SONEAS Chemicals Ltd. (Uquifa Group member)

Introduction:

In the pursuit of developing novel treatments for neurological diseases, the collaboration between chemical and biology teams plays a crucial role. This article sheds light on SONEAS's significant contribution as the chemical support in a consortium working towards the optimization of a New Chemical Entity (NCE) for neurological disease treatment.

Background:

SONEAS, as part of a consortium, assumed the responsibility of providing chemical support for targeting a novel NCE intended for the treatment of neurological diseases. The primary focus was to optimize the lead compound from its initial identification, ensuring it evolves into an effective chemically available molecule.

Aims:

The overarching goal was to streamline the lead optimization process, transitioning from traditional linear synthesis methods to a more dynamic and efficient approach. This involved identifying key intermediates and developing scalable processes that not only saved time and resources but also facilitated a swift response to biological results.

Actions:

- **Abandonment of Traditional Synthesis:**

The consortium decided to move away from old, traditional linear synthesis methods, recognizing the need for a more adaptive approach in the complex field of neurological disease treatment.

- **Identification of Key Intermediate:**

A pivotal milestone was achieved by identifying a key intermediate collaboratively with the biology team. This intermediate contained a base structure that could be easily modified to optimize biological properties.

- **Scalable and Robust Process Development:**

A scalable and robust process was developed for the key intermediate, emphasizing efficiency to save both time and money during the lead optimization phase.

- **Analytical Method Development:**

To ensure the quality of the synthesized compounds, analytical methods were developed to monitor both chemical and chiral purity. This step was essential for maintaining the integrity of the compounds throughout the optimization process.

- **Close Collaboration with Biology Team:**

A close collaboration system was established with the biology team, allowing for the daily delivery of new molecules. This enabled a rapid response to biological results, with the synthesis of new compounds occurring within a few days.

Achievements:

- **Lead Compound Selection in 12 Months:**

The collaborative efforts between the chemical and biology teams resulted in the selection of a highly effective lead compound within a remarkably short timeframe of 12 months. This success was attributed to the excellent collaboration involving three Full-Time Equivalents (FTEs) in the chemical part.

- **Scalable Synthetic Procedure for Pre-clinical Activities:**

A scalable synthetic procedure was developed, ensuring the readiness of the lead compound to support further pre-clinical activities. This laid the foundation for the compound's progression towards clinical trials.

- **Capability for Quantity Scaling at SONEAS Laboratories:**

SONEAS proved advantageous, as it enabled the capability to scale up the production of Active Pharmaceutical Ingredients (APIs). This positioned SONEAS to provide extensive support for delivering the lead compound at higher quantities, crucial for advancing into clinical phases.

Conclusion:

SONEAS' strategic actions and achievements in collaboration with the biology team underscore the importance of a multidisciplinary approach in drug development. The successful transition from traditional methods to an adaptive and collaborative framework not only expedited lead optimization but also positioned the consortium for further advancements in the treatment of neurological diseases.

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BACKGROUND

- Lead optimization from first hit to find an effective chemically available molecule

01

AIMS

- Lead optimization from first hit to find an effective chemically available molecule

02

ACTIONS

- Old traditional, linear synthesis was abandoned.
- Key intermediate was identified together with the biology team containing the base structure which can be easily modified to optimize the biological properties.
- Scalable and robust process was developed for the key intermediate to save time and money for the lead optimization.
- Analytical methods were developed to monitor boththechemical and chiral purity.
- A closecollaboration system was developed with biology partner to be able to deliver new molecules on a daily bases and be able to react on the biological results within a few days by synthesizing new compounds.

03

ACHIEVEMENTS

- A highly effective lead compound was selected in 12 months time as a result of the excellent collaborations involving 3 FTEs in the chemical part.
- A scalable synthetic procedure was available to support further pre-clinical activities.
- SONEAS could give further support to deliver the lead compound at higher quantities as the capability to scale-up APIs is readily avalable in SONEAS Laboratories and cGMP Pilot Plant

Flexible delivery model

A flexible delivery model enables clients to work closely with our technical teams. Our teams are preparing detailed regular updates followed by telephone conferences and detailed development reports to ensure transparency during the work and supporting the most efficient way to make decisions together with the partner even during the project.

