CHEManager INTERNATIONAL 2023

Founder
Samuel Benoni
Siegfried
(1848-1905)

SPECIAL ISSUE

Siegfried Celebrates 150th Anniversary

CDMO Market Trends

Trends in API Development and Manufacturing, Siegfried CEO Wolfgang Wienand Outlines the Company's Strategy and Future Growth Opportunities

HPAPI Manufacturing

Focus on High-Potency APIs: Siegfried's New Barcelona Sites, New Development Center für Complex Drug Products, Fill and Finish of Biologic Drugs

Sustainable Pharma Production

Efficient API Production: Siegfried Introduces Second-Generation Processes, Applies Green Chemistry, and Researches New Sustainable Technologies

WILEY

OQEMA

LET'S MOVE TOGETHER

OQEMA extends our warmest congratulations with the entire team to our esteemed and long-standing partner on their 150th anniversary! It is an incredible achievement and a testament to the strength and dedication of your team.

OQEMA celebrated his own 100th anniversary last year. It is an honor to be a part of an industry with such a rich history and to have the opportunity to contribute to its ongoing success.

Siegfried

100 years OQEMA

Content

On The Move …

Dear Readers,

There are only a few chemical and pharmaceutical companies that can look back at a history of 150 years. Certainly, many companies claim such a long legacy, but if you only count those that have been operating and thriving under the same name for a century and a half, the number boils down significantly.

This special issue of CHEManager International is dedicated to one of them: Siegfried. Once a fully integrated pharmaceutical company, Siegfried is one of the few suppliers today that can provide both the drug substance and the drug product development and production capabilities.

The journey of Siegfried began in 1873, when it was founded as a family company by pharmacist Samuel Benoni Siegfried in Zofingen, Switzerland — the city which, to this day, remains the company's world headquarters. The original enterprise had only 12 employees; now, there are over 3,600 of them spread across the globe from the United States to Europe and China.

Despite the company's long history, it is primarily the developments of the last 14 years that have created the Siegfried we know today. Since 2010, sales have almost quadrupled, and the workforce has grown fivefold. Siegfried has expanded its technological base and geographic presence worldwide in recent years. In the process, the number of sites increased from three to eleven.

In collaboration with the Swiss outsourcing partner for services and products along the pharmaceutical value chain (CDMO), we have compiled an issue to commemorate the extraordinary 150 year-long history and development of Siegfried. But as we appreciate our readers' demand for independent, high-quality information we have tried to highlight the past and the present situation of Siegfried in the context of the respective market developments.

The focus of this issue, however, is not on Siegfried's history, but rather on the company's expertise and offerings today, its position in the CDMO market, and its strategic alignment for further growth.

Therefore, on the following pages you will not only read an insightful interview with Siegfried's CEO, Wolfgang Wienand, on the company's presence and future vision. You will also find illuminating articles by our editorial staff about the prevailing trends in the chemical and pharmaceutical markets and about how the Swiss CDMO reacts and adapts to these trends in order to continue its success story.

You will read about the omnipresent trend of sustainability and how it challenges pharmaceutical companies and their suppliers and partners. You will also learn about the current trends in the areas of drug substance and drug product development and manufacturing.

This introductory overview provides the background against which we place Siegfried's current activities — e.g., the development of innovative and increasingly sustainable production processes — in the context of current market events.

And a graphic timeline provides you with an overview of Siegfried's impressive history based on important milestones in the company's development.

150 years of company history are proof of the fact that Siegfried has been able to withstand market disruptions and adapt to changing business conditions by not only being resilient and persistent but, first and foremost, being innovative and courageous. These characteristics and qualities are in demand even more today than 150 years ago. Business challenges have probably never been more numerous and serious than today; therefore, companies cannot stand still. They need to be on the move constantly.

With this, we wish you an insightful reading.

Michael Reubold und Ralf Kempf, Editors, CHEManager

Siegfried

When every drop counts

Siegfried is the most trusted partner for your biologics fill and finish projects – from clinical studies to commercial scale production. With unbeatable speed to market and proven quality compliance, we have built a successful track record of Covid-19 vaccines projects as well as a significant number of clinical batches for leading biological companies.

expect more

www.siegfried.ch

"We Want to Be a Big Fish"

Siegfried CEO Wolfgang Wienand on the Company's Strategy and Future Growth Opportunities

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The CDMO (contract development and manufacturing organizations) business has a bright future, of that Siegfried CEO Wolfgang Wienand is certain. The economic advantages, among other factors, speak in favor of outsourcing compared to in-house production by the pharmaceutical companies themselves. Although Siegfried has already reached sufficient critical size within its industry, he sees the company continuing on its growth path. The goal is to take over an even larger share of the value chain from pharmaceutical companies in the future.

CHEManager: In your view, what characterizes a good CDMO?

Wolfgang Wienand: It's the combination of various success factors. There is technology, capacity, regional footprint, cost competitiveness, to mention a few. However, the most important one is trust. That is important in any business of course, but it is especially true between a pharmaceutical company and a CDMO. Firstly, of course, because the products we manufacture ultimately end up in the bodies of patients. So, the expectations in terms of quality and reliability are particularly high, for good reason.

But there is also a commercial point. A certain product, manufactured by us, may generate sales in the tens of millions for us, but such a product can very well represent sales in the billions for the customer. This means that if we can't deliver, it's not good for us, but it's even worse for our customers, because they may lose hundreds of millions or billions as a result.

Since our customers can hardly reflect this risk contractually, for a pharma company it eventually boils down to the simple question: Do I trust this company? Do I trust these people, for them to stand up and make it work and deliver what they promised? Underpinning this trust with tangible actions and consistent performance is crucial if you want to be a strategic partner and successfully operate in the high-value segments of the CDMO market.

How do you establish this trust?

W. Wienand: Among other things, by a proven track record and by having critical size. This ensures that you have a high degree of stability on the financial side and don't fall over at the first gust of wind. It is also advantageous to have a global presence so that we can supply and support customers in all relevant markets. Since we have several locations, we are able to offer dual sourcing within the Siegfried network, i.e., the manufacture of a product at two or more different locations. This gives us redundancy in the network and flexibility on the capacity side.

What other factors play a role?

W. Wienand: Trust is of fundamental importance, but of course, it is not enough if you want to play in the most attractive CDMO segments. That's why there is a whole group of other important factors. These include technological breadth, i.e., the ability to offer customers a solution to their problems, whatever they might be. As a CDMO, you have to be able to handle the full range of chemical technologies. Otherwise, the customer ends up with a scattered supply chain in which one CDMO performs only one or two steps before the next one has to take over.

How important are the aspects of quality and cost?

W. Wienand: Price is not everything in our market. But of course, the customer wants to be supplied at competitive prices. While this is a relative measure, quality, in turn, is absolute. You have to be able to prove over decades that you really know how to manufacture safe high-quality APIs (active pharmaceutical ingredients) or drugs. The challenge, which only the few leading CDMO master, is to check the box for all of them and not only a few and fail on the others. Then and only then you qualify as a trusted strategic partner to the pharmaceutical industry to industrialize their most precious innovations.

You are one of the few suppliers who offer the manufacturing of active in-

gredients and finished dosage forms of drugs under one roof. What benefit does this offer to your customers?

W. Wienand: The synergies between these two segments in terms of equipment, technologies and qualification of personnel are limited. However, the integration of these activities in the hands of one supplier offers a compelling value proposition for our customers. Taking over such a large chunk of our customers' value chain leads to a maximum reduction in complexity on the customer side. This includes not only the manufacturing of APIs and Finished Dosage Forms (FDFs) for our customers, but also the management of the supply chain and a uniform quality management system. A large pharmaceutical company often has thousands of suppliers. This causes enormous complexity, as all these suppliers must be managed and kept on track. As an integrated supplier we provide everything from a C2 or C3 building block over the complex active ingredient to almost any finished dosage form from a single source and within consistent management of quality, processes and supply chain.

