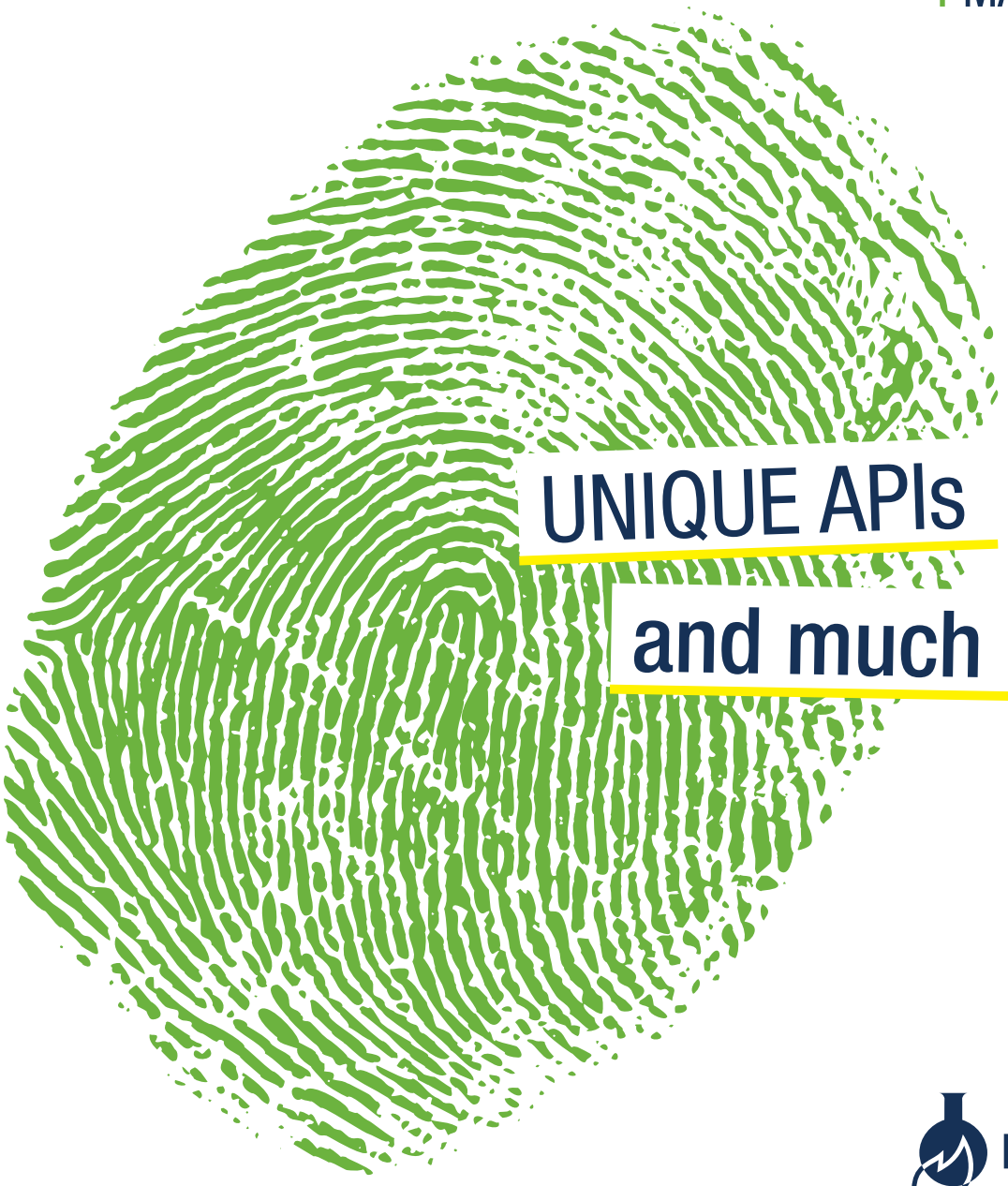
CONTRACT
MANUFACTURING



UNIQUE APIs

and much more...

