New Directions for Development:
A Latecomer's Guide to Navigating the Regulatory Thicket

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Abstract

For decades, scholars of the sociology of development have investigated how "underdeveloped" countries might be able to "catch up" to what have traditionally been considered the advanced economies. The developmental state literature is one well-established interdisciplinary subfield that emerged to explain development outcomes in newly industrialized countries (NICs) during the second half of the 20th century—a period when development was largely synonymous with industrialization. In the contemporary global economy, attempts to achieve sustainable economic growth have generally shifted from manufacturing towards economic activity centered on knowledge-intensive fields. If, previously, the definition of development focused on the promotion of industrialization, what does development entail today? What are the new strategies that latecomer states and firms can adopt in this ever-evolving context? Today, the accrual and dissemination of intellectual property and the globe-spanning activities of frontier technology firms make the role of the regulatory environment ever more critical for answering these questions. Using a knowledge-intensive sector, pharmaceuticals, in a country often advanced as a paradigmatic successful late developer, South Korea, as a primary case study, the dissertation explores how the regulatory landscape is now a key domain of government action for a developmental state. The dissertation also explores the Argentine agri-biotech industry to provide a point of comparison.

While regulation is by definition an application of state authority, how well a country navigates what I term an interconnected *global regulatory chain*—a worldwide chain of regulation that impacts many different stages of production processes—is what fundamentally determines its developmental trajectory in the knowledge economy era. Not all states are equally well-positioned to overcome the range of regulatory hurdles this process presents, however, and the difficulties are more pronounced for latecomer states lacking large domestic markets –the case of most late developers, which generally do not have a domestic economy capable of absorbing the bulk of their local production. This leaves them heavily reliant on export, and, therefore, on the global regulatory landscape. That does not mean that countries with little power to contest global standards remain mere passive regulatory-takers; rather, they regularly reorient domestic regulatory frameworks to cope with changing circumstances. By combining the global value chain (GVC) perspective with insights from scholarship on regulation and governance, this dissertation demonstrates that the contemporary developmental state strategically employs available regulatory means, depending on the links or segments in the relevant global value chain the state has the practical ability to affect, with the goal of supporting domestic firms in their efforts to participate in global market. The global regulatory chain perspective, in this sense, provides a new way to conceptualize both the possibilities and challenges that await latecomer states in the global knowledge economy.

Chapter One
Introduction

In March 2020, with the advent of the Covid-19 pandemic, life seemed to come to a halt. There was no end to the crisis in sight, as the world waited eagerly for the Covid vaccines that were then being developed by Big Pharma companies like Pfizer, Moderna, and Johnson & Johnson. Those who contracted Covid turned to antiviral medications, such as Pfizer's Paxlovid or Lagevrio, a drug produced by a joint venture between Ridgeback Biotherapeutics and Merck. And when vaccines and other treatments did become available, access to them was highly uneven, reflecting the latest example of how people living in developing countries suffer from "vaccine inequity" (United Nations 2022).

The pandemic further entrenched global hierarchies in science, innovation, healthcare, and even access to very basic supplies, such as personal protective equipment. But it also illuminated the urgent need for "pharmaceutical autonomy" (Flynn 2015) to reduce the world's dependence on a small number of multinational pharmaceutical companies, a dependence that severely constricted the distribution of vaccines to developing countries. Meanwhile, the two parties that claimed to have first developed the SARS-COV-2 mRNA vaccine, Pfizer-Genentech and Moderna, are in a legal dispute over intellectual property rights and the rents accruing from them.

As the pharmaceuticals industry has grown ever more concentrated and complex, the following question has become more urgent: what have drugmakers from countries other than the U.S. or EU been doing to develop this kind of autonomy? Are they still dependent on a few Big Pharma and start-up companies in advanced economies for accessing active pharmaceutical ingredients (API), the core innovation in vaccines, or are they making material progress in developing their own vaccines and treatments?

