SEQENS

Synthèse des principes actifs : une stratégie de relocalisation en Europe par l'innovation

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Section 1

SEQENS

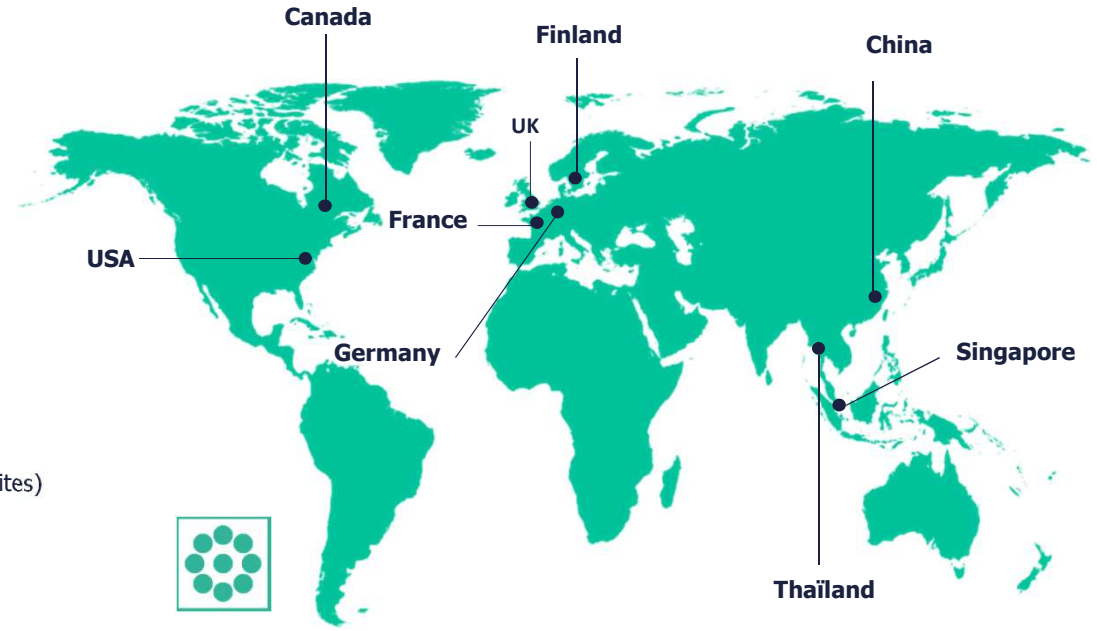
At a Glance

Global leader in small molecules API and specialty ingredients development and manufacturing

3,200
Employee

€1.0bn
Revenue

1000+
Clients



24
manufacturing sites (12 cGMP sites)

7 R&D centers
250 Research scientists & experts (120 PhDs)

2 main activities supported by transverse technologies, R&D capabilities and global assets

~70 % Pharmaceutical Solutions

- APIs and intermediates development and manufacturing
- Pharma solvents, hygiene & disinfectants solutions

Serving large, medium, small pharmacos, emerging pharma, biotechs, CDMOs, finechems

~30 % Specialty Ingredients

- Custom-specialties development and manufacturing

Supplies the most demanding industries: Cosmetics, Electronics, Lubricants additives

Strong R&D platform

- R&D centers of excellence in Europe and North America
- Technical engineering team with superior GMP knowledge based in Ecully (France)

