High Quality & Reliable Services

cerbios
Switzerland

Who We Are

Cerbios-Pharma SA (CERBIOS) specializes in the development and manufacturing of chemical and biological APIs for its partners worldwide from highly regulated markets (USA, Europe, Japan) to BRICS countries.

Our Vision

To be a leading company in distinctive chemical and biological API products and services

Our Mission

To provide excellent services, helping our partners achieve their core business objectives

CERBIOS is a solid, privately held, self-financed company located in Switzerland. It provides its stakeholders with the highest quality standards through continuous improvements, investments and innovation.

Active since 1976, CERBIOS has continuously grown and gained expertise in the following areas: **Small Molecules** within the Chemical Division and **Large Molecules**, as well as Probiotics, within the Biological Division.

In addition, CERBIOS has not only developed its own products, but also provided to its partners exclusive contract manufacturing services for the development and manufacturing of New Chemical Entities (NCE) or New Biological Entities (NBE) for clinical trials, registration and commercial purposes.

Thanks to its technologies and long-term experience, CERBIOS is active in providing products and services mainly in the following therapeutic areas:

(1) Oncology
(2) Dermatology
(3) Respiratory
(4) Ophthalmology
(5) Gastrointestinal

Our long-term partners appreciate CERBIOS' stakeholders' values, the commitment to **communicate** in an open and constructive manner, as well as CERBIOS' **responsiveness** and rapid decision making to meet their particular needs. This approach is essential in order to meet our partners' fast changing requirements, as well as those of regulatory authorities in different countries or geographic areas.

With almost 40 years of expertise, dedication and success in serving the Pharmaceutical Industry worldwide, we are proud to continue to innovate with a long-term strategy and partnership approach.

Chemical Division
Products & Services

Biological Division
Products & Services

With long-term expertise in the development and industrial scale manufacturing of classical APIs (since 1982) and know-how in handling High Potency Active Ingredients (since 1993), CERBIOS is the ideal partner for your New Chemical Entity whether it be APIs or HPAIs for preclinical, clinical and commercial worldwide supplies. Over the past years, CERBIOS has invested in infrastructure and technologies to strengthen and extend its activities and services in the field of HPAIs, maintaining the two large-scale API manufacturing facilities at the highest quality standards.

Contract manufacturing services for APIs and HPAIs include:

- Chemical process development and scale-up
- Analytical methods development and validation
- Comprehensive R&D support
- Production of material from clinical trials to commercial supply
- Regulatory proficiency for international submission (including eCTD).

Key starting materials can be developed by CERBIOS R&D and transferred under a confidentiality agreement to selected, reliable and qualified European and/or Far Eastern manufacturers.

High Potency Active Ingredients (HPAIs) Development and Manufacturing

Our HPAIs facilities are designed to operate below 30 ng/m^3 OEL level (SafeBridge category 4). This allows the safe handling of highly-potent compounds of all categories including cytotoxic APIs. Thanks to an innovative concept, the multipurpose plant can also operate as a dedicated manufacturing unit. Through our latest investments CERBIOS has strengthened its technology platform by providing access to additional services in conjunction with the production of HPAIs.

Continuous Flow Technology

Continuous flow chemistry and its application in micro-reactor systems is available at the CERBIOS site to enable and unlock the potential of this technology for purposes ranging from R&D to the cGMP production of HPAIs.

Particle Engineering

Access to Supercritical Fluids technology leads to unparalleled control of API Solid State features. This technology not only provides narrow distribution of custom particle size from micro to nanoparticles, but also

(1) patentable new polymorphs

(2) crystal shape design and control

(3) improved solubility and bioavailability for BCS class II and IV APIs

(4) pre-mix/pre-formulation options within the process for both small molecules and biopharmaceuticals.

Delivery System for Topical and Injectable Applications

Based on a water-free liquid delivery system, AKVANO™ opens up a new dimension of topical administration. With its simple formulation and manufacturing abilities, as well as excellent cosmetic properties, this innovative technology will create new opportunities for effective and convenient treatments in the dermatological field because of its excellent incorporation of “difficult” drugs and ease of administration.