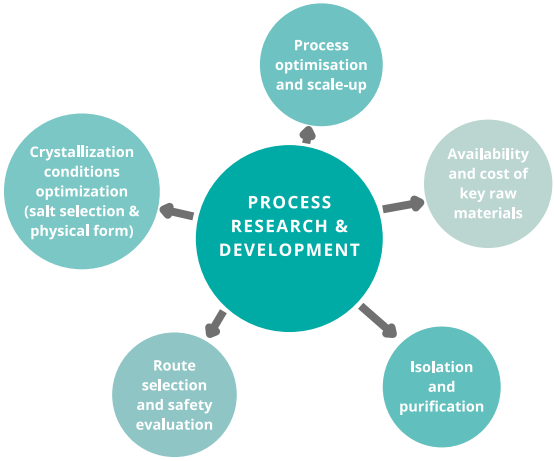
Our clients can choose from:

- Full-time equivalent(FTE)(mid or long term)
- Fee-for-service/Fixed Fee (FFS)

business models whichever-fits their requirements better.

PROCESS RESEARCH & DEVELOPMENT

We recognize the importance of understanding the chemistry and the processes. Putting a strong emphasis on process research and development means that we can minimize the risks associated with the scale-up of development chemistry routes. We pay attention on the requirements of large-scale manufacture already in the laboratory phase (such as price of raw materials, availability of raw materials, technology parameters of large-scale production).



Comprehensive development reports are provided. On completion of the work, customer will therefore have a technical package which adds value to the project and enables the smooth technical transfer of the process, if appropriate.

INTERMEDIATE AND cGMP API MANUFACTURE

The Illatos Site undertakes cGMP manufacture of APIs and intermediates from laboratory to pilot plant scale and is approved by the regulatory authorities for the manufacture of API from preclinical to commercial supply, supported by a fully qualified, well equipped analytical laboratories and comprehensive SOPs. Site Master Files are available on request.

KILO LAB

Equipments Reactors

- Glass reactors: up to 100L
- QVF glass lined reactor: 100L
- QVF crystallization reactor: 50L
- QVF reactor with DNISO Sulzer graphite distillation column:
  - 250L, theoretical plate number 20
- SCHOTT glass lined reactors: 63L
- Stainless steel mobile hydrogenation reactor: 20L, 10bar
- Rotary evaporators: 20L
- Filters and driers:
  - Stainless steel mobile process filter/dryer: 20L and 50L
  - Mobile filters: to 60L
  - Vacuum tray driers
- Centrifuge
- Stainless steel centrifuge (HEPA cl 100,000)
- Scrubber

LARGE SCALE MANUFACTURING FACILITY

The Large Scale Manufacturing ISO 9001 Certified (SGS) facility manufacture intermediates, starting and regulatory starting materials, speciality chemicals in commercial quantities and a variety of other products for pharmaceutical and non-pharmaceutical applications.

PRODUCTION UNIT - 1

- Copper lined: 1,000L
- Glass lined: 2,000L; 2x2,500L; 2x3,000L; 4x4,000L; 2x6,300L
- Stainless steel: 4,000L
- Paddle dryer: 1,000L
- Centrifuges: 2x1,000mm; 2x1,250mm

PRODUCTION UNIT - 2

- Glass lined: 500L; 2,000L; 3x2,500L; 3,000L; 10x6,300L; 2x8,800L; 10,000L; 12,500L
- Stainless steel: 2,000L; 2,500L; 8,800 L
- Filter-driers:
  - Comber: 4m²
  - Delta: 3m²
- Double cone dryer
- Centrifuges: 4x1,000mm; 2x1,250mm

PRODUCTION UNIT - 3

- Stainless steel: 2x2,500L

LARGE SCALE MANUFACTURING FACILITY

HYDROGENATION UNIT *

- Stainless steel: 100L, (10 bar); 500L, (10 bar); 1,000L, (6 bar)
- 3,000 L stainless steel reactor for dissolution and work-up
- Buss-SMS LB01100-type film evaporator

METATHESIS UNIT **

- Glass line: 6,300L; 2,500L
- Destillation/ rectification columns:
  - Stainless steel: 2x500mm
  - Glass line, Stainless steel: 350mm
  - Glass line, Stainless steel, Graphite: 150mm

