CHIMIA 49 (1995) Nr. 5 (Mai)

Chimia 49 (1995) 132–133

ISSN 0009–4293

*Helsinn Chemicals SA**

Active Ingredients for the Pharmaceutical Industry

The contract manufacturing business is a bazaar of many different players. Purchase managers of pharmaceutical companies should, therefore, have a rich choice of suitable active ingredient manufacturers. Most of these manufacturers offer particular chemical technology as competitive edge. But on the other hand, nowadays active ingredient manufacturers have to comply with a highly regulated environment, not only with respect to staff and process safety and environmental issues but in particular with quality assurance and regulatory support underlying a constant price pressure. The competitive edge has shifted towards these accessory services, and those companies which will be able to survive and prosper with both their know-how and experience in chemical-technical know-how and in accessory services will be the strongest players on this market.

Helsinn Chemicals SA is a medium-sized manufacturer of bulk active and intermediates for the pharmaceutical industry. It is part of the *Helsinn* group, whose headquarters are located in Pazzallo-Lugano, southern Switzerland. The *Helsinn* group consists of six operational companies in Switzerland, Portugal, and Ireland, and its core business is the in-licensing, development and out-licensing of pharmaceutical specialities. At present *Helsinn*'s major products are Fentiazac Acid (antirheumatic, analgesic), Nimesulide (non-steroid anti-inflammatory), and Brodimoprim (antibacterial).

The production plant of *Helsinn Chemicals* is located in Biasca, southern Switzerland, since 1984. It was expanded in 1990 and now occupies 5000 m^2 of the 17000 m^2 site. The technological advanced, multi-purpose production facilities have a reaction capacity of *ca.* 50 m^3.

Besides collaborating with other companies in the group for the production of pharmaceutical compounds for captive use, *Helsinn Chemicals* is involved in contract manufacturing. It also offers a range of services, including the study and scale-up of manufacturing methods. *Helsinn Chemicals* is interested in developing long-term partner relationships with pharmaceutical companies seeking for active ingredient manufacturers able to provide a high technology standard in chemical synthesis and the relevant know-how in quality assurance and regulatory support.

From the very beginning *Helsinn Chemicals* has dedicated its efforts to the development of a refined quality assurance system for its active ingredients manufacturing programmes serving the *Helsinn* Group to safeguard high quality of the successful pharmaceutical products Fentiazac Acid, Nimesulide, and Brodimoprim.

The equipment available includes six stainless steel and eight glass-lined reactors, with individual volumes of 1–6.3 m^3, which are controlled by either electro-pneumatic or computerized systems. All the reactors are designed to operate at pressures from –1 to +6 bar and have a closed circuit heating/cooling system for temperatures ranging from –15 to +150°. Apparatus for fractional distillation and thin-layer evaporation is also available. A completely modernized pilot facility will be operative by summer 1995 serving as development plant as well as small production unit with reactors from 20 up to 250 l working under cGMP conditions.

Solid products may be isolated in one of four centrifuges, for lots up to 500 kg, with automatic inertisation and in an inox pressure filter, treatment facilities include vacuum dryers and granulators. The plant is FDA approved and has been GMP audited several times. It has also passed different individual audits carried out by various multinational chemical and pharmaceutical companies.

Since it went into operation in 1984, *Helsinn Chemicals* has developed and produced more than 60 products for customers around the world.

Development and production know-how focuses mainly on multistage synthesis, routinely using most of the common organic chemical reactions. The company has particular expertise in

- a modified method of the *Rosenmund* reduction for aromatic aldehydes
- *Grignard* reactions
- *Friedel-Crafts*
- pure enantiomer synthesis.

Another important part of process development is the consequent minimization of environmental impact, complying with the strict Swiss environmental legislation. Where possible, hazardous materials are substituted by compounds with less environmental impact. New processes are subjected to a rigorous risk assessment procedure before being scaled-up to industrial scale.