Preformulation

Not all Drug Product manufacturers are capable of handling HPAIs. With CERBIOS’ pre-formulation service, offered in conjunction with HPAIs manufacturing, this issue is solved since the potency of the Drug Substance is highly mitigated. This allows the preparation of the final dosage form to be carried out already at the source in our established Drug Product manufacturing sites.

Further Expansion

Space is currently available and ready for the introduction of an additional production line or even of an additional building in a relatively short period of time. This could be of particular interest for strong partnerships where the project starts with an initial co-investment for the establishment of a dedicated production line for our partner.

Chemical HPAI Services

CERBIOS is highly qualified in process development of new APIs and HPAIs for preclinical, clinical and commercial production

Characteristics of API Production Units:

- Two independent facilities in Switzerland for batches from 50 up to 300 KGs
- Total capacity of 17 m^3 with reactors ranging from 2'500 up to 5'000 liters
- Horizontal peeler centrifuges for product isolation
- 1x Bicon Dryer and 1x Conical Dryer

Characteristics of HPAI Production Units:

- Two plants :
  (1) up to 100 grams/batch
  (2) up to 2 KGs/batch (upgradable)
- One Kilolab for the manufacturing of non HPAI cGMP intermediates
- High Pressure Liquid Chromatography system
- Photo chemistry
- Continuous Flow Chemistry with microreactors
- Preformulation know-how

Chemical Division

CERBIOS offers a high quality tailor-made development program for biopharmaceuticals

Conjugates

- A great asset of CERBIOS is its synergy between the Biological and the Chemical Division, thereby encouraging the opportunity to develop and manufacture HPAI conjugates with recombinant proteins or antibodies

Biological Division

By working with recombinant DNA technology to manufacture monoclonal antibodies, antibody fragments or recombinant proteins, CERBIOS will provide you with a competent and flexible team to help you achieve your project timelines and quality objectives. From cloning to cGMP production, CERBIOS will meet your product development and manufacturing needs with mammalian expression systems based on CHO cells.

The full service platform typically includes:

Cell Line Development

If required, CERBIOS can carry out a stable expression of therapeutic recombinant proteins or monoclonal antibodies with high yield within approximately three months.

RCB Evaluation and Cell Banks Manufacturing

CERBIOS assesses and evaluates the RCB (Research Cell Bank) thoroughly to obtain a target biologic analytical/proof of concept sample and to submit a process development proposal/plan. In addition, CERBIOS provides Master Cell Banks (MCB) and Working Cell Banks (WCB) in full cGMP conditions and the related regulatory documentation.

Process Development Activities

To obtain reliable process industrialization, CERBIOS will optimize the cell culture fermentation, identify, test and verify the best process conditions for the upstream phase. Moreover, the downstream process will be optimized in order to obtain high quality, purity and yield. Finally, we will provide a process development report and analytical/proof-of-concept material suitable for formulation trials.

Manufacturing of First Engineering Batch

The process reproducibility is accurately tested and engineering batch material is provided for pharmacodynamic and pharmacokinetic studies. The material can also be used for Drug Product development and/or toxicology studies. Reference standard material is provided with Certificate of Analysis and release documents.

Manufacturing of cGMP Batches

GMP material is provided with all the documentation required for clinical trials both at process level and at analytical level, following the different clinical phases up to commercialization (depending on quantities needed). All the manufacturing phases are carried out in a “state-of-the-art” cGMP plant conceived and set up according to international standards (FDA, EMA, PMDA). Moreover, the cultivation media used by CERBIOS for its CHO platform are “state-of-the art”, serum-free, protein-free, antibiotic-free and free of any component of animal origin. These completely synthetic media may be adapted to the cell line and the protein to be expressed. This allows the further optimization of key parameters including productivity and yield. In addition, CERBIOS offers other important services such as the manufacturing of conjugates.

CERBIOS is specialized in high quality cGMP manufacturing of APIs and HPAIs for clinical and/or commercial supply in different therapeutic areas, from oncology to dermatology including respiratory and others.