© Siegfried

Siegfried's headquarters are in Zofingen, Switzerland, where the company was also founded in 1873.

Is the combination of drug substances and drug products the CDMO model for the future?

W. Wienand: That is our conviction. Basically, with our integrated setting we are anticipating the future supply model in our industry as we expect it to evolve. We believe that in five to ten years, large CDMO companies like Siegfried will have taken over an even larger part of the pharmaceutical value creation for our customers comprising both, the development and manufacture of the active pharmaceutical ingredient and the finished dosage form of a drug. We want to and will be able to support our customers in the solution of as many of their tasks as possible.

The challenges for CDMOs are great: intense competition, cost pressure, constant technological developments, and consolidation—how do you respond to this demanding environment?

W. Wienand: We have set our sights on playing in the top segment of the CDMO market. This is where we see the greatest opportunity to differentiate ourselves and earn adequate returns. That was and is our strategic goal. We have achieved this step by step over the past decade through organic growth and acquisitions and are now number five or six in our market.

Why is it so important to play at the top?

W. Wienand: Pharmaceutical customers give their most important innovations and products, i.e., their most precious assets, to the strongest and most capable CDMO. To be strong and to be able to offer the broadest range of capabilities, a CDMO needs critical size in terms of capacities and breadth of technologies. In return, they expect efficient problem solving, highest quality and security of supply, but are also prepared to pay accordingly, because only then the CDMO have the necessary to invest in the necessary critical size.

How do you define critical size - is it depth of service, is it geographic distribution, is it measured by revenue?

W. Wienand: The critical size is derived as an imperative from the aforementioned success factors: Quality, financial stability, flexibility, capacity, technology breadth. Each individual criterion is always associated with size. So, how broad is our technology portfolio? It is only broad if we can afford to invest in a broad set of high-end technologies. To be able to afford a lot, we need a lot of sales with adequate profits.

On the capacity side, if I want to offer dual sourcing for security of supply, flexibility and capacity that is available also on short notice, we also need size. As a small CDMO with 200 cubic meters of capacity, I can't afford to have 50 cubic meters or 25 percent of my total capacity sitting around idle because a customer might request additional volumes on short notice. But if I have a total of 2000 cubic meters, then 50 cubic meters represents only 2.5 percent. I can afford that. That gives us spare capacity to help a customer if needed. A pharmaceutical company expects that from its strategic partner.

So, on the one hand you have this critical size, but on the other hand you also say that you want to continue to grow. What role will Siegfried play in the consolidation of the CDMO industry in the coming years?

W. Wienand: We want to stay in the top ten. And to advance further. We want to be the big fish and consolidate, not the small fish and be consolidated. That's our ambition, that's what our strategy is geared towards. To achieve this, we have the necessary will, ideas, know-how and the necessary financial resources..

How much money can you raise for this?

W. Wienand: Without having to increase capital, about half a billion Swiss francs.

You have a strong presence in the small molecule sector, and you repeatedly emphasize how important this is for you. Will you use acquisitions to diversify and put more emphasis on biologics, for example?

W. Wienand: In the area of M&A as well as organic investments, we are proceeding in three directions. First, it is part of our strategy to further strengthen ourselves where we are already strong, be it organically or

through acquisitions. Secondly, we are pursuing the approach of adding certain technologies to our portfolio. I am thinking here, for example, of particle technologies like micronization, lyophilization or spray drying. The same applies to drug delivery platforms in the area of formulation. The third field of action concerns entering CDMO market segments where we are not yet active. It is quite conceivable for us to enter the space of biological drug substances like proteins or antibodies. We would most likely not build this up organically but do this through an acquisition. In addition, there is cell & gene therapy, which is at the forefront of medicinal research. We can also imagine an investment there because we believe that this segment can be very attractive for Siegfried.

Siegfried is now 150 years old. According to your ideas, the company should continue to be active in the next 150 years. What will it take to achieve this?

W. Wienand: We need to retain and further develop our strong corporate culture. This is characterized, among other things, by a will to grow and, at the same time, to take good and sustainable entrepreneurial decisions which hold true not only tomorrow but far beyond. If you want to grow, you need a growth mindset in your teams and a positive attitude towards change.

Furthermore, of course, we need sustainable economic success. Because this puts us in a position to earn the financial resources we need to invest in our future and to capture the many opportunities in this growing market.

Are you confident that the large pharmaceutical industry will continue to need the services of CDMOs in the future? Or do you think it's possible that the trend could go back to more in-house production?

W. Wienand: I consider the basic logic of the CDMO model to be very conclusive and compelling. It is driven by the fact that pharmaceutical companies want to invest their cash in innovation and new therapies. They don't want to invest it in brick and mortar. So as long as they can find a reliable, capable, high-quality partner and the manufacturing process can be sufficiently well described, specified and controlled, there is a strong incentive for them not to invest in their own capacities but outsource. Incidentally, this is also what their investors expect.

In addition, from the point of view of diversification, we as a large CDMO can do something that even Big Pharma cannot: When pharma companies keep their own production facilities, they can essentially use them for their own drugs only. This means that even for large companies their in-house manufacturing portfolio is limited. This translates into a significant risk of underutilization or even write-offs of their expensive assets if an important product fails and the volumes disappear.

We as a large CDMO, on the other hand, can go to any pharmaceutical company in the world and thus can create a much larger portfolio of projects and products. These are of course inherently risky, too, but the individual risks are much better diversified in our larger portfolio leading to a much lower risk of underutilization and idle costs. In the end, this leads to greater capital efficiency at the CDMO as compared to in-house manufacturing by a pharmaceutical company. These economic benefits for our customers are tangible and real. And that's why I am so confident that the CDMO business model with its sound economic logic will continue to thrive.

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Small Substances with Big Effects

Trends and Drivers in API Development and Manufacturing

The market for APIs is expanding significantly. Experts predict annual growth rates between 4.5 and 7.6 percent by 2029. There are plenty of good reasons for this: Chronic diseases are on the rise — and with them the need for medicines and active ingredients. In addition, the economic upswing in several emerging countries means that more people can afford novel medicines. APIs are also benefiting from the trend toward personalized medicine and the growing understanding of diseases. Meanwhile, API developers and manufacturers are working on increasingly sophisticated methods to better handle these delicate substances.

The market for active pharmaceutical ingredients (APIs) has been on a growth trajectory for years. According to the report of market research specialists, the global API market was valued at approximately $168 billion in 2020 and $174.17 billion in 2021. Based on estimates of Fortune Business Insights it will grow to $272.44 billion in 2028 at an annual rate of 6.6%. The European Fine Chemicals Group (EFCG) takes a similar view. The association, which calls itself the forum and the voice of the European fine chemicals manufacturer, forecasts annual growth rates of 4.5% in the generic API sector and 4.8% in the custom sector in the coming years.

Chronic Diseases Fuel API Demand

For market experts the reasons for the expected expansion are clear: "The growing trend towards new high-tech therapeutics coupled with the emergence of novel and innovative delivery systems and the evolution of personalized medicines will only serve to further emphasize the growing demand for advanced APIs", argues EFCG. Fortune Business Insights, a market research company, adds that the growing demand for biopharmaceuticals, strong surge in the demand for cost effective drugs such as generic drugs, and technological advancements in API production are key drivers.

