UNDERSTANDING MODERN SWITZERLAND II

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SUPERVISOR: THIBAUD GIDDEY

Pharmaceutical Industry In Switzerland

Authors:
Arthur Vard
César Toussaint
Christopher Stocker
Emma Vernizeau

Scipper :
282302
273494
266575
282143

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Abstract

The chemical and pharmaceutical industry generated 5.4% of Switzerland's gross domestic product in 2019. The foreign commerce of pharmaceutical and chemical products was valued at around CHF 114 billion (47 % of total Swiss exports). These industries are the back bone of Swiss foreign trade. Furthermore, the pharmaceutical sector employs approximately 70,000 people in Switzerland and over 338,000 abroad.

By the turn of the 19th century the first chemical and pharmaceutical plants had appeared in Switzerland. These were initially involved in making color dyes for the textile industry. They further specialized into fabricating products with higher added value. With loose patent laws to protect intellectual property the Swiss textile industry successfully transformed into a pharmaceutical and chemical industry. With time, these industries were the first to create new serums, vaccines and other types of medication. The pharmaceutical industry enjoyed many years of growth but by the end of the twentieth century century it hit a financial crisis. This caused major restructuring and changes to these companies' core business. Since the 2000s the pharmaceutical sector has maintained a steady growth. Exports jumped from CHF 8 billion in 1990 to CHF 116 billion in 2020 despite the Covid-19 crisis.

Switzerland now hosts around 1000 companies in this sector. However the industry is largely dominated by a handful of key firms such as Novartis, Roche, Merck Serono, Syngenta, Firmenich and Givaudan. This paper seeks to answer the question of how these industry giants were formed, and why was Switzerland the birth ground. It also highlights the importance of the pharmaceutical industry to Switzerland at an investments level and its historical significance.

The short answer to this question would be Switzerland's localization in Europe and its capacity to adapt its industry to the local and global geopolitical landscapes.

Contents

1 Introduction

Switzerland is globally known for its beautiful landscapes, perfect ski slopes, smelly cheese, and of course, delicious milk chocolate. However, less known to the general public is its enormous pharmaceutical industry. In fact, Switzerland's largest exports come from the pharmaceutical and chemical sector. These sectors have grown so much that they make up about one third of all Swiss exports [1]. It is then of no surprise that two of the most valuable companies in Switzerland are the pharmaceuticals Novartis and Roche. These companies are not only relevant in Switzerland but also in the rest of the world. They place 3rd and 5th respectively in the top 10 biggest pharmaceutical companies in the world (2020) [1]. These Basel based companies have an outstanding gross revenue of more than CHF 100 billions and contributed to 5.7% of the Swiss gross domestic product [2].

Perhaps it is difficult to imagine Switzerland as a non wealthy nation but, back in the eighteenth century, a lot of the industries present today did not exist. One must then wonder how a small country like Switzerland transformed its chemical production into the pharmaceutical industry and establish itself as the world leader in the commerce of medicines?

One could say that several key political and economical factors contributed to the spurt of these industries. These factors alone however do not explain the grand success these industries came to encounter. The exponential growth and grand success can be attributed to important entrepreneurial risks and the men behind who took them.

In a first part, this paper will review the history of the Swiss pharmaceutical industry (SPI). It will explore the Swiss's early beginnings in the textile industry during the nineteenth century century to its transformation into the pharmaceutical giant. A key element in that success was Switzerland's capacity to adapt to pivotal moments in history to propel its industry on the center of the world stage.

Then, it will analyze the impacts the SPI has had on other domains: economy, politics, as well as its role during the COVID-19 outbreak.

Lastly, the challenges that the SPI faces today will be discussed. Such challenges include but are not limited to the questioning of the current pharmaceutical model with the explosion of competition due to globalization, the predominant role of patents, and the increasing role of smaller companies and start-ups. This paper will finally explore the ever-changing SPI and how new challenges could lead to collaboration of established industry leaders.

These three sections will aim at answering the following interrogation: *How did a small country like Switzerland transform its chemical industry into a pharmaceutical industry and establish itself as the world leader in the commerce of medicines? What part did the SPI play in the Covid-19 pandemic?*

2 History

The beginning of the Swiss pharmaceutical industry can be traced back to the beginning of the broader Swiss chemical industry. A specific aspect of the latter is that its existence is driven by the needs of other industries. Apart from some academic research (often linked to industrial innovation), the chemical industry's purpose is to provide resources necessary to other industries to thrive. Therefore, the development of industries like textiles, pharmaceuticals or food processing often come with the sprouting of a chemical industry or the importation of chemicals. During the second half of the nineteenth century, the development of the periodic table by Dmitri Mendeleev started a race in Europe between the most ambitious scientists to discover and understand the chemicals as well as their interactions and their possible combinations [3].