HYDROXYETHYLATION UNIT ***

- Stainless steel: 3,700L
- Glass line: 6,300L; 3,000L

PACKAGING UNIT

- OLSA paddle dryer: 1m³
- Tray dryer: 2m³



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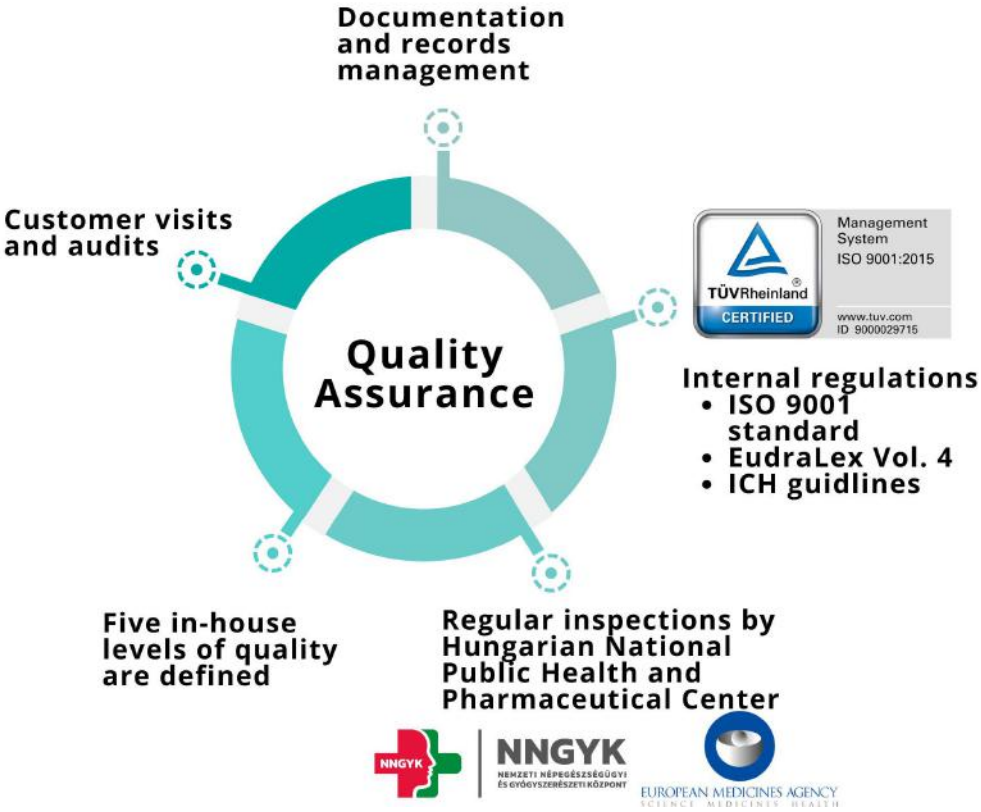
QUALITY ASSURANCE

At SONEAS Chemicals Ltd., (Uquifa Group member) all manufacturing procedures are carried out according to ISO 9001 standard in-line with our comprehensive quality management strategy. Besides that, at SONEAS Illatos Site we are following the cGMP regulations (the principles described in EudraLexVol. 4 and ICH guidelines) as well.

Our Quality Management System focuses on management of documentation and records, manufacturing procedures including material and laboratory controls, training, change control, out of specification (OOS), corrective and preventive actions (CAPA) and deviation management. SONEAS Illatos Site is regularty inspected by NNGYK, the Hungarian National Public Health and Pharmaceutical Center, member of the European Medicines Agency (EMA).



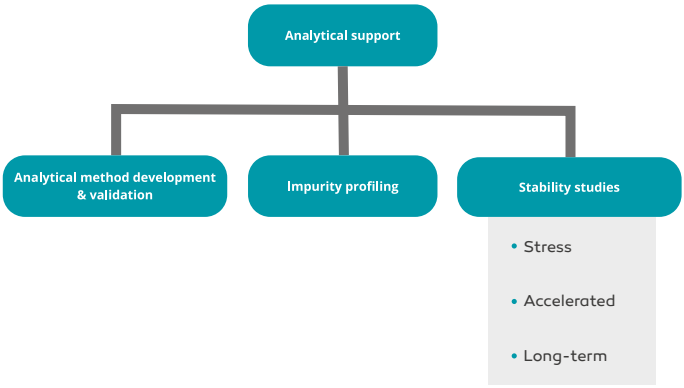
Five in-house levels of quality are defined. The level applied to a project is determined by several factors relating to the intended use of the product to be made. Along with the clinical development phase of the API, it is important to identify whether the compound given is a starting material, late or key intermediate or API. Each piece of manufacturing equipment is cleaned according to multilevel procedures of the chosen level and special requests of our customers.
Customer visits and audits are welcome. We are ready to provide detailed information about our Quality Management System during visits and audits.