Unique suite of solutions

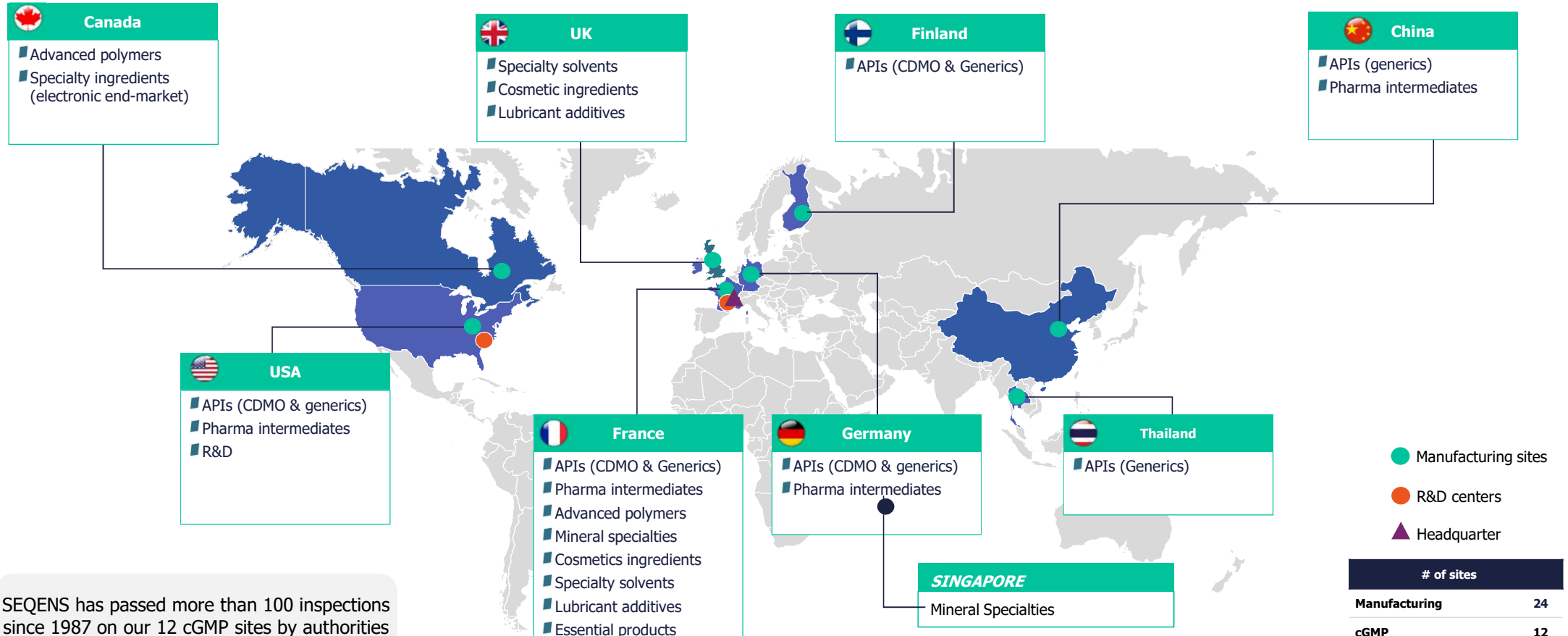
- Broad range of technologies spanning all our businesses
- Ability to manufacture most complex molecules
- Technical expertise from pre-clinical to Commercial

Global assets

- Worldwide footprint in Europe, North America and Asia
- Flexible facilities to manufacture complex molecules
- Supported by competitive facilities for intermediates and large-scale APIs

% de l'EBITDA

Global network of assets on 3 continents committed to development and manufacturing excellence



# of sites	
Manufacturing	**24**
cGMP	**12**
R&D	**7**

SEQENS has passed more than 100 inspections since 1987 on our 12 cGMP sites by authorities from all continents

Comprehensive global R&D platform with unique scientific skills combining a continuum of expertise (c.10% of group workforce)

Our R&D centers

North America

Boston (USA)

R&D center dedicated to early phase projects

- **Lab Surface: 2,000 sqm**
- **5 Kilo-lab suites**
- **1 Pilot Plant**

Montreal (Canada)

Electronics

- **1 Kilo-lab suite**

Europe

SEQENS 'Lab

Paris (FR)

Flagship R&D center

- **Lab Surface: 5,000 sqm**
- **3 Kilo-lab suites**
- **2 cGMP pilot plants**

Aramon (FR)

Drug Delivery polymers

Lahr (GE)

Accelerated R&D / Industrialization center

- **Lab Surface: 700 sqm**
- **3 Kilo-lab suites**

Middlesbrough (UK)

Custom + Cosmetics

proteus

Nîmes (FR)

Biocatalysis

- **Lab Surface: 1,000 sqm**
- **1 Kilo-lab (fermentation)**
- **Robotic platform**

Pharma

Specialty Ingredients

7 R&D centers of excellence in Europe and in North America

250 research scientists & experts (c.10% of group workforce), **120 PhDs**

Supported by **a Technical Engineering team with superior GMP knowledge** in Lyon (France)