This dissertation addresses the elusive search for pharmaceutical autonomy via a focus on innovation and industry development, focusing on the particular situation of latecomers to the global pharmaceuticals industry.

1.1 What Does Successful Development Entail in a Knowledge-Intensive Economy?

For decades, sociologists of development have been interested in learning how societies shift from a less developed to a more modernized economy, and have posited a variety of strategies to help effect that transition. Development, for most of the 20th century, has been understood largely as industrialization. The "developmental state" literature is a well-established sociological model that is frequently applied to explain development outcomes in a series of newly industrialized countries (NICs). Within this scholarship, there is a strain of thought stressing the role of the state in effectively facilitating economic growth and competitiveness in selected industries, with a group of East Asian countries comprising the primary cases for study (Amsden 1989; Chibber 2003; Evans 1995; Haggard 1990; Wade 1990). These scholars argue that many industrialized East Asian countries, including South Korea, Singapore and Taiwan, benefitted from becoming "developmental states", political economies characterized by a top-down, government-run interventionist approach, wherein states strategically and deliberately make management choices aimed at the development of selected industries.

In contrast, there is another literature that focuses on the global economy and historical capitalism as factors determining when and where national development is most likely to occur (Bair 2009; Hamilton and Gereffi 2009; Gereffi 1996; Wallerstein 1974). Rooted in the world systems approach, global value chain (GVC) scholarship highlights the importance of examining how a country's economic growth is shaped by international market forces and its interrelationships with other global actors, in particular multinational companies (MNCs). Studies building on the GVC framework challenge the developmental state explanation of the

"East Asian miracle". In its place, these scholars use a "buyer-driven approach" to explain how the "retail revolution" in the United States in the last half of the twentieth century increased demand for manufactured goods exported from East Asia, such as South Korea and Taiwan (Feenstra and Hamilton 2006). These accounts emphasize the "iterative matching" that occurred between global buyers and East Asian suppliers, which enabled South Korea and Taiwan to find distinct niches in the value chain, with South Korea specializing in mass-produced standardized goods, while Taiwan turned to production of component parts and goods with short product life cycles (Hamilton and Gereffi 2009). This recasting of South Korea and Taiwan as "demand-responsive economies" thus emerges from a combination of market, GVC, and institutional stories (Hamilton and Kao 2011).

Increasingly, however, in the contemporary global economy, industrialization is no longer a synonym for development. Attempts to achieve sustainable economic growth have generally shifted away from manufacturing to economic activities centered on such knowledge-intensive fields as information communication technology (ICT), biotechnology, nanotechnology and artificial intelligence, fields that prioritize research and development (R&D) (Breznitz, 2007; O'Riain, 2004; Wong 2011). This transition raises a crucial question as to what development has come to mean in this altered context, and also how the role of government in facilitating development has evolved (Boyd and Ngo 2005; Kennedy 2016).

Innovation is a central precondition of development in today's global economy, and contemporary innovation requires greater investments for longer duration than was the case in the past (Chorev and Ball 2022). As a result, it has become far more challenging for a developmental state to apply the kinds of tools that governments used to nurture and promote the competitiveness of "national champions" in the manufacturing sector. For this reason, some have argued that even East Asian development states have transformed themselves into something closer to the classic neoliberal state (Pirie 2018). Developmental state scholars have

responded by suggesting that the East Asian states have, rather, "adapted and evolved" (Wade 2018), with the state continuing to play a significant role in steering markets, identifying new growth sectors and deploying financial and regulatory support for corporations to meet international standards and to become leaders in frontier technologies (Haggard 2018; Thurbon and Weiss 2021).

While the degree of state involvement in contemporary high-tech industry is a matter of debate, there is a consensus that the role of the state has in any event been "reconfigured," and that previous state-industry alliances have been "reconstituted" into a new set of forms and institutions (Chu 2021; Gereffi and Sturgeon 2013). If, previously, the definition of a developmental state centered on the promotion of industrialization, what does it mean to be a developmental state today? What new strategies does it benefit "latecomer"[1] countries and firms to embrace in the ever-evolving context of the global economy? In other words, what are states doing to improve conditions for firms to succeed today?

