SUSTAINABLE DEVELOPMENT

SANOFI QUALITY STANDARDS

QUALITY & REGULATORY SUPPORT

WORLDWIDE COMMERCIAL NETWORK

IN HOUSE API MANUFACTURING

CEPiA SALES

BIOTECH & CHEMICAL SUPPLY

INTERMEDIATES & APIs
Within the Industrial Affairs Division of Sanofi, CEPIA (Commercial & External Partnership, Industrial Affairs) is an organization **fully dedicated to third party activities**. One of the key activities of CEPIA is to offer a **broad range of innovative solutions** including:

- Intermediates and Active Pharmaceutical Ingredients (APIs) supply
- Custom Synthesis & API Contract Manufacturing
- Pharma Contract Manufacturing

**CEPIA SALES AT A GLANCE**

- Around **200** APIs on catalogue...
- ...sold in more than **80** countries...
- ...manufactured in **16** Sanofi chemical & biotech sites
- **200** CEPIA collaborators close to you

**CEPIA Sales** is a Sanofi activity dedicated to manufacturing and supply of a broad range of Biotech & Chemical Intermediates and APIs available on a catalogue basis. By employing Sanofi exhaustive industrial capabilities and other resources expected of large pharma, CEPIA offers high quality pharmaceutical intermediates and APIs:

- From traditional chemistry to biotechnology
- From small scale to large scale production
- Various grades of physical quality of APIs (sieving, milling, micronization...)
- Knowledge & expertise sharing from Sanofi network
- Sustainable Development and Ethical Chart
- From Sanofi sites regularly inspected by international Health Authorities with success
- Regulatory & Quality standards
- Regulatory & Quality support with dedicated team

> CEPIA guarantees **REACH** compliance.
Five chemical and biotech Business Units at your service. Each Business Unit focuses on a specific expertise and offers dedicated Quality & Regulatory support.
FACILITIES AND TECHNOLOGIES

FERMENTATION & BIOTECHNOLOGY
- Vitamin B12 & derivatives
- Antibiotics & Antituberculosis
- Packaging customization
- Customized product grade

SYNTHESIS
- A portfolio of more than 60 APIs covering various therapeutic areas
- 12 Sanofi manufacturing sites involved to support this broad offer
- From mass production (Metamizol, Ketoprofen) to medium and small scale production

CORTICOSTEROIDS & HORMONES
- 30 corticosteroids manufactured on a ton scale
- Sustainable process for a long term presence
- Fully back integrated manufacturing
- Jet milling expertise

OPiates & Opioids (Francopía)
- From poppy seeds to APIs
- World number 1 Codeine producer & exporter
- 30 Narcotics & Antagonists in portfolio
- 80 years experience in Alkaloid extraction

PROSTAGLANDINS
- Supply of natural & modified Prostaglandins APIs
- Continuous evolution of product portfolio
- Process development and scale-up of new chemical entities
- Multipurpose production lines, batch sizes up to 10 Kg API
- cGMP compliance for all operations, with proven record of seamless regular FDA inspections and customer audits

EUROPE FOCUS

- Frankfurt
- Vitry
- Elbeuf
- Mourenx
- Vertolaye
- Frankfurt
- Prague
- Ujpest
- Garessio
- Sisteron
- Aramon
- Brindisi
- Ankleshwar
- Jurong
Sanofi Biotechnology expertise is based on a **large volume fermentation** technology used to produce complex APIs in **Europe** in a backward integrated manner, i.e. without intermediates from various origins. Sanofi inherited its **know-how** in fermentation from its roots in Roussel Uclaf, Rhône-Poulenc, Gruppo Lepetit and Sanofi.

Production of **vitamin B12** started in the 1960’s with Roussel Uclaf and has expanded with Rhône-Poulenc. This strong industrial background makes CEPIA today one of the world’s leading suppliers and Sanofi the **only Western producer** of vitamin B12.

CEPIA industrial footprint is also characterized by an integrated production of **antituberculosis and antibiotics** which started 40 years ago with Gruppo Lepetit. Specific **biotechnology projects** are also developed. Thanks to in-house expertise and capacity in bio-manufacturing, high tech APIs are produced through recombinant technologies, cell culture, protein engineering...

