UNIVERSITÀ POLITECNICA DELLE MARCHE
FACOLTÀ DI ECONOMIA "GIORGIO FUÀ"

Master's degree in International Economics and Commerce – Business Organization and Strategy .

Analysis of the international outsourcing processes in pharmaceutical industry.

Analisi dei processi di outsourcing internazionale nell'industria farmaceutica

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Tesi di Laurea di:
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Anno Accademico 2020 – 2021

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Abstract

L'elaborato ha come obbiettivo quello di analizzare il processo di outsourcing internazionale prendendo in esame l'industria farmaceutica. Inizialmente il lavoro di tesi si è sviluppato descrivendo i modelli teorici che descrivono gli aspetti rilevanti dell' outsourcing internazionale. Successivamente, si è descritto il mercato farmaceutico globale, la sua distribuzione geografica e le dieci aziende leader. In seguito, si è affrontato il tema della gestione del prodotto farmaceutico in tutte le fasi del suo ciclo di vita e della catena di approvigionamento analizzando le differenze emerse con l'implementazione di processi di outsourcing. Conseguentemente, si sono descritte le due tipologie di servizi di produzione in conto terzi, CRO e CDMO. È stata, poi, presentata la problematica della dipendenza da soggetti terzi, ponendo l'attenzione nella recente crisi COVID. Infine, si è sviluppata una analisi dati su importazioni ed esportazioni di prodotti farmaceutici finiti ma anche di principi attivi. Insime a questa, è stato sviluppato un modello regressivo basato sulla equazione gravitazionale di commercio bilaterale, che ha dimostrato la correlazione positiva tra quota di importazioni da paesi emergenti e esportazioni tra un generico paese i e un paese j.

INTRODUCTION

Pharmaceutical industry is a complex system of processes and operations. Organizations involved in this sector perform activities such as: research and development (R&D), manufacturing of active pharmaceutical ingredients (APIs) and drugs production. To grow, in the past two decades, outsourcing practices have been performed and the change of direction from the previous business model (vertical integrated supply chain) led to a transition of a new global supply chain. The aim of this project is to analyze the pharmaceutical industry, from an economic perspective, trying to figure out why international outsourcing became a prominent strategy. In addition, the thesis wants to understand the benefits and risks associated with this business model and highlights the fragility of such management practices during the COVID-19 era, focusing on US policy problems. The overall objectives of the projects are supported with a final case study, in which, through numbers, all the hypotheses are confirmed. The structure of the paper is divided in four chapters each of them with valuable information to understand the topic and support the conclusion. The first chapter depicts the theoretical economic approach of international outsourcing, explaining the reasons why this kind of strategy had become such performed in this sector. Few economic models are discussed to understand the phenomena touching positive and negative aspects investigating about the performance in short- and long-term perspective. The second chapter gives an overview regarding the pharmaceutical industry, understanding it through a general analysis of macro numbers of the sector and presenting the geographical distribution of import and export of

pharmaceutical. Then, the ten-principal players of the industry are presented. The third chapter analyzes the main steps through which the products take shape, and which are all the standards that the inventors must follow. Then, it goes on with the description of the supply chain with focus on the shifting from the vertical in-house structure to the current horizontal, analyzing in which step of the supply chain are done all the processes of the product life cycle. In addition, the business model of the new supply chain that characterize the phenomena of outsourcing in the pharma industry and, finally some references concerning the COVID-19 and related policy issues due to the precariousness of the outsourcing model. In the last chapter there is an original analysis done through the WITS database, with which the paper shows with figures the outsourcing trend to emergent economies. Finally, an econometric model based on the gravity equation of bilateral trade give evidence about the positive correlation between import from emerging economies and the overall exports of finished pharmaceutical products and active pharmaceutical ingredients.

CHAPTER 1

The first chapter highlights the economic theories behind the international outsourcing. It starts with the definition to identify the main topic of the thesis and then it begins to investigate through several theoretically model. The analysis is conducted to define the static and the dynamic effects related to this management practices.

1.1 Definition of Outsourcing

In economics, the concept of outsourcing has been identified as the phenomenon of hiring a third-party company that by contract will provide a service or the production of a particular good, giving it the responsibility of a specific process. The outsourcing practice makes it possible to purchase goods or services at a lower price, exploiting the advantage of importing things that are cheaper to produce outside the in-house process. In fact, the home company could shift part of their business outside and it can leverage the possibility of paying lower wages and reduce the cost of the total production of a good or service. This process can also benefit the consumers, lowering the price of the final product.

Outsourcing comes in two different location-based variations:

- Onshore outsourcing

Also known as domestic outsourcing, onshore outsourcing refers to outsourcing a business unit to a third company within the same country where the hiring firm operates. Benefits that come from onshore outsourcing are several such as cultural expectation, same time zone, lower travel expenses and finally a simpler legal approach.

- Offshore outsourcing

Offshore outsourcing is the activity of outsourcing a business department abroad, in other words, relocating the unit of business to another country. Essentially, it does not concern recruiting employers abroad but signing a contract with an external partner organization that will perform part of the business activity. However, if the relocation is done to a neighbouring country, we can refer to it as "nearshore outsourcing".

This paper is going to analyze the aspects concerning international outsourcing (offshore outsourcing) relating to imports and exports between developed and developing countries. Specifically, this chapter looks to theoretically analyze the economic approach of this business strategy.

1.2 Outsourcing model

In order to develop a theoretical model that can give us answers about the benefits and gains of shifting activities abroad, let's describe an outsourcing model

considering only two activities: R&D and components production. We suppose that R&D uses skilled labor and components production uses unskilled labor. The analysis aims to understand if there are some changes in benefits for the Home firm when it shifts from a no-trade situation to an outsourcing situation, in which it is allowed trade with foreign countries. Essentially, by means of economic concepts we are going to show how those concepts applied in the two different situations a)no-trade and b)outsourcing provide important economic results that justify some decisions taken by multinational corporations.

Assumption of the model

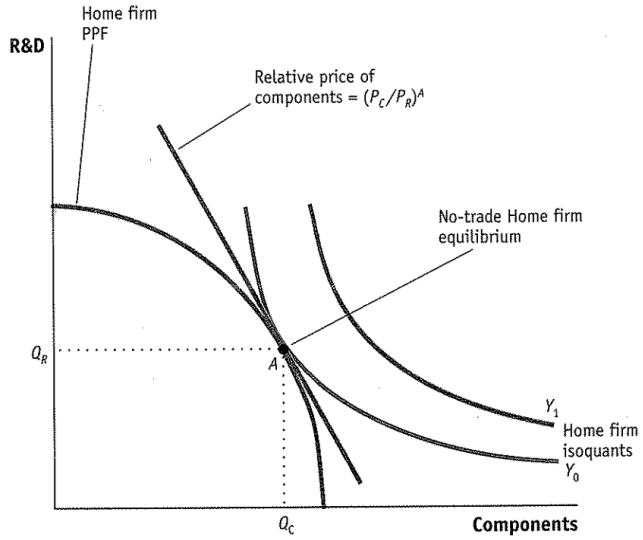
We assume that:

a) There are only two activities R&D and components production
b) Component production uses intensive unskilled labour
c) R&D uses intensives skilled labour
d) The cost of capital is equal in both activities
e) Skilled labour (S) and unskilled labour (L) are free to move between the two activities.
f) The home country is abundant in skilled labour and the foreign country is abundant in unskilled labour

1st situation: "Autarky"

Given R&D and Components as our two activities, we can introduce the Production Possibilities Frontier (PPF) to the model. We will use this PPF for the domestic company and through it explain the main economic reasons for the changes in skilled and unskilled labor in autarky and trade, and all the shifts that the graph will experience. After plotting the graph, we start to analyze the autarky situation and the main economical insights that are possible to understand from the graph.

Figure 1: Autarky Equilibrium for the Home firm



Source: *(Feenstra & Taylor, 2014)*

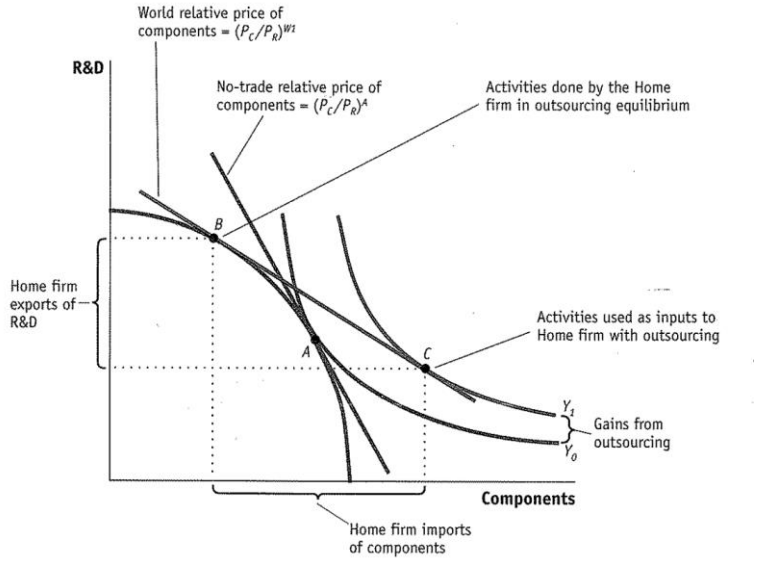
In this actual situation, the home firm cannot engage in trade with a foreign market. As a matter of fact, this implies that components production and R&D utilized at home are the ones that are going to produce final goods or services for Home, by definition. In addition, as illustrated in the graph, point A represents the amount of (Q_R and Q_C) used for R&D and components manufacturing. In order to understand

how much is produced by the firm and which combination of labour is utilized, the economic theory gives us "isoquant". In the graph this is represented by the curve Y_0, and along Y_0 the amount of product manufacture remains constant, but the combination of QR and QC differs. For instance, the isoquant in point A shows that the final goods produced are the combination of the quantity Q_R and Q_C respectively of R&D and Components. Moreover, if we observe the isoquant Y_0 we notice that it is tangent to the PPF in point A suggesting that Y_0 is the isoquant that gives to the model the highest amount of final products independent of the combination of Q_R and Q_C. As shown by the graph, the production resulting by isoquant Y_1 cannot be reached since the curve does not lie in the production possibilities frontier. Another relevant piece of data is the slope of the isoquants. Fundamentally, the slope indicates the value, in this case, the price of the components relative to the R&D, $(P_c/P_R)^A$. In conclusion, in the first step of "autarky" the home firm cannot trade, and all production done at home is used to produce the final good for home. The model explains this concept through equilibrium point A which is the point of tangency between the PPF and the isoquant Y_0. The result is the optimal combination of skilled and skilled labour given by Q_R and Q_C with a slope of the isoquants equal to $(P_c/P_R)^A$ that represents the relative price of components with respect to R&D.

2nd situation Outsourcing

In this case, with the same assumption, international trade is now allowed, and the home firm can import and export their activities through outsourcing. In brief, components that were previously made at home can now be done/produced abroad alike R&D.

Figure 2: *Outsourcing Equilibrium for the Home firm*



Source: (Feenstra & Taylor, 2014)

The correlated consequence of an open market where international trade is authorized consists of a total production that is no longer constrained within the production possibilities frontier (Home). However, it is possible to construct a

higher isoquant that allows the firm to produce more final goods through outsourcing practices. At this point, it is crucial to make an important assumption.

- $(P_c/P_R)^{W1} < (P_c/P_R)^A$, we assume that the relative price of components is cheaper Foreign than Home.

What does this assumption mean? Basically, it means that Home wants to outsource components because the relative price is lower. $(P_c/P_R)^{W1} < (P_c/P_R)^A$ that is strictly correlated with $W_S^*/ W_L^* < W_S/W_L$. As a consequence, if the relative wage in Foreign is lower, the Home firm is encouraged to import components from outside where it is cheaper. Furthermore, looking at the graph, it is noticeable that the equilibrium point is no more in A. Indeed, the straight line of the slope, world relative price of components, is now flatter than the previous one demonstrating the assumption that $(P_c/P_R)^{W1} < (P_c/P_R)^A$. So, in a no-trade situation, home cannot exploit the advantage that outsourcing offers by lowering the relative price of components. The lowering of price shifts the equilibrium point on the PPF, from A to B, where more R&D is produced with respect to components (the overall amount of skilled and unskilled labour remains unchanged). The actual situation allows the home firm to export R&D in excess and import components that now are produced foreign. Moreover, through outsourcing, the home firm is able to go outside the PPF, in fact, moving along the world relative price line we can notice that now it is tangent with a higher isoquant Y_1. The tangent point is shown by C indicating the

fullest amount of production of final goods and if we pay attention to the dotted line, the difference in the vertical axis between B and C gives the overall amount of the exports of R&D done by the Home firm. On the other hand, the difference in the horizontal axis between C and B gives the total amount of components imported by the home firm from abroad.

1.2.1 Results of Outsourcing

The analysis developed in the 2nd situation, with the outsourcing equilibrium, lead to interesting results. First, the increase of the total amount of production, shifting from the isoquant Y_0 to the isoquant Y_1, is significant because it measures the gain from trade exploiting outsourcing practices. Indeed, using the same amount as in autarky of skilled and unskilled labour, the Home firm now produces more final goods. In brief, Home having available the amount of Q_R and Q_C, is now more productive. Secondly, the general cost of production for the home firm decreases and therefore the interesting result we expect is the falling of the final price of products. In conclusion, the gain earned by shifting from the isoquant Y_0 to the isoquant Y_1 , was not only absorbed by the Home firm but also spread to final customers.

1.3 International Trade and Terms of Trade

To provide more value to our theoretical explanation another factor must be added, the “terms of trade”. Specifically, we need to identify what the effects are and how much they influence the country's terms of trade when a firm decides to outsource a unit of business.

Terms of trade is generally recognized as an economical measure that equals the price of country exports relative to the price of country imports. Applying this concept to our model, already built up, the Home terms of trade is: $(P_R/P_C)^{W1}$ because we have supposed that the home firm imports components from abroad and exports R&D. Consequently, we are going to briefly analyze two different situations occurring from outsourcing and that implies different outcomes with reference to terms of trade. The first situation led to a rise of the measure, which is correlated to a lower price paid for the goods imported or higher price requested for the product or service exported. The second one concerns a fall in terms of trade due to a higher price paid for its imports or a decrease in the price of the goods exported.

1st Case

Let assume the hypothesis that there is a fall in the relative price of components; the actual situation is the following:

- $(P_c/P_R)^{W2} < (P_c/P_R)^{W1}$

This assumption may be due to a strategic efficiency implementation in the production process of the foreign firm. Thus, the price paid by the home firm would be lower than before and as a consequence an increase in benefit for the home country.

The new graph shows how the rise of terms of trade or the reduction in the relative price of components implies an increase in benefit for the home country.

2nd Case

Let's assume, on the other hand, a different implication that can occur when a firm decides to outsource. The assumption is the following:

- $(P_c/P_R)^{W1} < (P_c/P_R)^{W3}$

The formula above indicates a higher relative price of components with respect to R&D and that means a lower profit in sales when those products and services are sold by the home country because the cost of production is now higher in a foreign country.

