The influence of local institutional and historical frameworks on a globalized industry: The case of the pharmaceutical industry in France and Quebec

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Abstract
In this paper, we combine the Varieties of Capitalism and the global value chain approaches, considering the interaction between lead firms' global strategies and national capitalism, to show how local pharmaceutical employment results from this interaction. Our analysis is grounded in the comparison between France and Quebec. The first part presents the relevant differences in both historical and institutional elements. Second, after highlighting the similarities that can be attributed to global dynamics, we detail the mechanisms by which local institutions shape the global value chain implantation, giving different forms to the employment structure and dynamics. We show that France is clearly oriented towards manufacturing activity because of industrial history and market features, whereas Quebec has a commercial specialty and an outsourced R&D as a result of high prices and the global organization of research.

Keywords: political economy; varieties of capitalism; industrial organization; local government; multinational firms

JEL classification: L650 Chemicals; Plastics; Rubber; Drugs; Biotechnology, P520 Comparative Studies of Particular Economies, P16 political economy

Résumé
Dans ce papier, nous combinons Variété des Capitalismes et chaine globale de valeur, pour faire apparaître comment l'emploi pharmaceutique local résulte de l'interaction entre stratégies globales et capitalismes nationaux. Notre analyse s'appuie sur une comparaison France-Québec. La première partie présente les différences majeures des cadres historico-institutionnels. Ensuite, après avoir souligné les similarités liées aux dynamiques mondiales, nous détaillons les mécanismes par lesquels les institutions locales influencent l'implantation de la chaine globale de valeur, donnant des formes différentes à l'emploi. Tandis que la France est clairement orientée vers l'activité de production du fait de l'histoire industrielle et des caractéristiques du marché, le Québec dénote par sa spécialisation commerciale et sa R&D externalisée, en lien avec le haut niveau des prix et l'organisation de la recherche mondiale.

Mots-clés : économie politique, variété des capitalismes, organisation industrielle, gouvernement local, firmes multinationales

1. Introduction

The pharmaceutical industry can be considered an emblematic case of the internationalization of the economy. Concentrated around a small number of very large players (65% of global sales are made by the 20 largest players), the pharmaceutical industry is organized around multinational groups that operate worldwide through subsidiaries in 150 countries, on average. Consequently, the major shocks that this industry has experienced during the last three decades, through its rapid financialization, the emergence of biotechnologies, the development of generics, and the tightening of regulatory requirements, can be considered from a global perspective.- Despite these major disruptions, the growth of the sector remains stable and continuous, pointing to the industry's adaptation to these shocks and the establishment of mechanisms to stabilize sales and profits (Belis-Bergouignan and *al.*, 2014, p. 18). By massively outsourcing certain activities, by developing partnerships, and by favouring external growth and open innovation, the dominant firms launched a complete reorganization of the global value chain, revealing a reticular organization (Foray, 2018, p. 32). In this new organization, multiple players of different sizes and specializations come together and interact according to a non-homogeneous distribution of value and of power relations, a distribution that is unbalanced in favour of pharmaceutical companies.

While the strategic orientations of the big pharmaceutical companies are highly centralized, their various research, production and commercial activities are, by contrast, fragmented and organized according to global networks. This opposition between centralization and fragmentation reveals the tension that can exist between the operative and the strategic levels in the case of a highly globalized industry. Moreover, the position occupied by regulation in this sector makes the characteristics of the activity closely dependent on the institutions that condition all three important attributes: supply, demand, and the price of a drug (Abecassis and Coutinet, 2008, p. 112); as a whole, this institutional system constitutes an "institutional order" (Belis-Bergouignan and *al.*, 2014, p.17). Although there is some harmonization of procedures (Labrousse, 2012, p. 182), states remain sovereign for much of their public health policies and regulations (De Mazières et Paris, 2004, p. 241), requiring pharmaceutical companies to deal with a variety of institutions in each country (Murray and Trudeau, 2004, p. 8).
How do these global and local scales interact? How and around which actors and institutions is this system of interactions structured?

Far from being a new question, this issue of global-local articulation places us in the field of study known as Comparative Political Economy, whose various contributions have been particularly focused on better understanding the way in which national economies evolve with globalization and on showing how local institutions can hinder the convergence process. In addition, the structuring of the pharmaceutical industry around large groups calls for an industrial economics literature centred on the strategies of companies (particularly multinational firms (MNCs)) involving the notion of global value chains and innovation networks (Balas and Palpacuer, 2008, 2010; Foray and Lhuillery, 2010).

In the vast field of political economy, the Variety of Capitalisms (VoC) approach has emerged as a singular branch whose object is based on the identification of dominant types of capitalism, given the shape and interweaving of institutions. In the founding book *Varieties of Capitalism* (2001), Hall and Soskice identify two major types that exist at two ends of a spectrum, "the Liberal Market Economy" (LME), of which the United States is the typical example, and the Coordinated Market Economy (CME), of which Germany is archetypal. In *Les cinq capitalismes* (2005), Amable offers another typology that preserves the model of market-based capitalism (Anglo-Saxon economies) but enriches the vision of the spectrum that remained unclear in Hall and Soskice. To do this, Amable offers four alternative models to the liberal model: social democratic capitalism (Finland, Denmark), Asian capitalism (Japan, Korea), continental European capitalism (France, Germany), and finally

Mediterranean capitalism (Greece, Italy). This second typology is based on the analysis of five institutional fields: product market competition, wage relations and the labour market, financial systems and corporate governance, social protection, and finally education and training systems.

In this article, we also rely on the theoretical contributions relating to global value chains (or GVC), as “major analytical tools to understand the new dynamics of international trade and the internationalization strategies of firms that massively fragment their production processes, leading to a deepening of intra-firm exchanges and an increased use of international outsourcing” (Durand and *al.*, 2018, p. 13). According to Gereffi (1994, 1995), global value chains can be characterized by four main dimensions : their input-output matrix which describe the set of incoming goods and services leading to the finished product, their geographical implantation, their governance and power structure which define the relationships between the firms of the chain, and the institutional framework in which they operate. Indeed, the latter can be a source of differentiation among territories. As such, Serfati (2006, p. 82) demonstrates that the MNCs, despite their global dimension, maintain special relationships with their national territory of origin, which can be captured with the notion of "national preference". The country of origin would generally be the main site of production activity, while relations built with customers, suppliers, governments and local elites would constitute barriers to entry for competitors.

Because it enables the identification of the places or links in the chain around which the extraction of value is organized and, the uneven distribution of value among actors, the GVC approach applies particularly well to the pharmaceutical industry, which is emblematic of an organizational mode in which the chain is led by the producers. Market-leading firms control the entire network, which executes upstream or downstream activities from which leaders want to disengage (production in particular) in order to focus more on marketing or financial management issues (Gereffi and *al.*, 2005, p. 79; Balas and Palpacuer, 2010, p. 92). While the disintegration of the production process of the drug is undeniable and is in itself an object of study (developed in other of our works), we intend in this paper to consider the pharmaceutical value chain in a wide meaning, in three segments: R & D, production, and commercialization. We defend the idea that R & D is the first moment of value creation, given the close links between "additional innovation level" of a drug (which depends on the R&D) and the ability to obtain a high selling price. At the other end, marketing is where the value materializes. This refers to the conclusions of Cristina Fróes de Borja Reis (2018), stressing the concentration of value in the pre and post production phases that are (R & D and marketing), particularly for the pharmaceutical industry. However, the pharmaceutical innovation model, affected in the same way as other high-tech industries, has also been progressively disintegrated, in parallel with the disintegration of the production process. According to Foray and Lhuillery (2010), the reorganization of R & D was characterized by the emergence of a new type of actor offering R & D services. In this new mode of organizing innovation, which took the form of a collaborative network, market mechanisms occupy an increasingly prominent place in coordination among actors, while property rights and licenses regulate the interactions. Technology transfers now occur among universities, industries, and new players in R & D services, the latter playing the role of a transmission belt. This arrangement has materialized spatially in the shape of clusters that bring together these three types of actors, even if each individual actor does not generate the same intensity of innovation.