medichem

MEDICHEM IN A FLASH

- Medichem S.A. is a privately owned company, based in Barcelona, founded in 1972
- Our activities:
  - Active Pharmaceutical Ingredients
  - Chlorhexidine, world leaders
  - Contract Manufacturing
- Process development and manufacture of non-infringing, cGMP Active Pharmaceutical Ingredients (APIs)
- FDA inspected since 1985 - Both Celrà and Malta plants are no “Form 483”
- ISO 9001 & ISO 14001 certified
- Manufacturing sites: Girona (25,000 m^2) and Malta (8,800 m^2)
- Medichem Manufacturing (Malta) Ltd. founded in 2005
- Nanjing Medichem Biopharmaceutical Development Co. Ltd. (NRC) founded in 2012
- Team of over 250 highly professional, committed and devoted people
- Full respect for the environment at all our sites

PROJECT MANAGEMENT

- Today, the drug development processes are under a high pressure regarding time and money. Our Project Management team and its availability allow us the possibility of accompanying our customers and understand in particular their needs and requirements to reduce both the costs and the time to bring their product to the market.
- The Project Manager will represent the relevant functions of our organization to guarantee the timely delivery of project’s requirements/the success of the projects.

CONFIDENTIALITY

- Before your experts and our technical staff get into a deeper conversation and exchange technical information regarding the project, **a Confidentiality Agreement is signed in order to protect your interests.**

RELIABLE PARTNER & TIMINGS

- **More than 40 years of experience in the API industry** make us as a reliable partner. The Project Management system ensures on time delivery of the project.

LEGAL, PATENT & REGULATORY SUPPORT

QUALITY ASSURANCE

Quality Assurance with Medichem is a fundamental and important aspect in our cGMP compliant production of APIs. Our quality system management and up to date manufacturing techniques **guarantee the consistent high quality of production through strict cGMP compliance,** being ISO 9001 certified since 1996.

- As Medichem applies cGMP concepts and guidance to every manufacture step, both on the production sites and in its research centres, **our personnel is continuously trained on the highest standards of cGMP** and therefore ensures constant cGMP compliance. Medichem respects the environment as it has its own waste water treatment plant, being ISO 14001 certified.

INSPECTION HISTORY

- Medichem has a long and **successful history of inspections** by clients and Regulatory Authorities from all over the world.

- Medichem's plants have received periodic **US FDA inspections with satisfactory results** since 1985 and **both plants are no "Form 483".** Last USFDA inspection in Malta was conducted in April 2012 and in Spain in September 2012.

GENERAL OVERVIEW

LEGAL, PATENT & REGULATORY SUPPORT

REGULATORY AFFAIRS

- Medichem has experience in submitting DMFs and Certificates of Suitability (CEP) to **National Regulatory Authorities in the US, Europe, Canada, Korea, Russia, Ukraine, Mexico and Japan** among others**.**

- Our regulatory department also constantly interfaces with decision-making bodies in the API field such as Health Authorities and industry association groups in the European Union and the US.

- Beyond the preparation of regulatory documentation, Medichem is ready to **support the customer from Investigational New Drug (IND), through New Drug Application (NDA) to market supply.**

IP AND LEGAL

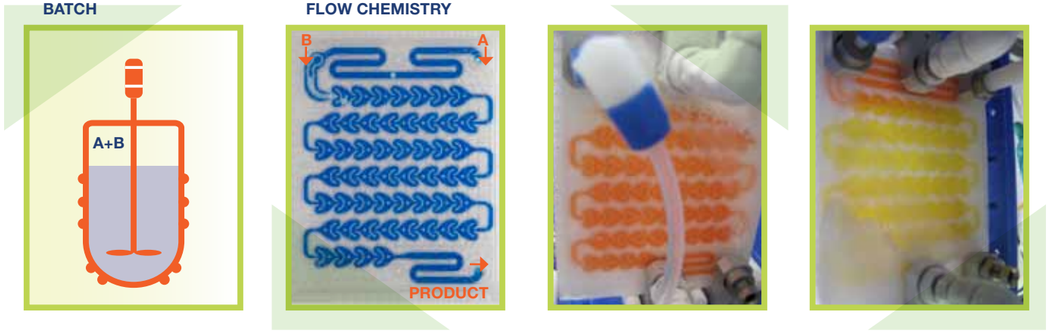
- Our policy is to design manufacturing processes that **do not interfere with any intellectual property.**

- Our experienced patent department together with an in-house legal affairs team are capable to **support you throughout the entire drug development process** and can assist you with their expertise in a special area.