Section 2

Flow chemistry

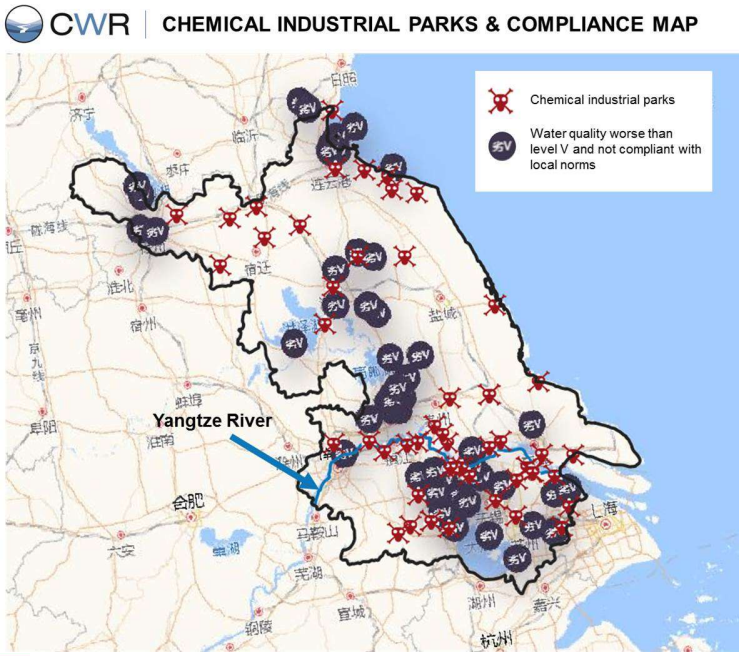
One of the main advantages of Flow Chemistry is linked to safety management – example of China…

On 21st March 2019, a major explosion occurred at a chemical plant in Chenjiagang Chemical Industry Park, Chenjiagang, Jiangsu, China

-> **78 people were killed and 617 injured**

Tianjiayi Chemical produces organic chemicals (pesticides, fertilizer), including some highly flammable compounds

- Park has since been shut down by the Jiangsu govt after which chemical material futures prices rose notably
- Jiangsu is a major chemicals producer but most industrial parks are either in water stressed or often flooded areas; the explosion happened despite many inspections



<u>Immediate decision by government:</u>

- Reduce the number of chemical enterprises to 2,000 by 2020, and 1,000 by 2022;
- Reduce the number of chemical industrial parks to 20;
- Stop production at chemical enterprises not fulfilling related safety/environmental norms; and
- Prohibit new projects on pesticides/medicines/dye intermediates

Chinese government have "forced" company to move to continuous process -> HSE notation from 1 to 4 and if 3 or 4, batch production is forbidden…

Main part of Corning's business is now in China !!

Integrate hazardous chemistry is a key element for the reshoring of strategic medicine

IMPACTS on

Attractiveness	✔
Competitiveness	✔
Quality standards	

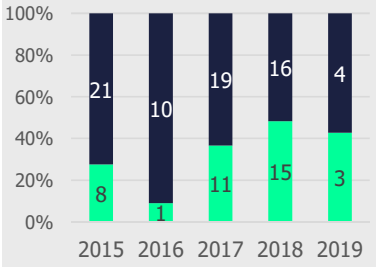
"*Almost 65% of APIs requires at least one nitration step in the whole process.*" Continuous flow nitration in miniaturized devices, Amol A. Kulkarni, 2014

"*Between 15% to 20% of all medicines and agrochemicals on the market contain at least one fluorine atom in their structure*" R. Antunes

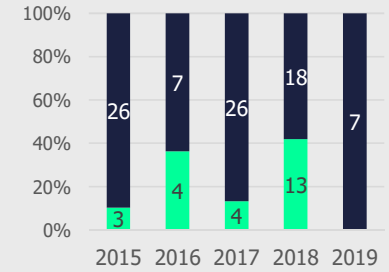
Nitration and Fluorination reactions are both quoted as strategic for us and our clients due to the production situation in Asia and good candidates for flow chemistry

Attractiveness gain: SEQENS integrated on nitration and fluorination RSMs and steps