The increase in chronic diseases, including coronary artery disease, arthritis, diabetes, asthma, and cancer has already been observed in the past decades across the globe. Experts attribute this to the increase in the geriatric population—by 2050, more than 20% of the global population is anticipated to be aged over 65 years. Also changing lifestyles and dietary changes are the main reasons for the rise of such diseases. Transparency Market Research argues in a report, that the surge in sedentary lifestyle and increase in geriatric population reflects in a higher demand of APIs.

But there are more factors influencing the API business. According to EFCG the market is increasingly a global business integrated in the supply chain of pharmaceuticals, in which APIs constitute the most important components in terms of clinical efficacy and value.

Furthermore, there is a growing investment in R&D for API production processes, as well in quality, environment and safety. This results in better, safer and cleaner technologies and in a substantial increase of pharmaceutical technology know-how and intellectual property.

Driven by the growth in oncology drugs, several CDMOs have made or announced capacity expansions to manufacture highly potent active pharmaceutical ingredients (HPAPIs) and drug products. One reason: Growth in the oncology drug market continues to spur demand for such products, writes DCAT Value Chain Insights, a not-for-profit business development association for global bio/pharmaceutical manufacturing companies. HPAPIs are effective at much lower dosages than conventional APIs, but their effective properties impose special handling requirements.

On the other hand, CDMOs benefit from the fact that pharma companies increasingly focus on large molecule operations and outsource their small molecule manufacturing activities. More than 50% of the global small molecules drug substances are outsourced to third party suppliers—similar outsourcing rates are assumed in the segment of oral solid dosage forms. Against this, sterile and aseptic drug products operations tend to be outsourced less due to higher level of criticality, which offers a significant upside potential for leading high-quality CDMOs.

Additionally, companies are increasing their size to face global competition. Mergers and acquisitions are taking place to pursue global projects. Finally, the demands on the patient side are changing. There is a continuous focus on patient convenience and quality of life, with treatments that require less frequent dosing and have minimal side effects.

This is reflected also in more personalized medicine.

Restraining Factors

However, the API world not only shines in bright light. There are also some restraining factors. Fortune Business Insides points to price fluctuations in emerging nations to restrict market growth. The periodic and unanticipated changes in the pricing policies of drugs in emerging regions, where most of the manufacturing companies are situated, is expected to hinder the market growth until 2028.

Dependency of the developed regions of the production of active ingredients on China has led to unforeseen changes in the pricing policy. This is projected to have a negative impact on the overall growth of this market. For example, in August 2018, the price of chlorpheniramine API shot up 57 times, as Hunan Er-Kang Medical Operation and Henan Jiushi Pharmaceutical were abusing their dominance as the only local supplier.

EFCG points out, that API manufacturers ask especially for global harmonized regulations with an increasingly strong relationship between the EU and the US. The European Fine Chemical association therefore advocates for strong regulatory measures to promote the use of quality APIs within Europe as an absolute necessity to protect public health and patients in Europe. One such measure would be to implement mandatory inspections of non-EU production sites whose APIs are sold within the European territory.

The organization also calls for EU authorities to encourage the removal of barriers such as regulatory or tariff-based hurdles to promote the entry of European products in higher growth non-EU markets.

Main Destinations: US and Asia Pacific

EFCG emphasizes that the API market is increasingly a global business integrated in the supply chain of pharmaceuticals, in which APIs constitute the most important components in terms of clinical efficacy and value. For many years North America has dominated the global API market, a trend which is anticipated to continue. The main drivers are the presence of major market players, significant healthcare expenditure, and early availability of new products. Additionally, a large patient base in the US and the surge in the number of API suppliers propel the market in the country. In this context healthcare experts predict that the increase in prevalence of lifestyle diseases and the increase in healthcare expenditure will boost the market in North America during the upcoming years.

Asia Pacific is expected to be the second largest market for APIs during the next years and is anticipated to expand at a significant annual growth until 2031. Favorable government initiatives, changing lifestyles leading to the development of diseases, rise in R&D investment, and technological developments in drug manufacturing processes are going to boost the market in the region.

The European region has traditionally a strong and important API manufacturing base. EFCG emphasizes the high level of technical competence and the range of skilled, highly qualified and experienced staff. Furthermore, some multinational pharmaceutical companies have taken the strategic decision to return to Europe for their API sourcing due to quality and reliability reasons.

For the future Europe is expected to witness a positive growth owing to the rise in funds for research programs along with the presence of major market players in this region. Also, the increase in R&D programs by various pharmaceutical and biopharmaceutical companies in Europe will fuel this market.

In-house Versus Outsourcing

In-house or outsourcing? — this is one of the key questions in API manufacturing. Market experts find arguments for both sides. They point out that some global pharmaceutical players prefer in-house production of APIs, believing that this provides control of the process from start to finish and offers the flexibility to adapt as and when required. This is especially useful when a company wants to respond to the market quickly and make a consumer-led change to the product, as it does not have to go through another company or rely on anyone else.

Nevertheless, there are also good reasons for contract manufacturing. Labor costs constitute most of any manufacturing process's cost. Outsourcing manufacturing eliminates the responsibility and costs involved in hiring the staff required to do the job properly.

Furthermore, quality is an important argument for outsourcing. "The trend towards outsourcing by big pharmaceutical multinationals is expected to continue growing, which will result in an increased demand for quality APIs," says EFCG. CDMOs like Siegfried could benefit from this trend. As specialists in their area, they can deliver what their clients ask for — quality and reliability — to avoid public health risks.

Quality is Key

Throughout the process, API producers face a number of complex technological challenges. "The most efficacious APIs are not always the simplest candidates in terms of solubility, bioavailability, and stability," say market experts. They argue that many APIs are not being commercialized as they are poorly water soluble, exhibit less stability, or become too viscous at higher concentrations.

A key factor to tackle these challenges is an advanced formulation, paired with high quality excipients. Taking advantage of the right and especially high-quality excipients is key and contributes to many factors such as stability, purity, and safety of the final drug product.

EFCG points out that clients are demanding more quality and more reliability from their API sources to avoid public health risks. Therefore, compliance, competitiveness and sustainability remain the most important drivers for the European API business with no compromise on quality.

One thing is for sure: the technological and regulatory requirements for API developers and manufacturers are becoming increasingly demanding.

Thorsten Schüller, CHEManager

Expanding Expertise in Highly Potent APIs

At its Spanish Sites Near Barcelona, Siegfried Specializes in the Production of Complex Drug Products Containing Highly Potent APIs. This Competence Will Now Be Strengthened by a New Development Center.

After acquiring the two Catalonian sites in Barberà del Vallès and El Masnou about two years ago, Siegfried is now significantly expanding its expertise in the production of complex Drug Products containing Highly Potent APIs (HPAPIs). In addition, the company has opened a new development center for oral solid dosage forms with active ingredients and HPAPIs as well as for ophthalmic sterile products. This not only strengthens Siegfried's position in the area of drug products, but also its global network and international competitiveness.

Drug products with highly-Potent APIs are a special species: these highly potent APIs are small, delicate and highly toxic. Handling them therefore requires an extraordinary expertise as it can be found in Siegfried's site in Barberà del Vallès in the northeast of Spain.

Carolina Bonifacio is the Head of Research and Development (R&D) in Barberà del Vallès and its neighboring site El Masnou. As an expert of this matter, she knows the requirements and challenges of HPAPIs: "These substances not only require particularly sensitive handling in the manufacturing process; the employees who work with them also need special skills, knowledge and protection to handle them", says Bonifacio. "Therefore, for HPAPIs, a thought-out risk and hazard assessment is needed." That is the reason why in Barberà del Vallès these products are manufactured in a separate area in isolated facilities, with the actual production process largely automated.