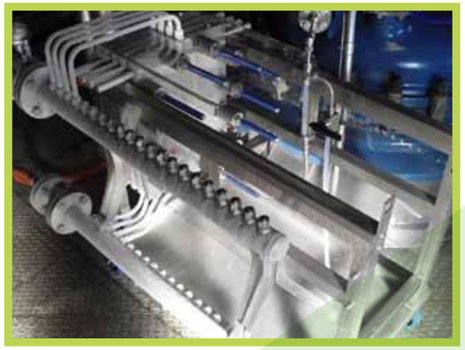
- Medichem's **confidentiality agreements** do strongly respect the intellectual property and thus protect your interests.

WHAT IS FLOW CHEMISTRY?

- Organic synthesis is generally conducted in a **batch mode.**
- The interest in Flow Chemistry has increased due to **economic and environmental pressures.**
- Medichem offers **this new technology in its Spanish Plant** in order to respond to this demand.
- Chemistry in Flow is one of the **newest technologies.**
- In a continuous flow system the chemical reaction is carried out with a continuous supply of starting materials. In others words, **two flows are pumped into a microreactor and they start reacting as soon as they mix.**



BENEFITS OF FLOW CHEMISTRY



Chemistry in flow provides exquisite control over reaction conditions:

- BETTER HEAT TRANSFER
- BETTER MIXING EFFICIENCY
- SCALE-UP ISSUES ARE MINIMIZED
- IMPROVED REACTION SELECTIVITY
- FASTER REACTIONS

Flow chemistry also allows:

- RAPID REACTION OPTIMIZATION
- PERFORMING DANGEROUS CHEMISTRY
- REACTIONS UNDER PRESSURE
- CRYOGENIC REACTIONS, LOW TEMPERATURE CHEMISTRY

WHY MEDICHEM MALTA?

- Malta offers many advantages for the pharmaceutical industry because of its **patent history and framework.**
- As a consequence of this, many companies in the pharmaceutical industry have established operations in Malta over the last decade. They can **take advantage of the absence of number of patents** which were not registered in Malta and thus develop and launch product batches to be the first on the market immediately when a patent expires in a given country.
- Medichem and Combino Pharm (its sister company) can benefit from this UNIQUE patent situation and are able to do **R&D work and produce generics drugs in advance of patent expiry.**
- Medichem can offer **unique non infringing processes and products** from its US-FDA (US Food and Drug Administration) inspected plant in Malta.
- This legal / IP framework allows us to offer a **first-to-market opportunity** to our customers worldwide.

IP SITUATION ADVANTAGE

OUR TECHNICAL INFRAESTRUCTURE & EQUIPMENT

PILOT PLANT

Our Pilot Plant is used for process validation, process scale-up and also for some small scale pilot production for lots ranging from 5 to 50 Kg.

QTY	Equipment description
	Reactors:
	Total number: **4**
	Total capacity: **1.5 m³**
2	Glass-lined
2	Stainless-steel
	Filters:
1	Stainless-steel centrifuge

PRODUCTION PLANT

Our Production Plant is a multipurpose facility that is fully equipped for the synthesis of APIs.

Reaction capacity 9 m^3 easily expandable to 30 m^3.

QTY	Equipment description	Reaction Capacity
	Reactors & tanks:	
	Total number: **3**	
	Total capacity: **9 m³**	
2	Glass-lined	**6.5 m³**
1	Stainless-steel	**2.5 m³**
	Filters:	
1	Stainless steel centrifuge	

THE FINISHING AREA

The Finishing Area is where the last steps of the process are performed.

It is equipped with HVAC, air filtration, differential pressure, air locks, etc. to prevent cross-contamination.

QTY	Equipment description
	Dryers:
2	Stainless-steel vacuum dryer
	Milling and sieving equipment:
1	Pin mill
1	Centrifuge sift
	Blenders:
1	Stainless-steel V blender
1	Stainless-steel drum blender

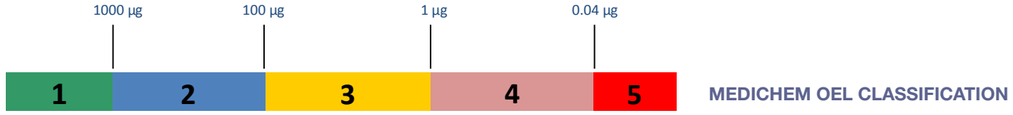
PRODUCTION FACILITY

- With the increasing interest in High Potency Active Pharmaceutical Ingredients and with over 40 years of experience in the API industry, Medichem understands the market needs and takes the challenge of **producing products like High Potency with all their specific potent characteristics** in its Malta Plant.