FDA approved small molecules with a nitration step

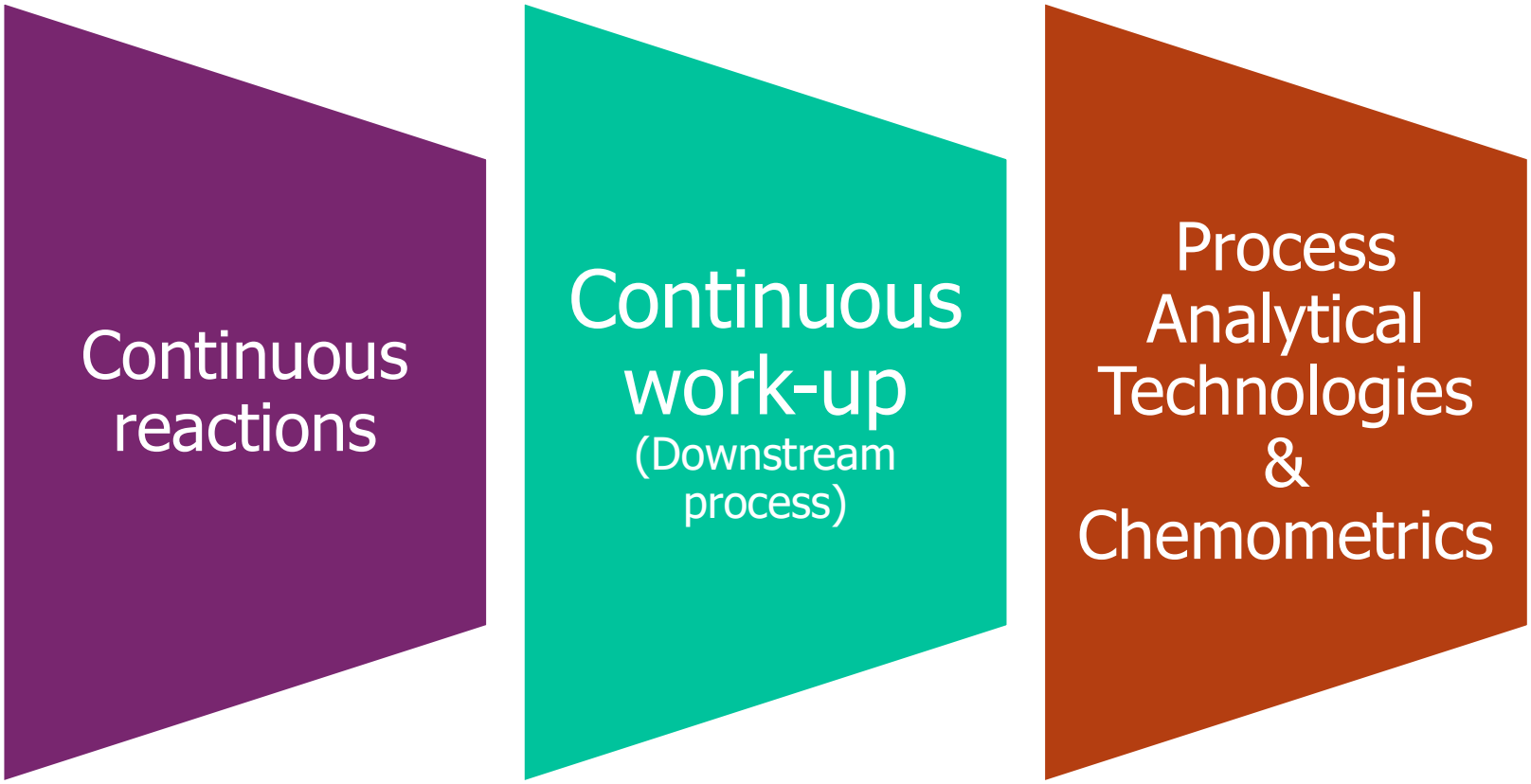


FDA approved small molecules with a fluorination step



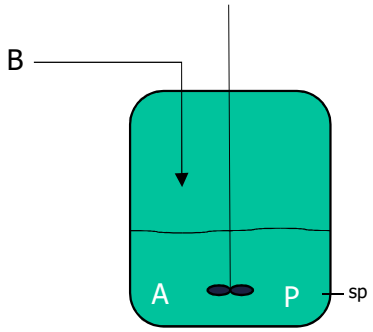
Already seen as a GMP intermediate player, SEQENS could integrate strategic intermediates that depend on nitration and fluorination

What is flow chemistry ?

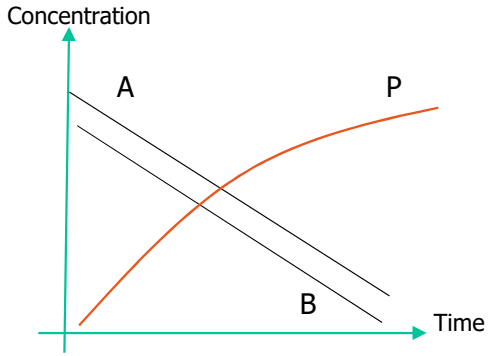


Batch vs Continuous reaction: basic concept

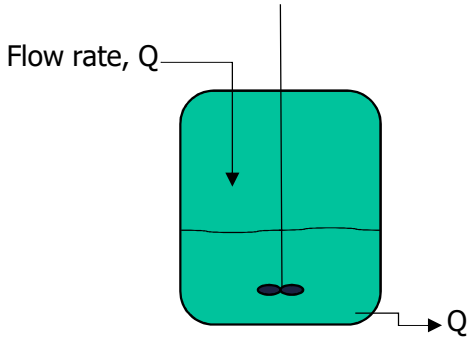
Batch reactor



KEY REACTION PARAMETER
Reaction time t
Reaction rate k
Concentration, P,T,
Mixing