Our policy of continuous investment in our employees and facilities and the improvement of our procedures combined with successful regulatory inspections have resulted in our company becoming an approved manufacturer of APIs from preclinical to commercial supply.
We are committed to complying with ISO 9001 standard at all Soneas Sites and with cGMP regulations at Soneas Illatos Site, to understanding the requirements of our customers and to providing high quality services for each phase of a project.

QUALITY CONTROL - ANALYTICAL SUPPORT

Our Quality Control Department utilizes a wide variety of analytical techniques to analyze and characterize intermediates, and final products. The evaluation of raw materials is an important starting point in ensuring final product integrity.

Production support is provided through in-process and intermediate testing, and rigorous final product release testing is undertaken. Our fully qualified analytical laboratories at our Pilot, GMP plant comply with cGMP standards. Additionally, stability testing and degradation studies are performed following ICH Q1A (R2) guidelines.



Our services include full analytical provision for regulatory filing purposes, including method development, validation, and reference standard qualification.

Soneas Chemicals continues to invest in additional analytical capability to support our growing synthetic capacity.

Analytical equipments

- Fully qualified cGMP analytical laboratory
- DSC
- FT-IR spectrophotometer
- UV-VIS spectrophotometer
- Flash chromatograph
- GC (headspace sampler)
- Titrators, Karl Fisher titrators
- Sulphated Ash
- Differencial scanning calorimeter
- Polarimeter
- LC-MS
- HPLC (Corona detectors)
- NMR Spectrometer (Bruker 500MHz Ultrashield)
- Power XRD
- UHPLC
- Stability chamber
- ICP-OES

HYDROGENATION

Catalytic hydrogenation is a versatile technology applicable to numerous synthetic transformations. Therefore, hydrogenation is routinely encountered in drug substance synthesis.

SONEAS Chemicals Ltd., (Uquifa Group member) has vast experience in developing hydrogenation processes using heterogeneous catalysis and operates this technology up to commercial scale. Our development team has a wide range of laboratory scale hydrogenators available for process development, optimization and scale up purposes. For subsequent scale up we have extensive large scale hydrogenation capacity.

Equipment

Reactor Capacity	Pressure Rating	Material of construction
100 L	10 bar	Stainless steel
500 L	10 bar	Stainless steel
1000 L	6 bar	Stainless steel

Supporting equipment's

- 3,000 L stainless steel reactor for dissolution and work-up
- Buss-SMS LB01100-type film evaporator

Flexible delivery model

A flexible delivery model enables clients to work closely with our technical teams. Our teams are preparing detailed regular updates followed by telephone conferences and detailed development reports to ensure transparency during the work and supporting the most efficient way to make decisions together with the partner even during the project.

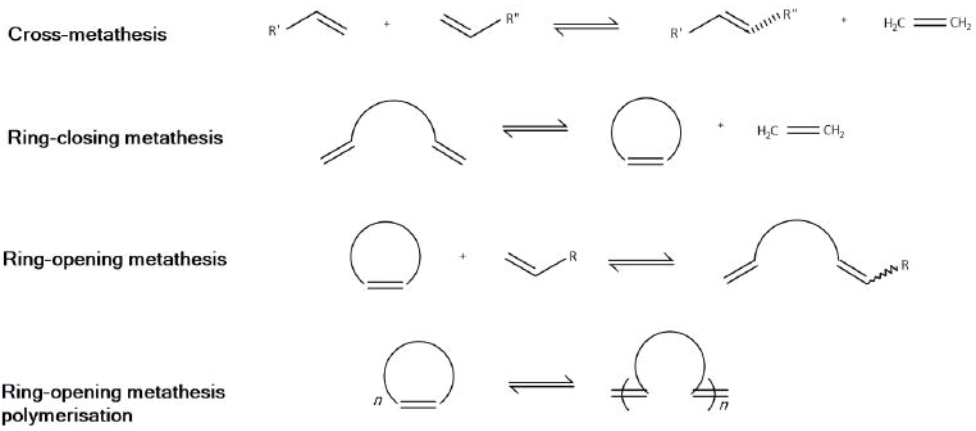
Our clients can choose from:

- Full-time equivalent (FTE), for laboratory development
- Fee-for-service/Fixed Fee (FFS)
- Time and Materials (T&M)

business models whichever fits their requirements better.