2.1 Before WWI

The Industrial Revolution brought drastic transformation to the agriculture and hands-craft economies. Few however imagine that during this period, a different type of revolution was taking place far from mechanized manufacturing: it was taking place in laboratories. New chemical products were being developed which eventually brought great wealth to the early scientists and entrepreneurs that backed them. During this period, the chemical industry in Europe began taking some importance with the industrial production of two base chemicals: sulfuric acid and sodium hydroxide. The production process of these two chemicals respectively originated from Great Britain (1746) and France (1791). These chemicals allowed for the production of derived chemicals such as hydrochloric acid among others. These derived chemicals were of particular importance for the production of synthetic dyes. [4]

Coincidentally Switzerland had a long standing textile industry during the seventeenth century century. Under French King Louis XIV new protectionist bans against imported "Indiennes" fabric and new religious persecution created a flood of French emigrants into Switzerland. These newcomers established their own textile factories near the french border in cities like Geneva and Neuchâtel. The demand for these affordable "Indiennes" fabric boomed and with it the Swiss textile industry. Being industrial, these production plants required a lot of resources, such as water and coal, which were initially too costly to import and justified local production, near natural deposits and rivers. In Switzerland, by 1850 most of the local manufactures lost their meaning: with the railway network expanding, transportation costs went down [5]. This was to be expected: in 1844 a federal commission realized that those small plants could not satisfy the demand for the booming transformation industry, notably for the textile industry [4].

2.1.1 Basel: the cradle of the Swiss chemical industry

Located next to the River Rhine and neighboring France and Germany, Basel became the nexus of two thriving economies. This city was historically a regional hub for the textile industry. It attracted the silk, cotton and calico printing industries. These textiles were not produced exclusively in Basel, but also in the the Jura, and Mulhouse regions with some production in the Lower Wiese Valley. The city's wealth made it the center for capital supply. The geography around the city initially allowed for the settlement of dye-making factories like the one seen in Firgure 1. Its proximity to France and Germany and the passing Rhine river made it a perfect production ground. Later these factories had to be further pushed to the river Rhine and to the outskirts of the city due to the harmful fumes and poisonous waste. This did not last long due to the development of the area and eventually these factories became industrial islands in the urban area. Ultimately, a relocation was needed and different companies started establishing themselves a bit further while staying in the area of Basel. Resource-wise, the starting materials were bought from Germany and the coal (necessary for energy production) was bought from the Saarland (south west of Germany) and later from the Ruhr region (west Germany). These were initially transported via train and later on via canals and the river Rhine. Initially, the sole domestic resource that was available was common salt [5].

Figure 1: The first industrial dye factory from Kern & Sandoz, in Basel, circa 1886 [4]

To resume, the reason for the existence of a cradle for the chemical industry around Basel boils down to a couple of factors: its proximity to the River Rhine and to a salt extraction plant, a nearby gasworks (industrial plant for the production of flammable gas), the proximity to the customers: the textile industry, and neighbors like Germany that allowed extensive commercial transactions. The natural demand of the local Basel-centered textile industry and its network of innovation and competition yielded the successful synthetic dye industry that sprouted the well know chemical and then pharmaceutical industry in the region.

In the 1780s, the textile region of the Upper Rhine Valley started collapsing due to the policy of French national protective tariffs: previously open frontiers were closed, thus impeding the importation and exportation of goods [5]. This was especially strange considering the fact that people and capital were not impeded until the first world war. Even before synthetic dyes were introduced, the chemical sciences were of clear interest to dye workers and calico printers because better quality attracted more business and generated higher revenues. Over the course of the eighteenth and nineteenth centuries, the acquisition of new processing techniques were pivotal for entrepreneurs to keep a manufacturing edge over their competition. Companies had to remain one step ahead of one another in the development of new dyes (synthetic or natural).

2.1.2 From political asylum to industry leaders

The year 1859 is often regarded as the year the Swiss chemical industry was born. This was the year that saw the arrival of the recipes for aniline (simple organic molecule used for the production of many chemicals like paracetamol [6]) from two places in France: Lyon and Mulhouse. Not only did a pivotal chemical came to Switzerland by the french: so did the men and their expertise. At that time, patent laws in France were restrictive: they protected the chemical and not the process. That meant that even if a cheaper process was found to synthesize aniline, the inventor could be prosecuted for synthesizing the element. Unlike France, Switzerland did not have such a law in effect for chemicals until the twentieth century. This situation benefited the local Swiss industry and the men set to elevate their social situation. The chemists working in Switzerland were entirely free to imitate, perfect and improve chemical processes from foreign countries without intellectual prosecution. These men founded their own factories, or became partners in existing ones. It attracted experts with valuable knowledge for sale. At this time, research had a negligible role: trial and error was the common procedure for innovation alongside with simply purchasing new recipes and making the most of them. [5]

2.1.3 ETHZ: where chemistry became science

In the last decades of the nineteenth century, Germany was the global hub for chemistry [3]. Chemistry textbooks were written in German and men eager of educating themselves in the matter of chemistry initially had to go to Germany to do so. Naturally, some these people radiated back to the Rhine valley where the chemical industry was thriving. At the acclaimed Swiss polytechnical school of Zurich ETH (Eidgenössische Technische Hochschule Zürich), German chemists were hired as teachers, allowing for the education of a new wave of scientists that changed the chemistry industry through modern and academic ways. Through this process, as well as through the employment of Swiss students and assistants in German labs that later returned to Switzerland, the Swiss chemical industry started being led by science rather that lucky discoveries [5]. From this point on, the Swiss chemical industry was scientifically auto-sufficient, and with the first world war as well as the implementation of the first patent law on chemicals in 1907, the industry evolved from being completely open to rather closed and competitive internationally.