Continuous Stirred tank reactor (CSTR)



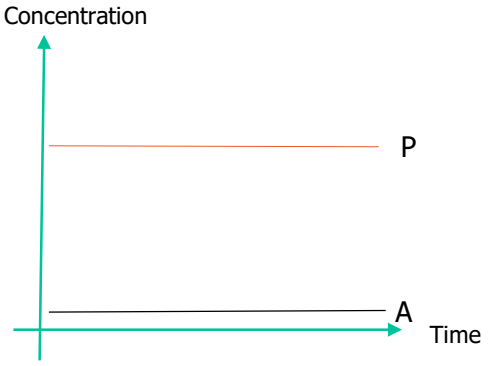
Residence time *t*
Reaction rate *k*

Continuous reaction key differences:

- Concentration of each species *vs* time
- Notion of Chemistry & Process (flow rates ratio, pumps,…)

Plug Flow reactor

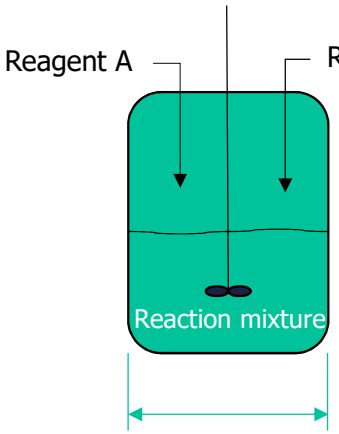
KEY REACTION PARAMETER
Residence time *t*
Reaction rate *k*
Molarity, T, P



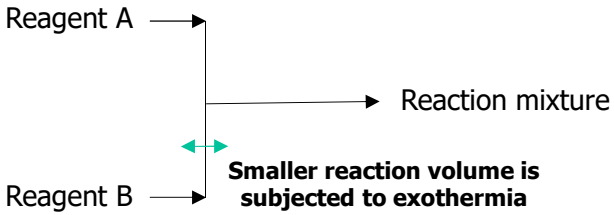
Flow Chemistry can allow both safer and more efficient processes

Definition: Flow chemistry (continuous process or continuous flow chemistry) begins with two or more streams of different reactants pumped at specific flow rates into a **single chamber, tube, or microreactor**.
A reaction takes place, and the stream containing the product is collected at the outlet.

SAFETY ASPECT



All the volume is subjected to exothermia



Smaller reaction volume is subjected to exothermia

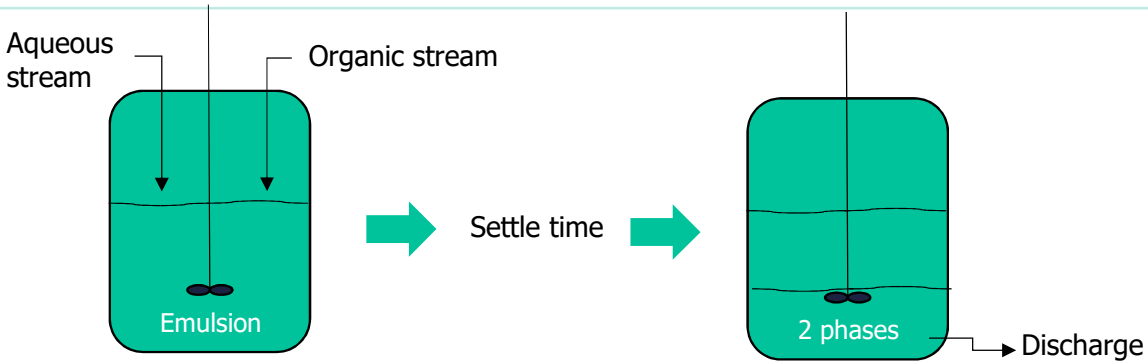
One example: Uniqsis coil reactors for homogenous reactions

SELECTIVITY ASPECT

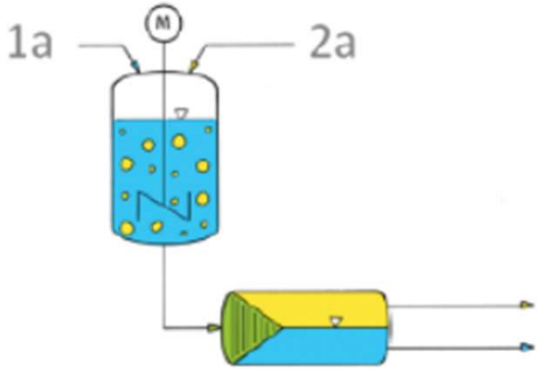
Narrow Residence time distribution so less impurities