But even beyond that, HPAPI production requires special requirements and skills: Investment in production equipment is high, manufacturing times are usually significantly longer and energy costs are higher than for conventional APIs. In contrast, production volumes are usually comparatively low. In addition, the transition times from one product or batch to the next are quite long, while cleaning and waste management are complex.

Siegfried brings its entire expertise in this area to the plant just under half an hour north of the port city of Barcelona. The company claims a successful track record of supplying complex Drug Products containing HPAPIs to Europe, US, Japan and many other countries. It has a team that brings decades of experience with these products. And it has a wide range of technologies - from dry & wet granulation process (including roller compaction) over blending, capsule filling, tableting, coating and blistering to bottling.

Due to the increasing importance of HPAPIs and its special expertise, Siegfried is focusing on further strengthening this area and gaining additional customers. Indeed, Highly Potent APIs are a rapidly growing segment of the global pharmaceutical industry. Some market estimates project that the global HPAPI market could reach 26 billion dollars by 2023 and close to 10% annual growth in this area. "Already today, more than 25% of all drugs in development fall into the HPAPI category," says R&D Head Bonifacio. Thereby the HPAPI market covers a wide range of product types across several therapeutic areas although oncology-focused medicines continue to lead in terms of innovative pipeline candidates.

© Siegfried

Aerial view of Siegfried's site in Barberà del Vallès, Spain

New Development Center

In addition to their HPAPI expertise, the northern Spanish sites gain further importance with the opening of a new global development center for drug products in spring 2023. From then on, highly qualified specialists will work there closely with Siegfried's customers in modern, purpose-built laboratories to transform their innovations into commercial products. For both sites, this is a qualitative step forward — from pure production of a limited number of drugs to development activities as well. In addition, employees are developing individual approaches to solving customers' problems.

Bonifacio points to the state-of-the-art laboratories that have been built on an area of around 1,500 square meters, and that even now, at the start of the new department, around 40 employees are working in product development. This involves, for example, determining how best to formulate an active ingredient so that it exerts its desired effect in the right part of the human body. The manager points out that in the development center they also carry out process development, provide drugs for clinical trials and develop analytical methods to be able to provide evidence for certain ingredients.

Furthermore, the tasks include pilot productions, but also enabling scale-up, i.e. the transition to the regular high-volume manufacturing process. In the end, says Bonifacio, the decisive factor is that the production process is robust.

Investment of €15 Million

Siegfried has invested €15 million in the new development center. Furthermore, development activities and equipment were moved from the

Siegfried's new development center in Barcelona, Spain.

company headquarters in Zofingen to Barcelona. The new facilities will be Siegfried's global research and development hub for its drug product sites, in addition to the development center for Biologics Fill & Finish in Hameln.

For CEO Wolfgang Wienand, this is an investment into the future, which will help to expand the competencies of the CDMO (contract development and manufacturing organization) and its service depth, as well as to win new customers: "The Center of Excellence for Drug Products development services at our Barcelona sites shows our strong commitment to invest in technologies and to development capacities for our customers."

Takeover in 2021

In Barberà del Vallès the lettering of the former owner Novartis is still slightly visible under the Siegfried logo, but the fresh wind that has been blowing through the plant with its approximately 550 employees since the takeover in early 2021 is clearly noticeable.

While the site, where solid oral dosage forms are produced in large quantities, served mainly its own internal production under the previous owner, under Siegfried they not only get additional competencies with HPAPIs and the new development center, they are also gaining new customers, each of whom has their own product requirements. This not only significantly expands the site's portfolio, but also demands a high degree of flexibility and expertise from the employees.

These skills they demonstrate, for example, in the inhalation products manufacturing area. Laura Moreno, Production Unit Head, is responsible for this area. She points to a high-precision capsule-filling machine that connects to a complex process control system. Every time the product is changed, the employees must completely disassemble the individual parts, clean them and then reassemble everything. Almost like completely disassembling and reassembling a car. "In the beginning, it took us a week," Moreno says. "Today, we do it in less than72 hours."

El Masnou: High-tech Near the Beach

Switch to El Masnou, a short drive from Barberá del Vallés and slightly elevated near the Mediterranean Sea. In the site's modern functional buildings, the focus of the nearly 400 employees here is on the production, filling, and packaging of aseptic ophthalmic products such as eye drops and eye ointments.

Access to the GMP (Good Manufacturing Practice) production of liquids and ointments is possible only in compliance with strong hygienic regulations. Also the manufacturing itself takes place under strict orders of absolute cleanliness: Materials are sterilized in autoclaves, 1,100-liter reactors produce fully automatically, the filling machine presses a cataract remedy into small containers, and in the packaging line, three robots connected in series, each with several arms, grab small vials from the assembly line at high speed and place them with equal speed and precision into passing sorting systems.

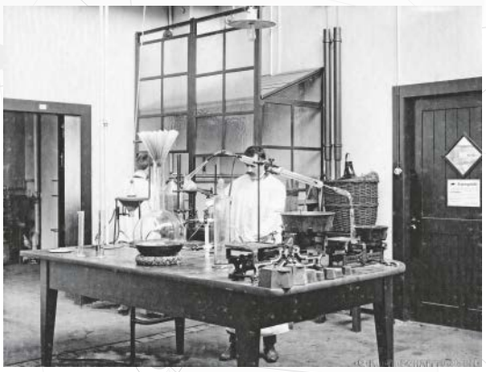
Ready to Master the HPAPI Challenges of the Future

As the HPAPI market is growing faster than the overall API market, for CDMOs a commitment to continuous investment in equipment and technologies is crucial to ensure that the most advanced manufacturing and safety systems are in place. Furthermore, a comprehensive HPAPI programme requires extensive planning, the use of risk management tools, and a corporate culture focused on quality and safety. Siegfried brings all this to Barberá del Vallés and El Masnou. With the new development center, the company is now further strengthening the capabilities of its global network in the Highly Potent API business.

Thorsten Schüller, CHEManager

On the Move Since 1873: Milestones in Siegfried's Company History

Siegfried has had to reinvent and fundamentally change itself several times in the 150 years of its existence. What has remained are the fundamentals of the company's business: chemistry and synthesis.



1873

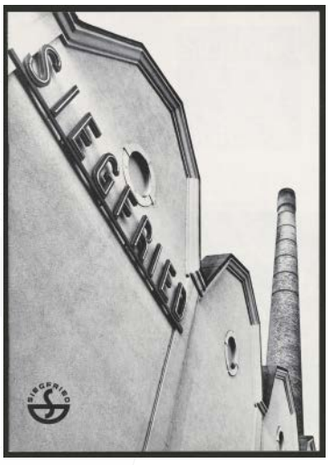
Foundation of the company "Siegfried & Dürselen, Fabrik Chemisch-Pharmazeutischer Präparate sowie Handel mit Drogen" by Samuel Benoni Siegfried – together with his brother-in-law and partner Johann Dürselen Wilhelm

1927

First subsidiary in the US, Ganes Chemical Works in New Jersey, founded together with the Ganes family

1973

Listing on the Swiss Stock Exchange (SWX) on the occasion of the company's 100th anniversary



1904

Transformation of his sole proprietorship into the "Aktiengesellschaft vormals B. Siegfried" by Benoni Siegfried

2007

Launch of a own pharmaceutical production facility in Hal Far, Malta

Sale of the Sidroga and biotechnology divisions

2001

Focus on outsourcing and split into two divisions: Siegfried and Sidroga

Foto(s): Siegfried

2005

Acquisition of Penick Corporation in New Jersey, USA

1879

B. SIEGFRIED ZOFINGEN

1887

B. Siegfried

1940

1948

SIEGFRIED

1955

SIEGFRIED

1973

SIEGFRIED

today

Siegfried

2010
Definition of the "Transform" growth strategy

New investors and capital increase

Sale of the Munich, Germany subsidiary Pulmojet to Sanofi-Aventis

2013
Construction start of a new production site in Nantong, China, and a new production building in Zofingen, Switzerland