2.2 World War Years

2.2.1 1914-1933: unsuspected economical growth

With the assassination of Archduke Franz Ferdinand in 1914, the "War to end all wars" started. With this event, Europe changed and was torn between the Allied Powers and the Central Powers. Economically and for the country of Switzerland, that meant a lot: tourism and commerce with Russia plummeted while the production of ammunition, aluminum, copper, cement and other ressources essential to the fighting sides rose considerably. Swiss industrials threaded carefully with both sides to maximize profit while hiding transactional details. Naturally, with a global conflict underway, the demand for pharmaceuticals rose and the Swiss companies managed to gain shares on the European market. Some industries, like the textile industry, never managed to get back up to the pre-war level. Other industries like the pharmaceutical one and more generally the chemical industry became driving sectors, despite the world crisis of the 1920s. [7]

2.2.2 1933-1945: Swiss chemical industries in the Third Reich

From 1933 to 1945, the Third Reich was led by the German national-socialist party. During this time period, the only companies active in the chemical industry sector in Germany were from Basel, Switzerland. These companies owned their own production plants, some of them in occupied Poland during the war. These companies were perfectly on point with the political and economic situation of the Reich: they adapted their board's decisions with the situation of the country and later the war. Moreover, they even complied with the "Aryanization" process, some from the very beginning, others later on. In 1937-1938 Roche complied to removed their Jewish staff and advisers under new German orders to become "non-Jewish firms". It is worth mentioning that Roche appears to have been the most reluctant of the Swiss Basel-based companies, to the point of hiring Poles in Warsaw to prevent then from being forcibly deported to work camps in Nazi Germany. Business-wise, that period was profitable for those companies. Ciba's pharmaceutical sales surpassed its dye sales from 1942 and on. The sales of Roche's subsidiaries close to tripled from 1939 to 1943 with a predominant place in Berlin's sales of synthetic Vitamin C and opiates. These companies had well established networks with the German officials responsible for their control. During the conflict, the plants from Ciba, Roche and Sandoz were categorized as "important for the war economy" and their pharmaceuticals were purchased both by the Wehrmacht and the SS (Schutzstaffel). [8]

2.3 Post War Expansion and Growth

After the world war era, pharmaceuticals had proved their value: medicines saved lives and deserved research. From that point and on, companies would invest in intensive R&D programs. Even though chemistry was already quite "serious" as a field with the German chemists from the late nineteenth and early twentieth century, the discovery of new drugs was achieved through "random screening", where thousands of potentially interesting compounds were tested, and if some sort of therapeutic potential was identified, a testing drug was made. Even though, this process was financially viable due to the fact that the amount of efficient drugs was low, and the fact the amount of identified disease was immense. One can therefore not be surprised by the fact that the drug R&D industry became a highly innovative and profitable one. From 1951 to the 1980s, the R&D to sales ratio evolved from 3.7% to 15-20% globally [9]. During this period, and with growing interests for local and global market shares, patents held an increasing importance, to the point were in 1980, generic pharmaceuticals represented 2% of the US market. In Europe, measures to implement more strict patent laws spread progressively, with two distinct outcomes. On one hand, countries like Italy and possibly France tended to avoid R&D when patent laws did not exist, whereas on the other hand, countries like Germany or Switzerland, the arrival of such laws did not affect much the tendency of companies to do research and development.

On the other side of the spectrum of the pharmaceutical industry in that so called "Golden Age" period, some companies began to invest substantial amounts in the marketing of their drugs, allowing them to sell them at a premium compared to generics. At the beginning of this period, prescription drugs represented about a third of the market (32% in 1929) whereas in the late 1960s this number had increased to over 80%. Following this, pharmaceutical companies started marketing themselves directly to physicians rather than to consumers. [9]

By the end of the Golden Age, companies started to align strategy-wise: R&D intensive and marketing intensive companies converged to the model what we more or less know today. By that time, companies became truly international: the companies strategies were so resource intensive that other markets had to be explored to make it worth it [9]. In Switzerland, companies progressively merged to become Roche and Novartis, two world leaders in the chemical and pharmaceutical industries.

3 Importance to the Swiss Economy

Compared to other countries Switzerland has a very diverse and robust economy. Taking into consideration the gross domestic product per capita Switzerland ranks among the richest countries in the world. The Swiss economy is built on various strong industries including: financial services, tourism, machinery manufacture, pharmaceuticals production, and watchmaking. These all play an important role in maintaining the total imports and exports. However, among these different sectors the pharmaceutical industry particularly stands out.

3.1 Present Day Overview

As previously mentioned, the Swiss export industry is largely driven by the pharmaceutical sector. In fact the export industry has grown increasingly dependent on the pharmaceutical industry. As of 2018 there were close to 1000 companies registered in this industry with 266 commercial companies manufacturing pharmaceutical goods in Switzerland. The chemical and pharmaceutical industry together have exported CHF 114,6 billion in 2019. As shown in Figure 2, these two industries surpass by far the rest of export goods. In order to produce these exports the chemical and pharmaceutical sector also lead in the number of imports made with 52.7 billion CHF in 2019. The Swiss pharmaceutical industry is so large it accounts for roughly one third of all income made abroad. [10].