In what way does the global pharmaceutical value chain, designed by the strategy of multinational firms and their geographical location, interact with the socio-institutional and historical configurations of the territories in which they're embbedded ? In this article, we propose to combine the institutional and industrial approaches, based respectively on VoC and on global value chains, to highlight the interplay between states and firms. We formulate the hypothesis that local pharmaceutical employment and its evolution result from this interaction between the global strategies of productive establishments and national capitalism.

Our analysis will be grounded in a comparison between two territories: France and Quebec. This choice is based primarily on the two territories' industrial histories, which are polar opposites. Indeed, the development of the pharmaceutical industry in Quebec is attributable to very attractive government policies enacted in this direction in the mid-1980s, targeting, in particular, the installation of large international pharmaceutical companies. Conversely, France has seen two centuries of building and consolidation in this sector, from small pharmacies and early chemical factories to integrated international firms. Given that health is a provincial prerogative in Canada, we focus our analysis on the province of Quebec, although broader references to the Canadian situation are sometimes necessary. On the other hand, according to the typology developed by B. Amable (2005), Quebec and French capitalisms belong to different types. Quebec belongs to market-based capitalism, with the caveat that it represents a variation on some aspects[1] where it is less liberal than the North American environment in which it evolved (Rigaud et *al.*, 2010, p. 32, 34). France, by contrast, belongs to continental European capitalism, whose two most commonly cited characteristics are the strong protection of employment and a high level of social protection linked to the State's intervention.

To what extent are the institutional and historical pharmaceutical industry frameworks different in these two territories? In light of these results, how should we analyse the evolution of local employment? Ultimately, the article seeks to make intelligible the differences in weight, of the three pharmaceutical value chain employment segments in the two territories: it implicitly raises the questions of the participation of France and Quebec in the chain of pharmaceutical value, and its determinants.

The first part of this paper will discuss the historical and institutional elements relating to product market competition, social protection and, to a lesser extent, financial systems for Quebec and France. The two regions exhibit very disparate frameworks:
- In Québec, late intellectual property rights are related to the attraction of foreign industry; the health system is based on the substitutability between public and private actors, which implies the segmentation of the drug pricing process, and the financial system is conducive to the development of biotech companies;
- In France, the pharmaceutical industry is an old one, and one from which some national players have emerged and play an important part in the world market; intellectual property rights are older than in Quebec, the health system is grounded in the complementarity between public and private, the State manages the whole pricing process, and the financial system has delayed the emergence of biotech companies.

In the second part, after underlining the similarities that can be attributed to the global dynamics of capitalism or sectoral dynamics, we detail the mechanisms by which the identified local institutions hinder the convergence process, giving different forms to pharmaceutical activity and employment in both territories. To do so, we analyse the evolution of pharmaceutical employment, divided into three categories according to the three central functions that have direct impacts on a drug: its discovery and development, its manufacture, and its commercialization. We show that the French pharmaceutical industry is clearly oriented towards production activity because of the industrial history and market features that make the French market attractive, whereas Quebec specializes in commercialization and outsources R & D in connection with the high price level of drugs and the global organization of research.

[1] Rigaud et *al.* refer in particular to the social policies implemented, or to the existence of labour standards offering much higher protection compared to the rest of Canada, and therefore also compared to the United States.

2. Actors and institutions shape heterogeneous local frameworks for pharmaceutical activity

Which parts of pharmaceutical activity depend on the local scale (respectively national for France or provincial for Quebec)? What are their territorial specificities? To answer these questions, we will discuss three themes: industrial dynamics, which combines industrial history, intellectual property rights (IPR) and industrial policies; the social protection system from which the pricing procedures are derived; and more briefly, financial regulation.

2.1 Inheritance of history, intellectual property rights and industrial policy

Intellectual property rights (IPRs) initially governed the terms of competition among firms and among products. Their industrial consequences are strong, as evidenced by the way in which the dominant firms in the industry pushed for these rights in the second half of the twentieth century. Like other industrial policies (protectionism, nationalizations, tax incentives), IPRs have been decisive in building up and consolidating the pharmaceutical industry.

2.1.1 Late intellectual property rights, industrial incentive policy and ex-nihilo creation in Quebec

Historically, Canadian property rights legislation has been much more favourable to generic manufacturers than to manufacturers of patented products. Indeed, since 1923, the law has allowed generic manufacturers to derogate from the monopoly conferred by the patent even before it falls into the public domain by producing their own drugs under "compulsory licensing[2]" as long as the active ingredients are made in Canada. Since 1969, the latter condition has not applied, offering the generic industry even better growth opportunities.

It was not until 1987, after inquiry and lobbying by Quebec, that the federal government decided to strengthen intellectual property rights through Bill C-22, which granted 7 to 10 years of patent protection to firms. Compulsory licensing definitively ended in 1993, following the negotiations of the North American Free Trade Agreement, while patent protection was increased to 20 years (Lexchin, 1997, p. 70, 2001, p. 2). In parallel with this reinforcement of intellectual property rights and consistent with lobbying in this direction, the Quebec government has developed targeted incentive policies, combining public subsidies, research tax credits, and what was called the "15 years rule," which authorized doctors to prescribe the branded drug for 15 years after the end of the patent even if a cheaper generic drug was available (Griller et Denis, 2008, p. 31).

The explanation of this shift lies in the economic and industrial structure of the province. In the mid-1980s, the Quebec government decided to develop three high-value-added sectors to revitalize the economy, including aerospace, information and communication technologies and the pharmaceutical industry (Griller et Denis, 2008, p. 1). This set of selective and strategic industrial policies (Hannon, 2016, p. 3, 6) specifically targets the pharmaceutical sector and targets large global players whose establishment in Quebec must allow the development of new jobs with high added value.

2.1.2 The pharmaceutical industry in France: a long tradition and support for an existing activity

The history of the pharmaceutical industry in France is intimately linked to the birth of the pharmaceutical business, of which it is one of the world's cradles. France indeed has a strong history in this field: at first, France was home to pharmacy practices dedicated to the artisanal preparation of medicine (Muller, 2014, p. 57); later, in the second half of the nineteenth century, another type of actor emerged, focusing on chemical pharmaceuticals that were not prepared at the pharmacy

[2] The compulsory license designates the exercise that forces the laboratories that manufacture a patented medicine to grant the generic manufacturers the right to produce the generic medicine under consideration.

(Chauveau, 2002, p. 178; Rasmussen, 2004, p. 19). Concentration took place gradually over the course of the twentieth century and accelerated during the 1980-1990s, consistent with the pharmacy industry around the world[3] (Chauveau, 2002, p. 169, 181; Bonnet, 2005, p. 125). French pharmaceutical companies have grown and changed during this last period; some have merged with companies of other nationalities and that perform other industrial activities, including chemical activities. The largest French pharmaceutical companies are now major players on a global scale.

In this scheme, the French public authorities, unlike those in Quebec, have encouraged and supported an already existing activity over the long term through significant protectionism, progressive intellectual property rights, and, later, nationalization. For example, between 1941 and 1972, only drugs produced in France could receive the necessary visa for marketing[4]. In addition to favouring French companies already established in the territory, this measure explains the rather early and important establishment of foreign pharmaceutical companies in France, especially with regard to production activities, since these companies wanted to market their drugs in France.

Patent law has existed in France since 1791, but drugs were excluded until 1959, the date the "special patent of medicine" (SPM) entered into force. Drugs did not join the ordinary law regime until 1968, although the latter (like the SPM) nevertheless allowed the use of compulsory licenses to preserve public health interests, although they have never been used. Subsequently, the significant strengthening of IPRs has been primarily attributed to external entities, such as the European Patent Office or the World Trade Organization.
The nationalization of Rhône-Poulenc for more than a decade, between 1982 and 1993, following major difficulties related to raw material costs and the textile crisis (Bonnet, 2005, p. 118), is another example of state intervention to preserve French national actors. On the other hand, as Sophie Chauveau (2002, p. 176) explains, French pharmaceutical companies have long been excluded from public aid for research, testifying to an ambiguous position *vis-à-vis* the sector (Cassier, 2004, p. 45).