- Thanks to our HPAI modular laboratory and our highly skilled team, we are able to **offer High Potency APIs from process development to large-scale manufacturing** in a cGMP and FDA inspected environment.

- Our HPAI modular Laboratory capacity allow us to **produce till Class 4 High Potency APIs with OEL down to 40 ng/m^3.**

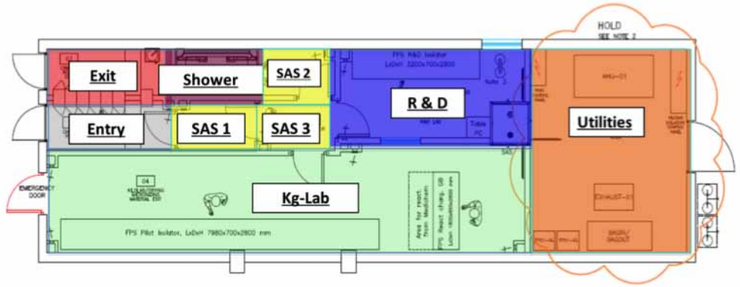
- **We also offer:**
  - R&D facilities
  - GMP Kilolab including:
    - Reactors
    - Filter
    - Dryer
    - Milling &/or micronizing



OUR TECHNICAL INFRAESTRUCTURE & EQUIPMENT

Our Production Plant is a multipurpose facility that is fully equipped for the synthesis of High Potency APIs.

QTY	Equipment
2	Reactors Total capacity: **30L**
1	Filter
1	Dryer
1	Mill
1	Micronizer



RESEARCH & DEVELOPMENT

- **Nanjing Medichem Biopharmaceutical Development Co. Ltd. (NRC)** was set up in August 2012 in Nanjing, PRC. NRC's main focus is the development of generic APIs.
- The R&D department is composed by a **team of 15 professional and dedicated chemists,** and equipped with state-of-art analytical equipments.
- **New synthetic routes are evaluated,** and reference standards of APIs and intermediates are prepared and characterized in R&D Department.
- **NRC TASKS:**
  - Design of synthetic routes
  - Optimization and development of existing processes
  - Synthesization and characterization of impurities
  - Development of analytical methods

MEDICHEM CHINA

KILOLAB

- GMP Kilolab designed to meet **FDA Quality requirements**
- It also **validates R&D process** and provides intermediates for R&D needs
- Hydrogenation capability from **100 mL to 5 L**

STRATEGIC PARTNER

- In 2012, Medichem has established a **partnership with a Chinese manufacturing company** which is currently supplying intermediates and APIs.
- This partnership will allow Medichem to offer to its customers the **manufacturing of intermediates and APIs in a low cost environment.**
- The Production Plant is **fully equipped for the synthesis of intermediates and APIs.**

QTY		Equipment
56	Currently	**Reactors:** 80.5 m^3 total reaction capacity **Operation capabilities:** · Temperature range: -20 ~ 200°C · Pressure range: -0.1 ~ 0.4 Pa
18	IQ2014	**Reaction capacity expansion to 240 m^3**
	Future (2014-15)	**Hydrogenation and special reactions workshop**

OUR CAPABILITIES

▶ MEDICHEM SPAIN

Set up: 1980

Location: Celrà Industrial Estate, located in Girona province, about 100 Km from Barcelona and 65 Km from the French border.

Total surface area:
25,000 m^2

Total reaction capacity:
150 m^3, easily expandable to 250 m^3

▶ MEDICHEM MALTA

Set up: 2005

Location: Hal Far Industrial Estate, located in the south of the island, about 3 Km from Malta International Airport.

Total surface area:
8,000 m^2

Total reaction capacity:
10.5 m^3, easily expandable to 30 m^3

▶ MEDICHEM CHINA

RESEARCH AND DEVELOPMENT CENTER IN CHINA NANJING MEDICHEM BIOPHARMACEUTICAL DEVELOPMENT CO. LTD. (NRC)

Set up: 2012

Location: Nanjing, PR China Nanjing Zijin Chemical Industry Park, located in Jiangsu province, about 1000 Km from Beijing and 300 Km from Shanghai.

Total surface area:
1,500 m^2

NRC's main focus is the development of generic APIs.

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