1.4 TOTAL OUTSOURCING, PRODUCTIVITY AND ORGANIZATIONAL INNOVATION

Generally, outsourcing shifts production or R&D services outside the barriers to an external provider. However, the relationship between total outsourcing and productivity highlights the presence of a paradox. Basically, it is proven with a theoretical model that in the short-run companies can reduce and cut costs, therefore in the long-run firms practicing outsourcing are involved in a lower productivity growth dynamic that is not experienced by the firms that do not engage in outsourcing. The main objective of this section is to highlight the weight that has the control over the firm activities rather than the activities per se; this is possible by analyzing the combination of each module composing the entire organizational architecture of the firm.

1.4.1 Model of organizational innovation and total outsourcing

The research process starts with a random selection of an activity where the management identifies a critical situation, and it can consider implementing an innovative strategy to increase Total Factor Productivity (TFP). The managers can opt for organizational restructuring or the improvement of an already existing activity's modules. The first is the phenomenon called "exploration" and consists

of an international identification of an external provider to outsource the activities altering the organizational structure. The second concerns the phenomena of "exploitation" and it suggests the improvement of the performance through the exploitation of the actual resources that the firms have, even in this case altering the current organizational structure.

1.4.3 Exploitation and Exploration

The model provides to the manager a set of strategies. The first is the strategy implemented in the exploitation case, where innovations are realized by the concept of learning by doing internally. On the other hand, the second is an exploration strategy and it consists of splitting complex activities into several less complex modules.

1.4.4 Decision process

First of all, managers are able to understand, whether to reject or accept an organizational innovation by looking at the profitability. Given the current profit, $\Pi_{d_t}(s_t)$, of the firm, they compare it with the expected profits that are likely to be generated by the new architectural structure, E[$\Pi_{d'_{t+1}}(s_t)$].

- $\Pi_{d_t}(s_t) \geq$ E[$\Pi_{d'_{t+1}}(s_t)$] Reject Innovation
- $\Pi_{d_t}(s_t) <$ E[$\Pi_{d'_{t+1}}(s_t)$] Accept Innovation

Furthermore, the firm, deciding which strategy to adopt, is influenced by the propensity to outsource.

- $E[\Pi_{d''_{t+1}}(s_t)] \leq E[\Pi_{d'_{t+1}}(s_t)]$ In house
- $E[\Pi_{d''_{t+1}}(s_t)] > E[\Pi_{d'_{t+1}}(s_t)]$ Outsource

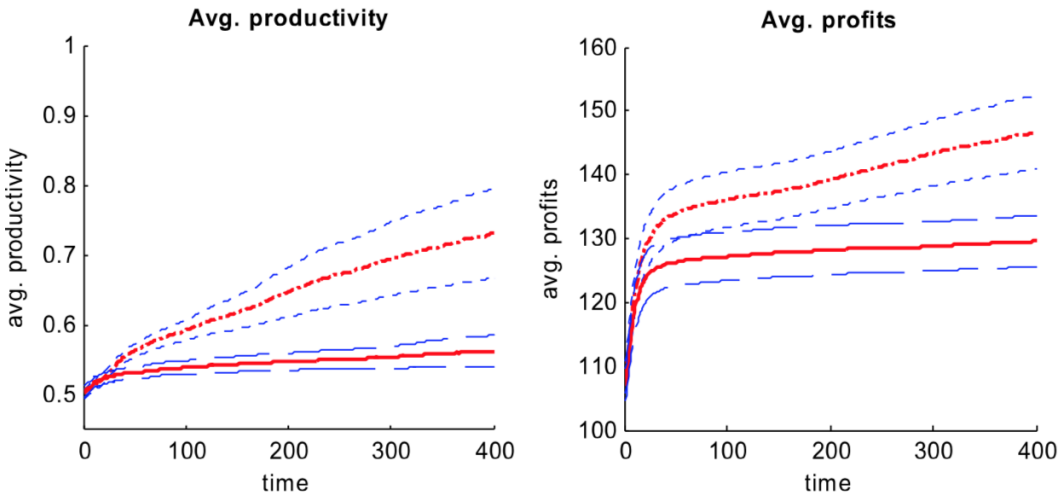
1.4.5 Results of the model

The simulation of the model led to the conclusion depicted by figure 3. The graphs describe two different results for the two scenarios taken into consideration above. The dotted line corresponds to "scenario 1" the others to "scenario 2". Basically, scenario 1 suggests that in-house coordination costs are influenced positively by IT. In addition, the development of the model describes through the graphs that in the long run there is an increase, on average, in productivity and in profits.

On the other hand, if we look at "scenario 2", which corresponds to outsourcing practices, IT provides cuts in costs for external coordination activities rather than internal coordination activities. The graph, indeed, suggests that after a short-run increase in productivity and profits than in the long run there is a stagnation of the trend resulting in lower total factor productivity.

To conclude, the model confirms the paradox that companies involved in outsourcing perform, in the long-run, lower productivity and profits, despite the companies not engaged in outsourcing practices. They succeed with higher productivity and higher profits.

Figure 3: Model results: Avg productivity and Avg profits



Source: P.Windrum · A. Reinstaller · C. Bull

1.5 STATIC AND DYNAMIC EFFECTS

Literature of outsourcing focus its debate too often on *static* effects paying less attention to *dynamic* ones that affect a firm's long-term performance. The two models together with "Naghavi and Ottaviano" paper show how the outsourcing processes are associated with a short and long-term perspective affected by internal and external dynamics occurring within the process. As already explained by the "Feenstra and Tylor" model, international manufacturing contracts can generate an increase in profit due to cost minimization such as low labor costs and reducing fixed costs derived from economies of scale. For instance, India, as a result of procuring multiple outsourcing contracts, was able to spread fixed costs over the production of larger volumes. Other reasons lay behind the short-term gains and this static phenomenon; for instance, practising outsourcing allows home firms to access resources that they are unable or unwilling to create leading to a big competitive advantage in terms of shorter time to market, which is a key determinant to short-term success. In addition, another reason is the resources leverage topic, which consists of better leveraging internal resources such as the high-value activities (core) and externalizing the low-value activities (non-core). Finally, contractors aggregate demand from different customers so their ability to diversify risks is better exploited than the home firm itself. However, as Naghavi and Ottaviano suggest international outsourcing occurs only if another variable,

transportation costs, does not negatively affect the gains generated by the delta between internal and external cost of production. Those facts explain the static effects provided by international outsourcing and why this business strategy spreads its presence over almost every industry and sector. Furthermore, in their model, Naghavi and Ottaviano did not conclude their research analyzing only static effects, but they also investigated the possible dynamics effects that affect the long-term. To summarize their model, they provide a scenario with two factors of production (labor and knowledge capital), two sectors (R&D innovation and production) and two geographical locations; North (where all workers and consumers come from) and South (simply production site, place where workers can be employed).

Basically, assuming South as a production site they want to study the offshoring consequences that come from it. They observed a productivity gain when production was shifted from North to South but only when shipping costs are less than the delta between internal and external costs. Analyzing those aspects of outsourcing they were faced with a new question. Does offshoring affect the marginal cost of in-house innovation?

Assuming that R&D innovation faces a learning curve, so that the marginal costs decrease with the number of successful products introduced in the past; it is clear that shifting the production abroad reduces the feedback from production to labs and the marginal cost, for the home firm, increases, because indirectly the products successfully introduced are developed by the foreign firms. This is the direct

consequence of knowledge spillovers, the involuntary leakage of all kinds of specialized knowledge within the industry. Indeed, outsourcing helps this kind of phenomenon leaving the home firm at the mercy of the barging power of suppliers. Nonetheless, offshoring prevents building competency within the organization, eroding the in-house knowledge, a critical point for long-term competitiveness. As a matter of fact, the dynamic effects of outsourcing have a negative impact on the profitability and the growth of the firm. Indeed, the two models, the Naghavi-Ottaviano thesis and the one regarding the organizational architecture structure agree with the final results that reducing feedback from plants to labs leads to dynamic losses because important news is not internalized by the home firms causing knowledge spillovers. As a consequence, it is more difficult to coordinate plants and labs when two different firms are running the businesses, and this will have an impact on the innovation and consequently the growth and productivity of the home firm.

1.6 Other Benefits and Risks of Outsourcing

Globalization and openness to foreign markets increased the opportunities to explore external trade where conditions allow increasing in profit and in firm's efficiency. Pharma companies decide to benefit from third-party partnerships for numerous reasons such as lack of infrastructure and facilities able to satisfy the requirements of the industry trends, assistance in the product and process development, possibility to explore a potential market without investing in the production structure. In addition, outsourcing can occur when a company is not able to satisfy the determined manufacturing schedule on time but also when sales exceed capacity. Nevertheless, this approach does not avoid risk, instead, multiple issues can arise, so it is fundamental to understand the benefits and risks caused by the practice of outsourcing and verify the trade-off between those two elements. Several benefits can be highlighted when outsourcing occurs such as:

Cost saving: Firms do not invest in facilities and equipment and can exploit the advantage of the low cost of labor. Long-term relationships can encourage lowering the price of services trusting in a lasting and constant flow of business.

Advanced skills: It can leverage the expertise and skills a contractor has but you are not able to reproduce without investing in it

Quality: The firm does not concern about quality in as much as the contracts owns an internal department focused on quality control. This permit to identify earlier problem or mistake in the production and value chain.

Focus: Freeing up available resources, pharma companies can concentrate on their main activities saving time and being more efficient.

Economies of scale: CRO and CDMO have a large portfolio of clients this implies huge production or R&D activities. Generally, economies of scale (are able to acquire) allow acquiring raw material at a lower price, reflecting on the final price of the service provided by the contractor to the sponsor.

Reduce time-to-market: Ready to satisfy a sudden request of the market without missing business opportunities.

On the other hand, it is coherent highlights the possibility to meet also risks like:

Lack of Control: Making agreement about production of their own products company loses the control on it. They are only able to provide strategy suggestion.

Trust: It is crucial to create a positive relationship with the contractor in order to work in a positive business structure, where the decisions are made cohesively

Quality concerns: When the sponsor decides to sign a contract, it has to be sure about the quality standards adopted by the contractor. Before signing the contract, the hiring firm should always observe that the methods to control quality match with their own.

Intellectual property loss: Once the strategy of outsourcing a unit of business is defined the pharma company starts sharing internal data and formulas with its contractor. It is fundamental that, all this information which is strictly private and could undermine the intellectual property owned by the Sponsor, is kept confidential.

General outsourcing risks: Language barriers and/or cultural differences.

Capacity constraints: The contractor may work with multiple clients so the sponsor could lose priority during intensive production periods. The risk is not being able to satisfy the demand because it does not have products on time.

Dependency of autonomy: The risk of being dependent on your suppliers and losing the flexibility gained by outsourcing when something unpredictable occurs.

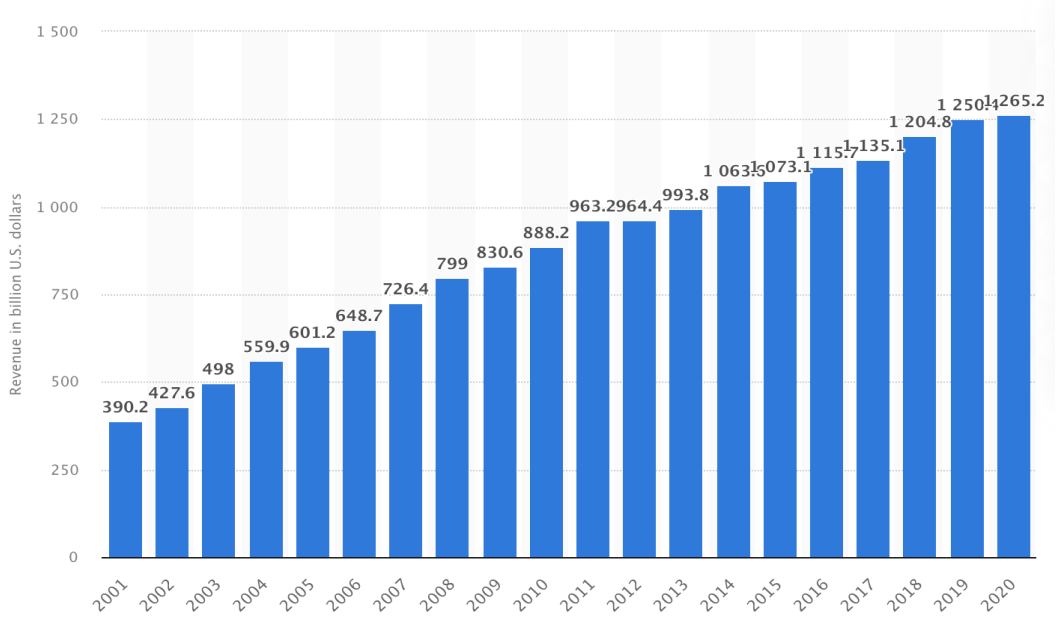
CHAPTER 2

This chapter provides a general overview of the pharmaceutical industry focusing on macro data and companies. Firstly, driven by figures it is possible to understand the dimension of the sector and how it is distributed through a geographical analysis of the main developed and developing countries. Then, an analysis aims to show the main pharmaceutical companies that are placed on the top of the industry pyramid.

2. The Pharmaceutical Industry in Figures

Today, the pharmaceutical industry is in the spotlight due to the pandemic situation. As a matter of fact, if we look back to recent history, compared to the current situation, it seems clear how the overall market value trend rises to an amount never reached before. Indeed, from 2001 to 2020, the revenue generated by this industry almost tripled. It was close to 400 billion dollars in 2001 (390.2) reaching the highest amount in 2020, 1265.2 billion dollars.

Figure 4: Revenue of the worldwide pharmaceutical market from 2001 to 2020



Source: Statista 2021

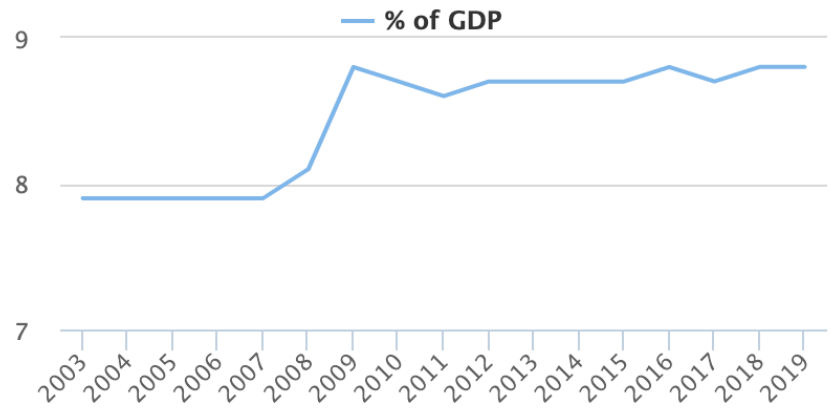
Basically, the rapid and fast globalization process and the increase in alliances and mergers led to this fast-growing trend in terms of revenue generated by the sector. In addition, this growth in revenue led to high intensity in competition where, in order to survive, companies have to perform a strategy of lowering price, discovering new products or increasing the efficiency of service through the implementation of new technology. Generally, the competition differs from patented and generic products, this implies a separate analysis in order to understand how competition works.