2012
Entry into sterile filling with the acquisition of Alliance Medical Products (AMP) in Irvine, California, USA

2021

Acquisition of two pharmaceutical production sites from Novartis in Barberà del Vallès and El Masnou, Spain

Establishment of a Center of Excellence in Barcelona, Spain

2014

Acquisition of Hameln Pharma in Hameln, Germany

Start of operation at facility in Nantong, China

Foto(s): Siegfried

2023

Groundbreaking for a new global R&D Center in Evionnaz, Switzerland

2015

Acquisition of three BASF production sites in in Minden, Germany; Evionnaz, Switzerland; and St. Vulbas, France

Every Drop Counts

At the German Site in Hameln, Siegfried Successfully Demonstrates Its Expertise in the Technologically Demanding Biologics Fill & Finish Segment. A Business with Future.

The Fill & Finish of biologic drugs is expensive and poses special technological challenges for CDMOs. At the German site in Hameln, Siegfried has successfully proven these capabilities over the past two years by producing Covid-19 vaccines and a significant number of clinical batches for several biological companies. By investing in its competencies, capacities and flexibility, the company intends to further expand this demanding but promising business area.

Siegfried entered new territory on September 14, 2020. On that day, the company announced that it had signed a collaboration and supply agreement with the German biotech company Biontech for the filling and packaging of commercial quantities of the innovative Covid-19 vaccine candidate BNT162b2. From mid-2021 to the end of 2022, the vaccine, which played a key role in the management of the Corona pandemic, was filled at Siegfried's German site in Hameln. For the aseptic filling and packaging ("Fill & Finish") of the vaccine, the company invested in a dedicated production facility and provided special storage capacity.

The next step followed in May 2021. Siegfried agreed with Novavax to handle the aseptic filling of the protein-based coronavirus vaccine NVX-CoV2373 for the US company in the future. The contract was extended the following year until the end of 2023.

The two vaccines are biologically manufactured drugs. In contrast to products with a chemical composition, biopharmaceuticals are characterized by a more complex molecular structure and a significantly more demanding production process. The demands on CDMOs like Siegfried are correspondingly high. Through these projects, the Swiss company demonstrated its ability to solve technologically demanding tasks even on short notice as well as to quickly ramp up capacities as required. With the investments in competencies and multi-purpose capacities in Hameln, Siegfried has already been able to support a number of customers with development and manufacturing services beyond vaccines.

Every Drop is Important

In the biological Fill & Finish process, every drop counts, because the production of the active ingredient is very expensive. For example, 30 liters of drug substance yields 1 million doses of drug product. In this context, Siegfried points out that it has the equipment and experience to limit waste and leftovers and to ensure no interruptions in manufacturing. With the new production line, the CDMO is also able to perform 100% inline check weighing.

In addition, the company is very flexible in producing a wide range of quantities. For clinical trials, for example, Siegfried has a special line for small batches with minimal losses. Here the CDMO can produce batches of only 4 to 8 liters and doses of just 0.2 milliliters. But Siegfried can also do big things: In one of its projects they produced 760,000 cans in 500 liters— the company claims it is the only one that can do that.

Even though they are used to dealing with complex processes in Hameln, some products present a special challenge. Like Biontech's Covid-19 vaccine, which had to be cooled down to minus 80 degrees. The problem: The stoppers that seal the vials become as hard as stone at minus 50 degrees, says Marianne Späne, Chief Business Officer (CBO) of Siegfried. Their ability to seal diminishes. That's why they developed their own solution. Which one? Späne only says: "IP"—intellectual property. Trade secret.

The Future of Biologics

Up to now, the liquid pharmaceutical products they fill in Hamelin have mostly been based on small molecules, i.e., chemically produced active ingredients. Biologics still account for a small proportion. But that is set to change in the future.

Given the growing pipeline of biologics, lack of technical expertise, and huge capital investment in the installation of Fill & Finish equipment, a rising number of pharmaceutical companies are turning to contract service providers in order to ensure the development of quality drug products. This surge in the demand for biologics Fill & Finish services has presented opportunities for service providers having such capabilities.

Digital screens at the entrances to the production halls in Hameln show, which products are currently being manufactured. Basically, they fill almost all sterile liquid pharmaceuticals, a total of more than 100 different products: anesthetics, water and also the Covid-19 vaccines from Biontech and Novavax, with which Siegfried has proven its capabilities "as one of the leading service providers in the CDMO sector for technologically demanding products such as Covid-19 vaccines," according to CEO Wolfgang Wienand.

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Sophisticated Process

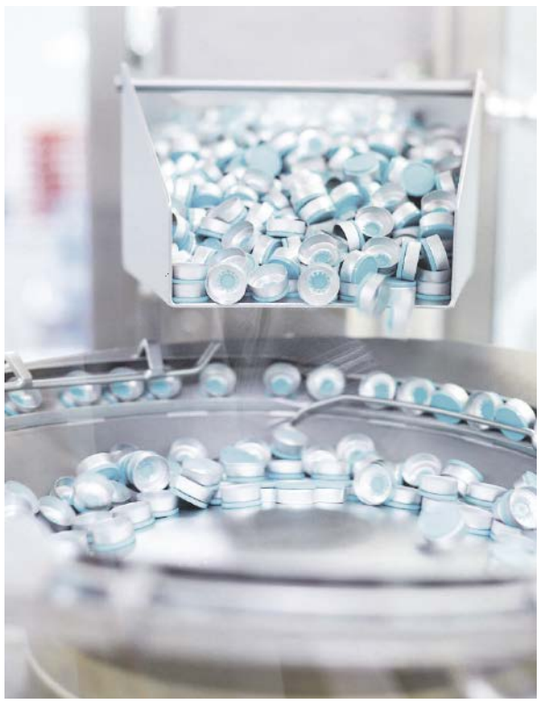
CBO Späne adds that the quality of the biologics and liquid drugs they produce in Hameln depends primarily on strict adherence to processes. One thing is to be avoided at all costs: That germs get into the production process or even into the drugs. After all, the products they manufacture here are highly sensitive. In addition to vaccines, they also include anesthetics that are injected into patients' bodies before operations. Nothing can be allowed to go wrong.

Sterile and aseptic production means germ-free production. This kind of manufacturing process is one of the most demanding procedures in pharmaceutical production and places highest demands on rooms, air quality, starting materials, surfaces and personnel.

There are two ways to ensure sterility or aseptic conditions: One is heating the liquid drugs. For 15 minutes at 121 degrees in so-called autoclaves. These are basically oversized steam ovens that can hold several metal boxes, each containing thousands of ampoules or vials.

But not all drugs can withstand these temperatures, including most biologics. Then the only option is to manufacture them in a germ-free environment. The problem is that people always carry germs with them. They stick to their clothing, but they also adhere to tables, walls and work surfaces. And: You can't make them visible. There is no spray that can be used to detect the germs as small colorful dots in the environment.

Accordingly, the Siegfried employees at the Hameln site make great efforts with regard to purity. It already starts in the warehouse—the incoming crates are transferred here from wood to aluminum pallets. Employees can only enter the actual production area through locks and with special protective clothing. Particularly sensitive production steps are carried out fully automatically in specially separated rooms.