2.2 Price setting process

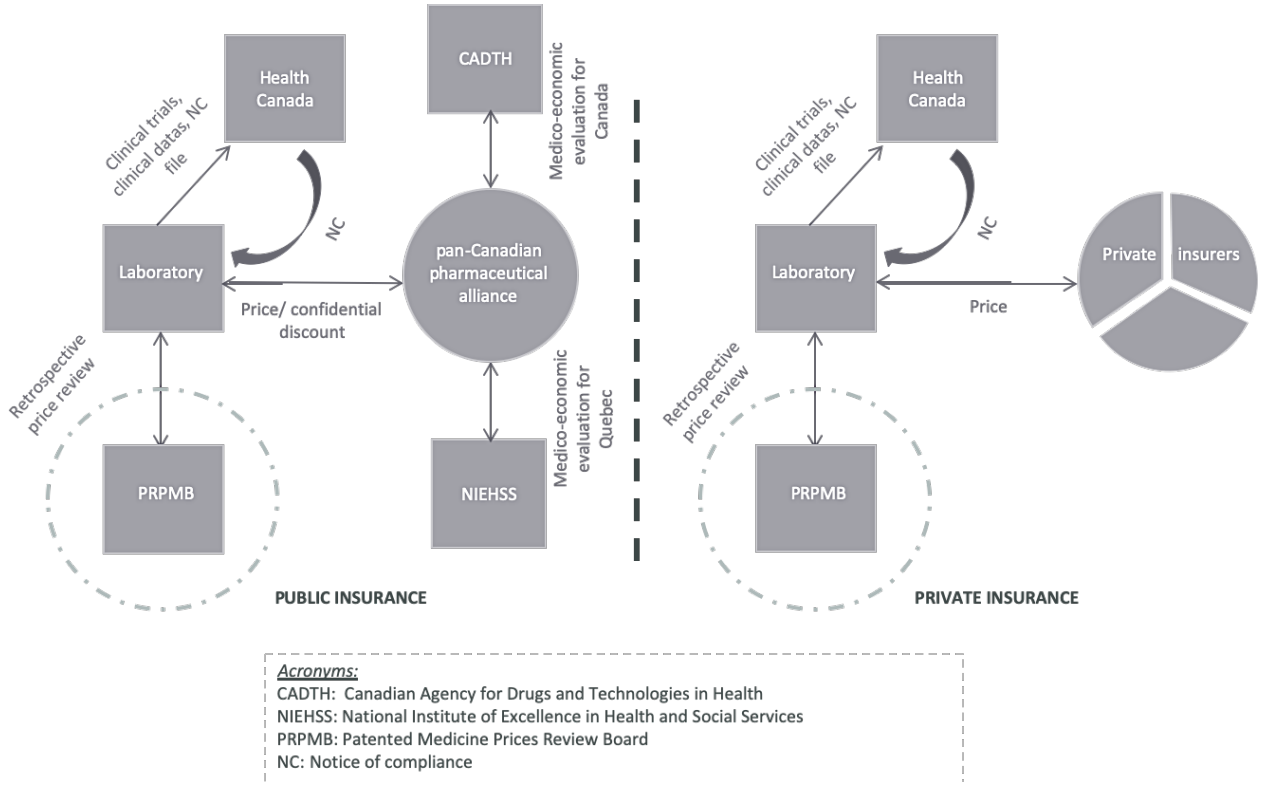
France and Quebec are opposites with regard to their health systems. The actors are identical, but their articulation differs. In economic terms, private insurers and health public insurance are complementary in France, while they are substitutable in Quebec.
As a direct result of each territory's health system, pricing procedures are very different. In Quebec, the price-setting process is split between public and private actors and also between patented and generic drugs, whereas the Economic Committee for Health Products (ECHP) centralizes the whole process in France. Moreover, the latter's role contrasts with the retrospective role played by the Quebec Patented Medicine Prices Review Board (PMPRB), which does not itself conduct price negotiations with industrial actors.
Ultimately, France has an advantage in terms of the solvency of drug demand by the state[5], while Quebec is distinguished by its high prices.

2.2.1 Fragmentation of the process and actors in Quebec

Figure 1 shows the various players and institutions involved in the price-setting procedure of brand-name drugs in Quebec.

Figure 1: The patented-medicine pricing process in Quebec

[3] This second, much larger concentration movement was mainly based on mergers and acquisitions (Danzon et *al.*, 2004).
[4] The visa policy came into effect in 1941 and ended in 1972, when foreign-made medicines became eligible for marketing authorization (Chauveau 2002).
[5] In 2016, French public health insurance covered 68.7% of drug expenditures (Leem, 2018).



Source: Ministry of Health and Social Services (Quebec)

In the case of the public plan (left part of the figure), when a pharmaceutical company wants to market a new patented drug, after dealing with Health Canada regarding the safety of that drug, it turns to the Pan-Canadian Pharmaceutical Alliance. Created in 2010, this Alliance is in charge of negotiating confidential discounts with laboratories for all public plans in Canadian provinces. The Alliance relies on the expertise of CADTH and NIEHSS. The price determined by each negotiation applies to all public plans in Canada, including Quebec.

With respect to private plans in Quebec (right part of the figure), each of the private insurers deals individually with industrialists. They simultaneously negotiate the registration of the new drug on the list of reimbursed drugs as well as its price. Faced with this segmentation, the continued increase in healthcare costs, and particularly the increased use of some very expensive treatments, private insurers have asked to join the pan-Canadian Pharmaceutical Alliance. This request has not yet been accepted, but the private insurers have changed their behaviour and are waiting for the recommendations of CADTH / NIEHSS before proceeding with any negotiations with industrialists.

This hybrid system ultimately gives Quebec's public and private plan administrators less bargaining power: each negotiates the prices of new patented drugs with industrialists, bilaterally[6]. In both cases, public and private, the PMPRB only intervenes retrospectively to ensure that the prices negotiated by the Alliance and applied to the market are not excessive according to its benchmark. Concretely, the PMPRB compares prices in Canada with those of seven other countries, including the United States and Switzerland, the two most expensive countries in the world with regard to drug prices, mechanically pulling the comparative element upward.

For generic drugs, the price-setting process is identical between public and private plans, according to the provisions of the public plan. Otherwise, generic manufacturers may be tempted to offer

[6] This idea is based on the economic idea that a producer has a greater propensity to negotiate prices down when the size of the market he can expect to capture is greater.

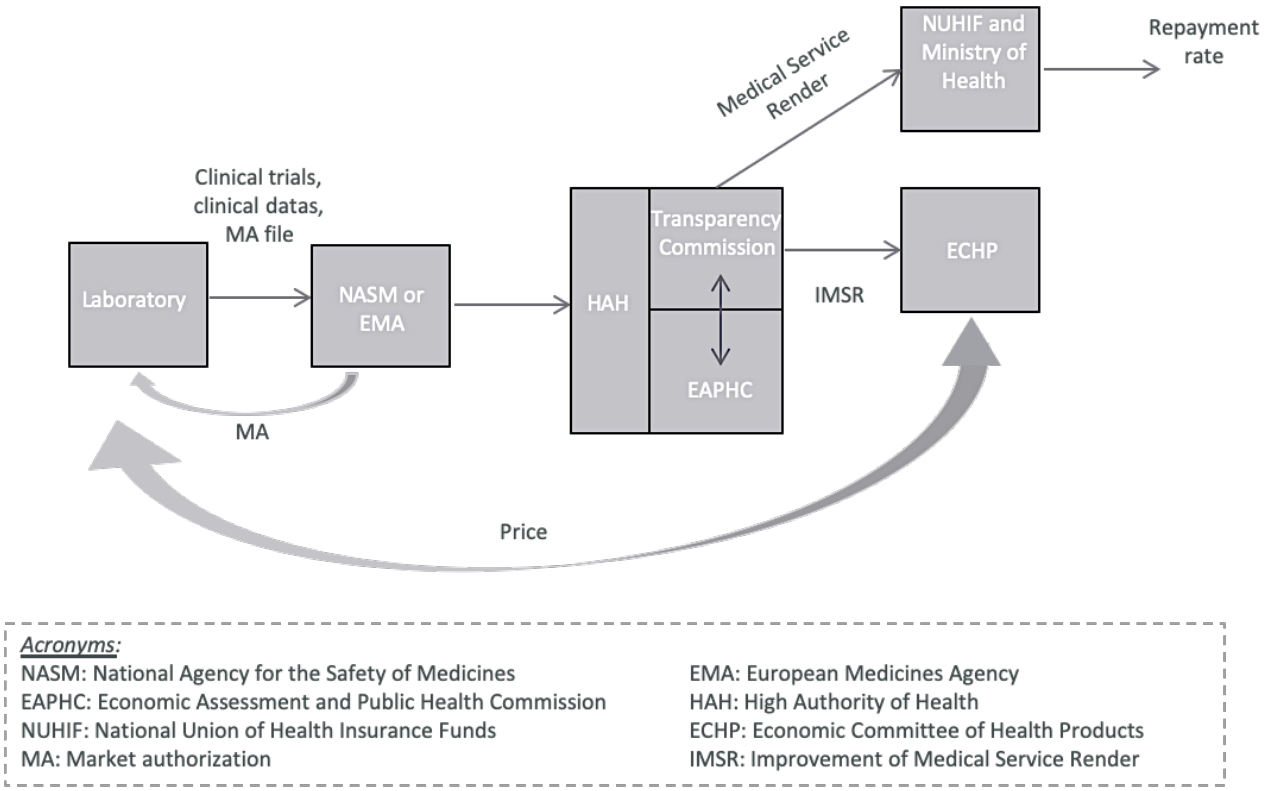
discounts to the public, partly or fully offset by higher prices in the private sector. Until 2016, the price of generics in Quebec was set relative to the best price offered in Canada. The adoption of Bill 81 by the Quebec government in 2017, allowing the use of competitive bidding, represents a significant change in the governance of competition among generic manufacturers and in pricing methods for generic drugs.