By combining “state-of-the-art” infrastructures with innovative technology platforms, CERBIOS generates Intellectual Property that creates value for our partners.

Reduced Folates

Over the years, the expertise of the Chemical Division has turned CERBIOS into a world leading company in the field of Reduced Folates. These compounds, which are mainly used in the therapy of colorectal cancer as well as in the prevention and treatment of vitamin deficiencies, are sold to pharmaceutical companies worldwide, including highly regulated markets (Europe, USA and Japan). In the oncological field there are two main uses for Reduced Folates: (1) as antidotes to Folic Acid antagonists, such as Methotrexate (“rescue therapy”), and (2) as biochemical modulators enhancing the cytotoxic activity in well-known regimens (like FOLFOX and FOLFIRI), widely used therapies in the treatment of colorectal cancer. Another important use of Reduced Folates is in cases of Folate Deficiencies, which can typically occur under conditions such as malnutrition or malabsorption, after treatment with high doses of folate antagonists, or when increased intake is required as a result of pregnancy, lactation or malignancy. Folate Deficiency can cause birth defects such as split spine (spina bifida), megaloblastic anemia and some types of depression. In this area CERBIOS offers not only the largest product line for Pharmaceutical use, but also products for Nutraceutical use.

Vitamin D Derivatives

CERBIOS introduced the development, scale-up and commercial manufacturing of High Potency Active Ingredients (HPAIs), and in particular of Vitamin D Derivatives in 1993, and it has continued to grow and evolve ever since. Two key compounds, Calcitriol and Calcipotriol, are manufactured in our “state-of-the-art”, US-FDA-inspected facility, and have been used in commercial products for many years. Specific products for the Japanese market have also been successfully developed and launched. Extending the portfolio of this category of HPAIs and related derivatives, including innovation on new synthetic routes, chemical processes and polymorphs that could lead to improved bioavailability, is important for CERBIOS. It is thanks to this expertise and activity that CERBIOS has successfully provided some exclusive services for NCE in this area, which are available for third parties (see Chemical Services). The most recent additional activity in the area of Vitamin D Derivatives is the availability of pre-formulated products, providing our partners with a “diluted” HPAI that will dramatically reduce their need for containment while handling the product in the formulation phase. For those of our partners considering life-cycle-management, an innovative sprayable drug delivery system is now available to substitute creams and ointments. This modern alternative has successfully met clinical trial Phase I and IIa primary and secondary endpoints.

Future Products

CERBIOS is not only working on the expansion of its product pipeline in the therapeutic areas of historical presence, but also in the area of manufacturing expertise, mainly in the handling of HPAIs and in particular, products that have specific pharmacological activities at very low dosages (<0.1mg) or high containment requirements (Category 4 SafeBridge).

Therapeutic areas include:
(1) Dermatology
(2) Oncology
(3) Respiratory
(4) Ophthalmology
(5) CNS and others

CERBIOS APIs and HPAIs

A leading company with over 30 years of experience in Reduced Folates and 20 years handling and manufacturing Vitamin D Derivatives with highest containment levels

Reduced Folate

- Calcium Folinate
- Calcium Levofolinate
- 5-Methyl-tetrahydrofolic acid calcium salt
- (6S)-5-Methyl-tetrahydrofolic acid calcium salt
- Folinic acid
- Levofolinic acid
- Sodium Folinate
- Sodium Levofolinate

Vitamin D Derivatives

- Calcitriol
- Calcipotriol
- Several more under development

Other HPAIs

Please Contact us

Chemical Division

CERBIOS is considered to be a leading company worldwide in the field of pharmaceutical probiotics

Probiotic Manufacturing Capabilities

- Fermentation
- Microencapsulation
- Probiotic Active Ingredients
- Probiotic Intermediates
- Probiotic finished products such as hard gelatin caps in bottles

Biological Division

With more than 35 years' experience, CERBIOS is considered to be a leading company worldwide in the field of probiotic pharmaceuticals. The most important probiotic products produced by CERBIOS are based on its proprietary active ingredient *E. faecium SF68*® and are commercialized under different trademarks in countries all over the world.