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From 5,000 to 30 Million Vials

The site has belonged to Siegfried since the takeover of the former family-owned company Hameln Pharma in 2014. Around 500 employees work here, in the southern part of Lower Saxony, in three shifts five days a week, sometimes seven days a week, in sterile and aseptic filling. They are specialists in this.

Hameln, says Späne, is the largest sterile filling site in the Siegfried family. Here they produce on eight filling and four packaging lines for about 30 to 50 pharmaceutical customers. Some have had production for years in the town known for the Pied Piper saga, others for just one production run. The volume of orders also varies greatly: sometimes it's just 5000 units for biopharmaceuticals, sometimes it´s 50,000 or even 30 million ampoules or vials per customer and year.

The El Masnou site in northern Spain, 20 minutes north of Barcelona, also specializes in handling aseptic products, in particular opthalmics. Nearly 400 employees here manufacture and package sterile ophthalmic products including eye drops, eye ointments, ear and nose sprays. The Siegfried sterile and aseptic filling network also includes the US site in Irvine, California. The plant with its more than 120 employees has been part of the company since 2012 and primarily serves customers from the US market. watch.

Constant Control, Constant Cleaning

Production is one thing, checking processes and sterility is another. At Siegfried's Hameln site, they check constantly, in the running process, so to speak. Employees take measurements on surfaces, they measure air quality, and employees are „wiped down". Data is continuously collected and documented to prove that the batches are germ-free.

Visual inspections also have an important function. With an alert eye, employees check whether the heat-formed vials are properly sealed. Do they have a bulging head, i.e., is the glass around the top too thin? If so, the vials are sorted out by hand. It is a strenuous job that requires constant attention and is exhausting. That's why the inspectors take turns every 20 minutes.

Elsewhere, however, machines check whether the vials contain the correct amount of liquid and are really free of particles. To do this, the vials are set into rapid rotation, followed by an abrupt stop. And in order to test the tightness of the vials, they are subjected to high voltage.

Twice a Year the Big Check

Twice a year, each production line undergoes a major check. The process is called Mediafill. In this process, a solution capable of strong growth is brought into contact with the surfaces of the production line. It is a demanding and technically challenging procedure. Contamination must be avoided at all costs. That's why cleaning, always cleaning. "In sterile production, they literally clean themselves to pieces," says the Chief Business Officer.

60 Employees in Quality Control

At the Hameln site alone, 60 employees work in quality control. Added to this are the production employees, who also make sure that processes and quality fit in the daily workflow.

In addition, they attach importance to service. Späne: "Our principle is: If someone comes to us with a problem, we'll find the solution." Or as Siegfried's corporate slogan says: "Expect more." In Hameln, this is brought to life in a very concrete way.

Thorsten Schüller, CHEManager

Sustainability—The Many Facets of Action

The Pharmaceutical and Biotech Industry Already Contributes Significantly to Reduce Its Environmental Footprint. Nevertheless, Even More Can Be Done.

Climate change, energy crisis, the call for a more environmentally compatible production method and socially responsible action do not stop at the pharmaceutical and biotech industries. Sustainability is becoming a central competitive and reputation factor and carries a high economic value. This need not be to the industry´s disadvantage. It helps companies to make processes more efficient, reduces energy consumption and keeps costs in check. But is the pharmaceutical industry already doing enough in this regard?

It's just a small word, but simultaneously a big term: hard to grasp, a bit fuzzy, ambiguous, yet on everyone's lips and increasingly important: sustainability. Some call it a megatrend.

Sustainability is so elusive because it includes several dimensions such as fair trade, social commitment, prudent use of resources, natural ingredients, animal welfare, environmentally friendly packaging or regional production. Also, governance, compliance and integrity are an important part of sustainability. Last but not least compliance issues such as product quality, transparency in collaboration with healthcare professionals as well as patients, and anti-corruption remain important.

As with nearly every industry, pharmaceutical and biotech companies cannot avoid dealing with the contents and implications of this term. The European Federation of Pharmaceutical Industries and Associations (EFPIA) admits that there are many risks associated in the whole life cycle of a medicinal product that impact the environment negatively. Further understanding of these impacts and the interface between society, health and the environment is the key to guaranteeing that the pharmaceutical industry can form and execute actions.

For its part, the consulting firm PWC emphasizes the need to set the right priorities when it comes to sustainability. Even though many healthcare companies have committed to stricter climate protection targets, the industries still emit significant amounts of greenhouse gases. Adjusting production and supply chains would not only benefit the environment, but also add value.

Importance of Social Criteria

In addition to environmental aspects, social criteria also play an important role, i.e., above all access to medicines for humans and animals for food security. According to PWC this topic is receiving a lot of attention, but there remains substantial untapped potential. Decision-makers need to develop a focus on the issues that fit their strategy, using all available levers—from research and development to pricing strategies and capacity building. The focus here in the future will be particularly on developing countries with immature agriculture and healthcare systems.

Digital Integrity

PWC also highlights the importance of digital aspects when it comes to sustainability: The industry is currently undergoing a transformation from traditional value chains to a patient-centric business model. Data plays a central role in this. For this model to be sustainable and for patients to trust companies, a high level of data protection must be ensured, argues the consulting company. High ethical standards and consistent implementation are therefore necessary to successfully shape the digitalization of pharmaceutical and life science companies.

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What Pharma Is Already Doing

A closer look shows that the healthcare industry is already making a lot of efforts in terms of sustainability. Although research driven pharmaceutical companies do not typically belong to high energy consuming companies, they are at the forefront of numerous ground-breaking initiatives to help reduce CO_2 emissions, according to EFPIA.

The German Association of Research-based Pharmaceutical Companies (Vfa) points out that pharmaceutical manufacturers are committed to the guiding principle of sustainability. Thanks to their "long-standing and international commitment to the environment," they are well positioned to meet the challenges of the future.

And Bengt Mattson, chair of the Interassociation Industry Pharmaceuticals in the Environment Task Force, says in a blog for EFPIA the

industry has already taken "strides forward in minimizing its emissions and driving environmental sustainability. Every stakeholder concerned must play its fair part and the industry has taken a leading role in this respect."

Target: CO_2-Neutral

In fact, many companies want to become CO_2-neutral in the coming years, or at least significantly reduce their CO_2 emissions. Roche has set itself the strategic goal of halving its environmental footprint between 2020 and 2029. On the way there, CO_2 emissions per employee are to be reduced globally by 40% by 2025. Boehringer Ingelheim aims to become climate-neutral in its operations by 2030. And Novartis wants to achieve CO_2 neutrality in its own operations by 2025 and complete CO_2 neutrality by 2030. Siegfried has set itself the goal to reduce its CO_2 footprint by 50% by 2030. In addition, the CDMO will introduce long-term activities conforming to the so-called net-zero target 2050 to limit global warming to 1.5 °C via the reduction of greenhouse gas emissions.

Moreover, industry experts emphasize that innovative technologies are key to their success in environmental sustainability. Such technologies enable high output in next-generation facilities with a smaller physical footprint, smaller carbon footprint, and less water usage.

Less Wastewater, Less Waste

In this context the German Vfa points out, that the consumption of energy and raw materials has already been declining significantly for years; less wastewater and waste are being produced, and greenhouse gas emissions are also falling. The industry is therefore not only meeting the increasing requirements of environmental legislation. In many cases, the companies are even going above and beyond the prescribed level to protect the environment, climate and natural resources.

This also applies to the European pharma and biotech scene. According to information from EFPIA, the members of the association take responsibility for reducing environmental risks from manufacturing emissions, through implementation of risk-based containment procedures in their manufacturing Effluent Management Programs. They also pursue extended producer responsibility (EPR) programs for waste pharmaceuticals and support the meds disposal campaign and other take-back schemes.