Competition for patented pharmaceuticals is essentially based on new

pharmaceuticals placed on the market. However, only a small number of organizations can compete in this segment, due to the barriers of the R&D process and financial costs. In fact, the competition is made up of innovation, intellectual property rights and product patents. Other factors do not influence the competition, for instance, packaging and marketing are subordinates compared to the exclusivity gained by the patents and the range of business is worldwide. On the other hand, competition for generic pharmaceuticals is restricted to countries where the patent of the original pharmaceutical has expired. In general, the competition is based on price and marketing because now anyone can try to produce the pharmaceutical according to the expired patent.

Rapid and fast globalization and competition on the other hand were the main drivers to achieve this stunning result in less than 20 years.

Figure 5: *OECD health spending as a share of GDP, 2003 to 2019 (estimate)*



Source: Organisation for Economic Co-operation and development

If we look at the health expenditure in relation to GDP, the figure remains unchanged after the economic crisis of 2008 and 2009. In fact, OECD data shows a sizable jump during that period but since then, the trend has remained quite stable until now. OECD reports that the average expenditure in percentage in 2018 was 8.8% of GDP (OECD countries). Analyzing the data from the OECD regarding the healthcare expenditure and financing, they show us that from the very beginning of the 21 century until now there has been a general growth in the healthcare expenditure of 2%.

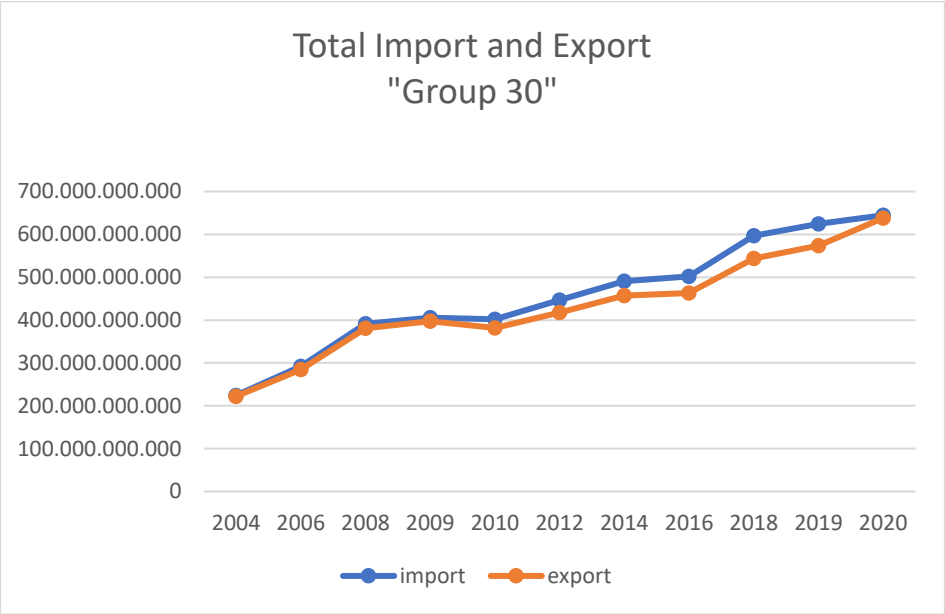
2.1 Geographical Distribution of Import and Export of Pharmaceuticals

The pharmaceutical industry plays a relevant role in the economic scenario, and it is experiencing constant growth. For instance, the graph below (Figure 4) illustrates imports and exports of pharmaceutical products concerning the code 30[1]. The vertical axis shows the value in US dollar of pharmaceutical products imported and

[1] (30.01 Glands and other organs for organo-therapeutic uses 30.02 Human blood prepared for therapeutic prophylactic and diagnosis uses, 30.03 Medicaments consisting of two or more constituents which have been mixed for therapeutic or prophylactic use NOT PUT UP in measured doses, 30.04 Medicaments consisting of mixed or unmixed products for therapeutic or prophylactic uses, PUT UP in measured doses, 30.05 Wadding, gauze, bandages, and similar articles, 30.06 Other pharmaceutical goods).

exported, instead, the horizontal axis represents the year in which the study was conducted from 2004 to 2020. Overall, both imports and exports have slumped since 2004 demonstrating the general health and prosperity of the industry. However, while the general trend is in constant improvement, during the economic world crisis in 2008, the lines seem to remain steady to the value of 400 billion dollars for both. Then in 2010 the positive rise in trade started again. In fact, starting from 224 billion dollars of import and 222 billion dollars of exports in 2004, now in 2020 they reached 644 billion dollars in imports and 638 billion dollars in exports almost three times the initial value. The reasons are multiple like numerous discoveries during the last 20 years, increasing the demand for any health product.

Figure 6: World import and export from 2004 to 2020



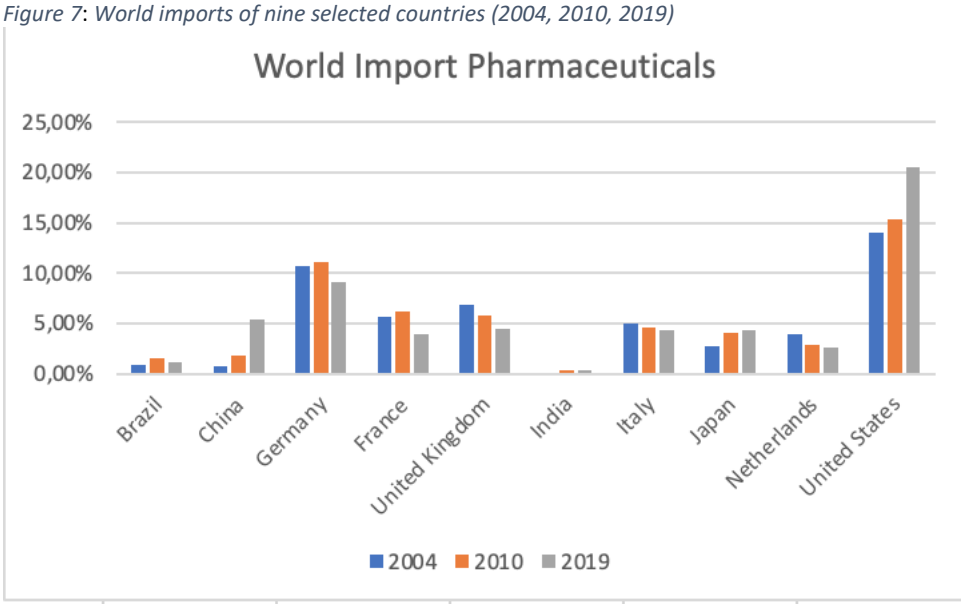
Source: Own elaboration

Considering the values of the overall exports and imports of pharmaceutical products, it is reasonable to compare those values with the principal players and emergent ones to analyze how the trade of the industry is geographically spread. The followings figures analyze the percentage of imports and exports of Brazil, China, Germany, France, the United Kingdom, India, Italy, Japan, the Netherlands, and the United States.

To begin, Figure 7 allows us to understand the percentage of imports related to the total, considering the countries described above.

- Reporters: Brazil, China, Germany, France, the United Kingdom, India, Italy, Japan, the Netherlands, and the United States.
- Partners: World
- Trade Flow: Import
- Years: 2004. 2010, 2019

Figure 7: *World imports of nine selected countries (2004, 2010, 2019)*

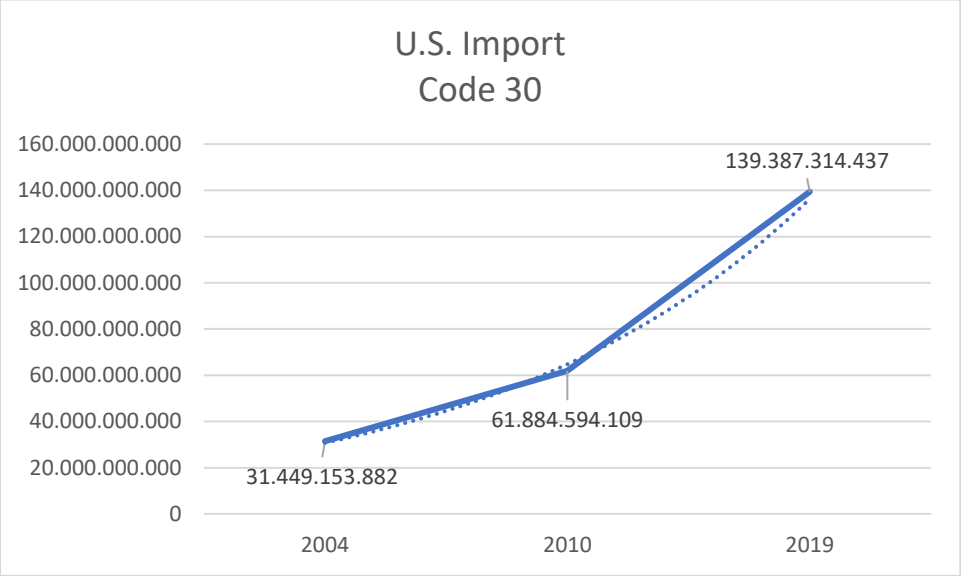


Source: Own elaboration

The U.S. bar shows a significant increase over the years starting from 14.01% reaching its peak in 2019 with an overall value of 20.51%. The United States is the leading country in the pharmaceutical industry, therefore the general rise in imports suggests that outsourcing practices were done in the period taken into analysis and in addition, it gives information about the always increasing dependency of the US on foreign suppliers. Furthermore, it is relevant to mention that, as Figure 7 depicts,

an increase of around 6% in terms of dollars is a very large improvement; in fact, 14.01% in 2004 corresponded to 31.5 billion dollars of pharmaceutical products imported, the 20.51% corresponded to 139.3 billion dollars.

Figure 8: *U.S import of pharmaceutical products*

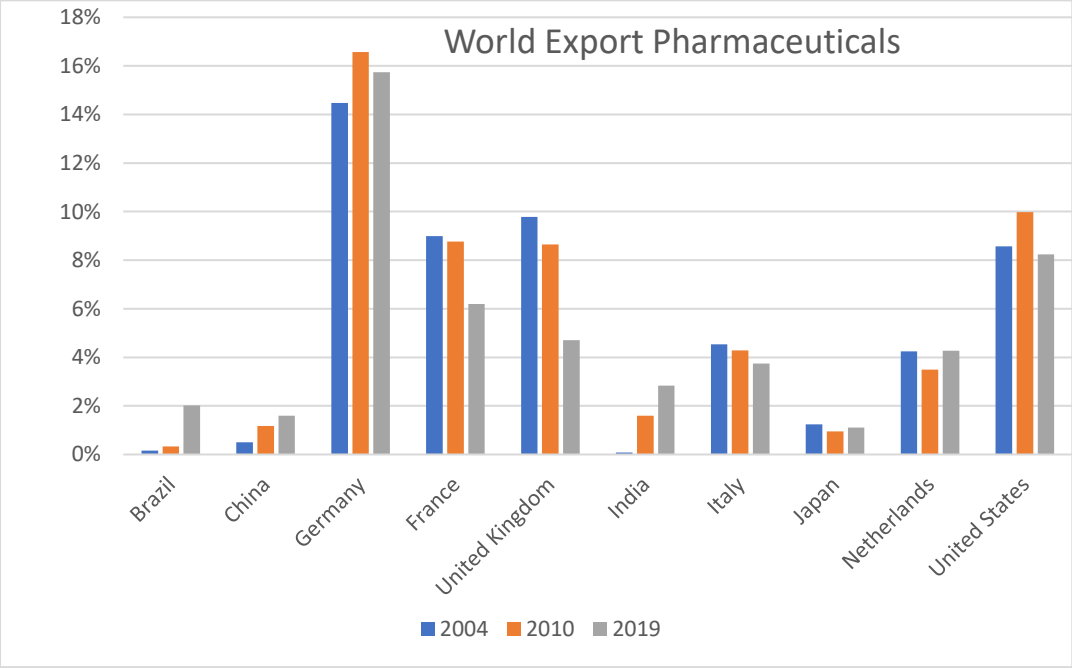


Source: Own elaboration

Another interesting result is what tells the China's bar in Figure 7. Basically, starting from a percentage of 0.70% of the overall share of imports it slumped to a stunning 5.37%. The reason behind this flow of values is the constant growth of China's pharmaceutical market, that can be considered as the second-largest market in the industry, indeed even if the import value is a synonym of dependency on external economies, it is true that when a market growth necessarily variable of

quantity tend to increase. Other relevant values are shown by Germany, France, and Italy (three of the major players in Europe) that altogether account for 17,43% of the total pharma products imported. Finally looking at India, it is clear how the total amount of pharmaceutical products imported is not so relevant, indeed it increased slightly from 2004 but overall value was less than 1% in 2019, more precisely 0.40% starting from a value of 0.13%. India is one of the major manufacturers in this industry and in fact it counts the majority number of manufacturing plants authorized by the FDI. Going throw the analysis the export of the subgroups 30.04 will give some justification for that.

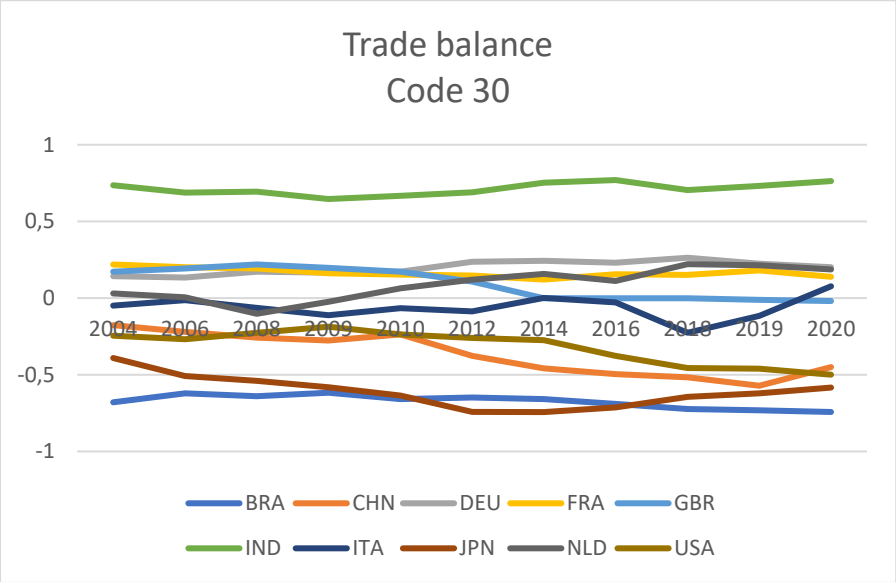
Figure 9: World exports of nine selected countries (2004, 2010, 2019)



Source: Own elaboration

Concerning Figure 9, at first glance there are less evident results than before, however, they confirm how the industry is moving. For instance, if the imports of the US reaches its highest point in 2019, the table illustrates a negative stable trend on the export reaching the lowest percentage of 8.24%. This small decrease in dollars of pharmaceutical products exported, is probably due to the pandemic situation nonetheless, this highlights a situation where imports exceed exports resulting in a negative balance of trade (BOT). It is also interesting the percentage resulting from the three European countries, Germany, France, and Italy respectively with a total export percentage of 15.75%, 6,20% and 3.74% reaching an overall value higher than the imports results, meaning of a positive balance of trade. China and India increased their exports; however, it is difficult to find relevance only through this data. Following the "case study" in the last chapter, more specific data will clear up and will give a more defined analysis of these two countries. In addition to the three representations above, a line graph has been produced to describe the trade balance of the nine countries referring to group 30.