In summary, high prices are the central interest of this market. Of all Canadian provinces, Quebec has the highest total drug expenditures (Gagnon and *al*., 2017, p. 5), while Canada is the third most expensive country in the world in terms of medication (Patented Medicine Price Review Board - PMPRB, 2017, p. 34-35)

2.2.2 Centralized process in France

Figure 2 shows the French equivalent.

Figure 2: The medicine pricing process in France



Source: Ministry of Health and Social Services

Unlike in Quebec, the French pricing process is not segmented among several actors: the ECHP is the only one who negotiates with the industry, and it does so for all products marketed and reimbursed in France. The French pricing process is also based on the assessment made by the internal agencies of the High Authority of Health, which enriches the negotiation and reduces information asymmetries. According to Chauveau (2002, p. 175), the rigorous regulation of prices, and of which medicines are reimbursed, result from the fact that French Social Security covers more than 2/3 of medicine expenditures. Moreover, this strict regulation explains the French ability to benefit from significantly lower prices than those offered in other countries. Different pricing systems have been used successively since 1948, and they progressively introduced negotiation aspects in a highly administered framework, starting in the 1980s[7]. Today, the ECHP can conclude bilateral agreements

[7] This so-called "conventional" policy is based in particular on the three-year framework agreements concluded between the State and the industrialists.

with industry, which may include retrocession to Social Security if a threshold of prescriptions is exceeded, or conditional payment for an innovative treatment in terms of real-life performance.
In contrast to Quebec, France is characterized by the centralization of the price-setting process and by high state coverage of drug spending, which almost mechanically implies lower prices.

2.3 Financial regulation

This section is essentially based on the work of Foray and Lhuillery (2010, p. 408). They show that since the 1980s, changes in financial regulations of the New York Stock Exchange, the main stock exchange in North America, renewed in-depth access to capital for firms at risk. By allowing pension funds to invest in risky companies, by allowing non-beneficiary companies to float on the stock market, and by making possible the valuation of intangible assets such as patents, this new regulation allows NASDAQ to specialize in the rating of innovative firms. On the other hand, European financial regulation, and in particular French regulation, adapted to these changes only fifteen years later, in 1996.

Finally, table 1 summarizes all the levers of differentiation identified in France and Quebec, the details of which were provided in part 1.

Table 1: Summary of the differentiation levers of local pharmaceutical activity

		Quebec	France
Industrial determinants	**Industrial history**	Implantation since 1980s	Old implantation ≅ 1800
	Industrial policies	Late active policies (subventions, tax credit, 15 years rule)	Long-term support, between protectionism and nationalization
	Intellectual property rights	Late: 1987 then 1993	No patent until 1959, intermediate patent until 1968, common law patent after
Health system	**Nature**	Liberal but… hybrid public-private	Mixed: Bismarkian foundations, and Beveridge logic
	Actors and articulation	State, or private insurers = substitutable	Social Security, and complementary health = complementary
	Identified advantage	High prices	High coverage of medicine expenditure by the State (68%)
Price setting process	**Centralization/ decentralization**	Separate between public and private, and between brand-name and generics	Centralized
	Institution and power	Pan-Canadian pharmaceutical alliance vs PRPMB (retrospective role)	ECHP (effective role)
Financial system		Favorable to biotechs companies' development since 1980	Unfavorable to biotechs companies' development until 1996

Ultimately, the implantation and the operating environments of pharmaceutical activity in France and Quebec are quite different. With regard to industrial policy, while Quebec has created its pharmaceutical industry from scratch by means of attractive policies, giving it a very polarized spatial form, France has encouraged and maintained a preexisting industrial network. In addition, because industrial policies and health policies cannot be isolated, Quebec's healthcare system and the resulting pricing method offer pharmaceutical companies high price guarantees, whereas the French system guarantees high coverage of medicine expenditures by the State, which constrains price levels.

Finally, between the two territories, there is a fifteen-year gap in financial regulation with regard to introducing new and relaxed measures.

How do these different identified levers influence the form of the local pharmaceutical industry in France and Quebec? How do they materialize in the evolution of local pharmaceutical employment?

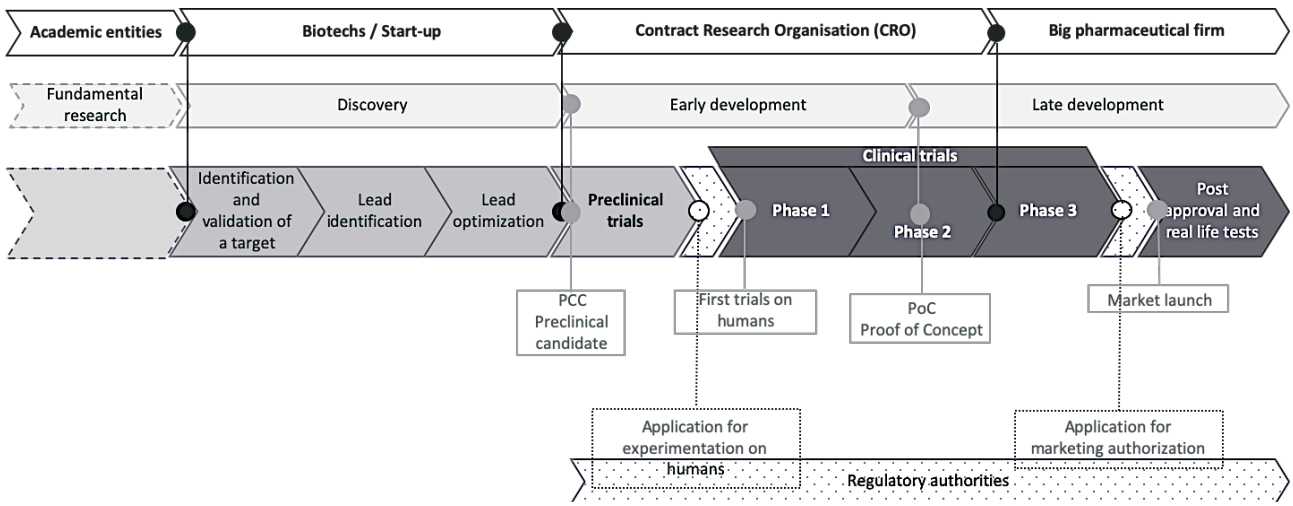
3. Employment and its evolution: a visible phenomenon of the articulation of global strategic dynamics and local particularisms

While some of industrial dynamics are common and linked to global dynamics, the levers identified in the first part have different influences from one territory to another and lead to varied trajectories in job categories.

3.1 Common trends shaped by global pharmaceutical dynamics

Two main orientations are found in both territories: the decline in overall employment after 2008 and the new organization of the value chain that began in the 2000s. While these two dynamics feed into each other, the former is more closely linked to sectoral dynamics, the patent cliff[8] and the period of uncertainty surrounding it. The second, on the other hand, is part of a broader, cross-sectoral and global reorganization of the innovation model of high-tech industries (Foray, 2018[9]). Figure 3 illustrates the new positioning of the actors during the research and development process in the case of pharmacy.