Beyond this, even small steps can have a big effect. Many companies offer bike-to-share stations to their employees, use green electricity from biomass power plants, build solar panels on its plant roofs, operate beehives on their premises, or offer only food that comes from the region in the plant cafeteria.

For Siegfried for example, sustainability has been one of the company's five core values since 2019. In 2021 the Swiss CDMO called into life the Corporate Sustainability Board, an interdisciplinary body that coordinates and pools its sustainability activities. These efforts are being recognized by external parties and independent institutions. In addition to certifications such as the ISS ESG Rating and the MSCI ESG Rating, Siegfried has also been included in the Dow Jones Sustainability Index Europe in 2021.

More Can Be Done

Nevertheless, more can be done. EFPIA believes, a cooperative approach with broader stakeholders to be the way that will allow to expand the common knowledge and comprehension of the industry on how to proactively handle any potential risks imposed by the existence of Pharmaceuticals in the Environment (PiE). Consequently, EFPIA along with AESGP and Medicines for Europe have established the Eco-Pharmaco-Stewardship (EPS) framework with the focus on PiE and is executed across the industry and with broader stakeholders in the healthcare and environmental sector.

As part of the pharmaceutical legislative review, the Commission will adopt legislation looking at strengthening the environmental risk assessment for medicines. Minimizing the impact of pharmaceuticals on the environment, the extended Environmental Risk Assessment (eERA) concept was proposed by the pharmaceutical industry to address the challenges and strengthen the Environmental Risk Assessment process in the EU.

As pointed out in a blog on the EFPIA website, ERA should be reviewed and, if necessary, updated throughout a product's lifecycle to reflect the latest information on the medicine's potential impact on the environment, while avoiding duplications of submissions for off-patent drugs. However, the focus should be on the active pharmaceutical ingredients (APIs) entering the environment and not on each single product, as a single API can be used in multiple products. Regulatory, academic and industry resources and associated environmental mitigation strategies should be prioritized on those APIs that pose a potential risk to the environment.

German Supply Chain Act Heats Tempers

In parallel, the framework conditions are also being adjusted, for instance in Germany. The new Supply Chain Sourcing Obligations Act (LkSG), which came into force at the beginning of 2023, heated tempers in the run-up.

Supporters see the regulation primarily as a necessary instrument to push companies toward more sustainable practices; others argue that the legislation will not bring any noticeable changes in society. The LkSG focuses on the social aspects of sustainability, such as human rights, child labor, working conditions or fair pay, and only marginally addresses specific environmental issues.

Especially for highly regulated industries like the pharmaceutical industry, it can be assumed that they know better how to deal with administrative efforts, since topics like the traceability of each batch already have to be ensured today. Thus, it can be expected that the documentation processes are well established and can be applied or adapted. Risk-based assessments are also known and proven in the pharmaceutical industry from approvals, validations and qualifications.

Communication is Key

In addition to all active measures in sustainability, another aspect also plays an important role: communication. "Sustainability doesn't work without transparency," says Robert Paffen, Partner at PWC Germany. "The last decade has seen a steady increase in public demand for transparency for pharmaceutical and life science companies on their environmental, social and governance performance, including their contributions to the local economy." According to the proverb: Do good and talk about it.

Thorsten Schüller, CHEManager

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Increasing the Sustainability of API Production

Efficient Production Processes Not Only Have a Positive Impact on Economic Parameters, but Also on Sustainability.

For Siegfried, sustainability is much more than a phrase with a green coating. The term, which encompasses social and economic criteria in addition to ecological aspects, is one of five central corporate values. One of the biggest levers for reducing energy and resource consumption in the pharma supply chain lies in the efficient production of active ingredients and pharmaceuticals. The company therefore works consistently on optimizing its processes.

Sustainable entrepreneurial action has many aspects - social, environmental and also economic. For a CDMO like Siegfried, a key lever for sustainability is in particular in a more effective production of active pharmaceutical ingredients, so-called APIs.

One person who is instrumental in ensuring that Siegfried's sustainability goals—which in fact are also derived from the ambitious goals of customers—can be implemented in concrete terms, is Chief Scientific Officer (CSO) Jürgen Roos. He outlines the main measures: "We introduce second-generation processes, apply green chemistry, and continuously research new sustainable technologies. With these efforts, we reduce energy consumption, produce less waste, and at the same time, maximize our products' safety."

Reducing Resource Consumption in Production

A significant leverage for reducing energy and material consumption in particular he sees in the API (active pharmaceutical ingredient) production. APIs ultimately derive from petrochemical starting materials, which are converted in complex and energy-intensive syntheses. Roos is therefore concerned with the question of how the synthesis of APIs, i.e., their production, can be carried out at Siegfried with less effort. The company has developed and implemented various measures to achieve this. One lever, for example, is the implementation of green chemistry. This involves minimizing or completely eliminating the use of hazardous substances. "We target the simple things first as they can have a big impact. Some processes can operate just as effectively with less reagent and higher throughput. We design experiments to see how far we can 'green-shift' an existing process to reduce inputs."

In some cases, Siegfried goes further and fundamentally redesigns a manufacturing process by using more creative and innovative chemistry – a so-called 'second-generation process'. Thus, the company rethought the API synthesis route and optimized manufacturing processes for selected multi-client products. Such a method replaces the original API synthesis with more efficient approaches, e.g., shorter synthetic routes and more selective catalytic processes. Roos uses the example of the German Siegfried site in Minden to illustrate what this looks like in concrete terms: "For one of our multiclient products, the synthesis route was shortened from 17 to 10 process steps, producing the API faster than the traditional method. The raw material and energy consumption were also reduced by half. At the same time, the process generated 50% less waste and thus had a smaller environmental impact. Ultimately, all these benefits lead to higher product yields for our customers."

Computer Modelling for Scaling-up

Not only shorter processes, but also the tool of computer simulations

contribute to a better environmental footprint in active ingredient production at Siegfried. For example, data analysis enables Design of Experiments (DoE) for efficient laboratory development and Quality by Design (QbD) to achieve optimal product quality. And Big Data (process data) analysis helps to improve processes and to stabilize them at an optimum.

Computer modelling is also being used for 'scaling-up' from small lab equipment to large reactors in the production plant. This allows, for example, to predict heat transfers or flow conditions in the large reactor. Roos: "In the past, scientists would use an intermediate-scale reactor as a steppingstone, because quite a lot of things can go wrong with chemical processes as the reactor gets bigger or changes shape. Nowadays however, our laboratories have accurate, small-scale models of the large production reactors, and we combine these with computer modelling to guide us. This allows us to go straight to the desired manufacturing scale from the lab, without the wasteful and time-consuming experimentation at the intermediate pilot scale."

Membranes Reduce Waste

One example for a new process technology in API production processes is pervaporation. This is a sustainable solution for the removal of water and methanol from solvents during API manufacturing. This method uses semi-permeable membranes that allow water or methanol molecules to pass through them. "Through this process, we can reduce the waste produced by up to 15 times compared even to distillation", says Roos. "In addition, this approach has a smaller carbon footprint than incinerating the waste created in traditional methods. The use of pervaporation membranes offers an environmentally responsible way of managing solvent drying with lower energy requirements. At the moment, Siegfried is testing this technology to deploy it in the near future."

Enhanced Distillation Techniques

Distillation processes that have been in use for centuries and are a common method for separating chemical compounds, also offer the potential for greater efficiency and sustainability thanks to modern and sophisticated technologies. For example, enhanced distillation techniques enable higher product quality, yield, and a more efficient process while reducing waste. At Siegfried, distillation is used in numerous process steps of an API synthesis.