Probiotic Pharmaceuticals

Production of probiotic pharmaceuticals is both a core competence as well as a core business of the Biological Division of CERBIOS. The products are manufactured in our facilities in Lugano and are supplied in different forms including:

- active ingredients
- intermediates
- finished products, such as hard gelatin caps in bottles.

CERBIOS' partners appreciate its high quality standards and insight into cGMP manufacturing of probiotics. Its expertise includes fermentation, drying and stabilization of living microorganisms.

Probiotic Feed Additives

The probiotic feed additives produced by CERBIOS are defined as microbial feed additives that stabilize the intestinal microflora. They are based on its proprietary probiotic active ingredient *E. faecium SF68*® (strain deposit E. faecium NCIMB 10415) and are sold under the trade names Cernivet® and Cylactin®. These products have been successfully used in broilers, calves and pigs for more than 35 years in many countries and in different climatic and rearing conditions. The pellettable product forms are the result of CERBIOS' specialized expertise in the field of microencapsulation. The protective microcapsules have been specially developed to improve process stability and to release the metabolically active SF68® once it reaches the gastrointestinal tract of the animals. The various formulations (microencapsulated and granulated) of the Cernivet® product range meet the requirements of the modern feed industry and have been developed for use in premixtures, milk replacers, water, mash feed and pelleted feed.