Commercial scale

Flow technology is also applied for work-up : helps to free reactors capacities
Example of continuous flow extraction



Batch extraction



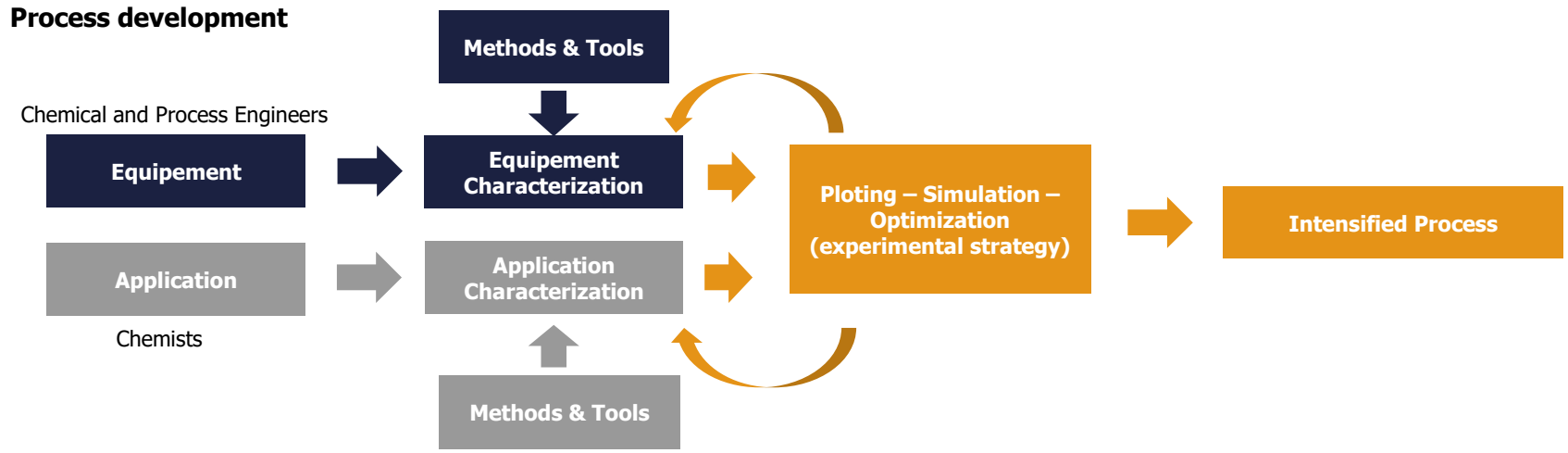
Mixer settler

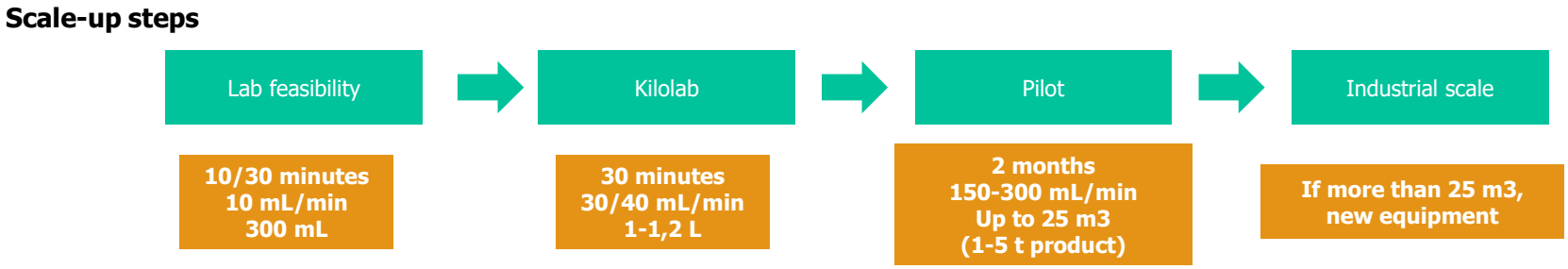
Continuous flow extraction advantages:

- Time savings
- Equipment availability savings

Requirements: Basic data (equilibrium, solubility, kinetics, …)

Development requires equipment and application characterization
In some cases, Flow Chemistry allows a safer/faster scale-up