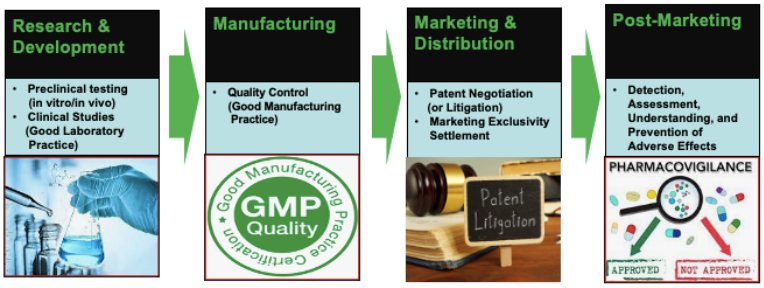
To better conceptualize the evolving dynamics of economic development in the contemporary era, this dissertation explores a knowledge-intensive industry, pharmaceuticals, in what is often advanced as a paradigmatic successful late developer: South Korea. Given the pace and industry-specific nature of innovation in today's leading sectors, states that must compete in international markets can no longer simply incubate *domestic* firms. Instead, they aim to support integration of local firms into *global* networks (Bair 2009; Gereffi 2019). And, as the dissertation will show, one key way states do this is by mobilizing the regulatory arena. Sociologists have long treated the regulatory environment as a part of a country's domestic institutional context, given that regulation is by definition an application of state authority (Carruthers and Babb 2013; Evans 1995; Nee 2005). However, as the case of pharmaceuticals

[1] The question of how to refer to countries that are not home to leading multinationals in knowledge-intensive industries is a complicated one. Obviously, South Korea is difficult to place in the global South, as it is clearly an upper income country. At the same time, it is a latecomer to pharmaceuticals industry, as are, in essence, all countries outside of the G7.

makes clear, the regulatory landscape extends beyond national borders to make itself felt at every stage of the global value chain, from R&D (e.g., patent claims), through clinical studies (ensuring that researchers follow safety and ethical guidelines, for instance), and into the distribution and marketing phase (e.g., recalls or cancelled drug renewals) (Wong 2011; Tewari 2017).

Using the South Korean pharmaceuticals industry as its primary case study, this dissertation argues that latecomer states and firms today must learn how to navigate what I term an interconnected *global regulatory chain*—an intertwined set of regulatory measures and organizations that spans national borders and impacts multiple stages of the production process in global industries. Take a new cancer drug to be sold in a European market: first the developer must determine whether it violates any patent claim or market exclusivity clause in Europe (the intended market) and also in the country where the drug is produced. The drug company must produce the medicine at a facility that regulators have determined to have good manufacturing practices (GMP). Once a sample is produced, it undergoes clinical trials in several countries, each of which has its own regulatory guidelines, depending on the demographics of the markets into which the medicine is to be sold. Finally, even after the medicine enters those markets, it remains under surveillance by regulators for possible recall and/or renewal requirements. All countries involved in international trade are unavoidably part of a chain of regulation that spans the globe, impacting all different stages of the pharmaceutical value chain (See Figure 1.1).

Figure 1.1 Regulatory Barriers By Stage of the Pharmaceuticals Value Chain



Source: Author's own elaboration

Yet not all states are equally well-positioned to overcome the range of regulatory hurdles this process presents. In particular, the impact of *global* regulatory chains on *domesti*c decision-making is especially pronounced for latecomer economies, particularly when they lack sizable home markets. Large countries like China and India are relatively less sensitive to regulatory changes in the United States and the European Union, and may even challenge their policies on occasion (Quark 2021; Rault-Chodankar and Kale 2022), something they are able to do because they have a domestic market large enough to absorb a substantial percentage of local production, as well as vibrant south-south trade relationships (Chorev 2023).