**1960**
Vitamin B12 production in Romainville site (Roussel-Uclaf), France

**1966**
Vitamin B12 production in Saint-Aubin-lès-Elbeuf site (Rhône-Poulenc), France

**1972**
Rifampicin (Rifadin®) production in Brindisi site (Gruppo Lepetit), Italy

**1987**
Teicoplanin (Targocid®) production in Brindisi site (Gruppo Lepetit), Italy

**1995**
Deflazacort (Calcort®) production in Brindisi site (Hoechst Marion Roussel), Italy

**2007**
Artesunate (Coarsucam®) production in Garessio site (Sanofi), Italy

**2012**
Launch of the semi-synthetic Artemisinin production in Garessio site (Sanofi), Italy
BIOTECHNOLOGY INTEGRATED OFFER

A comprehensive offer from production by fermentation to delivery of APIs
2 major poles dedicated to integrated productions of traditional compounds.
The total industrial fermentation capacity is more than 6,000 m³ with a fully computerized control system and state-of-the-art downstream equipment (filtration, concentration, crystallization, chromatography...).

VITAMIN B12 & DERIVATIVES
2 sites in France:
• Saint-Aubin-lès-Elbeuf
• Aramon

ANTIBIOTICS & ANTITUBERCULOSIS
1 site in Italy:
• Brindisi

BIOTECHNOLOGY
Purification of recombinant proteins in a controlled environment as well as biochemical synthesis.
2 sites focused on specific biotech projects:
• Aramon / France
• Garessio / Italy

All sites are certified FDA, cGMP, ISO 14001 and benefit from regional and specialized certifications such as ANSM (France), AIFA (Italy), ANVISA (Brazil), KFDA (Korea)...
Packaging customization
- Customized number of batches to minimize quality control and avoid extra costs
- Specific certifications (e.g. Hallal, Kosher)
- Customized product grades (particle size distribution, impurity profile…)

15 APIs out of which 9 are suitable for injection

More than 280 customers in 62 countries

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HISTORY OF CHINOIN

The tradition of chemical and pharmaceutical academic sciences in Hungary provided a stable background for the foundation of several pharmaceutical companies. Amongst these, Chinoin’s more than hundred year tradition is unique. Chinoin has been the fountain of innovation since its establishment in 1910, owning numerous patents worldwide and providing new drugs to patients and high-tech solutions for its partners. The dedication to the discovery of new therapeutical fields resulted in an intense research and development activity on Prostaglandins in the late 1970s. Chinoin was acquired by Sanofi in the mid 1990s. The Prostaglandin activity is managed by a dedicated "Prostaglandins Business Unit" within CEPIA.

Until today, the Prostaglandin Business Unit has successfully developed and industrialized several synthesis routes for natural and modified Prostaglandins. Thanks to the high level of expertise and diverse portfolio, we are now supplying high quality Prostaglandin APIs in 5 continents, in partnership with more than 50 companies.

PROSTAGLANDIN EXPERTISE

1980
PGF2 α production

1998
PGE1 & PGE2 production

Since 2000
Leading generic Prostaglandin supplier of Japan
APCs: Beraprost Sodium and Limaprost Alfadex

Since 2005
Development of pulmonary arterial hypertension (PAH) portfolio
APCs: Epoprostenol, Iloprost, Treprostinil

Since 2008
Development of Ophthalmology portfolio
APCs: Latanoprost, Travoprost, Bimatoprost

2012
17 Prostaglandin APIs available from regular production
THE PROSTAGLANDIN OFFER

For many years, we have produced one of the most complicated entities nature has ever created with industrial state-of-the-art chemistry. Our production is based on our own intermediate tree, so we are totally broad from external sources or suppliers.