Figure 3: Structuring of the new innovation model of the pharmaceutical industry: positioning of the actors, key steps and assumed functions[10]



Source: Summary of regulatory bodies, author's graphic

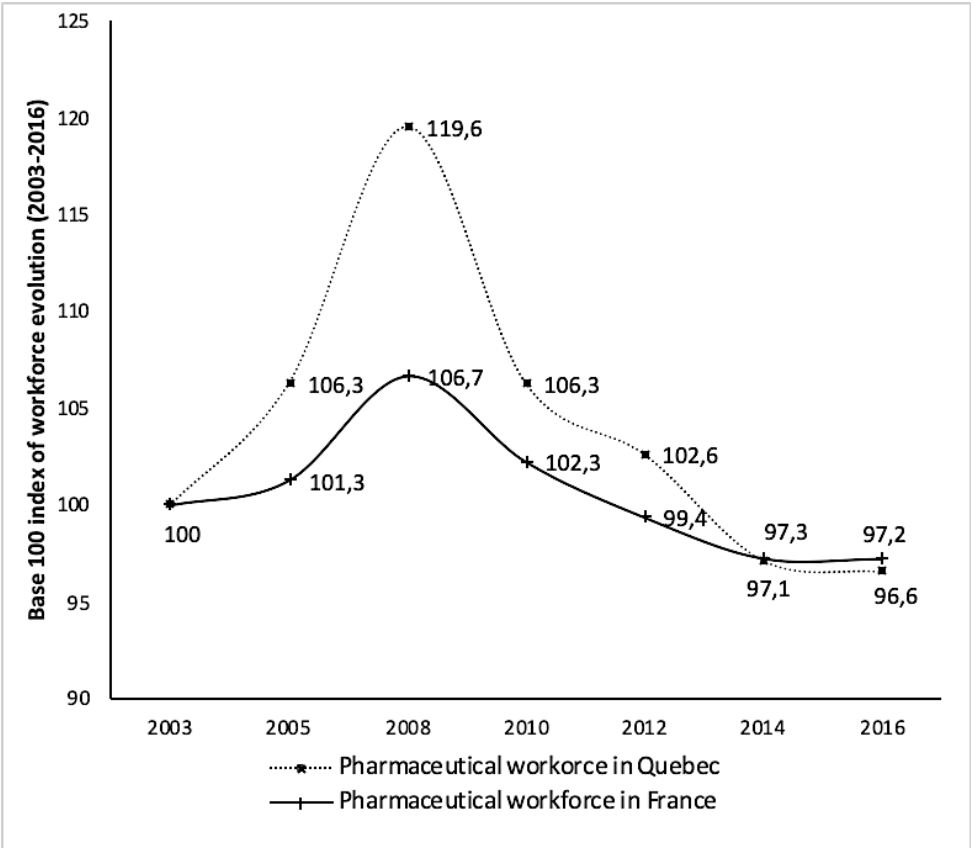
[8] The patent cliff refers to the expiration of a large number of blockbuster drug patents in a concentrated time period, exposing laboratories to generic competition with the products concerned.

[9] Foray describes the transition from a "relatively simple innovation model made up of two big poles - the public research domain and that of the large vertically integrated firm - to a much more complicated model where many actors have inserted, to assume very specialized functions" (p.32).

[10] In the network organization of R & D, four actors can be inserted during the process, assuming specific stages whose margins can nevertheless vary by integrating or eliminating a step depending on the case. Although the linear representation mode is not optimal, Figure 3 shows the most common organizational modality, but in practice, for some products, the large pharmaceutical companies may be present throughout the whole process, from experimental research to late development.

Overall employment in the pharmaceutical industry reached a peak in 2008 in both France and Québec, followed by a steady decline after the economic crisis (see Figure 4). After a period of significant growth over the 1997-2007 decade (+18,000 jobs), the French pharmaceutical industry lost 10,000 jobs over the next decade. The hardest years were between 2008 and 2014, while employment stabilized with approximately 98,700 employees thereafter. In Quebec, there was the same significant increase between 2003 and 2008 (+3,425 jobs), followed by an even larger drop (- 4,025 jobs) between 2008 and 2014, reaching 16,900 employees in 2016.

Figure 4: Evolution of pharmaceutical employment in France and Quebec, base 100 index in 2003



Source: LEEM and Ministry of Economy and innovation (Quebec)

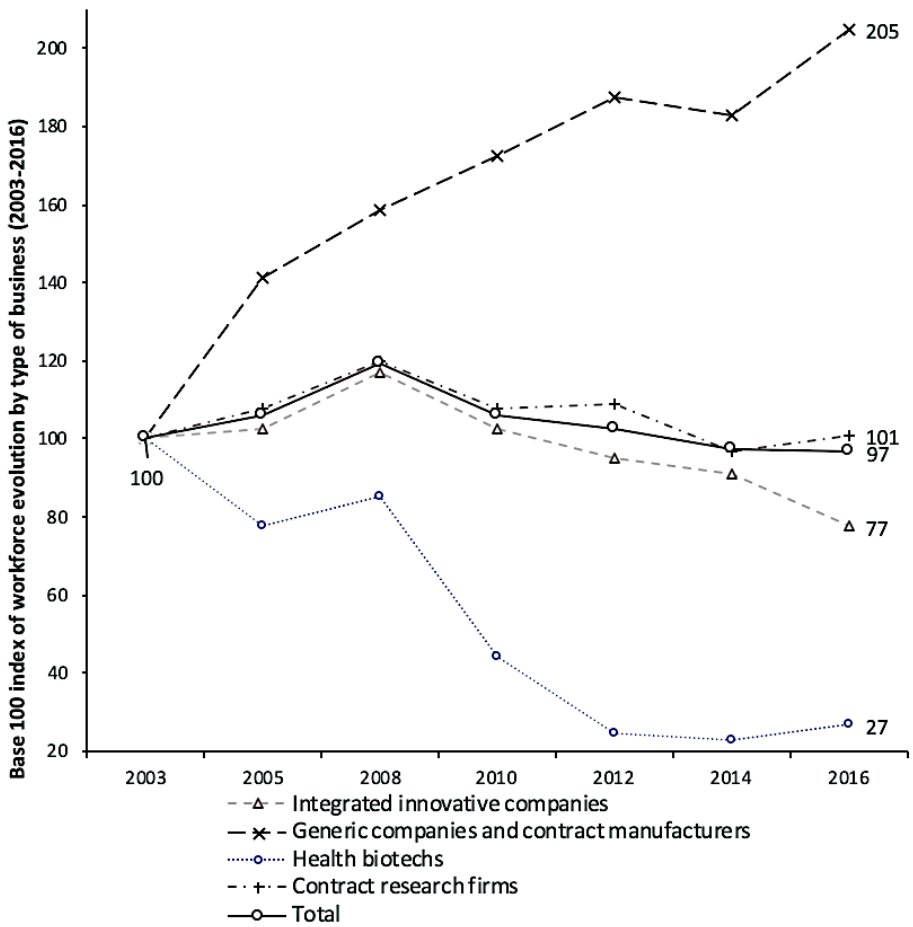
This overall finding, however, hides very heterogeneous situations from one business category to another and provides information on the massive disengagement of multinational firms from the sector. In Quebec, these firms lost one-third of their workforce between 2008 and 2016. Such downsizing in the dominant firms would have mainly affected employees in research and development. According to Pharmabio Développement[11], 652 jobs of this type were eliminated in Quebec between July 2010 and the end of 2012 (Ouellet, 2015). Indeed, the amount of R & D done within the pharmaceutical companies is declining significantly[12], as shown by the closures of their integrated research centres.