Figure 10: Trade Balance of the nine countries selected



Source: Own elaboration

Figure 10 describes net exports which is a measure of a nation's total trade. The formula used to calculate those values is the following:

$$Trade\ balance = \frac{(\ Export\ -\ Import\ )}{(\ Export + Import\ )}$$

The graph suggests once again that the U.S. (brown line) is a net importer rather than a net exporter. On the other hand, India (green line) is a net exporter with a positive coefficient throughout the whole period.

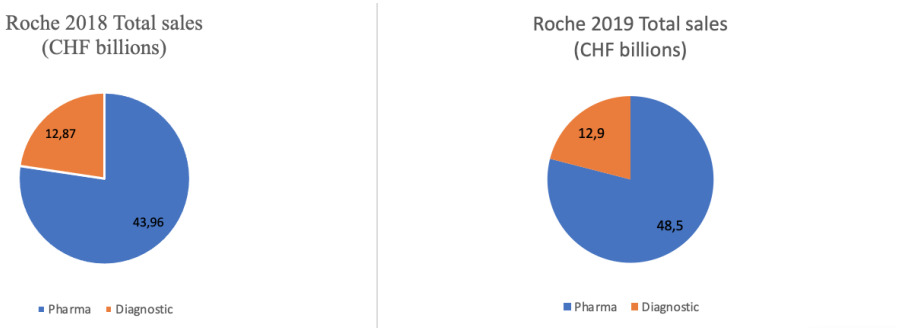
2.2 Main Pharmaceutical Players.

To begin, this part of the thesis is going to analyses the biggest pharma companies, per revenue, in 2019. The main players are the following: Roche, Pfizer, Johnson & Johnson, Merck & Co Inc, Novartis, AbbVie Inc, GlaxoSmithKline uplc. The companies mentioned above are part of the so called “Big Pharma”. Big pharma is one of the most powerful industries in the world, with a turnover of more than one thousand billion dollars. Four out of seven are American companies

2.2.1 Roche

Roche is a pharmaceutical company which focuses on patients by responding at the right time with the right treatment. The company has a combination of Pharmaceutical and Diagnostic departments and through them can deliver unique personalized healthcare. In 2019 Roche experienced very impressive results, indeed group sales rose by 9% from the previous year reaching 61.5 billion CHF. If we look at the Pharmaceutical Division sales increased by 11% achieving the highest amount of the company until that moment, 48.5 billion. The reason behind the increment in sales was the speed at which Roche managed the innovation of new medicines and brought them to patients. As a matter of fact, the main drivers were the multiple sclerosis medicine Ocrevus, the new haemophilia medicine Heamlibra and cancer medicines Tecentriq and Perjeta. Roche is divided into two main business segments: Pharmaceuticals and Diagnostics.

Figure 11: Roche Turnover



Source: Roche Annual Report 2019

2.2.2 Pfizer

Pfizer is a pharmaceutical company, and its primary objective is to apply science and its resources to find solutions and provide new technologies and medical treatments that are consistently helpful for patient lives. They want to achieve these results through the discovery, development, manufacturing, and distribution of pharmaceutical products like medicine and vaccines. Basically, the operation structure is composed of three main business areas: Pfizer Biopharmaceuticals Group (Biopharma), Upjohn and Consumer Healthcare. Looking at the financial highlights, 2019's total revenue experienced a decrease of 4% compared with 2018 (51.8 billion in 2019, 53.6 billion in 2018). However, a more precise analysis reports that the pharmaceutical manufacture and sales revenue from 2018 to 2019 demonstrates a quite stable trend.

Figure 12: Revenue by operating sector (2018 and 2019)

Source: Pfizer Annual report 2019

Indeed, the revenue resulting from pharmaceutical sales is the sum between Biopharma area and Upjohn area. As a matter of fact, the sum in 2018 is 93.3% of total revenue, corresponding to 50.01 billion dollars while in 2019 the sum is 96% of total revenue corresponding to 49.728 billion dollars. Furthermore, Pfizer, and more specifically Biopharma, is looking for a long-term strategy that takes into consideration long-term growth opportunities. For instance, growing life expectation implies an increased demand for new medicine in order to address unmet patients' needs. Moreover, investments in new technologies and biological science to deliver the best solution for the final consumer.

2.2.3 Johnson & Johnson

Johnson & Johnson was incorporated in 1887 in the State of New Jersey. The company is structured in three main divisions: Consumer, Pharmaceutical and

Medical Devices. Furthermore, the pharmaceutical segment can be divided into six specific areas: Immunology, Infectious Disease, Neuroscience, Oncology, Cardiovascular and Metabolism and Pulmonary Hypertension. Looking at the sales revenue, the annual report gives a precise insight about each operating segment.

Figure 13: Sales by segments (2018 and 2019)

Source: Johnson & Johnson annual report 2018 and 2019

As shown by the pie chart, there is a clear positive trend in the overall sales figures. But more interested in our analysis is the evident increase by 1.5 billion dollars in revenue for the pharmaceutical areas. In fact, if we look at the financial statement reported in the annual report, all the subareas that make up the pharmaceutical division experienced an increase in sales during 2019 except cardiovascular and metabolism which decreased by 10.7% between 2018 and 2019. To sum up, total pharmaceutical sales gained 1.5 billion dollars corresponding to an increment of 3.6%.

2.2.4 Merck & Co Inc

Merck & Co Inc is a corporation working in the healthcare field mainly focused on health solutions such as medicines, vaccines, biologic therapies and animal health products. The company is divided into four different segments: Pharmaceutical, Animal Health, Healthcare Service and Alliances. As usual in this analysis, we are focusing/concentrating on the pharmaceutical division. The table below gives some figures relating to the years 2018 and 2019

Figure 14: Total sales Merck & Co Inc.

Source: Merck & Co Inc. Annual report 2019

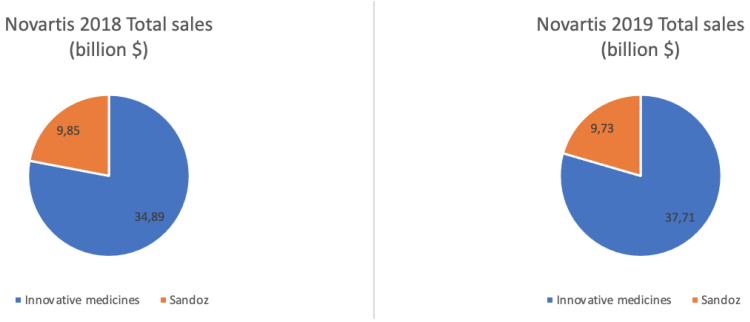
The table describes the total revenue generated by the company in 2018 and 2019. As analysed in most of the previous corporations, even in this case the total sales increased (+10,74%). The second raw of the table shows the specific figures about the pharmaceutical segment and in this case, anyway, there is a positive trend between the two years. From 37,689 billion dollars in 2018 to 41,751 billion dollars in 2019 with an increment of more than 4 billion. The pharmaceutical division

includes human health pharmaceuticals and vaccine products. The first concerns the medical treatment of human disorders instead the second consists of preventive products for children, adolescents, and adults.

2.2.5 Novartis

Novartis is a leading company in the pharmaceutical sector, it is one of the ten largest corporations worldwide. Novartis' strength is the ability to adapt innovative science and technologies therapies to the most difficult healthcare issue and deliver them to as many patients as possible. The multinational is made up of two main specific business divisions: Innovative medicines (patent-protected products) and Sandoz (generic and biosimilars). In 2019 a new separated company, a spin-off Alcon was established/opened/founded/set up. Moreover, the general financial trend of Novartis in 2019 achieving 47.4 billion dollars revenue in sales increasing their previous financial year by 6% and by 9% considering the change in constant currency. This increment is the result of the launching of 5 new innovative molecular products.

Figure 15: Net sales to third parties segments



Source: Novartis Annual Report 2019

Figure 7 describes net sales divided by segments and compares them between 2018 and 2019. As above mentioned the two segments are Innovative medicines and Sandoz. As a matter of fact, looking mainly at the pharmaceutical patented products it seems clear how the introduction of the new molecular entities had an impact on the turnover. Indeed, three more billion dollar have hightened the total net sales to third parties regarding Innovative Medicines moving out of 34.892 billions to 37.714 billions.

2.2.6 AbbVie

AbbVie is a biopharmaceutical company established in 2013 after the separation from Abbott Laboratories. Like the other big corporations, AbbVie's objective is to utilize its expertise and knowledge to make a difference in the healthcare battle against serious diseases. AbbVie technologies and medicines treat conditions including chronic autoimmune diseases in rheumatology, gastroenterology and

dermatology, oncology including blood cancer, virology, immunodeficiency virus (HIV), neurological disorders and metabolic diseases. Furthermore, opposed to the previous analyzed corporation AbbVie is composed of only one business segment: pharmaceutical products. As for the other multinational companies, the below figure 9 is going to consider the main financial figures to understand in broad terms how was, financially and economically, the business years 2018 and 2019 comparing a series of items that depicts the situation of AbbVie at the end of the 2019.

Figure 16:General financial data

Source: Annual report AbbVie 2019

Approximately, the positive growth trend is clear (even if we look at the previous year), from 2018 to 2019 where net sales increase by $500 million and, we note the jump in items per share. This strong financial performance gives AbbVie the power

to invest in their pipeline and R&D departments.

2.2.7 GlaxoSmithKline

GlaxoSmithKline has 99,000 employees across 95 countries with strong expertise in technologies, medicines, intellectual property and marketing of healthcare products. Together with these strong workforces, GSK has joined relevant strategic partnerships over the years to enlarge their actual know-how. There are three business units in which GSK operates in order to discover, develop and manufacture new products like pharmaceuticals, vaccines and consumer healthcare. Pharmaceuticals is composed of several medicines concerning the respiratory system, HIV, immune inflammation, and oncology. On the other hand, GSK is the biggest producer of vaccines with a range that covers all stages of life. Finally, consumer healthcare is about the ability to create brands that are trustworthy through specific scientific knowledge, indeed in 2019 GSK finalized a partnership with another colossus, Pfizer, to combine their two-consumer healthcare business.

Figure 17: Pharmaceutical and vaccine turnover

Source: GlaxoSmithKline annual report

Figure 10 shows the total revenue generated in 2018 and 2019 by business unit division, precisely the pharmaceutical and vaccine net sales. Both together generated around 24,7 billion in 2019, respectively 17,55 billion for pharmaceuticals and 7.15 billion for vaccines with an increment of 6,6 % compared to 2018.

CHAPTER 3

The goal of this third chapter is to highlight the steps that compose the pharmaceutical product life cycle from the discovery until the final entrance to the market. Furthermore, this part of the project analyses the structure of the industry comparing the old supply chain with the modern one indicating the changes, during the past two decades, owed to different global context and different strategies adopted. Then the analysis proceeds with the corporate strategy adopted in order to exploit the practices of outsourcing. Indeed, the project illustrates how outsourcing is performed abroad and which kind of contract organizations play a relevant role to connect the home firm and with the country destination. In other words, the thesis wants to show which are the contract organization, what characteristics they have and in which step of the supply chain they are positioned. And finally, a consideration about COVID-19 issue in U.S. due to outsourcing precariousness.

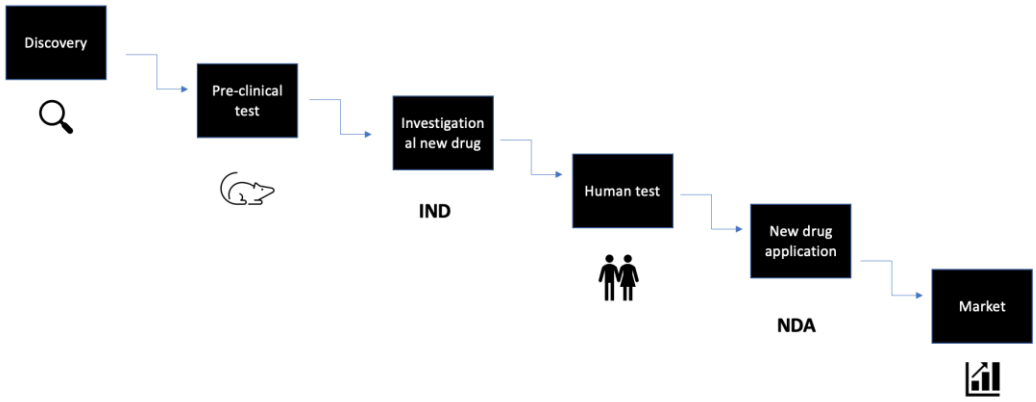
3.1 Pharmaceutical Product Life Cycle

In general, the pharmaceutical life cycle presents these four fundamental steps:

1) Drug discovery
2) Pre-clinical and clinical trials
3) Post-market drug review
4) Generic competition

The process starts after the discovery of a new compound. However, before setting up the pre-clinical and clinical trial, the manufacturer must apply for a patent that will be issued by the Regulator (Food and Drug Administration or European Medicines Agency). In the meantime, while the manufacturer is waiting for the patent to be granted, the pre-clinical phase begins. This is a period of laboratory or animal testing that precedes the submission of the investigational new drug (IND) application to the Food and Drug Administration (FDA). Once the regulator approves the application, the manufacturer moves to the next step, human testing, or clinical trials. This stage is made up of three phases called I, II, III; if the drug is able to pass through all the three phases then the producer can submit another drug application, the new drug application (NDA) and a description of all the outcomes resulting from the trials. Now, the role of the regulator is to control and verify that the molecule is safe and if it fulfils all of the requirements needed to enter the market.

Figure 18: Pharmaceutical product life cycle



Source: Own elaboration

3.1.1 Drug Discovery

While in the past scientists used to discover drugs randomly, now the process is more rigorous following a defined scientific and logical method. This new way of searching for molecules adopted by pharmaceutical companies is called “rational drug design”. Basically, it refers to a new process of understanding where scientists try to find the right molecule by analysing the cause. It is no longer a process of trial and error; they try to theoretically identify the reason why a drug could work for a particular disease. Once the design process finds the right molecule the inventor requires the patent, instead of relying only on corporate secrecy.

3.1.2 Pre-clinical and clinical trials

The development of the process begins with the pre-clinical trial, this step has always been conducted before testing the molecule in people. Indeed, scientists through these studies have to find out if the drug could be dangerous in terms of what they call toxicity. Basically, the pre-clinical trial could be done in two different ways:

- In Vitro (laboratory test)
- In Vivo (animal test)

Generally, different analyses are done during the pre-clinical testing, and each of them brings a unique set of data important in understanding what might be a safe dose for the first human test. More specifically, the pre-clinical test aims to understand what the drug does to the body (pharmacodynamics); what the body does to the drug (pharmacokinetics); the absorption, distribution, metabolism, and excretion (ADME) which is done to verify the drug exposure to the tissue and the performance of the compound as a pharmaceutical. Now, that this first process of testing is done the inventor needs to submit an investigational new drug application (IND) to the regulatory agency. Investigational new drug applications must include:

- Animal study and data toxicity
- Manufacturing information
- Clinical protocols for studies to be conducted
- Information about the investigator

Once the IND is issued by the regulatory agency, the producer can pass to the next step, the clinical trial.