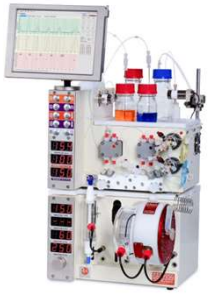




Process Analytical Technologies (PAT) coupled with Chemometrics expertise generate a large amount of data for process optimization

Continuous flow reactor

P, T
Flowrates



On-line analysis
Spectral technologies, Chromatography…

Concentrations
Kinetics

Data fusion
and
Chemometrics / Statistical Data treatment

Multivariate Curve Resolution - Asymmetric Least Squares (MCR-ALS)

PLS (Partial Least square regression)

Improved Design Of Experiment
(10s – 100s experimental points)
-
Quality By Design

The main advantages of Flow Chemistry are linked to sustainability (Economic, Environmental and Social impact)

ADVANTAGES OF FLOW CHEMISTRY

- Better temperature and exothemic control
- Reaction conditions not possible in batch
- Lower reaction volume and safer handling
- Narrow residence time distribution: less impurities
- Scale up issues are minimized
- Reaction time can be reduced (P, T)
- Often coupled with in line analytical control
- Smaller equipment and lay-out
- Cost effective

Key advantages	Why?	Impact for Seqens	Positive impact for our customer
Safety	Low reaction volume No accumulation Steady-state conditions	Dangerous chemistry could be done safely: exothermic and/or fast reactions CSR: employee's safety	- Environmental (risk decreased) - CSR: responsible and reliable supplier Secure sourcing (less sourcing required) in EU
Productivity	No washings between batches Easy automation Continuous separations	More capacity usage	- Production costs - QC (less batch failure)
Multi-steps reaction	Continuous process	No / Less storage of instable product	- Reliability of delivery
Reaction selectivity	Rapid diffusion mixing (vs slow diffusion in large vessel), narrow residence time distribution	- Potentially less purification needed - OPEX	- Competitivity (Production costs as Yield increase) - QA/RA constrain (less impurities)
Constant production quality	Potentially larger "batch" size	Less analysis	- Reliable and constant quality
Reduce wastes	Less washings Less impurities	Waste treatment (OPEX)	- Environmental
Footprint	Smaller size of equipment	CAPEX/project investment	- Project investment (in case of co-investment)

Preconceived ideas

- Flow Chemistry is a lab academic "toy"
  - **Lonza already used it since 2003 and since 2006 at industrial scale**
  - **Seqens used it since 2018 at lab scale.**

- Flow Chemistry is only for small scale reaction
  - **No, Flow Chemistry doesn't mean only micro-reactors and small scale product**
    Coil reactor or NiTech reactors are suitable for Flow Chemistry > 100s t/year can be envisaged
    Many industrial large scale process already exist and are continuous

- Flow Chemistry require complex equipments
  - **No, a "simple" pipe (coil) can be also used as a continuous reactor in some cases**

- All reactions can be done by Flow Chemistry
  - **No, Flow Chemistry is not a miracle technology**
  - Solid/Liquid reaction are difficult to manage (solid transportation) => still, there is a high potential with continuous cristallization to be investigated at a later stage

- One Flow Chem equipment can do all chemistries
  - **No, Flow Chemistry is not a single equipment but various technologies exists for various chemistry**

- If reaction is continuous, everything must be continuous
  - **No, we can combine continuous reaction and batch work-up or batch reaction and continuous work-up!**

Flow Chemistry at Seqens: a key R&D and industrial asset for optimal process design & chemistry « reshoring »

Continuous reactions
Nitration
Halogenation
Fluoration
Hydrogenation

Continuous work-up (Downstream process)

Process Analytical Technologies & Chemometrics

A sustainable approach

- Increased temperature control & reduced reaction volume
  - ➡ **safe handling of exothermic chemistry** (nitration…)
- Better residence time control
  - ➡ **Higher selectivity & optimal product quality**
- Improved downstream process & better capacity usage
  - ➡ overall **economics improvement**
- Reduced scale-up steps & risks
- Technology **promoted by FDA**

Multi-disciplinary expertise

- **Long-term experience** in continuous pharma reactions and separations
  - Ex: Salicylic acid, solvents separations and recycling…
- A dedicated task force combining **process, chemistry & chemometrics**

- A toolbox for data acquisition & process design
- Robust development methodology based on DoE and QbD, allowing **optimal technology choice**

- Scale-up from lab to pilot & multi-tons industrial scale within Seqens EU-based CDMO facilities, for **GMP APIs, intermediates & pre-GMP RSM**