METATHESIS

Olefin metathesis is an important catalytic reaction that is perfect for making carbon-carbon bonds and building molecules. Carbon-carbon double bonds are simultaneously broken and re-formed as the reaction progresses, along with a substituent exchange, ring closing, ring opening, or polymerization. This essential family of reactions now makes a wide range of small-, medium-, and large-ring carbo- and heterocycles and a variety of acyclic unsaturated compounds. These reactions need catalysts.

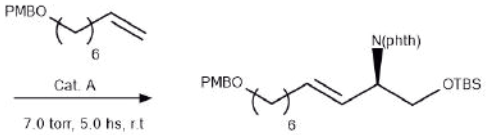


The molybdenum (Mo) and tungsten (W) catalysts that represent a new generation of metathesis catalysts are based on the breakthrough scientific research of the two founders, Amir H. Hoveyda, Richard R. Schrock, co-winner of the 2005 Nobel Prize in Chemistry. Presently these are the most popular metathesis catalysts.

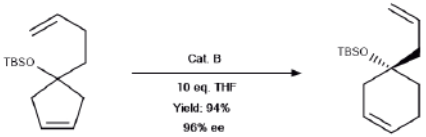
Mo and W catalysts are particularly efficient and valuable catalysts in various selective transformations (including regio-, stereo- and enantioselective/asymmetric metathesis reactions) of industrial interest. From relatively simple intermediates to complex natural products synthesis, those catalysts can be widely used.

The types of reactions, that can be carried out using different Mo and W based catalysts, are the following:

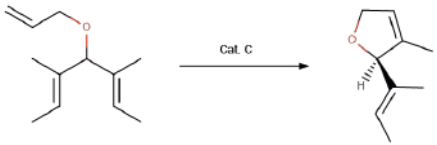
Z-selective metathesis reactions



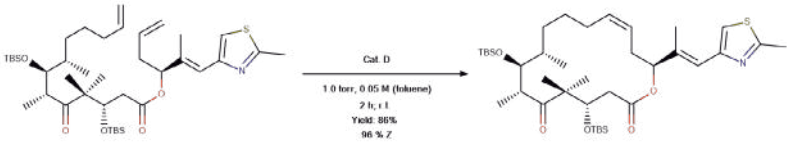
Enantioselective Metathesis Reaction



Asymmetric Ring-Closing Metathesis (RCM)



Z-selective catalytic ring-closing metathesis (RCM) reactions



SONEAS Chemicals Ltd., chemistry team can perform metathesis reaction in laboratory scale, scale up and perform multi tone scale.

Reactors

Reactor Capacity	Material of construction
6,300 L	Glass line
2,500 L	Glass line

Destillation / rectification columns

Column diameter	Material of construction
500 mm	Stainless steel
500 mm	Stainless steel
350 mm	Glass line, Stainless steel
150 mm	Glass line, Stainless steel, Graphite

Flexible delivery model

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Our clients can choose from:

- Full-time equivalent (FTE) (mid or long term), for laboratory development
- Fee-for-service/Fixed Fee (FFS)
- Time and Materials (T&M)

business models whichever fits their requirements better.

ETHYLENE AND PROPYLENE OXIDE CHEMISTRY CAPABILITIES

Hydroxyethylation and hydroxypropylation are versatile technology applicable to numerous synthetic transformations. Therefore, hydroxyethylation and hydroxypropylation are routinely encountered in drug substance synthesis.

SONEAS Chemicals Ltd., has vast experience in developing hydroxyethylation and hydroxypropylation processes and operates this technology up to commercial scale. Our development team has a wide range of laboratory scale hydroxyethylation and hydroxypropylation available for process development, optimization and scale up purposes. For subsequent scale up we have extensive large scale hydroxyethylation and hydroxypropylation capacity.

Equipment

Reactor Capacity	Material of construction
3700 L	Stainless steel
6300 L	Glass line
3000 L	Glass line

Supporting equipment's

- Ethylene/Propylene oxide treatment system

Flexible delivery model

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Our clients can choose from:

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- Fee-for-service/Fixed Fee (FFS)
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business models whichever fits their requirements better.

CONTENTS

R&D Laboratories:
Berlini utca 47- 49., 1045 Budapest, Hungary

Pilot, GMP Plant, Headquarters:
Illatos út 33., 1097 Budapest, Hungary

Large Scale Manufacturing Site:
Bányalég utca 47-59., 1225 Budapest, Hungary

www.soneas.com
sales@soneas.com