The human test, is a selective one, in fact, it is classified in three different phases:

- Phase I
- Phase II
- Phase III

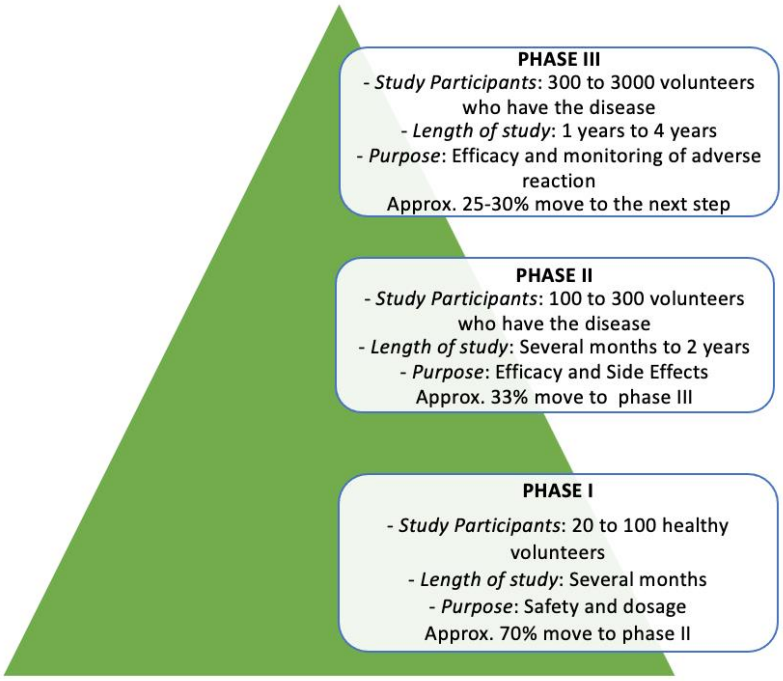
Each of them provides specific results to the inventor and they are done with different approaches. Let's investigate each of them. Phase I is the first test after the approval of the investigational new drug application; generally, it is done to healthy volunteers to verify the safety of the compound. The group of people could vary from twenty to one hundred, where not only the safety is considered, but they also try to define the right amount of dosage for the next phase. According to empirical data, the Food and Drug Administration allows approximately 70% of drugs to pass from phase I to phase II and several months are necessary to conclude the study. Phase II is conducted on people with the disease for which the drug is studied, it can be stated that the number of volunteers is from one hundred until a maximum of three hundred. The purpose of this second phase is to prove the efficacy and the side effects due to the application and usage of the drug. Normally, the length of the study ranges from several months to a couple of years with a success rate of approximately 33% moving to the third and last phase. Going on to phase III, also known as "pivotal" trials, the study needs several participants, in the range of three hundred to three thousand, that are affected by the disease. Here, the length of the study is longer because it could take up to 4 years. The purpose of this step is to monitor the safety and the effectiveness of the new treatment against the current standard medicaments. In phase III, the new drug should be tested against the best current prophylactic, diagnostic and therapeutic methods. However, the use of placebo or treatment in studies where no proven efficiency exists is not excluded.

As for the placebo control trial, this type of method should only be used when no proven treatment exists. Given these methodologies, some risks can emerge from comparing the new drug. First of all, if the comparison is with an active comparator, the risk is to find a lower efficiency and safety from a treatment already used. On the other hand, comparison to a placebo leads to the risk that clinicians and payers will fail to recognize the trial. However, when a drug is able to pass every phase, the inventor can submit the NDA (new drug application); it has to contain the whole life of the drug through reports, analysis, data and all the results of the pre-clinical and clinical phases. It has to include:

- Proposed labelling
- Safety Updates
- Drug abuse information
- Patent information
- Any data from studies that may have been conducted outside the country where the regulatory agency acts
- Direction for use

Once the document has been submitted the sponsor has to wait for the approval of the regulatory agency. Then, when the NDA is approved the drug is ready to be launched on the market.

Figure 19: Clinical trials



Source: Own elaboration

3.1.3 Post-market drug review (Phase IV)

The launch of the drug on the market does not end the process of development and testing. As a matter of fact, phase IV is conducted in the "real world market", this means that if the drug performs well, it demonstrates its safety and efficacy behind the laboratory and the other artificial trials. During months but often years after the launch on the marketplace, regulatory agency reviews reports and feedback about the performance of the drug, and if necessary, they can decide to amend the dosage or usage information or apply even more severe measures. For instance, Food and

Drug Administration provides tools to allow professionals, consumers and producers to leave feedback about issues related to a newly approved drug. MedWatch and Medical Product Safety Network (MedSun). The first is a platform where you can report problems with drugs and devices related to the medical field. The second, Medsun, acts as a monitoring network where the FDA controls the safety of medical devices throughout the USA, publishing a report giving information about this every month. Furthermore, phase IV is characterized by the introduction of a new drug on the market that is patent protected. This means that only the manufacturer or sponsor who owns the Intellectual Property has the right to do business with it. This generates an Oligopolistic Competition that will end with the expiration of the patent. In the figure below the timeline will be clear.

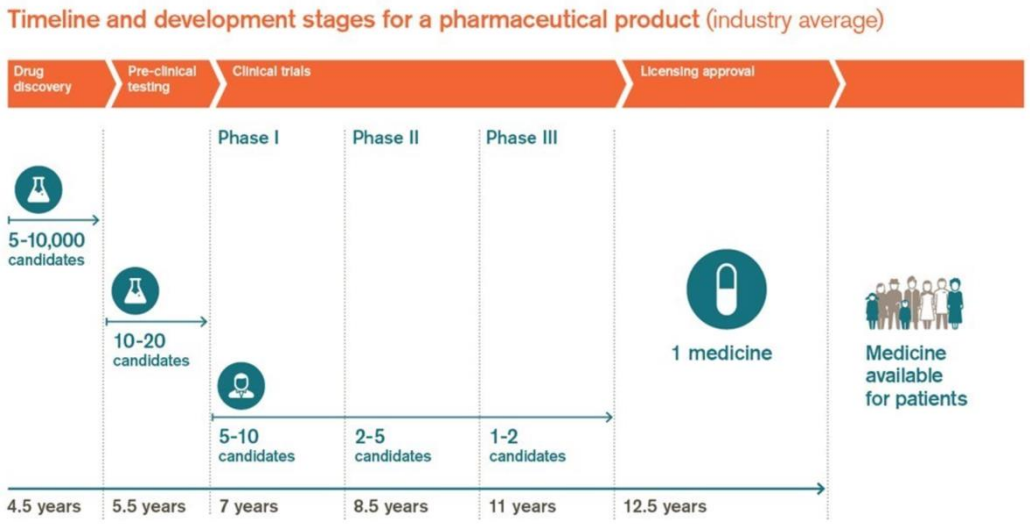
3.1.4 Generic competition

Once the patent expires, other corporations have the right to produce the same product also known as “generics”. However, if the manufacturer wants to produce the same medicine it must respect some restrictions.

- Dosage form
- Strength
- Safety
- Quality

- Performance characteristics
- Intended use

Figure 20: Pharmaceutical development timeline



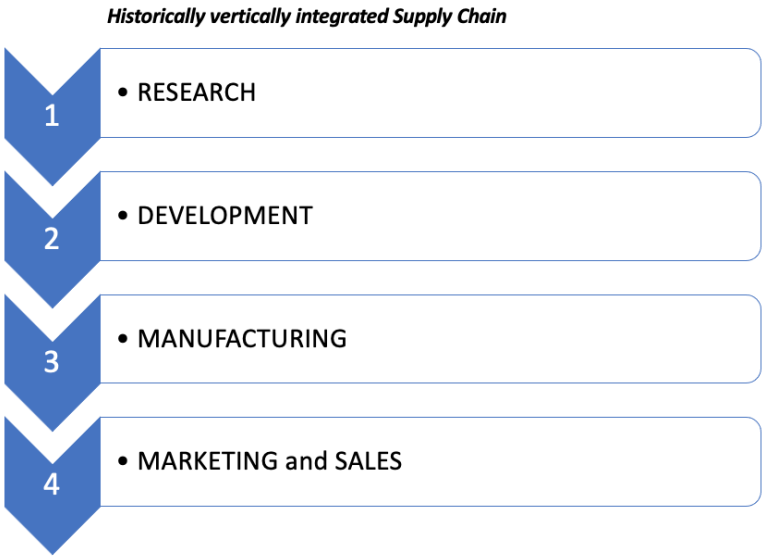
Source: GlaxonSmithKlein website

3.2 Supply chain in the Pharmaceutical Industry

The pharmaceutical industry has experienced a profound transformation regarding the allocation of R&D, manufacturing infrastructures, commercial activities, controls and saving cost policies. The innovation in technological tools and new methods of discovering drugs together with the need to meet shareholders' demands for greater profitability have changed and influenced the structure of the supply chain. This is because the increase in new drug discoveries is synonymous with

high cost in terms of investment; for this reason, the once vertically integrated structure is now being renewed with the influence of many players within the chain.

Figure 21: Vertical integrated supply chain

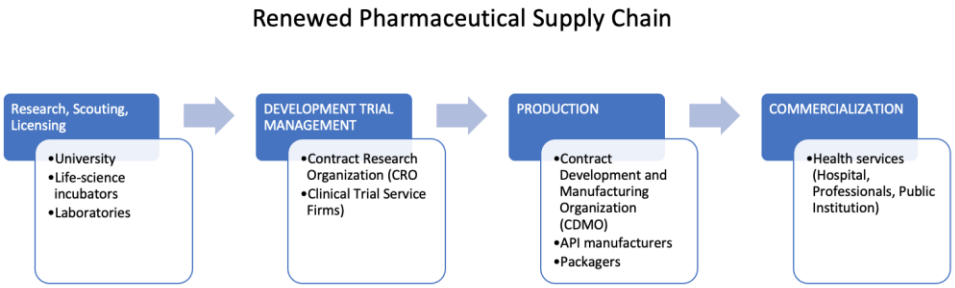


Source: Own elaboration

Pharmaceutical firms have handled their multi-stage supply chain, through a concept of vertical integration, as shown by the figure above. However, evidence suggests that vertical integration leads to the underutilization of manufactured products, excessive and increasing costs in terms of investment. Indeed, capacity utilization depends on market demand, usually in pharma industry generic drugs, when the intellectual property expire, can completely erode the demand leading to underutilization of the real capacity of the plant. This scenario studied by the management of the big pharmaceutical corporation produced a change of direction,

closing in-house plants and starting to apply outsourcing policies. In addition, it is true that this change in the way the business is handled has led to some amends resulting in a redesign of the supply chain.

Figure 22 :Current pharmaceutical supply chain



Source: Own elaboration

The figure above demonstrates how the supply chain is now a settlement of blocks in which different players have a specific role. Starting from the research to the commercialization, the end of the chain. Basically, each firm can decide which part has to be outsourced, there is not a conventional rule that suggests and gives a specific configuration. However, the tendency seems to achieve a divestment strategy focused on the transfer of business units such as: R&D to CRO and CDMO, production to CMO and CDMO. Management applying these actions allows the firm to fix the issue of overproduction, save money from capital investment and increase flexibility.

To sum up, it is evident the switch from a vertical and in-house supply chain to a multiplayer supply chain, where profit and flexibility are the key drivers responsible for such changes.

3.3 Outsourcing and Risks of Dependent Autonomy

Practicing an outsourcing policy allow firms to gain autonomy and to focus on their core business, however, this condition can expose them to unwanted risks, one of which is becoming dependent on the new supply chain structure. Indeed, the risks associated with relying on an external entity may be represented by:

- The availability of supplier
- The loss of internal capability

It is interesting to analyses these risks during the COVID-19 pandemic, because they help to understand the dynamics developed due to the precariousness of the dependent autonomy associated with outsourcing practices. In fact, after theoretically explaining why the availability of suppliers and the increase in loss of internal capabilities are risks that have to be managed by the corporate governance; the following part is to understand which issues have emerged during the Coronavirus crisis due to the dependent autonomy.

3.3.1 The availability of suppliers

When a firm decides to outsource a unit of business, it indirectly agrees to sign a contract with a third business party. This partnership allows the sponsor or home firm to free itself from some responsibilities and at the same time, to satisfy tasks performed at home with more accuracy. So, the contractor is committed to meeting the request of the partner and the sponsor becomes dependent on the performance of its supplier. The issue arises when the foreign firm is no longer able to respect the contract for several reasons like external unexpected events or internal inefficiency. Therefore, this unavailability can occur of course before having established a business relationship but also when a contract is already signed. Studying why the unavailability could be problematic, some important points to consider have emerged. For instance, sponsors are obliged to handle operations without parts, which have been outsourced, necessary to complete the process, or even stop the process itself. Another point to take into consideration is the difficulty of changing suppliers as it costs time, money and resources to find another service provider. Furthermore, they have to start internal production again losing the advantages gained by outsourcing. To sum up, in situations of crisis or unpredicted events the power of contracting suppliers emerges in the new configuration of the value and supply chain undermining the stability and efficiency of the outsourcing business model.

3.3.2 Loss of internal capabilities

As explained in the above paragraph outsourcing frees corporations from some activities in their value chain, which means losing control over internal resources such as human, physical, and informational. Consequently, internal capabilities are no longer applied for tasks intended for the outsourced market and that support the thesis of dependent autonomy. Indeed, when sponsors are no longer able to perform activities in-house they expose themselves to the risks of being dependent on someone. In this case, they need to rely on specialized contractors to perform research, development, manufacture, and logistics tasks.

The corporate governance of the sponsor together with the regulatory party have to understand and manage these situations in order to minimize the risks when they occur. However, sometimes unpredictability shakes the stability of the outsourcing practices causing policy problems like those that emerged in the USA during the pandemic situation.

3.4 Contract Organizations (CRO and CDMO): General Overview

Contract Research Organizations and Contract Development Manufacturing Organizations (CRO and CDMO) have been managed and exploited as a valid business strategy to build a different way of conceiving in-house development and making units of pharmaceutical products. Indeed, the overall increase of

outsourcing over the years shows the effectiveness of this business policy and the efficacy that it can leads in terms of profit and growth. Formerly, the pharma industry and in particular companies operating in this sector were required to be vertically integrated, so the structure had to be vertical and the company owned or controlled the entire supply chain, substantially reducing errors and increasing efficiency. However, with the process of globalization and the improvement of the way of communication, the practice of outsourcing can be a valid alternative to the conventional vertical system used in past. In addition, year by year stakeholders and investors demand continuous and more consistent financial performance which leads pharma companies to make important decisions concerning how, where and which type of contract sign to outsource a unit of business abroad. Here, two different types of contractors already mentioned above: CRO and CDMO.