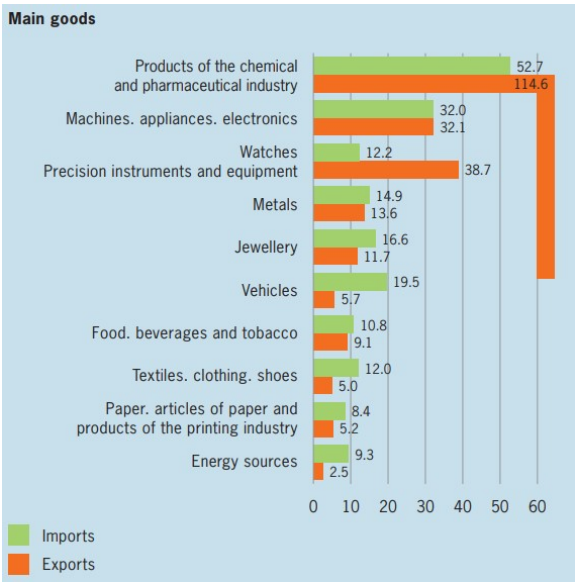

Figure 2: Imports and exports in CHF million (2019)
Source: Federal Statistic Office

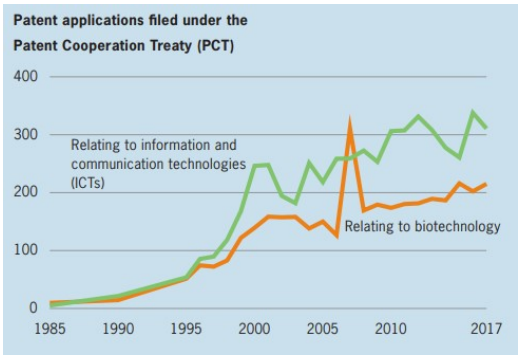

Figure 3: Yearly filed patents from 1985-2017
Source: Federal Statistic Office

Switzerland's strong industries ranks it among the highest with the highest share of foreign trade in the gross domestic product. To maintain this competitive edge, pharmaceutical and chemical companies are constantly investing in new research and development (R&D). In fact much of the business surrounding the chemical and pharmaceutical industry today involve research and patent filings. The number of patents related to biotechnology filed under the Patent Cooperation Treaty (PCT) have steadily increased in past years as shown in Figure 3. To accomplish this, these companies invest heavily on intramural R&D expenditure spending close to 5.8 billion (2019). To put this figure in perspective, the Swiss government spent only 13% more than the pharmaceutical sector to fund all public university research. Despite funding their own research, the pharmaceutical industry benefits from government funded university research.

3.2 Impact Outside Switzerland

At the global stage the Swiss pharmaceutical industry is at the forefront of the international competition. In 2020 alone out of the top 5 largest pharmaceutical companies in the world with respect to revenue two were Swiss 3rd Roche & 5th Novartis. The Swiss pharmaceutical industry is a cornerstone of research and development. In turn the Swiss pharmaceutical industry is one of the largest exporters in the world for package medicament. According to the OEC (Observatory of Economic Complexity) Switzerland was the 2nd largest exporter of packaged medicament in 2019, with a global market share of 11.9 % worth 36.5 billion USD. Figure 5 shows the percentage each country exports in packaged medicaments [11][12].

3.3 Strength during COVID-19 crisis

On March 11th, the COVID-19 outbreak was characterized as a global pandemic by the World Health Organization (WHO). It quickly spread around the world, contaminating more than 150 million people and killing over 3 million. The COVID-19 pandemic, even if it is not finished and can still bring its share of surprises, had a major impact on the pharmaceutical industry. This pandemic brought an urgent need for research and supply for medicines.

3.3.1 COVID-19: The golden goose of the pharmaceutical industry

Covid-19 has certainly taken the world by surprise. Many business and industries have taken a hit from the global pandemic as consumer spending dropped. However, during this trialing period pharmaceutical and chemical industry have been able to fair well in comparison. They have been classified as some of the few "winners" of Covid. The need of anesthetic products has jumped by 2000 % [13] during spring of 2020 in response to unprecedented flux of patient in reanimation sectors. New Consumers behavior, like panic buying which was very present during the early onset of the COVID-19 pandemic, also help the industry with the depletion of pharmaceuticals for chronic disorders. In March 2020, panic buying is estimated to be responsible to an increase of +8.9 % [14] of sales for chronic disease medication. In the US, ,asthma medications spiked by 65%, and type 2 diabetes medications increased by 25% [15]. Another impact can be seen in research and development. With more than 53 vaccines in research, about 924 ongoing trials in the world for the treatment of COVID-19 [16] and a large funding from the states (For instance Moderna received more than 2.5 billions as a help from the US government for the development of a vaccine [13]) . The pandemic is a good opportunity for the industry to test its R&D system and its ability to innovate. And the benefits of such a global investment in research can be enormous for the sector. Indeed, big winners for this race (Moderna and Pfizer) developed their vaccine based on messenger RNA, a still new technology with very promising applications in other domains (HIV or cancer) [17][18]. Therefore the effort put in the development of this vaccine could lead to other big discoveries that could benefit all the pharmaceutical industry. However, this strategy also raised ethical consideration: As mentioned before, the industry received a lot of money from states and therefore, from the public sector to find a solution to the pandemic. Profit made by these companies are huge: they are estimated to 26 billions for Pfizer and 18 billions for Moderna[19]. But the access to the vaccine is still complicated for some countries and we can start to see an unequal repatriation between rich vaccinated western countries and the others. That is why more than 100 countries led by South Africa and India are currently asking to the World Trade Organization to suspend intellectual property rights on COVID vaccines in order to accelerate their production worldwide [20]. These patent restrictions raise ethical questions concerning the intellectual property during a global health crisis. Countries like India could ramp up the production of Covid vaccines if these patents were release giving access to poorer countries to this life saving medicine.