However, the classical distillation step is often long and thermally intensive. This results potentially in product degradation and yield losses. With increasing inefficiency and resource use, the sustainability of the process also decreases. To address these limitations, Siegfried optimizes the distillation with the help of subject matter experts and computer simulations. By doing this the chemical processes can be optimized significantly, and carbon emissions are going to be minimized. Furthermore, the use of solvents can be substantially reduced by selecting the right distillation equipment and conditions.

However, Roos points out, that many APIs are unstable and thus not suitable for standard distillation. Continuous distillation can be applied in these cases, as it minimizes the residence time at elevated temperatures - a few minutes compared with several hours for standard batch distillation. Roos: "Therefore, we decrease product degradation and increase quality, yield, and efficiency."

Limits of Sustainability

But Siegfried's sustainability efforts go far beyond optimizing processes. One of the core goals here is: by 2030, the company wants to halve its carbon footprint compared to 2020. On the other hand, the drive to optimize and thus reduce resource and energy consumption also has limits. This applies, for example, to the operation of cleanrooms, in which sterile or aseptic drugs are produced. Sterility in these environments is paramount. This requires a certain number of resources and energy, which cannot be dispensed with.

The CSO also points out that not every measure that would reduce the ecological footprint of pharmaceutical production can be implemented immediately. In many cases, approval must be obtained from the regulatory authorities. According to Roos, it can take as long as one year before this is obtained.

And whether a measure that is good for the environment is also good for the company in financial terms cannot always be guaranteed in advance. After all, more efficient production methods initially require substantial investments. Whether and when these will pay off in the form of lower costs cannot always be predicted.

Recognition by Rankings

All efforts and initiatives of Siegfried in terms of sustainability have been recognized by external parties and independent institutions. In 2022, Siegfried was again rated positively in the ISS ESG and the MSCI ESG Ratings, and was, for the second time in a row, included in the Dow Jones Sustainability Index Europe.

These awards are more than a nice figurehead for Siegfried. Nowadays, many customers expect the CDMO to operate and act sustainably. This also benefits the customers. "With our expertise in process optimization, we help our customers to develop greener production processes for their products and to achieve their ambitious sustainability targets," says Roos.

In 2023, Siegfried celebrates its 150th anniversary. Management's goal for the company is to continue to operate successfully for the next 150 years. One thing is clear: this will not be possible without a focus on sustainable action.

Thorsten Schüller, CHEManager

"Investments Always Pay Off"

CSO Jürgen Roos on Opportunities and Limits of Sustainability

CHEManager: How do you improve the environmental footprint of your production processes at Siegfried?

Jürgen Roos: We prioritize our sustainability efforts based on environmental impact. For example, we experiment with alternatives to harmful chemicals. Or we fundamentally redesign a manufacturing process by using more creative and innovative chemistry. This includes bio-transformations, in which enzymes catalyze highly selective reactions.

How much sustainability is possible? Where are the limits?

J. Roos: To give you an example: With our expertise in process optimization, we have reduced the number of process steps in the production of one of our APIs from 17 to 10, saving large amounts of solvent, energy and raw materials, and reducing process waste. The limit is often time: this research effort took over six years and cost nearly 2 million dollar.

What are the biggest challenges? And do investments in sustainability outweigh the financial benefits that you ultimately gain from them?

J. Roos: Sustainability and operational efficiency go hand in hand and investments always pay off over the long run. However, the optimization of production processes is resource and manpower intensive, one reason being that a new process requires a new regulatory approval. More regulatory flexibility would incentivize companies to revisit their production processes to make them more sustainable.

Thorsten Schüller

Jürgen Roos, Siegfried

Siegfried's Global Production Network

As a leading CDMO, the Siegfried Group builds on a finely tuned global development and production network of eleven sites in seven countries on three continents, both in the area of drug substances and drug products.

DP Drug Products

DS Drug Substances


Zofingen, Switzerland [Headquarters]
Active pharmaceutical ingredients (API), Intermediates, Controlled Substances
DS
Evionnaz, Switzerland
Active pharmaceutical ingredients (API), Intermediates
DS
St. Vulbas, France
Active pharmaceutical ingredients (API), Intermediates
DS
Minden, Germany
Active pharmaceutical ingredients (API), Intermediates, Controlled Substances
DS
Hameln, Germany
Active pharmaceutical ingredients (API), Intermediates
DP
Hal Far, Malta
Solid oral dosage forms
DP
Barberà del Vallès, Spain
Solid oral dosage forms
DP
El Masnou, Spain
Sterile filling
DP
Nantong, China
Active pharmaceutical ingredients (API), Intermediates
DS

"The Only Constant Is Change"

The ancient Greek philosopher Heraclitus of Ephesus is credited with the idea that the only constant in life is change. Against the backdrop of megatrends such as digitalization and globalization, as well as challenging macroeconomic climate, this idea seems as relevant today as it did some 2,500 years ago. In the 21st century, companies are confronted with increasingly complex and rapidly changing environments in the face of which competitiveness must be ensured. To thrive in this age of rapid change, an increased level of agility is required. And agility is one of Siegfried's core principles. During the company's history, the Swiss CDMO has transformed itself into a complete, fully integrated drug substance and drug product partner with a broad portfolio – and inherited knowledge in both of those parts of the pharmaceutical industry. The nature of the pharma industry means it has to constantly react and adapt to changing market conditions, navigating uncertainties with consequences for patients if continuity of supply is interrupted. Siegfried works closely with its customers, suppliers, service providers and other cooperation partners to ensure a resilient pharmaceutical supply chain. Some of the company's longstanding partners are featured here exemplarily to congratulate Siegfried on its 150th anniversary. (rk)

Congratulations on Siegfried's 150th Anniversary

150 Years of Pharmaceutical Excellence — Congratulations, Siegfried!

Hartmut Zeller,
Head of Pharma & Medical
Biesterfeld Spezialchemie

Knowledge and the spirit of innovation, that has been a tradition at Siegfried for 150 years. You have always thought pharmaceuticals and chemistry together. With customized solutions for services in development and production and your own products, you are one of the most important drivers for the pharmaceutical industry today — and globally. We would like to congratulate you on your anniversary and are pleased to have had a strong and trustworthy partner in you for many years, one that appreciates and utilizes our application technology expertise and consulting services, our comprehensive portfolio and know-how in regulated pharmaceutical markets, as well as our international network and sales strength. Here's to many more years of exciting, innovative projects, product developments and customized solutions with and for our international customers and our industry!
Your HealthCare Team of Biesterfeld Spezialchemie

We Tackle Challenges Together

Bernd Striegel,
Business Unit Director,
Bilfinger Engineering &
Maintenance North-West

Siegfried is celebrating its 150th anniversary. As a group with a long tradition, we at Bilfinger know the relevance of such a milestone. Only those who, like Siegfried, combine tradition with innovation, who constantly reinvent themselves and offer their customers added value over generations, make it this far and can look to the future with optimism.
„If you want to go fast, go alone. If you want to go far, go together," says an African proverb. We are honored to partner with Siegfried on its journey to success. Together, we are tackling the challenges of the future at Siegfried's sites in Minden, Zofingen and Evionnaz to balance efficiency and sustainability efforts with the pharmaceutical industry's demanding regulatory requirements.

Philippe Jaques, CEO,
Bilfinger Industrial Services
Switzerland

The maintenance partnership between Siegfried and Bilfinger has been a proven success for many years and has been expanded several times. In addition to repairs, maintenance and inspections, many other activities have been added for Siegfried to date — from warehouse management and plant security to mobile order handling via app. Companies on the move are the ones that last and thrive.
We congratulate Siegfried on their anniversary and look forward to being a strong partner at their side for decades to come.

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