3.4.1 Contract Research Organization

A Contract Research Organization is a third-party firm that provides services to another firm that wants to outsource a particular part of its business. CRO, in pharmaceutical industries, is also called Clinical Research Organization indeed those realities supply big pharma through high skilled services such as:

- Clinical monitoring

- Biostatistics
- Medical writing
- Regulatory affairs consulting

Before the emergence of these kinds of organizations, pharmaceutical firms used to perform the early stage of the process of studying and discovering in house. However, the incumbent increase in demand for new drugs leads pharma companies to rely on third-party producers to reduce costs of maintaining medical facilities which are prone to sudden changes, due to market volatility and the need to rapidly satisfy what the market requires in that precise moment.

CROs perform services and activities previously mentioned in the early stage of the development of a drug; indeed CROs are positioned in the phase of drug discovery and preclinical analysis, they overlap and become complementary to CDMOs in clinical phases I to III.

3.4.2 CRO Business Model

The peculiarity of the pharmaceutical sector is that within the main industry a subindustry emerges increasing the efficiency and the profitability of an already rich sector. CROs have a very specific business model characterized by a contract between two entities, the Hiring firm, and the Contractor. Firstly, the hiring firm approaches the contractor and based on the negotiation with a CRO or a CDMO the

process of selection can be different. For instance, the main criteria for a CRO selection are the following:

- Specific therapeutic area
- Team member experience
- Responsiveness
- Quality/Consistency of performance/Financial Stability
- Value
- Transparency
- Project management
- Cost/ Profitability

Collaborative agreement between pharma companies and CROs arises from the need to exploit technologies held by other realities, share the risks of the development and discovery process, and finally enlarge the portfolio of drugs to meet increased customer demand. However, when the process of negotiation with a CRO starts it is crucial to build a sustainable strategic value, where the final objective is to deliver value to both partners. This final objective passes through those intermediate goals; creating a process to simplify the relationship, support within units of business and trying to establish a long-term relationship. Furthermore, to create strategic value between both parts there are some best

practices. First of all, an internal system that involves stakeholders, making the key information decisions available. Then, take into account the cultural aspect when evaluating a potential partner and after that manage and resolve internal conflict in order to establish a long-term contractual relationship. Promote collaboration within the business units focusing on shared goals. Once these best practices have been established, it is vital to monitor the effectiveness and health of the working relationships and try to anticipate changes in order to satisfy the benefit of both parties, the hiring firm and the contractor.

3.5.1 Contract Development Manufacturing Organization

A Contract Development Manufacturing Organization is a firm, that provides services to pharmaceutical companies such as drug development and manufacturing services. Pharmaceutical corporations make partnerships with CDMOs in order to outsource units of business abroad. Specifically, CDMOs provide two different main activities regarding manufacturing:

1) Primary manufacturing
2) Secondary manufacturing

On the one hand, primary manufacturing concerns the synthesis of drug substances such as the mass of active ingredients. On the other hand, secondary manufacturing

is more related to the production of the final drug product such as tablets and capsules.

Furthermore, a contract manufacturer could be classified as a supplier or toller, here the difference between the two. First, if the CDMO is recognized as a supplier it means that its main objective is to provide to the hiring firm (pharma company) products that it has in its inventory. Secondly, if the CDMO is a toller, the work performance relates to a customised order sent by the hiring company. Indeed, the toller receives the raw material, then converts it into a formulation and finally gives the product back to the hiring firm.

In summary, the services that a CDMO can perform are as follows:

- Drug product development
- API manufacturing
- Drug product manufacturing
- Packaging

Where pharmaceutical product development represents clinical phases I to III, the remaining three services are more concerned with the production and commercial part, from the production to the labelling.

Recently, these two providers already described have started to become increasingly complementary; contract development and manufacturing

organization have started to provide services more inclined to the sphere of contract research organizations and vice versa. Therefore, there is an increasing tendency towards the concept of "one-stop shops" which economically means a firm that offers a range/group of services or products together in a unique establishment. In this way, a firm can handle a variety of customer requests all together from the start to the end of the process, from the discovery to the commercial part. CRAMs, contract research and manufacturing services, reflect the concept of the one-stop shop where contract research and contract manufacturing merge in a unique firm that carries out jobs concerning the two depicted type of contract organizations.

3.5.2 CDMO Business Model

In the case of CDMOs, the business model due to the fact that the different task provided by the contractor could be a little be different. The hiring firm engage in a deal with the contractor and the process of selection starts by going through some conditions:

- Quality product
- Technological experience
- Flexibility
- Available capacity

- Risk management
- Reliable product supply
- Cost / Profitability

However, these conditions must be included in the Request of Proposal (RFP). This kind of document is the first touchpoint between the two parties that allows both to initiate a relationship based on rules, requirements, information, and schedule. The goal of the RFP is to inform the contractor as best as possible of the details of the activity to be undertaken so that the CDMO can deliver a cost-effective and competitive bid. Basically, a well-formulated RFP will provide the sponsor with the correct way to identify suppliers through a detailed initial requirement, a very precise Project Budget, and organizers project personnel. To sum up, a correct and exhaustive RFP contains the following main components:

- Project Plan
- Intellectual Property
- Financial Information
- Product Manufacture
- GMP Compliance Records
- Roles and Responsibilities

After the request of proposal is completed and the contractor is chosen, the two parties have to start a period in which the supply and quality agreement has to be

established and signed. First, the supply agreement establishes the quantity, the reference of the product payments terms and the time schedule planned in the contract. On the other hand, the quality agreement is more about "Good Manufacturing Practices" regulation, which means that the two parties have to draw up a unique document, different and detached from the first one, where all the services and operations are in compliance with the guidelines described by the GMP. GMP rules require the CDMO to focus on and follow Standard Operating Procedures (SOPs), to hire highly knowledgeable and trained employees for the tasks the contract assumes, independent quality control and quality assurance (QC and QA).

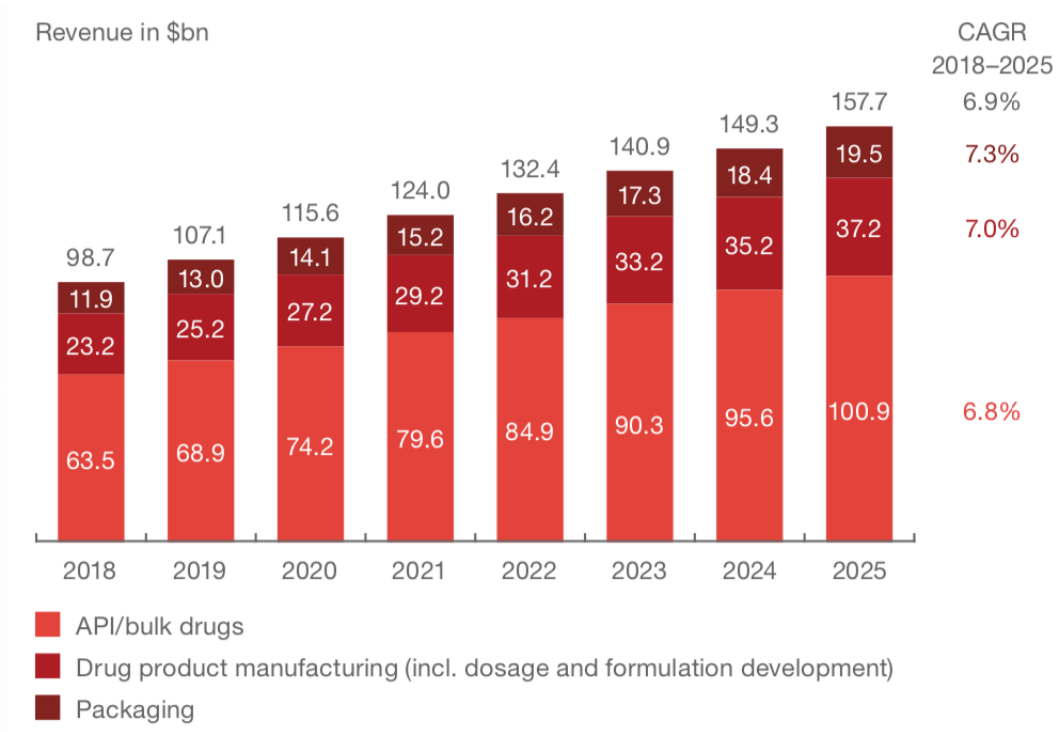
However, even if all the rules are followed the contract manufacturer could change procedures during the course of the project that could undermine the quality, safety and/or efficacy of the product. Each amendment of the plan needs a communication in which the contractor justifies the new strategy and it is subsequently approved by the regulator. The implementation of the new procedure could be immediately effective or needed 30 days after the notification. Therefore, the CDMO has to share the intention to change the production with the Sponsor.

3.6 Key Figures in CDMO Market

Therefore, CDMO can be identified as the most widely used alternative of

contracting to outsource in the pharma industry. PriceWaterhouseCoopers provides a meaningful analysis that shows us trends and figures useful to give some insights about this internal market in the pharma industry. Indeed, according to Grand View Research CDMO business reaches almost 100 billion dollars in 2018 demonstrating how the pharma market has to be aware of the growth of this specific business. In addition, Grand review research estimates an outstanding positive expansion until 2025 where they said that the market could reach 157.7 billion dollars. As a matter of fact, if that happens, another indicator to take into consideration is the compound annual growth (CAGR) which indicates an overall increase of 6.9% over those 7 years (2018-2025). Basically, due to the pandemic happening in 2020, it seems logical to think that those forecasts will not occur with such accuracy even if the pharma market was one of the few not affected by this unusual pandemic situation. The trend described by the graph below highlights that the overall turnover by year is composed of three different elements respectively: API/Bulk drugs, Drug product manufacturing and Packaging. It is evident that the most outsourced are the active ingredients, while the least outsourced is the packaging which is usually done in-house. On the next page, there is a graph that summarizes the evidence described above.

Figure 23: CDMO market in billion



Source: PWC report, Current trend and strategic options in the pharma CDMO market (Grand View Research estimates)

Continuing with this analysis, this stunning increase over the past years and the increasing showed by the forecast cannot only be the results of pharmaceutical needed due to the rise in global population and in the amazing step forward done by the technological innovation. However, it is proof that big pharma companies rely on the business model of outsourcing trying to exploit benefits deriving from it such as: saving time, saving costs, reducing complexity, and reallocating internal resources. Furthermore, the report shows how the CDMO market is dominated by

Asian countries. In fact, in 2018 the Asian market made about 44 billion in revenue from CDMOs and it is supposed to reach over 80 billion in 2025. This is possible due to the low cost of manufacturing but also the favorable regulations. In support of this growth, it is also valuable to mention the fact that China and India are the top producers of active ingredients.

3.7 COVID-19 and US Policy Problems due to Outsourcing Practices

The previous paragraph analyzed how, and in which configuration the pharmaceutical industry changed the structure of its supply chain. However, the recent COVID-19 pandemic reveals the downsides related to such actions, showing how the dependency of autonomy can influence emergency operations. In fact, an unpredictable shift in demand and uncertainties in production and distribution create alarmism and show the precariousness of the drug supply chain. Focusing on the USA pharmaceutical supply chain we are going to identify five policy problems revealed by the pandemic, strictly related to the past several years committed to implementing outsourcing business practices.

1) Unexpected increase in demand for drug products

COVID-19 led to an emergency characterized by shortages of drugs important to prevent and to dab the pandemic. As a matter of fact, shortages during the epidemic are due to an unexpected increase in demand for the specific drug required to fight the difficult situation. The growth of the demand was so great that it exceeded the capacity of manufacturers to supply the right number of products needed to maintain equilibrium. In fact, data reveals that in the second half of January, precisely on 31st 2020, when the Department of Health & Human Service announced the state of emergency, over 100 drugs were under production level according to the Food and Drug Administration. So, the pandemic highlights, as a determining factor, the problems related to supply when unexpected events suddenly increase the demand.

2) Disruption of production

The excessive increase in demand for drugs, has literally exhausted the stocks of the final drug and raw materials. Indeed, the supply arrangements are done based on predetermined projections to meet client and customer needs. For this logical and reasonable cause, the unpredictability of the pandemic event and the long-lasting high demand have exceeded the forecast made by managers causing an

unmatched situation between the drug available and the one requested by the market. In addition, another fundamental variable that facilitated the disruption of production was the international business relationship between the USA and three other world powers, Europe, China, and India. As a matter of fact, the United States imports a huge amount of raw materials and finished pharmaceutical products from these places. The temporarily closing of manufacturing infrastructures around the world, but above all in China where Coronavirus started, decreased the procurement of products causing the shortage of vital medicines needed to provide first aid. In addition, factories that were open or could reopen were short of employees because government restrictions such as lockdowns and quarantine measures were put in place in order to limit infection as much as possible.

3) Delayed regulatory surveillance of pharmaceutical production

A supporting factor in drug procurement is the Food and Drug Administration's surveillance of producers. However, during the pandemic, travel restriction did not allow inspectors of FDA to reach factories oversees and, therefore increased the delay related to the checking of products ready to be shipped. Furthermore, planned inspections organized by the regulatory party were suspended until further notice causing, as a domino effect, a general shortage in house market (USA). The relevant

issue, caused by those delays, is the fact that regulatory oversight is necessary and the product, useful for a first aid, needs specific control over the sterility standards. Those kinds of drugs were fundamental to support the huge effort needed to fight the first wave of coronavirus, a period in which no one knew of a specific treatment and medications were the most logical choice. By medication, we intend injectable preparations also known as intravenous preparations.

4) Interruption of global trade in medicines

The paragraph, about the dependent autonomy, had already anticipated the risks concerning the loss of power over your production if the supplier is no longer able to satisfy what was agreed in the contract. During the COVID-19 crisis, the interruption of global trade in medicines for a period of time demonstrated the overdependence of the Unites States of America for Active Pharmaceutical Ingredients production and finished drugs. Here are the reasons:

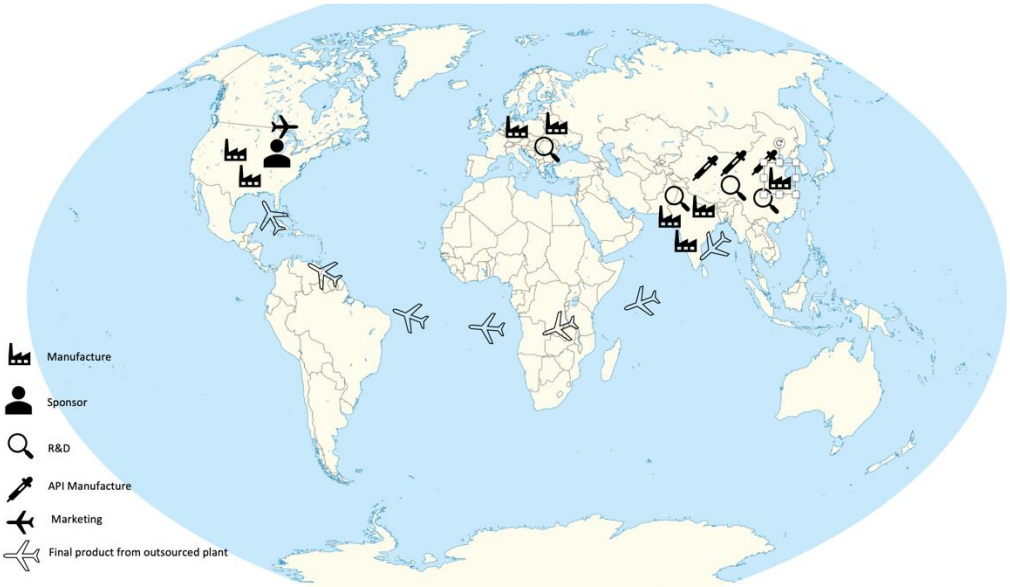
- Delays of regulatory inspection in outsourced foreign plant
- Transportation uncertainty
- The country, where the US outsourced the production, prevented the export of medical treatments to satisfy their own demand.