3.3.2 The case of Switzerland

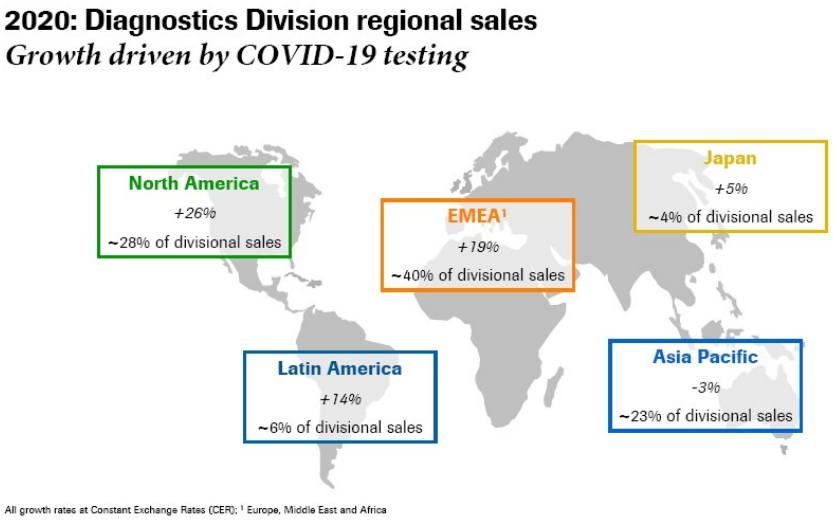

Figure 4: Roche's diagnostic division regional Sales
Source: Roche Fourth Quarter Results

Swiss pharmaceutical companies have also benefited from the situation. The chemical and pharmaceutical industry exported an impressive 116.40 billion CHF in 2020. These industries saw their exports grow 1.6% in 2020 compared to 2019. They achieved this despite having equally reduced their imports by 2.8% during this period[]. As in the global picture, the increase was largely due to the spike in demand for vitamins and Covid-19 diagnostic tests. Figure 4 shows the regional growth of diagnostic sales for Roche alone. These two products were able to compensate the loss of other products and exceed the sales performance. While industries were hindered by production delays, and low sales, the pharmaceutical and chemical industry were able to maintain and increase their sales. For this reason these two sectors alone accounted for 44% of the total Swiss exports for 2020. By comparison typically percent share of exports from these two industries are at around 30% of the total Swiss exports. This was a significant jump from last years highlights how other sectors struggle to sell their products most notably the watch and machining industry whilst the chemical and pharmaceutical industries remained strong.

The pandemic's strain on global production and demand brought to light important revelations to the Swiss and European markets: the reliance on foreign production. The international market is built on the cooperation and optimization of costs. This has led to an intricate network of production assembly lines and supply chain. However, the bottlenecks in supply chain brought to light important European dependency on foreign markets. Most notably six strategic areas were critically highlighted: raw materials, pharmaceutical ingredients, semiconductors, batteries, hydrogen, and cloud technologies [21]. For the production of antibiotics and medicines both Europe and the US are dependent on the supply chains in China and India. Particularly in Switzerland the Federal Office for National Economics Supply FONES has devised new measures for both short-term and long-term supply shortages. This was put in place in order to alleviate initial difficulties of medicine management. The reporting obligation with the BWL (Federal Office for National Economic) and BAW (Federal Office of Public Health) from cantons, pharmacies, enterprises and hospitals proved pivotal in preventing medicine shortfalls. This new regulations permitted the shortage crisis to be further managed and has been working effectively since April 2020. This however was possible thanks to major efforts and determined agreements on communication [22] .

The major export region during this time was the EU (European Union). Roughly half the total sales accounted to countries in the EU, contributing to roughly CHF 54 billion. The next large buyer of Swiss chemical and pharmaceutical products was North America with roughly CHF 29 billion CHF. Asia comes in third with roughly CHF 20 billion [22].