In contrast, countries like Korea, which are highly reliant on exports to the global North, and, partly for that reason, lack the power to contest the policies of the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), find themselves under constant pressure to reorient their regulatory environment via an "adaptive approach" (Whittaker et al. 2020). Countries with little power to contest global standards, however, do not remain mere passive regulatory-takers, as some of the literature argues; rather, they regularly reorient and reconstruct domestic regulatory frameworks to engage with changing circumstances (Cho and Büthe 2021; Desai 2020; Dubash and Morgan 2013; Samford 2015). Along the way, latecomer states may adopt more stringent regulations at home than are expected in foreign markets in order to ensure quality control and minimize the risk of losing opportunities in foreign markets (Jeon 2022).

Likewise, the extent to which latecomers can overcome regulatory hurdles is a key determinant of developmental trajectories in the contemporary era. I use the term "regulation"[2] broadly to indicate not only regulatory edicts and policy (usually discussed in connection with drug safety), but also legal frameworks (e.g., patents and market authorization) that act to define, obligate, constrain, or even promote certain activities by relevant actors. A primary

[2] In the dissertation, I use such phrases such as "regulatory landscape", "regulatory arena", "regulatory environment", and "regulatory context" interchangeably.

reason for broadening the definition of the regulatory landscape in this way is that regulatory conditions at one stage are so subtly intertwined with those arising at subsequent stages of the value chain. Sometimes what happens in a particular regulatory domain (i.e., advanced economies) or an international standard-setting body may also impact various countries' regulatory decision-making.

In a frontier technology like pharmaceuticals, as we will see, even after relevant regulatory approval is received, commercialization of an innovation can still easily be blocked or delayed due to unresolved patent issues or market exclusivities that intentionally extend protection for original producers. Such regulatory hurdles are often imposed not in the name of caution with respect to emerging technologies, but mainly as an effort to consolidate the power of existing innovators, mostly MNCs and other companies from advanced economies. This dissertation aims to provide a more comprehensive understanding of how the global regulatory chain operates, the existing constraints with which latecomers (essentially new competitors in the field) have to cope, and how they navigate the hurdles created by the dominant incumbents (primarily U.S. and European MNCs), all with the goal of finding their own niches in the global market and ultimately upgrading their domestic pharmaceuticals industry.

1.2 Why the South Korean Pharmaceuticals Industry?

Among the newly industrialized countries (NICs) in the latter half of the 20th century, South Korea is often described as a successful late developer. South Korea experienced an unprecedented rate of growth and shifted from the category of "underdeveloped" to "developed" country in only three decades. Some sociologists have pinpointed the essential strength of its state apparatus, featuring a nodal agency capable of coordinating and reining in other bureaucratic organizations, as the key factor that enabled South Korea to effectively facilitate development (Chibber 2003). Others have argued that the South Korean state's "embedded

autonomy" from capitalist interests was behind the country's success in developing a high-quality manufacturing sector (Evans 1995).

The developmental state literature has also emphasized the importance of centralized nodal bureaucratic agencies (e.g., Japan's Ministry of International Trade and Industry) that act as a "control tower", coordinating various development projects to achieve planned goals. These peak agencies, however, no longer exist and, therefore, there is no single ministry in charge of promoting one particular industry.

In today's knowledge economy, there are multiple agencies with differing regulatory power and interests. Decentralization of government authority has simultaneously led to increasing tensions among them.[3] In the case of the pharmaceuticals industry, while government agencies generally act to further the development of domestic technological innovation, each individual agency will have its own set of priorities. As I will discuss in greater detail in subsequent chapters, Korea's Ministry of Science and Technology stresses the importance of innovative activities and profits generated via the new technology for the overall development of the country. These goals, however, are likely to come into conflict with those of other organizations, such as the Ministry of Health, whose central aim is to facilitate the effective functioning of the universal health care system. The dissertation thus advances our understanding of how those competing interests with respect to emerging technologies shape the experience of firms and, more broadly, of knowledge-intensive industries overall.