STRENGTHS

- Anticipation of market needs by continuous overview of worldwide marketed Prostaglandin APIs status
- High level service of individual customer needs
- Flexible, quick supply of broad range of Prostaglandin APIs
- Worldwide marketed APIs
- Broad experience in laboratory, pilot plant and commercial scale manufacturing
- Multipurpose production lines, batch sizes up to 10 Kg API
- Equipment sizes from 2 L up to 4000 L
- All operations are cGMP compliant, with proven record of seamless regular FDA inspections and customer audits
- Quick and flexible development and scale-up of Prostaglandin production technologies
A COMPLETE OFFER

- Supply of natural and modified Prostaglandin APIs from regular production
- Flexible contractual relations: custom synthesis, exclusive agreements, capacity contracts
- Process development and scale-up of new chemical entities
- Furnishing impurities, degradation products, working standards to support partners in analytical activities
- Constant high quality, in-house specifications above monograph levels
- Regulatory process support, DMF filing

SERVICES

The team of Prostaglandin Business Unit is committed to meet the growing demand of API market with:

- Trained staff of 120, including 45 professionals with Masters and Ph.D. degrees
- Multiple manufacturing and service areas providing flexibility and short lead-time
- Development department specialized in experimental synthesis and scale-up
- Analytical department highly skilled in method development, validation and stability studies
- Quality Control department ensuring the high quality of the products
- Marketing & Sales department with decades of routine in the field of international trade
- Continuous evolution of product portfolio, containing most of the worldwide known Prostaglandin APIs

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Sanofi is a resulting combination of mergers and acquisitions of famous historical pharmaceutical companies that all contributed to the richness of our intermediates & APIs.

**Rhône-Poulenc** was the first company to synthetize the antipsychotic drug Chlorpromazine, which served as the prototype for the Phenothiazines class of drugs including Levomepromazine and Promethazine.

**Sanofi** is the originator of the well known antiepileptic sodium Valproate and Valproic acid.

**Hoechst** on top of its expertise in Insulins, developed the anti-pain pharmaceuticals Metamizole and brought to the market the local anaesthetic Articaine HCl.

**Synthelabo** launched the famous hypnotic drug Zolpidem.

All the intermediates & APIs proposed by the dedicated «Business Unit Synthesis» within CEpiA (more than 60) are still successfully marketed by Sanofi as Drug Products all around the world. All CEpiA customers benefit from the same highest quality levels, industrial know-how & expertise of the Sanofi Group.
PHENOTHIAZINES
A wide range inherited from Rhône-Poulenc R&D

- For both Oral and Injectable applications
- Regulatory documentation for EU, US, JP
- Efficient packaging to protect products from light & humidity.

METAMIZOLE
Sanofi, the sole European API manufacturer fully integrated

- 2 different salts offered: Na and Mg
- Large volumes production
- Several types of particle sizes adapted to various dosage forms (liquids, semi solids and solids)
- Several packagings from cardboard folder boxes to Big Bags

ANALGESICS & NSAIDs*

- Ketoprofen

METABOLIC DISORDERS

- Ciprofibrate

ANAESTHETICS

- Fexofenadine

ANTI-ALLERGICS

- Cromoglycate

SYSTEMIC & CARDIOVASCULAR

- Furosemide

OTHERS

- Ramipril

* NSAIDs: nonsteroidal anti-inflammatory drugs
HUMAN RECOMBINANT INSULIN FOR CELLS CULTURE

Get the benefit of one of the most important Insulins manufacturer to maximize the performance of your mammalian cells lines

- Same Insulin as the one used as API
- Reproducible and consistent production
- Regulatory compliance (EU and US Pharmacopoeias, US DMF)
- Animal Free product
- Various packagings/ from 50g to several kg.
- Directly from manufacturer to customer with full control of the cold chain (-20°C)

ARTICAINE HCl

CEPiA: the leader of the Articaine API market

- A dental local anaesthetics highly efficient with limited side effects thanks to its additional ester group
- A full regulatory documentation to support worldwide registration
- Very low iron content specifications, suitable for a use in combination with epinephrine
- Manufactured in a Sanofi dedicated and high capacity FDA approved workshop

More than 60 APIs & intermediates
12 manufacturing sites in 8 countries
35 CEP
25 USDMF
15 JMF

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Founded in 1932, Francopia is now one of the major international players in opiates production. Being a world leader in the supply of narcotic active pharmaceutical ingredients, Francopia is at the forefront of the global fight against pain.