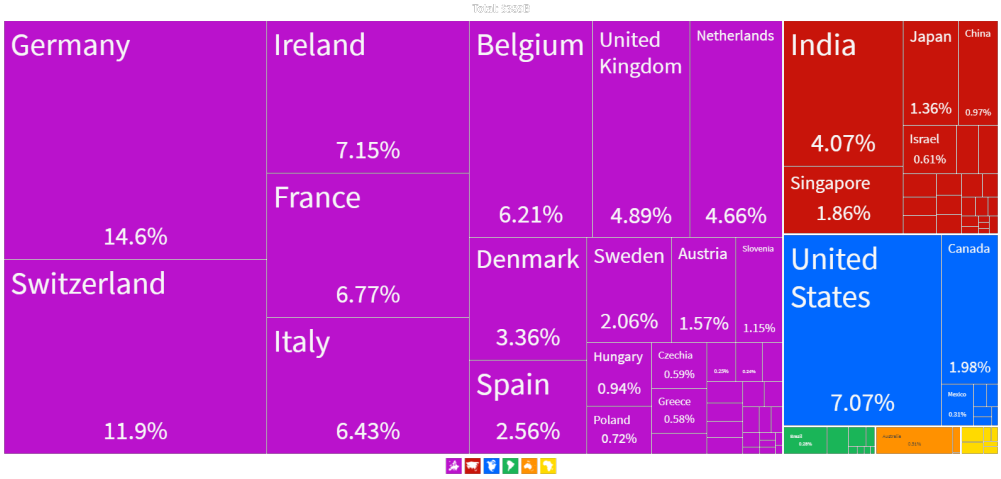

Figure 5: Packaged medicaments exports by country (2019)
Source: OEC

However, although they have benefited from the general health situation, they seem to have missed the big opportunities created by the situation and have remained in the background. The small role of the two Swiss giants remained at only providing some ingredients of the molecular test for the detection of the virus and to do some trial on already existing medicine [23]. But they are totally absent on the vaccine research front. This is a consequence of the politic of withdrawal of Swiss companies from vaccinal research at the beginning of the 2010s, considered not profitable enough, and which is symbolized by the acquisition of Novartis vaccine department by Glaxo-SmithKline Pharmaceutical in 2015 [24]. This could be a first sign of the decrease of the inovativity of the Swiss industry. Indeed Novartis and Roche are in 2021, ranked respectively 36th and 48th in the world ranking of the most innovative companies by the Boston Consulting Group [25]. Their concurrent Pfizer and JohnsonJohnson are ranked 10th and 20th respectively. We can however mention the accord between Moderna and the Swiss company Lonza for the production of the vaccine in the canton of Valais, creating more than 1'200 jobs and a huge economic development for the city of Viège [26].

4 Pharmaceutical landscape

4.1 Big Business, Small Competition

Like most industries, Swiss pharmaceutical companies must adapt to a new context brought by globalization. This includes the opportunities offered by new markets with diverse needs. This is, for instance, the case of the Chinese market, where the export of Swiss medical products where multiplied by four, reaching 4,1 billion francs in 2016 [27]. Globalization also initiated market competition not only among external markets but internally as well [1]. Among the biggest competitor were companies from the US and several European countries (France, Germany, Sweden). However, there is a growing emergence of companies from the Global South such as China and India. The name of this phenomenon is "pharmerging"[28]. A good example of it is the Shanghai Pharmaceuticals Holding that was considered to be the 10th biggest pharmaceutical company by revenue in 2020. [29]

Furthermore, pharmaceutical industries have suffered since the beginning of the 2000s due to an increasing uncertainty concerning the business model developed during the Golden Age (The 1940s to the mid 1970). This industry has suffered over disputes over intellectual property and has declined in research productivity. This vacuum led to the emergence of smaller companies and start-ups. This will be described in the following sections. Big companies reacted to this challenge through a wave of mergers and acquisitions [9].

The most recent acquisition from Warner-Lambert by Pfizer for more than 100 billions USD in 2000 clearly exemplifies the merging of companies. Similarly in Switzerland, Ciba and Sandoz shook the world announcing there merger into what is now known as Novartis in 1996 [30]. This similar trend was followed by other Swiss pharmaceuticals. For example, Roche acquired several big companies spread all around the globe including: Genentech in the USA, Chugai in Japan, among others. These subsidiaries play a massive role in the outreach of the company and on its financial stability. It is because of the products developed by Genentech for Roche that the latter is now the world leader in oncology. This Californian company represented around 30% of this group's revenues back in 2008 [31].

These companies have grown so large that rumors have even surfaced concerning a possible fusion between Novartis and Roche [3]. This fusion would catapult Switzerland as holder of the largest pharmaceutical company in the world. These groups have already shared investments: Novartis holds one third of Roche's shares and the companies already cooperate on numerous activities. An example of this collaboration is the partnership of the two companies with the Research Center for Clinical Neuroimmunology and Neuroscience that is based in the University Hospital of Basel working on multiple sclerosis research [32]. Notwithstanding, several sources indicate that this fusion is actually very unlikely to happen, or at least not in the near future. This intention to stay separated was reaffirmed by Novartis president Jörg Reinhart in 2014 during an interview with the SonntagsZeitung [33]. Even without a merge, cooperation and communication between Swiss pharmaceutical companies is notoriously embodied by Interpharma. Interpharma is an association situated in Basel that regroups all Swiss pharmaceuticals doing research in cooperation with the other actors of the Heath domain and global public communication.

Therefore it can be seen as indicated by the title of the section, the pharmaceutical industry is huge by the money it generates and the weight it represents in GDP of the countries. However, all the power is concentrated in the hands of a few companies that maintain their hegemony through the purchase of smaller ones, but also sometimes through mergers between them.

4.2 Research modalities

Pharmaceutical research and development (R&D) is highly regulated to guarantee public health. That is why it must follow the precise steps and rules described below. These will be emphasized in the following paragraph prior to addressing the specifics of said regulation.

4.2.1 How ?

The process begins with basic research and early discovery phases. This can consist of targeting, testing, or modifying a lead compound by organic synthesis. A lead compound is a molecule with proven medicinal properties that needs to be modified to promote better body absorption or increased efficiency. This is followed by pre-clinical studies, which consists of testing the product in cells and animal models. This process is followed by clinical development, which constitutes three different phases:

- Phase I involves the first application of the drug to human volunteers.
- Phase II consists of testing the drug on more patients to assess the efficiency of the drug compared to one that is already on the market and a placebo.
- Phase III requires many more patients and is pursued to label medication and instructions for drug use.