For instance, India decided to stop the export of 26 finished drugs and 13 APIs, in order to have them available for their own purposes.

5) Limited understanding of local shortages

The US regulatory party rely on an online database where all drug shortages from the past to the present are recorded. However, the software takes data from the manufacturers who note when certain disruptions hit production and warn of possible drug shortages on a national scale. On the other hand, there is another entity called American Society of Health-System Pharmacists (ASHP) that owns a database with the current and past shortages, however in this case the database is uploaded by end-user's feedback like local pharmaceutical stores and any entity that provides drugs. In both cases, the shortage has a national resonance. The solution is to adopt a tracking system that connects the sponsor, outsourced manufacturing, and all the stakeholders involved in the supply chain, to monitor the requirement of any drugs even at a local level. The figure below is a contextualized representation of the US supply chain, with a main focus on the Indian, European and Chinese market.

Figure 24: U.S: supply chain with China, India and, Europe



Source: Own elaboration

CHAPTER 4

This last chapter describes the outsourcing phenomenon from an analytical perspective. It has been downloaded data from different database such as WITS, BACI and GeoDIst; through them it has been conducted a graphical analysis to show the increment of Chinese and Indian exports of two selected four-digit products. Then a model builds up on a log-linear regression analysis consisting of a gravity equation explains and investigates the correlation between import from emerging countries and export from country I and country j.

4.1 Case study: Understanding Outsourcing through Figures

The analysis aims to report and study the pharmaceutical trade data of the most important geographical players. Through these figures, we are going to detect and find some answers about the general trend in which the pharmaceutical industry is moving.

First, the dataset, where the analysis is conducted, is the World Integrated Trade Solution database. It allows to advance queries of trade data, giving the possibility to choose the following variables: Reporters, Products, Partners, Years and Trade Flow. Indeed, for this study multiple reporters were chosen, from different geographical locations, such as: Brazil, China, Germany, France, the United Kingdom, India, Italy, Netherlands, and finally the United States. After choosing

the reporters, two different groups of products were taken: Organic Compound (listed under number 29) and Pharmaceuticals (listed under number 30). Within those groups there are subgroups, which can be selected and studied individually. For instance, inside group 29, to develop the case study, the subgroups 29.36 that contains "Provitamins and Vitamins, natural or reproduced by synthesis (including natural concentrate), derivatives thereof used primarily as vitamins, and intermixtures of the foregoing, whether or not in any solvent" was taken into account. On the other hand, subgroup 30.04 was chosen for group 30, which consists of "Medicaments; consisting of mixed or unmixed products, for therapeutic or prophylactic uses, packaged for retail sale".

Regarding the variable related to partners, most of the time, the one called "World" has been used, indicating the partner with which the reporters export or import the previously selected product. Furthermore, was decided to choose data from 2004 until 2020; then, as trade flows, import and export have been selected as the main drivers to conduct the study.

The configuration of the pharmaceutical supply chain, as described before in the paper, changed the structure from a vertical, in-house structure, to a more integrated and global multiplayer chain. Globalization, international trade, and technological innovation were the main reasons that led to this worldwide scenario and, therefore, even if the biggest pharmaceutical companies are American and European, the

whole industry relies on China and India, respectively for active ingredients and finished drugs supply. In fact, from a broad perspective, the supply chain consists of two main steps:

- Production of active pharmaceutical ingredients (API)
- Finished Pharmaceutical Products (FPP)

The two main players that supply those services are China and India. The first is the largest producer of active pharmaceutical ingredients on the other hand India is the largest producer of pharmaceuticals.

4.1.1 API manufacturing

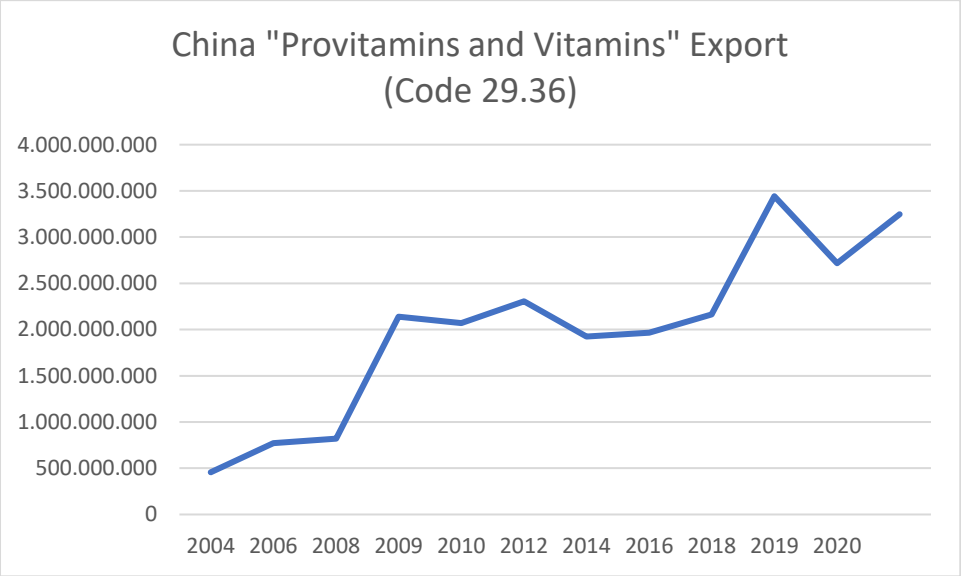
The World Integrated Trade Solution allows to make some research into these fields helping to understand the scenario and verify who imports and exports such products. Group 29 on the database contains several organic compounds, one of these is 29.36 and it contains data about “Provitamins and Vitamins” considered as API. Active pharmaceutical ingredients are defined as follow:

“Any substance or combination of substances used in finished pharmaceutical product (FPP), intended to furnish pharmacological activity or otherwise have direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease,

or to have direct effect in restoring, correcting, or modifying physiological functions in human being"

The analysis of "Provitamins and Vitamins" shows how effectively China is the leading country of API production. Figure 24 illustrates a huge increase in Chinese Exports from 450 million to 3,245 billion in 2020.

Figure 25: China Export Provitamins and Vitamins (API)

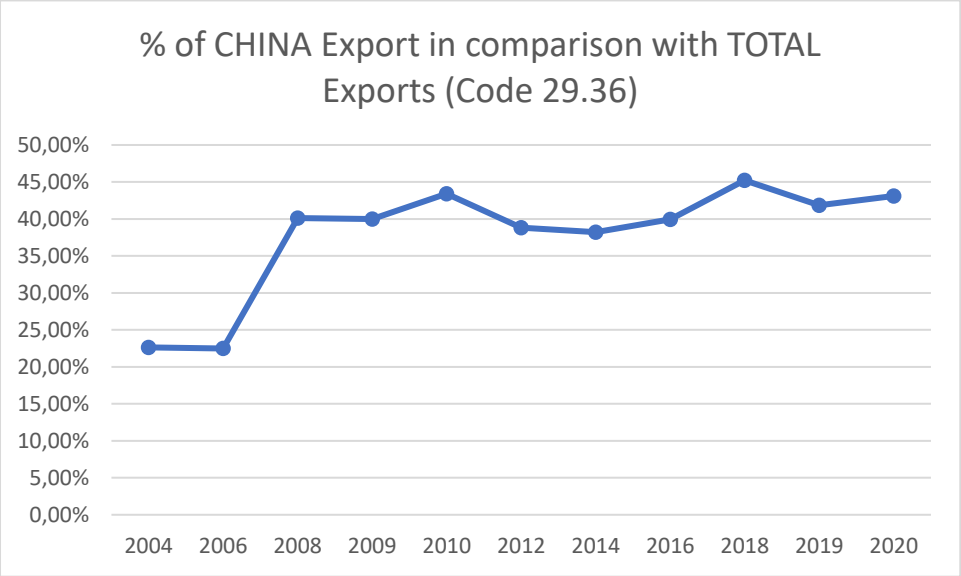


Source: BACI database. Own elaboration.

Indeed, the graph confirms the fact that before the world crisis the major producer of API was elsewhere than China, then a rapid growth led China to become the biggest manufacturer of API holding about 40% of the market share.

As a matter of fact, plotting another graph and comparing the total export of "Provitamins and Vitamins" worldwide with that made by China, confirms the dominance of the Chinese API market. The chart depicts a stable trend in a high percentage share (average 40%) after a jump from 20% to 40% between 2006 and 2008. Indeed, the total export market value of Provitamins and Vitamins in billions in 2020 amounted to 7.5 billion dollars compared to 3.2 billion for Chinese exports.

Figure 26: Percentage of China export (Code 29.36)



Source: BACI database. Own elaboration.

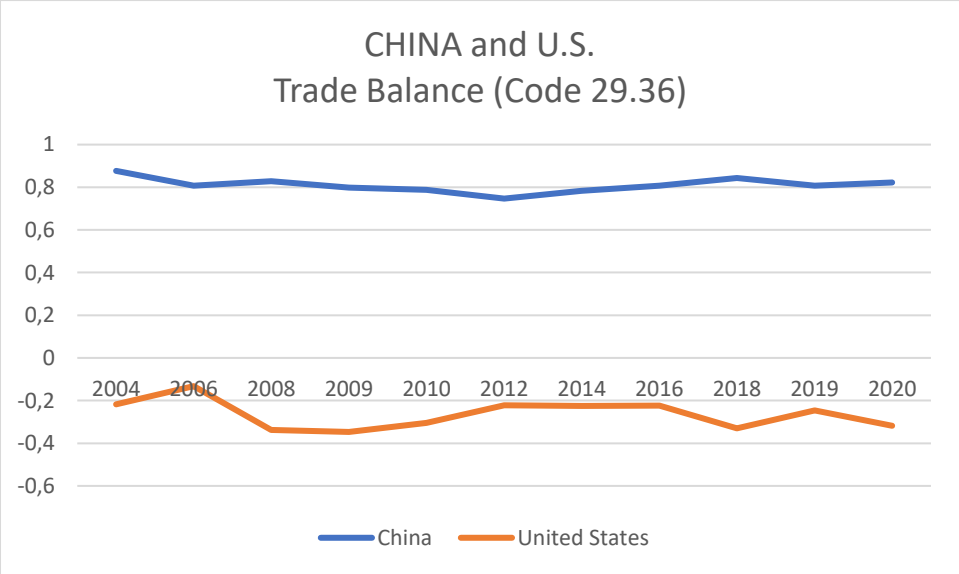
Interestingly, in the two past decades the number of API facilities in China has risen exponentially, as a consequence of the outsourcing policy implemented by the

major pharmaceutical players with the desire to cut costs and deal with less stringent regulation in terms of environmental law.

Furthermore, to confirm the outsourcing theory and the data already analyzed, the trade of balance (Code 29.36) of China and the USA provides fundamental information.

China has a stable positive coefficient over the years, synonymous with being a net exporter, on the other hand, the USA, (once again) demonstrates the tendency to be a net importer.

Figure 27:China and U.S. trade balance Provitamins and Vitamins



Source: BACI database. Own elaboration.

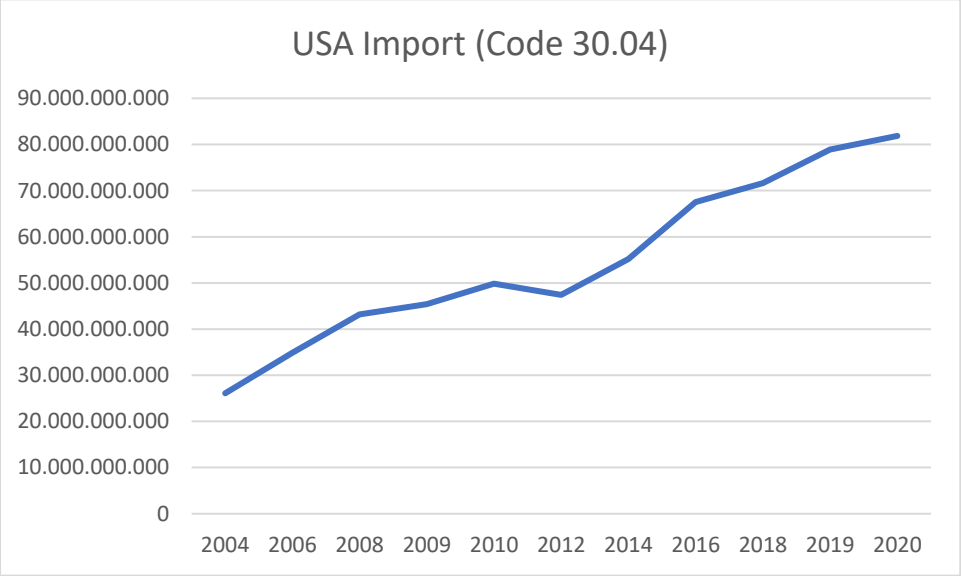
Certainly, Americans are prone to making this deficit with respect to API manufacturing because the lower cost of production and the flexibility that the

suppliers provide big pharma to make more profits and be ready to new challenges. However, it is not always true, and the COVID-19 pandemic has demonstrated the fragility of this scheme, the dependency of autonomy before described undermines the industry when something unexpected happens. In fact, the centralized supply for API in China makes the market vulnerable. When a disruption occurs, like the COVID-19 crisis, all the countries including the USA have to wait in line to obtain what they ordered. Moreover, if the disruption, again as with COVID, is global in scale China can maintain production for itself while securing medicines for its own citizens.

4.1.2 Finished Pharmaceutical Product (FPP)

After having analyzed the API market, the case study is going to focus on another specific variable coded as 30.04 in the WITS database which stands for "Medicaments mixed or unmixed, put up in a measured doses", basically, pharmaceuticals prepared for retail sale. Looking at the import data, the USA has experienced a tremendous increase in imported finished pharmaceutical products. Indeed, the line graph reports the value in billion dollars from 2004 to 2020 of the total US import purchases of finished pharmaceuticals.