Thus, in response to global changes, the dominant firms have undergone successive reorganizations, combining redundancy plans and outsourcing activities now carried out by subcontractors, as

[11] The sectoral committee on manpower of the pharmaceutical and biotech industries of Quebec, bringing together employers, union and government actors around the stakes of the sector.
[12] See current R & D expenditures by types of research entities in the various editions of the PMPRB Annual Reports. For example, pharmaceutical companies accounted for 66.6% of R & D expenditure in 2004, compared with 53.8% in 2010 and 46.9% in 2016.

illustrated by the preservation or the rise of subcontracting companies (contract research and contract manufacturing). Firms have adopted open innovation strategies based on the acquisition of promising innovative assets outside their borders, assets generally held by a multitude of small and medium-sized biotechnology companies (Labrouche and Kechidi, 2016, p. 67). This reorganization is visible in data from the Ministry of Economy and Innovation (see Figure 5): contract research firms have lost nearly one-fifth of their workforce between their highest level in 2008 and that of 2016, but the number of contract research firms tripled between 2005 and 2016, highlighting the dynamism of this activity in Quebec, despite the tightening of the workforce. Generic companies and contract manufacturers have experienced sustained and steady growth in their workforce since 2003 as a result of the outsourcing of production activities and the context of healthcare spending control, which promotes generics. The hardest-hit companies are health *biotechs*: they lost 71% of their workforce between 2008 and 2012. Renowned as intensive fundraisers from venture capitalists or equity markets but very risky in terms of return on investment considering the high probability of failures (Montalban, 2007, p. 391; Abecassis and Coutinet, 2018, p. 44), they constitute a neglected form of investment in times of economic uncertainty.

Figure 5: Evolution of pharmaceutical employment in Quebec by type of business, base 100 index in 2003.



Source: Ministry of Economy and innovation (Quebec)

As in Quebec, the shrinking of the French pharmaceutical workforce is attributable to large laboratories. Indeed, unlike the large groups in which employment is eroding, only firms with fewer than 100 employees are net creators (Leem, 2013). Moreover, of the 20 to 30 redundancy plans that occur each year, impacting an average of 2000 jobs in total, large pharmaceutical companies are the

most present and eliminate the largest number of jobs. The trend persists: in 2016, for example, 70% of companies with more than 1,000 employees lost employees (LEEM, 2017).

France is experiencing the reorganization of the value chain related to the transformation of production activity. Indeed, the latter has been progressively divided between two types of actors: pharmaceutical laboratories or drug manufacturing specialists under contract. Between 1999 and 2014, more than 30 production sites were sold by pharmaceutical companies to manufacturers under contract, and the employment of pharmaceutical production sub-contractors grew rapidly, from 7,213 employees in 2006 (Grau and Pouquet, 2013, p. 4) to slightly more than 12,000 in 2014 (PIPAME, 2017, p. 39). Similar outsourcing is also seen in the field of R & D, but there are fewer examples.

At first glance, the synchronism of the decline in employment in the pharmaceutical sector and the financial crisis raises questions. However, Perez et *al*. (2015, p. 73) showed that pharmaceutical companies were characteristic of a type of company that exploited the cause of the crisis to make opportunistic adjustments, even though it did not experience a turnover decline. Downsizing would therefore meet two complementary objectives: that of maximizing shareholder value, echoing the conclusions already made by Lazonick and O'Sullivan under the banner « downsizing and distribute » (2000, p. 22); and that of risk and cost reduction in times of uncertainty, linked to the development of generics[13] and the patent cliff.

The analysis of employment dynamics in the pharmaceutical sector in France and Quebec shows similar trajectories in the two territories, with a comparable level of decline (approximately 20%). Multinational firms have a central role in reducing employment, as they shrink their workforces through outsourcing, mergers and acquisitions in the pursuit of increased profitability and reduced exposure to risk. At the same time, secondary actors emerge, who position themselves along the progressively disintegrated value chain.

Thus, this analysis of overall employment dynamics does not seem to indicate a strong influence of the historical and institutional environments because major trends are found on both sides of the Atlantic. However, this global approach hides differentiated evolutions in structure, relating to the local implementation of the pharmaceutical global value chain and to different commercial strategies that depend on the region.

3.2 Trajectories of major job categories: between industrial organization strategies and the influence of local frameworks

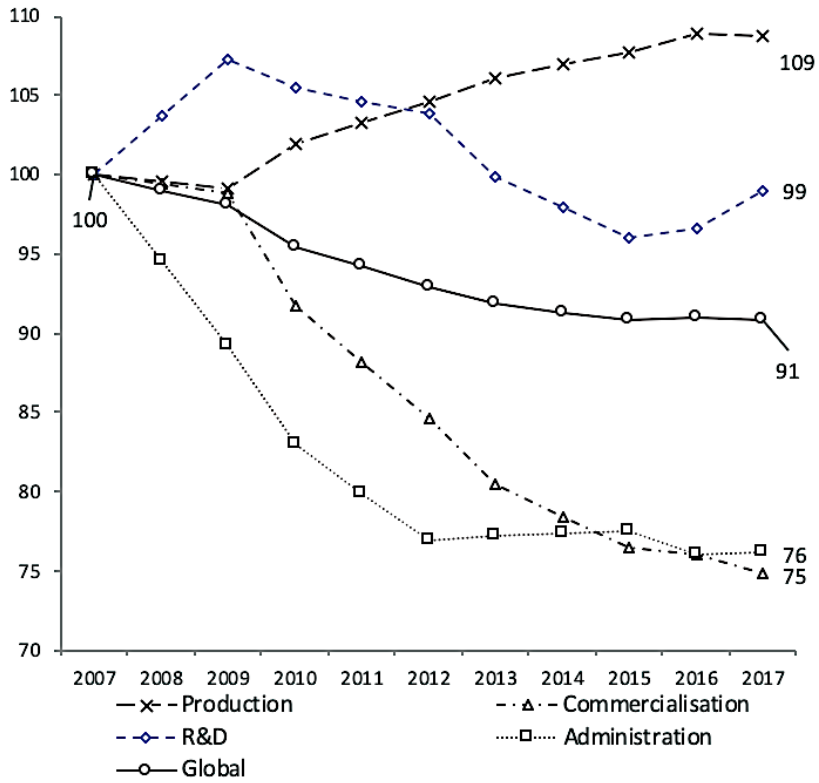
To go further, we distinguish the three central functions with direct impacts on a drug, namely, its discovery and development, its manufacture, and its marketing. The aim of the following section is to link the dynamics of these three categories of employment in France and Quebec with changes in local institutions and historical industrial determinants as well as with multinational firm strategies and behaviour.

Because value chains are by definition global, their disintegration, and their counterparts in terms of location, cannot be observed inside national borders. It is only possible to analyse what type of actors carry out each of the three activities in our two territories.
France appears to be mainly a country of drug production: 45% of its workforce is thus affected, based on 271 production sites, which positions France as 4th in the European ranking of producing countries (LEEM, 2018, p. 6). Conversely, Quebec stands out in terms of R & D, particularly because it is mainly this segment of the pharmaceutical business that 1980s government policies have targeted

[13] The Astra Zeneca site in Reims, which is 60% occupied by the manufacturing of Crestor©, whose patent expired in 2017, was, for example, sold to a US buyer in 2016, in anticipation of the commercialization of the corresponding generics.

through research tax credits on R & D wages, or through the fifteen-years rule (Ouellet, 2015, p. 23). Taking note of these specializations, how can we explain the finding that jobs eliminated in Quebec are mainly affecting R & D activity, whereas France has mainly lost support and commercial functions (Figure 6)? To shed light on these heterogeneous dynamics, we go back up the drug cycle.

