

Is Switzerland Still a Lucrative Place for Manufacturers of Drug Substances to Produce Their Products?

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Abstract: Pharmaceutical manufacturers are coming under increasing pricing pressure as a result of healthcare reforms and are therefore looking to low wage countries in the Far East. Often, the outcome is a process that is not fully mature in economic terms. Contract synthesis manufacturers, such as Siegfried, offer assistance here with its comprehensive pharmaceutical know-how in order to establish efficient and low-cost processes at an early stage. Siegfried's strengths lie in its many years experience in the pharmaceutical industry and in the network of contacts it has built up over the years with technical and material suppliers. Therefore, as far as Switzerland as a location for manufacturing is concerned, Siegfried looks to the future with confidence.

Keywords: API manufacturer · China · Healthcare reform · Pricing pressure · Siegfried · Switzerland

Increasing Pressure

The price of medication produced from original compounds has recently come under increasing pressure. On the one hand, the health system in various countries can no longer cope with the accrued costs, as a result of which patients are having to pay extra and on the other hand there is enormous competition between generic manufacturers after patent expiry. To withstand this pricing pressure more and more large pharmaceutical manufacturers are either moving their production sites to the Far East or are having their products manufactured there by sub-contractors. Previously, this practice was essentially confined to raw materials and intermediates. In the meantime, APIs and fine chemicals are also be-

ing manufactured there. India and China are in the foreground. The decision to opt for the Far East is primarily determined and driven by price and certainly has some justification as China is currently still a low-wage country. In addition, China is a large future market.

The reason for outsourcing APIs for established market products to the Far East mostly lies in the fact that it was not always possible for manufacturers of the original products to establish a low cost and efficient process in the early phase of the drug life cycle. The pressure to gain approval for the drug as quickly as possible in order to secure market share ahead of competitor products was too great. Once approval was granted, the market was supplied with products from the current process, but unfortunately the manufacturer usually failed to follow-up with a second-generation process.

Siegfried knows this problem only too well and therefore offers specific services and preventive measures to avoid shifting production to the Far East at a later stage of the drug life cycle.

Services and Other Aspects for Manufacturers of Active Ingredients

What are these services and what other aspects are there for API manufacturers who favor Switzerland/Europe?

Our services include taking an early decision as to which route to take (from clinical phase I/II) for the synthesis of the substance in order to achieve a low cost and efficient process. If the regulatory approval of the drug is under great time pressure, we offer the manufacturer of the original product the parallel development of a second-generation process from clinical phase III onwards or immediately after market launch. This avoids unnecessary project delays and having to make so-called 'compromises' with a view to gaining rapid approval. Both services ensure low ex-factory costs (relating to APIs).

There are few providers in the contract synthesis business who are able to offer a total package, from chemical synthesis through to the formulation of solid dosage forms, including packaging. Siegfried offers this total package as a former manufacturer of original drugs. Furthermore, Siegfried can look back on many years experience in the pharmaceutical industry and is therefore very familiar with the requirements of a drug and the associated services. The importance of long-term experience is usually underestimated and is a real plus point, especially for spin-offs or start-ups. This customer group is therefore happy to have a partner with a high level of technical competence and who plays an advisory role. Our competitors in the Far East do not include such a comprehensive service package.

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Fig. 1. Upgrade of production plant. The upgrade encompasses the dryer and discharge in GMP cabins.

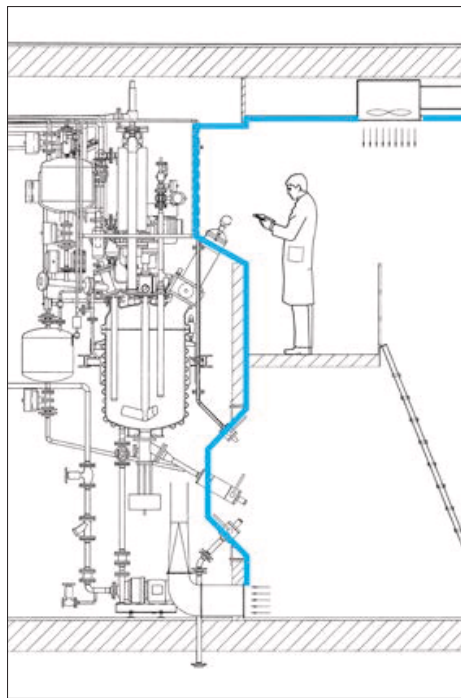


Fig. 2. cGMP wall: Separation of work room from the technical installations

Proximity to the Customer

An important aspect for Siegfried is the proximity to the customer as a lot of technical on-the-spot discussions help to ensure that processes and decisions can be specifically and frequently queried and optimized. Misunderstandings and wrong decisions can thus be minimized. When production is outsourced to the Far East, these technical

discussions are usually kept to a minimum due to cost and time.

Switzerland and Central Europe also have qualified (well trained) specialists at all levels (from chemical process/laboratory technicians to chemists). They make a major contribution to efficient and faultless process handling and, on the basis of their sound training, they are also far sighted and are therefore able to point out potential er-

rors. In the long term, this always pays off.

The European network that has developed over decades between Siegfried and our suppliers of raw materials, material and plant technology is another highlight. Raw materials are available very quickly and the plant technology's pool of experience means that we are always able to offer our customers a solution, even when faced with difficult problems.

Switzerland also ensures clean chemistry. In the last few decades, numerous efforts have been made by the chemical and pharmaceutical industry to ensure that the activities of the chemical industry are in keeping with the needs of the environment. This challenge still has to be met in China.

Opportunities

In spite of the strong pricing pressure and the increasing assimilation of technological know-how in the Far East, we certainly see opportunities for maintaining our position in this area.

Therefore, at the end of the 1990s, Siegfried already invested CHF 38 million in building a new development facility for the manufacture of key intermediates, APIs and solid dosage forms.

Between 2000 and 2003, a further CHF 200 million was spent on the construction/extension of state-of-the-art production plants. This resulted in the establishment of a milling and mixing plant that operates in conformity with GMP and the upgrading



Fig. 3. Milling and mixing centre. Automated and closed drum infeed system in the new milling and mixing centre.



Fig. 4. Filter dryer in pilot laboratory. The filter dryer is located immediately next to the crystalliser. This ideal solution allows product losses during isolation to be kept to a minimum. The closed system prevents product contamination and makes the plants easier to operate and to clean. The systematic separation of workroom and technical installations is totally new in the area of small-volume production. This separation simplifies the cleaning operations, which are confined only to the workroom and the reactor room. This allows rapid product change.



Fig. 5. Milling and mixing centre. Automated and closed filling station in the new milling and mixing centre.



Fig. 6. Centrifuges and drying room. In the pilot, two automatic horizontal centrifuges and a ball dryer are installed. The centrifuges are made of chemically resistant Hastelloy C22 and are therefore also suitable for handling hydrochlorides. All installations are computer-controlled. The workrooms contain only a minimum of technical installations. All surfaces are chemically resistant.

of various production facilities (dryer with cabin).

Reports published only recently on the business and industrial region of Shanghai confirm that this was the right decision. According to these reports, the commercial centre of Shanghai has, in the meantime, become more expensive than locations in Central and Western Europe.

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