Pilot PCV - mid 2021
Capa : 2 kg/h
GMP (development only)

Production plant CTN – S1 2023
Capa : 1OO T/y
Non-GMP

Section 3

Nous rejoindre

SEQENS is led by permanent commitment to the society and the world

SEQENS has established a comprehensive sustainable development strategy which relies on:
Sustainable development policy at corporate and business units' levels

- The implementation of a common sustainable development framework, based on 4 axis and 14 commitments) and a relevant management system and organization
- The definition and monitoring of key performance and progress indicators with clear objectives
- The implementation of specific action plans with efficient follow-up to ensure objectives are met
- A network of site managers coordinated by the group Industrial department
- An annual reporting to our shareholders

These 14 commitments are clearly aligned with Seqens CSR priorities:

PUBLIC ENGAGEMENTS

Responsible Care®
OUR COMMITMENT TO SUSTAINABILITY

THE GLOBAL COMPACT
WE SUPPORT

SEQENS is supported by a Scientific Advisory Board with recognised personalities who help guide the group's innovation strategy

- **Missions of the Scientific Council of Seqens**
  - Stimulate Seqens' Research & Development activities by proposing innovative lines of work.
  - Ensure a technological watch in order to provide recommendations on the group's innovation strategy.
  - Accelerate and secure development programmes by critically reviewing their scientific content.
  - Support Seqens' scientific press releases.
- **External and internal members of the Scientific Council of Seqens**

President

Bernard Meunier
Former president & Member of the Academy of Sciences

Janine Cossy
ESPCI

Gilles Auffret

Philippe Catroux

Christophe Gourdon
ENSIACET

Pierre Luzeau
CEO

Jean-Louis Martin
Industrial and Human Resources Director

Christophe Eychenne-Baron
R&D Director

Gérard Guillamot
Scientific Director

Frédéric Schab
Innovation Director and Secretary of the Scientific Council

Dominique Audoux
Technical Director

SEQENS and the French Academy of Sciences

Since 2017, Seqens and the French Academy of Sciences implemented a partnership with the "Seqens prize." This award targets the field of "therapeutic chemistry and/or pharmacochemistry related to the mechanisms of chemical drugs." It honors an innovation, a breakthrough or a new approach in the field of small synthetic molecules with therapeutic value. This prize is awarded to a scientist working in a public or private French laboratory.

2017

Géraldine MASSON
November 21st, 2017
2nd class Research Director at the CNRS, at the **Institut de Chimie des Substances Naturelles** of Gif-sur-Yvette. Geraldine Masson received the "SEQENS Prize" for her work on **new and effective methods in the field of catalysis, mainly organic.**
See the video:

2018

Julien NICOLAS
October 16th, 2018
Research Director at the CNRS at **the Institut Galien Paris-Sud.** He received the "SEQENS Prize" for his outstanding contributions to the design of **new Polymers & materials for biomedical applications.**
See the video

2019

Sébastien LECOMMANDOUX
October 18th, 2019
Director of the LCPO Organic Polymer Chemistry Laboratory and professor **at Ecole Nationale Supérieure de Chimie, Biologie et Physique of Bordeaux INP**, who receives the Seqens Prize for his research on **therapeutic polymers.** See the video

2020

Ruxandra GREF
November 24th, 2020
CNRS Research Director, CNRS Silver Medal in 2019, **was awarded for her work on nanomedicines for the treatment of infections and cancer.** She was among the pioneers to propose, in this field, nanoparticles not recognized by the immune system, and organic-inorganic hybrids. **She has also developed nanoparticles with intrinsic properties to fight disease**, acting in synergy with incorporated drugs.

NOUS REJOINDRE…

Chez Seqens nous avons la conviction que nos talents sont le moteur de nos réussites et nous offrons des perspectives à la hauteur de vos ambitions :

- Des opportunités internationales, des missions stimulantes et la possibilité de grandir au sein de nos équipes de plus de 300 scientifiques, ingénieurs et experts.
- Chaque année nous recrutons des **alternants** et **jeunes diplômés** sur nos sites de production. (Ingénieur Chimiste, Ingénieur Méthodes, Ingénieur Projet & Procédés, Chargé(e) de missions en Innovation, Ingénieur R&D…)

Découvrez nos offres sur notre site internet :
https://www.seqens.com/fr/emplois/

Et sur JobTeaser :
https://www.jobteaser.com/fr/companies/seqens/job-offers

Et retrouvez nous sur : Seqens channel Seqens_group Seqens

EMPLOYEUR DE CHOIX ENGAGEMENT JEUNES 2021

SEQENS

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