Figure 6: Evolution of pharmaceutical employment in France by type of activity, base 100 index in 2007



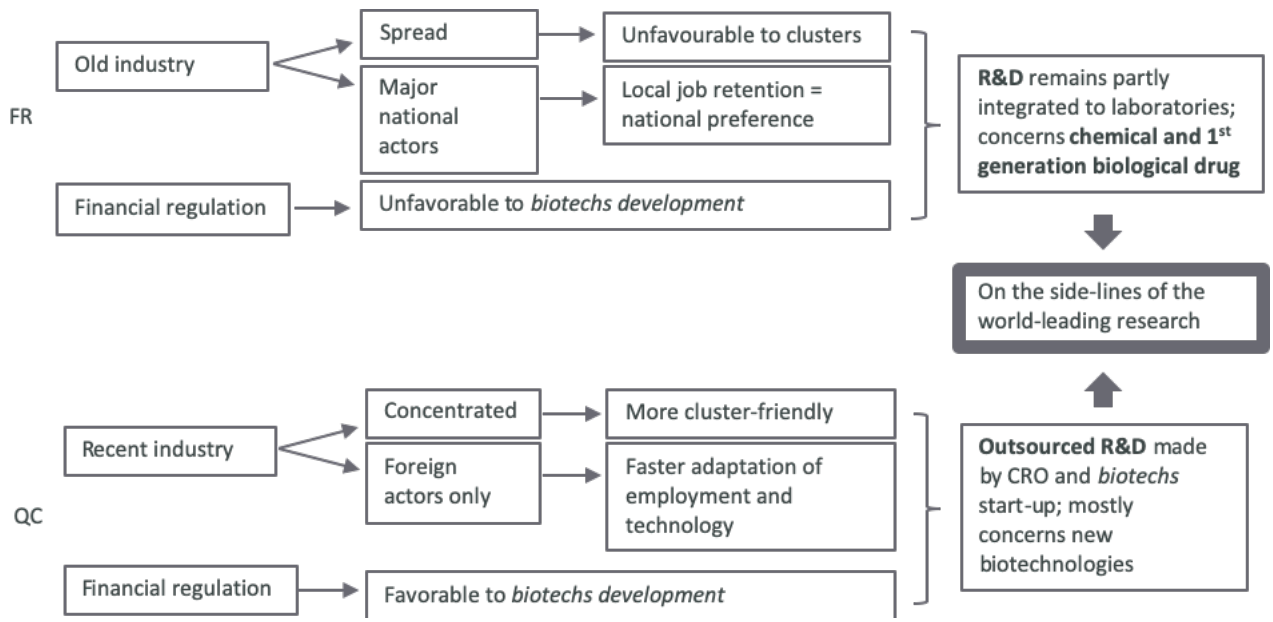
Source: LEEM, data from Employment-Salary Survey

In France, the evolution of pharmaceutical employment can be observed in light of its major activities. While the rise in production remains significant (+ 8.7%), and R & D is stable over the period, administrative and commercial functions fall sharply, losing 23.8% and 25.1% of their workforce, respectively.
We do not have such data for Quebec. However, previous figures on segmentation by type of business can provide approximate estimates.

3.2.1 Research and development: the importance of industrial history

Figure 7 summarizes the determining factors in the evolution of R & D.

Figure 7: Differentiating factors of R & D employment



Let us start with the French case. In connection with what has been the foundation of the sector (small pharmaceutical shops and scattered family factories), with the sector's consolidation, the actual pharmaceutical industry is distributed over the whole territory, while important national actors have positioned themselves on the world stage. This sprawl does not allow the emergence of strategic nodes in the form of clusters, and the few competitive or innovative poles that hatch capture only a small part of the research activity. The presence of national actors seems to favour local R & D employment retention through the exercise of a national preference (in the sense of Serfati) because of historical links with local authorities and direct consequences in the case of behaviours deemed deleterious. As an example, Sanofi's R & D workforce alone accounts for 30% of French pharmaceutical R & D, despite numerous site transfers to outsourcing[14] and partnership development[15]. The situation is rather mixed between foreign and national actors: while the French players are still well established, the large foreign laboratories located in France are few to keep research sites[16]. This would partly explain why the R & D workforce was not the hardest hit in France compared to the marketing and administration categories. On the other hand, French R & D is mainly old and centred on chemical drugs or first-generation biological drugs. France's comparative advantage over chemical activities (Amable, 2005, p. 268), already identified in the analysis of the scientific, technological and commercial systems of Amable and Boyer, is evident in the pharmaceutical industry.

On the Quebec side, the rapid and significant implantation of R & D activities by large foreign firms, concentrated around the cities of Montreal and Quebec, following the attractive government policies implemented in the 1980s, has corresponded in some way to the comet tail of the integrated research model, which was centred on the screening of chemical molecules. The latter was quickly shaken by the arrival of biotechnologies and generic competition described above, resulting in its almost complete disappearance, as brief and compact as its implantation, without any expression of national preference. Moreover, this quick adaptation is one of the characteristics of the liberal capitalism enunciated in *Les cinq capitalismes* (Amable, 2005, p. 140). This disengagement from large laboratories was concentrated overall between 2010 and 2015 and concerned all the multinational

[14] Examples include the sale of the Porcheville site to Covance in 2014, and the sales of the Toulouse and Marcy l'Etoile sites to Evotech in 2015 and 2018.
[15] Sanofi indicates that 50% of its development projects are the result of scientific partnerships, while it is the first private partner of the National Alliance for Life Sciences and Health, which brings French public research into life sciences and health.
[16] For example, GSK and Astra-Zeneca (both English laboratories) sold their latest French R&D sites in 2015 and 2012, respectively.

firms that came to Quebec twenty years ago. In parallel, these firms have sought to develop cooperation with semi-public structures[17], such as NEOMED, the Quebec Consortium for Drug Discovery (QCDD), or the Quebec Health Research fund, or directly with university labs (Ouellet, 2015, p. 21). Even as they were cutting off internal R & D jobs for reasons unrelated to financial difficulties, the big pharmaceutical companies were investing millions in these public-private structures, to which governments have redirected aid formerly granted to laboratories, with the aim of reinvigorating Quebec and Montreal areas through the benefits of spillover effects (Cheval, 2003, p. 164). R & D in Quebec is therefore mostly external to laboratories, relying more on research subcontractors, parastatals, and biotechs, and mainly concerns new biotechnologies, unlike in France.

Ultimately, although it takes different forms, research activity in both France and Quebec remains on the sidelines of the new organization of world research. The persistence, in France, of integrated research focused on the chemical aspect of pharmaceuticals, combined with the weak breakthrough of clusters and biotechs, keeps this activity away from the clearly biotechnological orientation of current research. Despite Quebec's greater propensity to conduct biotechnology research, the Montreal and Quebec City clusters are failing to attract leading research.

In fact, leading research is mostly based in two places in the world: in the United States around Boston and in China around Shanghai. In both cases, it is simultaneously the size of the markets (they are the first two pharmaceutical markets in the world), the constraining nature of the standards of the Chinese and American health authorities, and the proximity to concentrations of biotechs, university centres and academic density that determines this implantation. To follow up on the example of Sanofi, the opening of two research centres in Shanghai and Boston in 2014, both of key importance in the internal R & D system, illustrates this movement. In the case of Quebec, the example of the American laboratory Merck is meaningful. The Merck research centre in Montreal occupied a central place in Quebec's industrial landscape before its closure. Following Merck’s 2009 acquisition of Schering-Plough, which owned a newer research centre in Boston, the research centre in Montreal was thus drained of its activities, which were transferred largely to Boston. Deletions of duplication and the search for synergies contribute to the disappearance of the research centres of large laboratories, especially when establishments based in the country of origin are competing with establishments abroad.

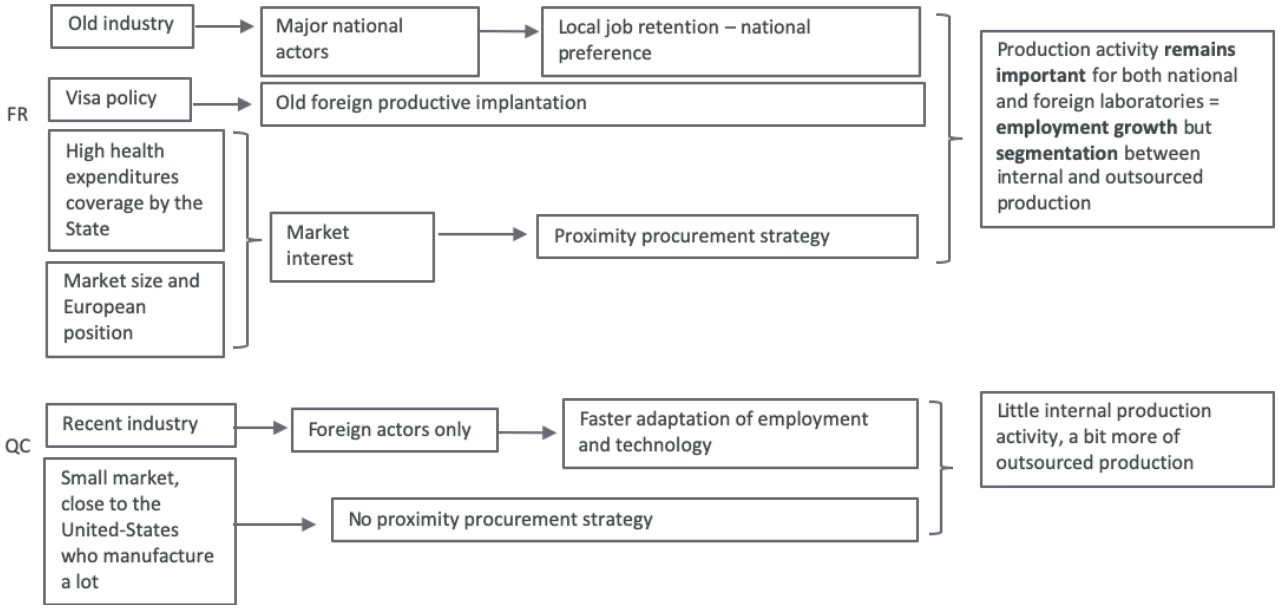
In summary, Foray and Lhuillery's (2010, p. 405) work on structural changes in European and US innovation models between 1980 and 2000 highlighted a new and growing US specialization in medical, biochemical, and genetic sciences. On the other hand, France and Canada would not have succeeded in forming a new specialization.