All these clinical phases are followed by the application for FDA approval, which can be accelerated in certain cases depending on the urgency of a treatment. The last step of the development process is the FDA (Food and Drug Administration) Adverse Event reporting system where all the parties in this particular drug use (manufacturers, health professional, consumers...) report possible problems that may occur consequent to their consumption. Even though the FDA is considered to be the reference authority in drug regulation, the Swiss government relies on its own equivalent organization: Swissmedic. This organization regulates drugs that can then be integrated into the Swiss market.

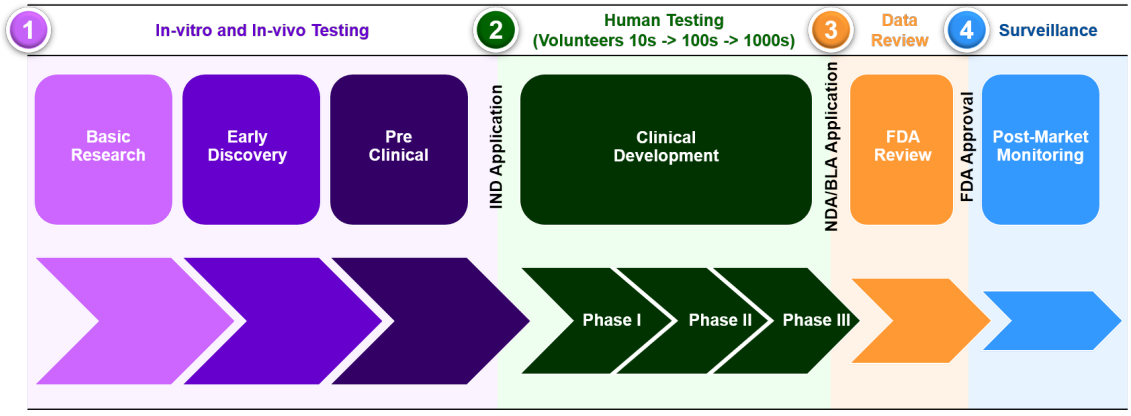

Figure 6: Drug development process
[34]

4.2.2 What?

The total investment in R&D of all pharmaceutical companies based in Switzerland and members of the Interpharma Industry Association was reportedly 7 billion francs in 2019, representing almost twice as much as their reported sales in Switzerland [35]. This indicates the great interest in researching Swiss pharmaceutical companies. Research has been in Swiss Pharmaceuticals' interest for years, yet the process of development and studies have certainly developed with time.

At an early stage of development, pharmaceutical industries primarily designed vaccines to fight off viruses and bacteria. They also focused on small molecule production. Small molecules drugs are those simple and light enough to easily enter cells for the treatment of specific diseases. A great example of it is Aspirin, a well-known anti-inflammatory drug. With new advances in the biological field, pharmaceuticals have added new forms of treatment known as bio-pharmaceutics. Bio-pharmaceutics utilize biological tools to combat and treat diseases as opposed to traditionally used chemical components. These new bio-pharmaceutic therapies enabled the production of new proteins and antibodies. A clear example of this was the breakthrough of Insulin back in 1921. Today, a big part of bio-pharmaceutic research is directed towards the treatment of cancer. This type of research is highly expensive with no promise of returns. Because of this, successful treatments carry a heavy price tag. For example, the price tag for Novartis' new lymph gland cancer treatment surfaces around 475,000 USD.

Over the past years, cancer and orphan disease treatments were still the biggest subjects of research and led to most patents. Moreover, other areas tend to be developed as well, such as genetic therapy or even cellular therapy. The first consists of introducing genetic material (in the form of DNA or RNA for example) into a cell to cure a disease. Cellular therapy, on the other hand, involves introducing cells (embryonic or stem cells) to cure an organ or an organism.

While these techniques are still thoroughly investigated, others subjects of research have taken the spotlight. A major one nowadays is biotechnology [36] which includes all technological tools that use biological systems, living organisms, or parts of them to develop different products. Switzerland now counts on more than 250 biotech companies as seen on Figure 7 and is considered one of the biggest biotechnological hubs in the world. With these biotechnological and genetic tools being developed, many companies specialize themselves in personalized medicine. This consists of checking patient data (genetics, clinical...) to take appropriate diagnostic and therapeutic measures that correspond to a particular patient's need.

Figure 7: Biotech companies in Switzerland [37]

Historically, big pharmaceuticals and R&D services were the main sources of innovation. This was especially the case in the 50-60s with the development of many small molecule drugs by big Swiss pharmaceuticals. Great examples are ascorbic acid (Vitamin C) or Valium developed by Roche at that time [3]. Throughout this time frame, 80% of “new molecular entities” (future drugs) approved by the FDA came from large companies. In the years 2005-2006, these proportions became 50/50, shifting in favor of small businesses. Thus, innovation is now primarily in the hands of small businesses rather than in those of big pharmaceutical companies. The latter are now positioned predominantly as buyers of possible drugs than as creators of them. Research risks are, in that case, taken by small companies, yet larger companies now find greater difficulty in discussing the price of new drugs [36]. This is particularly the case in Switzerland, where many small companies and start-ups working on pharmaceutical innovation are present, especially in the Geneva lake coast and in the region of Basel. Research subjects of these startups are as diverse as can be, ranging from small molecule drugs to the study of biotechnological products.