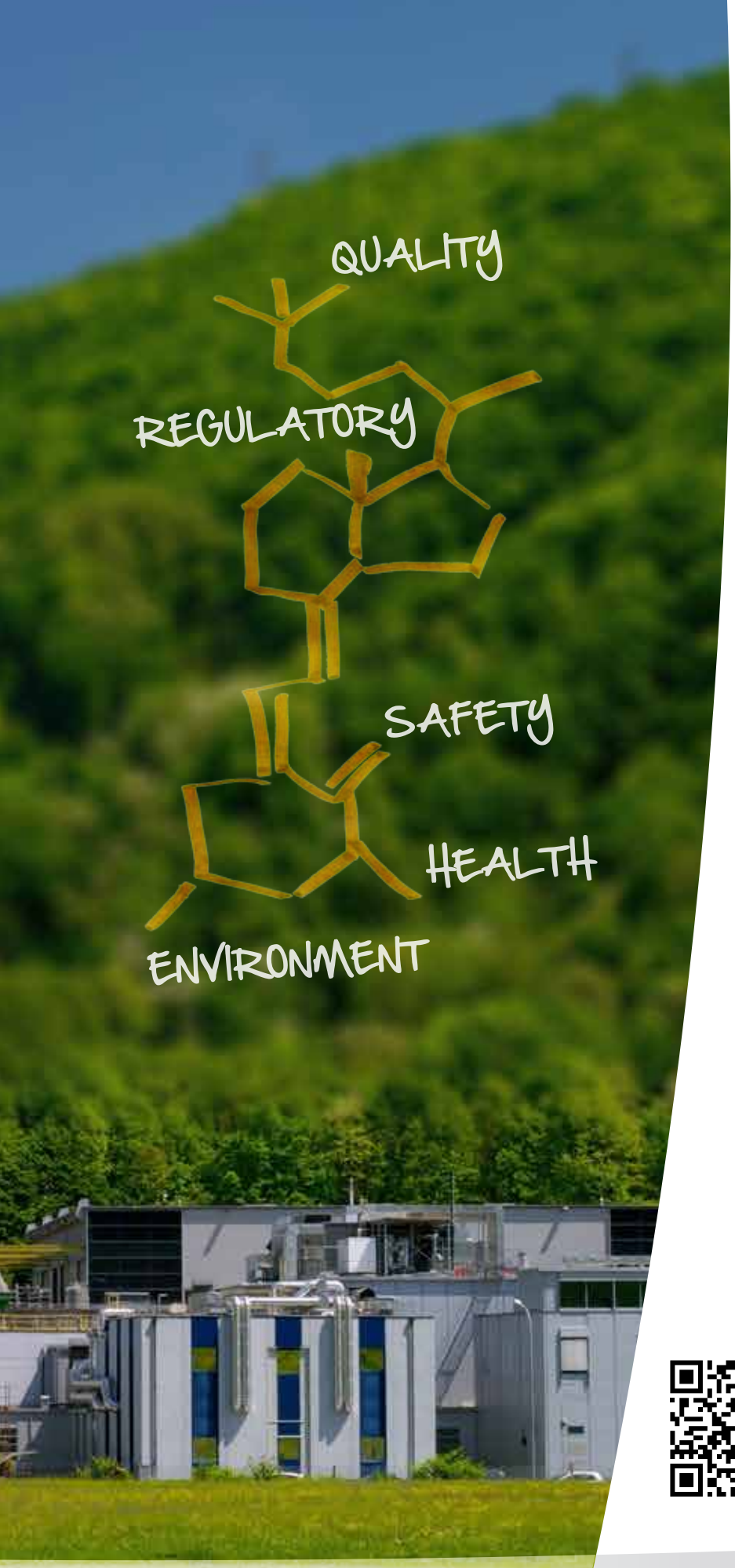
Contract Manufacturing Services

CERBIOS produces probiotic active ingredients of pharmaceutical quality as a third-party manufacturer for renowned global companies. The "full service" it provides, starts from the selection of raw materials through to manufacturing, quality control and the release of the API or the finished product.

This includes :

- Tech transfer
- Analytical development
- Medium optimization
- Preparation of Master & Working Cell Banks (MCB & WCB)
- Fermentation
- Biomass concentration
- Drying
- Formulation
- Validation & DRA documentation
- Finishing/packaging

Probiotics : Products and Services



CERBIOS supports its partners in their projects worldwide in full compliance with international standards (FDA, EMA, PMDA, OSHA, ECHA, ...)

SWISSMEDIC

Provides an internationally recognized cGMP certificate every two years

FDA

For products sold in the USA or under registration (successful inspections with no 483)

PMDA

First site accreditation in 2005, renewed in 2011. Several DMFs active and approved for APIs and HPAIs

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The aim of our Quality System is to maintain the highest quality standard for our production units, manufacturing processes and products, in accordance with the latest cGMP guidelines and requirements. An essential element of this process is the great care taken by the CERBIOS' HSE System in maintaining its workshops, equipment and procedures in order to prevent any accidents and injuries to operators and avoid potential environmental pollution by making a careful risk assessment for each product introduced in its plants.

Regulatory Support

CERBIOS has almost thirty years of experience and knowledge in successfully submitting DMFs for APIs and HPAIs to the major authorities worldwide. The submission of Type II DMFs to the US-FDA, DMFs or CEP documentation to regulatory authorities in Europe, and translated DMFs to the Japanese PMDA through CERBIOS' agents, are common practice. Services are available for our biotech partners that need this expertise in-house without the involvement of additional consultants.

Submissions can be made either on paper or electronically as eCTDs.

Health, Safety & Environment (HSE)

CERBIOS has developed and implemented an outstanding Management System to provide the framework and tools to manage evolving issues efficiently, while meeting high levels of HSE performance in addition to gaining the satisfaction of both our customers and regulatory authorities. With the support of external partners a structured approach is followed in the management of risks, based on design quality, risk assessment, and continuous training. Since CERBIOS handles HPAIs with very low OEL, SafeBridge Consultants have been chosen to challenge the system in order to confirm that there are no risks to our operators. The assessment has confirmed the highest containment level for CERBIOS: Category 4 (OEL < 10 ng/m^3) for both HPAI production units (up to 2 KGs/batch).

			CONTAINMENT CATEGORY			
	Plant	Capacity / Batch	1	2	3	4
	R&D	100s grams	✓	✓	✓	✓
API	Kilolab	< 5 KGs	✓	✓		
API	CERBIOS	10 - 80 KGs	✓	✓	(✓)	
API	GMT	10 - 200 KGs	✓	✓	(✓)	
HPAI	Small Scale	5 - 100 grams			✓	✓
HPAI	Large Scale	0.2 - 2 KGs			✓	✓
HPAI	Preformulation				✓	✓

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