A TEAM OF
200
INTERNAL & EXTERNAL
OPiates EXPERTS ON HAND

80 YEARS
IN ALKALOID EXTRACTION

40 YEARS
OF INDUSTRIAL SCALE
POPPY
CULTIVATION IN FRANCE

30 YEARS
OF EXPORT EXPERTISE
A FULLY INTEGRATED ACTIVITY
FROM POPPY SEEDS TO ACTIVE PHARMACEUTICAL INGREDIENTS

1 - AGRONOMIC RESEARCH
Developing new poppy breeding programs thereby creating new plant varieties

2 - AGRICULTURAL PRODUCTION
Cultivating over 11,000 hectares of poppy fields in France

3 - INDUSTRIAL PRODUCTION
Manufacturing close to 30 intermediates and active pharmaceutical ingredients

4 - DISTRIBUTION
Exportation of narcotic materials to over 80 different countries

Guaranteeing safe, reliable traceability products at every stage of our operation

TAILOR-MADE SOLUTIONS DRIVEN BY CUSTOMERS’ NEEDS...

- Custom built services (e.g.: packaging, labelling, sieving, milling, micronization, specific analysis)
- Operational responsiveness and reliability in the supply chain
- A fully dedicated team (commercial, supply chain, quality and regulatory)

... Aiming at developing and maintaining long term partnerships
Francopia is a world leader in the production of a wide range of active pharmaceutical ingredients used in the treatment of both moderate and severe pain. Long years of experience have allowed Francopia to develop a range of 30 APIs from traditional molecules to the very latest in synthetic opioids, all complying with highest worldwide standard (15 CEP, 4 USDMF...).

**Pain management**

- **Moderate pain Level 2***
  - Codeine, Dihydrocodeine
  - Ethylmorphine

- **Severe pain Level 3***
  - Morphine, Hydromorphone

**Other Treatments**

- **Apomorphine**
  - (Parkinson’s Disease/ Erectile dysfunction)

- **Naloxone**
  - Naltrexone
  - (antidote, management of alcohol dependence)

- **Methadone**
  - Levomethadone
  - (Anti-addictive)

**MORPHINE DERIVATIVES**

- Codeine, Dihydrocodeine
- Ethylmorphine

**THEBAINE DERIVATIVES**

- Buprenorphine
- Nalbuphine

**SYNTHETIC OPIOIDS**

- Tramadol
- Fentanyl

* World Health Organization pain ladder

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Over the years, corticotherapy has become the reference treatment for inflammation and allergies. More recently, corticosteroids have been used in combination with anti-cancer drugs.

The 1950’s were the starting point for the development and commercialization of the principal corticosteroids.

Roussel Uclaf (part of Sanofi Group) has been a pioneer in this field and has been providing the medical community with corticosteroids in various forms and doses.

Since that time and still today, Sanofi, one of the world leaders in biotechnology, keeps on offering innovative processes with fully back integrated manufacturing.

Today CEPiA offers a large product portfolio of around 30 corticosteroids manufactured on a ton scale.
Over 700 people experienced in corticosteroids

- About 300 vessels (reactors, spin dryers, ...)
- 7 chemical workshops + 1 finishing workshop (powder homogenization and micronization)
- More than 70 APIs and hundreds of isolated intermediates
- Successfully inspected by Health Authorities (French ANSM, FDA, PMDA, KFDA, GMED)
- HSE and sustainable development committed (ISO 14001 certified)
ANTI-INFLAMMATORY

Non fluorinated glucocorticoids and derivatives:
hydrocortisone, prednisone, prednisolone,
methylprednisolone to treat inflammatory diseases,
allergy and asthma

Fluorinated glucocorticoids and derivatives:
dexamethasone, triamcinolone, fluorometholone
for the same indication at lower dosage and with
a longer onset of action

For various formulations: creams, tablets, injectables,
nasal sprays and inhalers

ANTI-HYPERTENSIVES

Mineralocorticoids:
spironolactone, canrenone
and potassium canrenoate
used as diuretics and blood pressure regulators

JET MILLING EXPERTISE

Center of expertise and industrialization
for Sanofi Group

Homogenization capacities from
one kg to one ton scales

A various range of particle size
distributions from one micrometer
to hundred micrometers

Class C / or class 10,000

Ability to handle up to OEB 4 level
products

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