4.2.3 With What Protection?

Patents are filed by a laboratory to protect a product or a process from being used by others for a certain period of time (usually twenty years). These are usually specific to a region, such as Europe or the US, although these restrictions are usually accompanied by established agreements between the parties involved. In most cases, a patent is filed once a drug passes all the clinical trials necessary to be validated by regulation authorities, such as the FDA or Swissmedic. The patent is filed by the laboratory and is protected even before authorities’ approval. When a patent reaches the end of its protection, the laboratory can ask for an extension in certain conditions (for instance, if the authorities’ approval takes longer than expected). A strategy sometimes used to extend this market exclusivity is to file a patent for a particular process used for drug development or production. When the time of protection is over, some generic products may be produced by other companies.

This patent system is supposed to encourage research of new treatment because R&D involves considerable expenses for a company. As many drugs were developed in the ’80s-’90s, the 2000-2020 years were commonly referred to as the “patent cliff,” alluding to the end of most pharmaceutical patents and the loss of profit that this entailed, representing almost 20% of the worldwide turnover of this sector [38]. This highlights that, even though patent protection is limited in time and space, it takes great importance in the pharmaceutical companies economy.

In their report named “La place pharmaceutique suisse en 2030," published in Zurich in 2019, Interpharma, the association of Swiss pharmaceutical companies carrying out research, discussed the future of Swiss pharmaceutical industries. More specifically, as one of their ten proposed ways of ensuring the strengthening of the Swiss pharmaceutical, they suggested to: “Guarantee a modern patent protection system so that the pharmaceutical industry can continue to invest in research focused on innovative drugs.”[31]

Some companies take advantage of the fact that their countries do not protect intellectual property as others do. This was, for example, the case of Indian companies: until India joined the WTO (World Trade Organization), their pharmaceutical companies focused on the drug copy industry. This is due to various factors, including the low cost of production, the protection of fabrication processes for a small amount of time yet not the product, and the absence of investments by producers in R&D [39].) This makes it possible to manufacture cheaper drugs (ex. drugs for AIDS) rather than the ones produced by European companies which then become noncompetitive. This period is now over for India, who now recognizes patents. Nowadays, India put greater effort and investments into R&D, making Indian companies serious rivals of the Swiss pharmaceutical industry in the race for innovation. Interestingly enough, the development of the Swiss pharmaceutical industry is quite similar to that of India, as they once copied German innovation.

4.3 Future Perspectives

While it is difficult to accurately predict the future of pharmaceutical companies, there are certain patterns that indicate what the upcoming years may look like. The general trend predicts increased collaboration between different companies in research, forming alliances both with without hospital or university collaboration instead of merges between them. Small companies and start-ups will continue being the first actors of R&D, which are then bought by these big pharmaceuticals. The most dynamic research domain nowadays is biotechnology. This trend does not seem to be declining and we can confidently predict that it will continue to be the case for the upcoming years. Development of small molecule drugs and biopharmaceutics will most likely continue, yet biopharmaceutics will probably grow in relevance as the price of development is decreasing with the development of innovative techniques (ex. DNA sequencing that cost millions at first are now obtained for a few dozen dollars). This R&D is boosted by patent protection that is economically attractive for companies, and it continues to strengthen as it gets recognized by almost every country.

The pharmaceutical industry, being one of the few that profited from the Covid crisis, will most likely continue to thrive. Even though Switzerland's big pharmaceuticals were not the first to respond to the Covid crisis in medicine development, mainly due to their little or no vaccine research, they still participated in proposing treatment and diagnostic tools. This speaks to the power of Switzerland as a big research center, continuing to be the first country with a high number of patents per inhabitant. It must, however, reaffirm the authoritative power of Swissmedic over the FDA, which is still used as the global reference today.

5 Conclusion

To conclude, the SPI is born from the eighteenth century textile industry. It grew to the rank of a world leader of the sector by taking advantages of some key historical moments and by using the advantageous localization of Switzerland: in the heart of Europe, between France and Germany.

Today, the pharmaceutical industry is a very active participant in the Swiss economy. It is the leading exporting and importing industry. Switzerland is now positioned as the country filling the biggest number of patents per inhabitant among all countries. This is mostly due to the large investment put in R&D by both public and private actors. The Covid-19 pandemic situation is used here as a case study to how resilient the pharmaceutical industry has been through this troubling situation. Drug sales having increased and R&D as been greatly stimulated. However, Swiss companies did not benefit as much as other companies like in the USA with Pfizer and Moderna because they did not participate in vaccine development and only played a passive role.

One can thus see that global competition takes more and more importance and that Swiss pharmaceutical industries constantly need to adapt to this new situation, collaborating on projects and leaving innovation to start-ups. Innovation itself is very coded, and individual property is kept by patents. All of this makes it possible to predict the next few years of this industry which keep doing well focusing on biotechnologies and start-ups development.

The maxim of pharmaceutical industries could be: when things are well, the industry goes well; when thing are bad, the industry goes better.

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