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In addition to these currently standardized features of a modern chemical pharmaceutical manufacturer, *Helsinn Chemicals* provides the support to work out the necessary documentation needed for product registration and makes available its considerable know-how in this field to its clients.

To conclude, the chemical composition and the medical indication of a product is determined by the client. The contract manufacturer has to comply with his technology otherwise he will not be able to enter a collaboration.

However, the quality level of the product and the services provided are in the hands of the contract manufacturer and can be offered at different levels determining the point of difference between the competitors:

- quality of the compound
- quality of reaction control
- quality of environmental compliance
- quality of project management
- quality of regulatory support

chemical purity, analysis method development
risk assessment
trying to achieve lowest impact on the environment already during process development and implementation
speed and precision of commercial and technical information
the ability to work out Drug Master Files and to help the client to bring the final product to the market

During its ten years of operation, *Helsinn Chemicals SA* has continuously improved its capacities at the above mentioned levels and uses its know-how and experience for the production of the active ingredients for the *Helsinn* group and for its contract manufacturing partners with the same engagement. Infrastructural improvements and a dedication to quality management will be the guidelines of *Helsinn Chemicals* also for the years ahead.

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*IBSA Institut Biochimique SA**

Established in 1945 by a group of Swiss biologists, *IBSA Institut Biochimique SA* with headquarters in Lugano-Massagno, celebrates this year its 50th anniversary of uninterrupted activity.

Founded with the main aim of developing products of biological origin, the company eventually turned to manufacturing patent-free pharmaceutical specialties, subsequently introduced successfully into export markets of the Middle and Far-East. The ever-changing political and economic conditions of some of those countries engendered a heavy reduction of *IBSA*'s turnover and the Company was faced with a revision of its policy. In 1985, following a corporate reorganization, the number of managerial and scientific staff increased significantly. Substantial investments in new modern production equipment resulted in compliance with European GMP regulations.

To date *IBSA* is equipped with appliances for the production of solid pharmaceutical forms (capsules, tablets, granules), non-injectable liquids (eye-drops, syrups), injectables (ampoules, vials), as well as creams and ointments.

Recently, a new equipment for the sterile filling of injectables was installed, providing the means for computerized control of the main parameters pertaining to sterile environments. Meanwhile, a new Research & Development Unit was created and progressively expanded, with the main target of setting up a range of new and original specialties to be put on the Swiss market through *IBSA*'s own sales organization, a unit that was also created with new staff in 1985.

IBSA's essential strategy, is the accomplishment of new original specialties, through the modification of known chemical entities, or the production of new pharmaceutical forms protected by international patents. Following this principle,

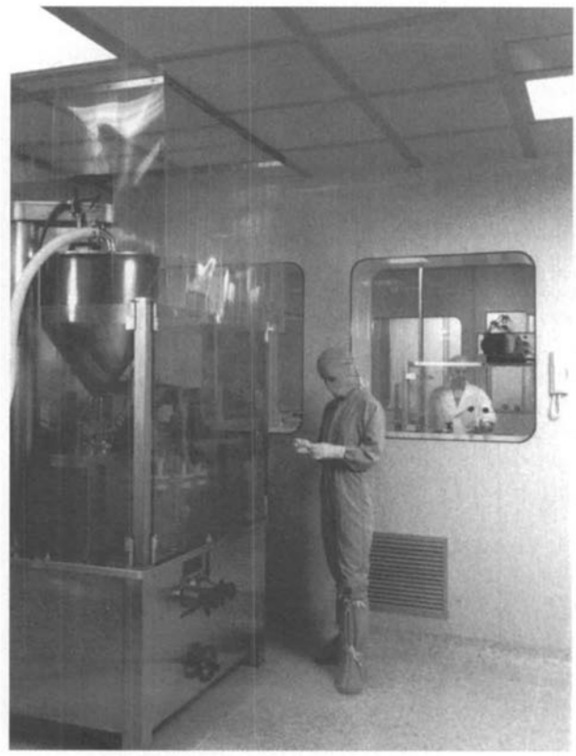

Figure. *The production of cream and gel under sterile conditions*

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