3.2.2 Pharmaceutical production: inheritance of sectoral history and the procurement logics of national markets

As with R & D, there is a certain national preference for production. However, this activity is also sensitive to other factors (see Figure 8).

Figure 8: Differentiating factors of production employment

[17] In the sense that these are financed by both private actors and government entities: "The NEOMED Institute is jointly funded by the pharmaceutical industry, by the Ministry of Economy, Innovation and Exports. of Quebec and Canada's Networks of Centers of Excellence (NCE)", as we can read on Neomed website www.neomed.ca.



On the one hand, the establishment of productive activities by foreign firms is linked to the history of industry in France (see I-1-b). On the other hand, the strengths of the French market are the solvency of drug demand insured by Social Security, which secures sales, a significant market size (for a long time the largest European market), and a position at the heart of Europe. These strengths favour supply strategies that enable close proximity to the market: for reasons of transport and conservation costs, or even different standards, the proximity of the production zone to the consumption zone remains decisive. Indeed, the establishment of foreign laboratories producing in France is much more varied than the establishment of laboratories for research and development activity. There is even a mono-implantation phenomenon: the Danish group Novo Nordisk, whose global production system only has a small number of sites, has, for example, chosen to install one of them in France.

In addition, pharmaceutical production is designed in the medium or even long term because it requires significant investments amortized over time. Because it is adapted to the few drugs that are specifically produced there, a plant receives dedicated investments for production that will last at least as long as the life cycle of those drugs. A specific drug production is thus difficult to transfer because it includes spatial issues and regulatory compliance well above what is required of R & D activities. Therefore, production sites are more solidly anchored territorially than is R & D activity.

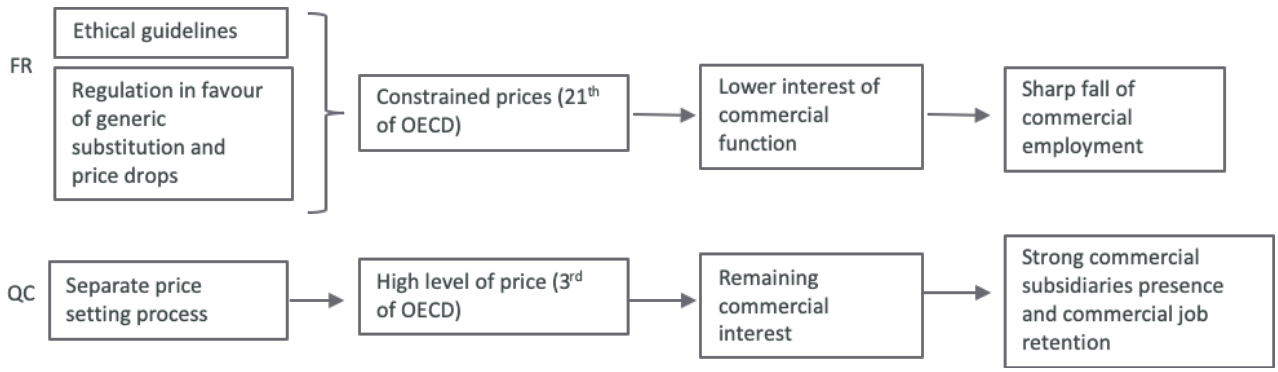
This importance of production activity in France, for both French and foreign laboratories, is illustrated by a continuous increase in employment in this category over the last decade. Nevertheless, this activity has gradually been segmented between integrated firms that retain production activity and subcontractors. This outsourcing, practised as much by national laboratories as by foreign laboratories, and both in Quebec and France, indicates a desire to retain production activity in those two locations.

On the Quebec side, the small size of the market (8.5 million potential consumers) and its proximity to the United States, which produces a large volume, discourage local supply strategies. In particular, the United States occupies a central place in the worldwide production of biological drugs. The significant increase in the category of generic and sub-contract manufacturing companies shows that on its soil, Quebec produces mainly generics and mature products through subcontracting, organic production being carried out elsewhere. Ultimately, Quebec hosts little internal production in its laboratories; activity is more supported by generic companies and subcontractors.

3.2.3 Commercial activity: high sensitivity to regulatory framework, health system and pricing process

Commercial activity is, in principle, based on an economic logic that is more than industrial: firms locate themselves where they want to sell (see Figure 9). To maximize sales, companies need to adjust their commercial strategies to local contexts (Jullien and Smith, 2012, p. 109)

Figure 9: Differentiating factors of commercial employment



The blockbuster model was based on an intense commercial marketing model for doctors and patients (Abecassis and Coutinet, 2008, p. 112; Bergouignan, 2014, p. 101) and on a specialized sales force[18] (Abecassis and Coutinet, 2009, p. 156).
In France, the control of health spending is based on price decreases, volume decreases, and a growing substitution of generics via mandatory substitution. Combined with the reinforcement of ethical rules that targeted conflicts of interest or gifts to doctors (Abecassis and Coutinet, 2008, p. 130), this set of measures has strongly contributed to the obsolescence of the model based on specialized sales forces, as these forces could no longer persuasively promote drugs for which cheaper equivalents exist. Because these sales forces were a substantial expense item[19], their use declined as soon as their effects appeared insufficient: 8,000 commercial jobs were eliminated between 2007 and 2017, i.e., a quarter of the commercial workforce.

In contrast, in Quebec, the atomization of payers, the lower propensity to consume generics in the private sector than in the public (Aviseo Conseil, 2016, p. 10), as well as the segmented pricing mode guaranteeing high prices, reinforced (until the 15-year rule takes effect) the continued prescription of brand-name drugs despite the existence of generics; this situation has preserved the interest in selling in Quebec. These various elements, combined with the observations made previously concerning R & D and production, lead us to formulate the following hypothesis: large foreign laboratories remaining in Quebec, following the liquidation of their internal research centres and the outsourcing of parts of their production, mainly retain their commercial and support functions, leading to a configuration very different from the French case.

[18] This specialized sales force can have an informational role, or a purely commercial objective, targeting mass prescriptions by doctors and extending the life of the drug.
[19] According to Bras et *al.*, from 8 to 11% of turnover.

4. Conclusion

This comparison of France and Quebec, based on the Varieties of Capitalism approach and a managerial literature centred on the strategy of multinational firms and the organization of global value chains, aimed to analyse local pharmaceutical employment and its evolution with regard to overall strategies for productive implantations, as well as local institutional and historical contexts. Overall, pharmaceutical employment in France and Quebec, resulting from the interaction between these two dimensions, shares many features in common: overall employment declines with the disengagement of the dominant pharmaceutical laboratories, which itself is guided by sectoral issues and accompanied by the emergence of specialized actors while the pharmaceutical value chain disintegrates. However, this common trend is modulated by some of the local specificities, which exercise a form of long-term stabilization and act as a brake on convergence: the persistence of production and research activities that are integrated with laboratories in France, while foreign laboratories in Quebec retain mostly commercial activities, is proof. The gap in the variation of local employment is thus a sign of firms' adaptation to these local contexts and to the institutional changes that occur.

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