Figure 28:U.S. import Finished Pharmaceutical Product (FPP)



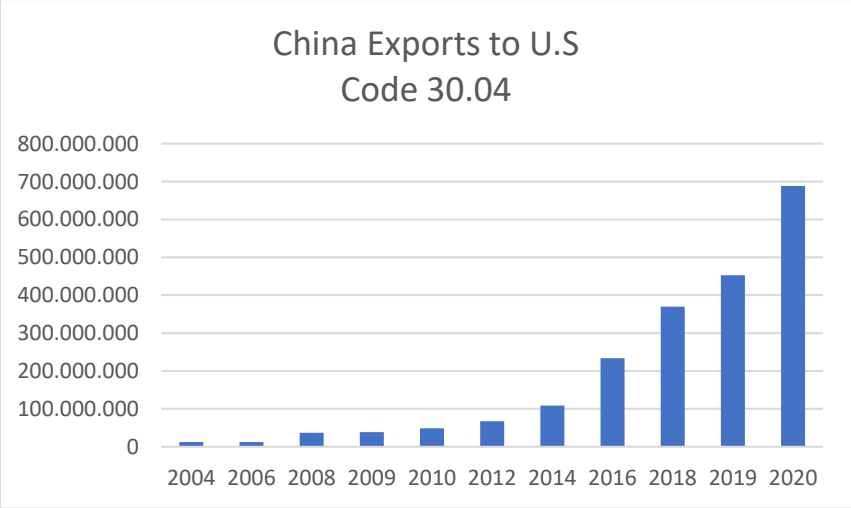
Source: BACI database. Own elaboration.

The graph suggests that even for FPP, the United States relies on external suppliers for most of its demand. Below, three graphs of countries experiencing a big improvement on exports (India, China and EU25). The three charts have a common lowest point, the increasingly higher value in terms of products exported. This trend is justified by the general health of the sector but even more so by the outsourcing practices, as is the case for the API market in particular for provitamins and vitamins as explained in the previous paragraph.

Figure 29: India export to U.S (30.04)

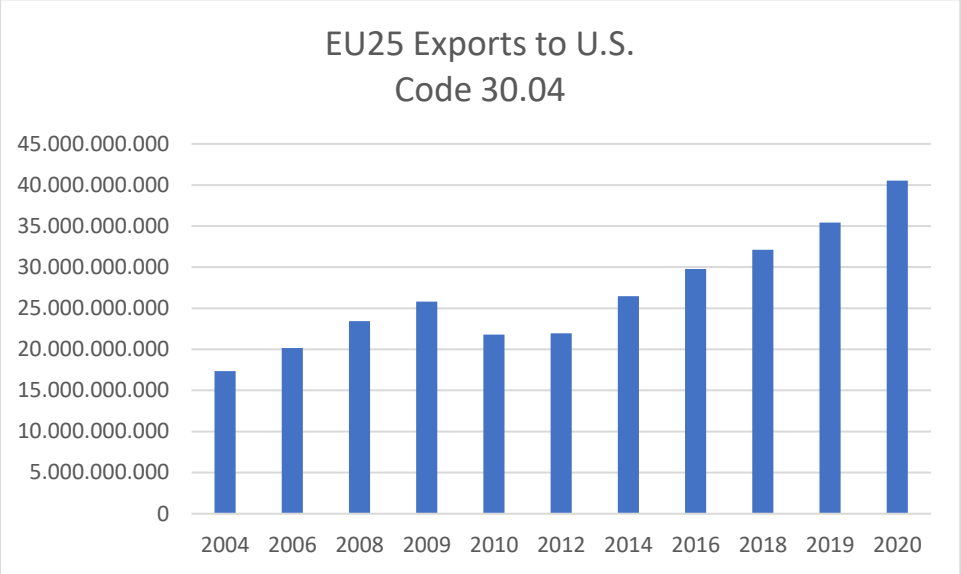
Source: BACI database. Own elaboration.

Figure 30: China export to U.S. (30.04)



Source: BACI database. Own elaboration.

Figure 31: EU25 export to U.S. (30.04)

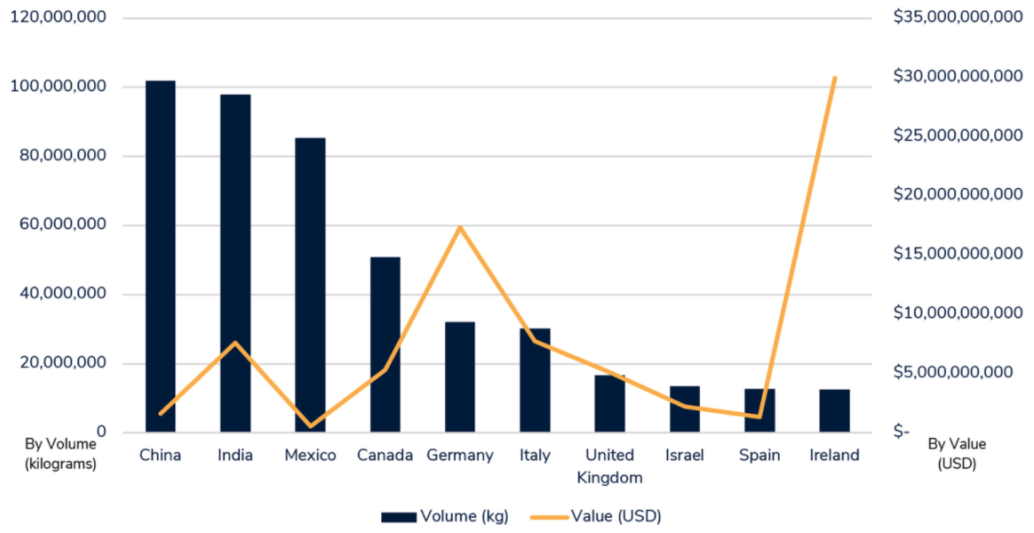


Source: BACI database. Own elaboration.

At first glance, it seems clear that the European countries reach the highest level of pharmaceutical exports, in economic terms, to the USA. However, even if a lot of multinationals have established their manufacturing plants in Europe; China and India play a fundamental role in the industry being the second and third large producers of pharmaceuticals. Looking at the three graphs, it is noticeable how the bar charts for China and India have experienced a greater increase in exports, demonstrating the importance and significance of the other side of the economic world, the developing countries. Therefore, by paying attention to the data a misunderstanding could emerge; the values are in terms of dollars and not in terms

of volume of pharmaceuticals exported. Now, another graph from the U.S. International Trade Commission gives some suggestions about how to interpret the big picture.

Figure 32: U.S 2019 import of pharmaceuticals



Source: Public Citizen Foundations

The bar and line graph illustrate the 2019 situation in the U.S., it depicts the US import value in quantity (volume) and in dollars from each country. It is crucial to highlight that China, India and Mexico export in the U.S. three of the lowest dollar values (yellow line) but the highest number of pharmaceuticals products (blue bars). This happens because the quantity value indicates the effective volume of pharmaceuticals, while the dollars figure also reflect the high price of already patented pharmaceuticals.

To sum up, the results of the analysis demonstrate the constant increase during the last decade of pharmaceutical imports made by the U.S. with a strong implication of outsourcing both for active pharmaceutical ingredients and finished pharmaceutical products. In addition, this strategy trend allows us to validate the hypothesis of dependent autonomy risk that occurred due to the pandemic crisis, demonstrating that the COVID-19 policy issues are linked with such management practices. Furthermore, the data confirms the dominance of the API market by the Chinese pharmaceutical sector, exporting 43.09% of the overall market value. Again, proving the dependency on China of the entire world for the supply of Active Pharmaceutical Ingredients. Then, it is also relevant to mention the information illustrated by Figure 32 that highlights the over dependency of the U.S. on China and India for general pharmaceutical products and the assumption that China and India have a low export value in dollars simply because products exported are not covered by intellectual propriety and the price is not influenced by it. Indeed, the graph demonstrates how this small amount of dollars, in case of China and India, corresponds to the highest quantity of pharmaceuticals exported to U.S in terms of volume

4.2 Empirical analysis: The gravity model

After having discussed the analytical review conducted through a research of import and export data and implication about outsourcing practices; now, this last part aims to understand the possible correlation between imports of four digits products (29.36 and 30.04) from emerging economies and exports from country i and country j. To verify this statement, it has been conducted and it has been constructed a model based on a regression analysis where the gravity equation explains the results.

The gravity equation states that exports are directly proportional to the exporting and importing countries' economic "mass" (GDP), and inversely proportional to the distance between them. In other words, larger countries trade more, vice versa countries further apart are expected to trade less. Through descriptive statistics and geographical techniques applied with the gravity model the paper wants to investigate about bilateral trade of the four digits selected products and suggests a mathematical result coherent with the previous conclusion. The general and basic gravity equation take this log-linearized form:

$$\ln (X_{ij}) = \beta_0 + \beta_1 ln(GDP_i) + \beta_2 \ln(GDP_j) + \beta_3 \ln(\pi_{ij}) + \varepsilon_{ij}$$

Where X_{ij} explains the exports from country i to country j, GDP explains countries gross domestic products, π_{ij} explains the distance between the two countries and

finally the random error (ε_{ij}) . However, based on our needs it has been developed a model starting from the theory but adjusted to what the thesis wants to highlight. Our multiple regression equation has the dependent variable X_{ijpt}, that measures the exports of product p by exporting country i to importer country j at time t, others regressors and some more added fixed effects. The equation as stated in the beginning of the paragraph wants to understand how much a variation of the regressor ImpShEM (share of imports from emerging countries by product category HS4D) influence the dependent variable. The data to construct the model are provided by CEPII a website that gather data from different sources. Precisely, to conduct the analysis two different database inside CEPII has been utilized BACI and GeoDist. BACI contains bilateral trade flows for more the 5000 products and 200 country, on the other hand GeoDist provides geographical variables regarding bilateral distance.

The model is formalized by the following log-linear equation:

$$\ln(X_{ijpt}) = \beta_0 + \beta_1 ln(ImpShEM_{ipt}) + \beta_2 \ln(Distance_{ij}) + \\ + \beta_3 \ln(Controls_{ijt}) + m_{it} + n_{jt} + q_p + \varepsilon_{ijpt}$$

Where :

- β_0 = intercept, the coefficient that determines the level of the regression line

- β_1= The slope $\beta_1$is the variation of X_{ijpt} associated with a variation of $ImpShEM_{ipt}$, β_2 and β_3, as well, describe the variation of X_{ijpt} based on a variation of $Distance$ and $Controls_{ijt}$
- $ImpShEM_{ipt}$ = (share of imports from emerging countries by product category HS4D)
- $Distance_{ij}$ = Variable that explains the distance between country i and country j
- $Controls_{od}$= It is composed by the following variables,
  "imp_{ijpt}"= the log of the import of product p from the export destination country
  "contig"= 1 for contiguity
  "comlang_off"=1 for common official or primary language
  "comlang_ethno" = 1 if a language is spoken by at least 9% of the population in both countries

- m_{ot} , n_{dt} , q_p = fixed effects (Origin- year, Destination-year and product)

The empirical results coming from this model are quite compelling, indeed running the model interesting findings give us suggestion about the validity of the thesis. The model has been utilized with a sample composed by 200 countries and then with a restricted sample where bilateral trade was done only by rich economies. In both cases, the variation of the regressors Distance and ImpShEM influence the dependent variable in the same way. As expected by the gravity theory, the distance variable has a negative impact on the export from country i to country j. Indeed, as can be seen on the table the coefficient β_2 is always with a negative sign. On the other hand, the share of import from emerging countries shows a significant positive

effect on the dependent variable X_{ijpt} and the positive sign of β_1 confirms, with both populations taken into account, the actual results, the positive correlation.

Figure 33: Gravity equation results

	All Sample		Rich Economies to Rich Economies		All Sample		Rich Economies to Rich Economies	
Imp_shEM	0.522***	0.497***	0.944***	0.840***				
	[0.016]	[0.016]	[0.024]	[0.022]				
Distance	-0.712***		-0.643***		-0.714***		-0.644***	
	[0.005]		[0.007]		[0.005]		[0.007]	
Imp_shCI					0.359***	0.348***	0.849***	0.722***
					[0.019]	[0.018]	[0.027]	[0.026]
Observations	857,891	855,765	427,678	427,465	853,291	851,177	425,236	425,028
R-squared	0.491	0.557	0.534	0.585	0.490	0.556	0.534	0.585
Fixed effects								
Origin-Year	yes	yes	yes	yes	yes	yes	yes	yes
Destination-Year	yes	yes	yes	yes	yes	yes	yes	yes
Product	yes	yes	yes	yes	yes	yes	yes	yes
Controls	yes	yes	yes	yes	yes	yes	yes	yes

Source: Own elaboration

In addition, another equation has been run on the statistical software:

$$\ln(X_{ijpt}) = \beta_0 + \beta_1 ln(ImpShCI_{ipt}) + \beta_2 \ln(Distance) + \beta_3 \ln(Controls_{od}) + m_{ot} + n_{dt} + q_p + \varepsilon_{odpt}$$

The only difference is the regressor $ImpShCI_{ipt}$, that consist of share of imports from China and India by product category HS4D. Even in this case, the effects of the independent variable on the dependent one is positive. Demonstrating a positive correlation between imports from developing country and exports.

To sum up, the gravity model gives us evidence about the influence that emerging economies have on trading active pharmaceutical products and finished pharmaceutical products showing the positive correlation between the two variables.

Conclusion

The objective of this thesis is to provide evidence on international outsourcing phenomena within the pharmaceutical industry. The elaborate tries to underline theoretical and structural aspects of the outsourcing with the aim to investigate the effective use of this managerial practice in the pharmaceutical sector. First of all, the paper analyzes the theoretical approach of the outsourcing phenomenum developing a clear freamwork, where static and dynamic effects depict the consequnces of this business strategy. On the one hand, in the short-term the company, that apply outsourcing policies, experiences increase in profit due to cutting in costs, on the other hand in the long-term, knowledge spillovers can emerge causing a loose of control over the activity and the company became increasingly relayant on the contractor. In fact, analyzing the structure of the supply chain, it is evident the change from a vertical integrated supply chain to an horizontal decentralized one. Indeed, data from BACI depic a situation where the USA has a negative trade balance of the four digit products, while countries such as China and India show a positive trade balance demostrating to be net exporters. In addition a systemic analysis was carried out and it demostrates the positive correlation beetween import from emergent country and general export from a country I to a country j. Those results reflect the change of direction from the oldest to the new supply chain. To support this structure, Home firm have to engage with

external providers, CRO and CDMO, in order to avoid risks and other negative sides. Those providers allows the home firms to rely in a trustworthy third-party outside the country for the development and/or the production. However, this condition of dependency to another entity shows during the pandemic the precauriousness of the horizontal supply chain and it rises the issue explained in the first instance of the dynamic effects. Finally, it is relevant to conclude by saying that international outsourcing is a foundamental economic practice which serves to meet the constantly increasing in demand of pharmaceuticals. However, should not be encouraged a policy of a total outsourcing because Home firm can loose the autonomy and it can be voulnerable when something unexpected occurs.

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Abbreviation INDEX

ADME = Absorption, distribution, metabolism, and excretion

API = Active Pharmaceutical Ingredients

CDMO = Contract Development and Manufacturing Organization

CRO = Contract Research Organization

FDA = Food and Drug Administration

FFP = Finished Pharmaceutical Product

IND = Investigational New Drug

NDA = New drug application

OECD = Organization for Economic Co-operation and Development

PPF = Production Possibilities Frontier