State-firm interactions in the knowledge economy have evolved, as well. If once the state played a leadership role in helping domestic firms emerge into the global market, firms today usually take the initiative in becoming participants in GVCs. Since research and development (R&D) is a key factor in the knowledge economy, there are numerous avenues

[3] Existing literature has accounted for the negative effect of competition among bureaucratic actors on achieving development goals (Chibber 2003), and also the reverse case wherein such competition can lead to regional growth (Ang 2017).

whereby firms can enter a value chain: start-ups and university labs often engage in technology transfer or collaborate with overseas partners, while in recent years medium and large-scale pharmaceuticals firms join GVCs as contract manufacturers or even contract research organizations. Increasingly, local firms are also becoming "head[s] of GVCs" (Gereffi 2019), outsourcing downstream activities to companies in their target export countries. The natural association of the term "lead firm" with MNCs has led some GVC scholars to use the concept of "head companies" to refer to any non-MNC firm that might potentially be the lead firm in a value chain. The kinds of support firms need from states are likewise transformed in connection with changing trade dynamics and GVC patterns.

Therefore, by combining the global value chain (GVC) perspective with insights from the scholarship on regulation and governance, the dissertation illuminates how state support has evolved over the past 30 years and the extent to which it has been effective in facilitating growth in the pharmaceuticals industry. Specifically, to better understand the regulatory context as a key domain for government action today, the dissertation asks: 1) How, where, and to what extent can states use regulation to shape prospects for upgrading in knowledge-intensive industries? 2) What are the potential implications of a state's ability to influence global value chains in the contemporary era?

1.3 A Shadow Case: The Argentine Agri-Biotech Industry

As described above, power differences among countries matter for how the regulatory process plays out in any given case. The striking differences in innovation outcomes in Argentina and Korea, viewed in relation to the relevant *foreign* regulatory frameworks, are well worth exploring in this regard.

East Asia and Latin America are frequently compared and contrasted in terms of their different development pathways and outcomes. Development scholars have identified a host of important distinctions between the two regions, including, among other things, in initial

factor endowment, historical legacy, external shocks, geopolitical linkages, and sources of foreign aid that can explain the divergent development outcomes so apparent today (Amsden 2001; Gereffi and Wyman 1991; Haggard, 2018; Hamilton and Feenstra, 2006).

Among the comparative cases for study, the South Korea-Argentina juxtaposition stands out. Both countries have economies heavily dependent on exports. While Korea is a high-income country and Argentina a high middle-income country, both can be conceived of as successful latecomers with prominent domestic firms in their economies' knowledge sectors. South Korea is a classic late developer that was able to grow domestic companies into multinationals that, in some sectors, rival those from the traditional core countries. In the highly concentrated global pharmaceuticals market, Korean firms have produced over 36 innovative drugs to date[4], and have become known for producing world-class biosimilars, which are off-patent versions of branded biopharmaceutical drugs. Similarly, Argentina has been developing numerous biotech seeds, including but not limited to new genetically modified (GM) strains and other forms of transgenic crops. To show how the global regulatory chain affects not only the South Korean pharmaceuticals industry, but also other knowledge-intensive sectors in different regions, the dissertation dedicates a chapter (Chapter Six) to the agricultural biotechnology industry in Argentina as a "shadow case". Specifically, I compare how South Korea and Argentina navigate the regulatory hurdles of the respective target markets in which they hope to obtain regulatory approval for their innovations – for South Korea, this is primarily the EU and the U.S. (depending on the type of medicine), while in the Argentine genetically modified organisms (GMOs) case it is Brazil.

In contradistinction to the manifold regulatory approaches in the global regulatory landscape for pharmaceuticals, GMO regulatory schemes fall broadly into two basic categories.

[4] This number doesn't include drugs developed by Korean firms that have only been approved outside of Korea (e.g., XCOPRI).

Some countries take a "liberal" approach (e.g., the United States), approving GMOs absent a compelling reason not to, while others adopt standards based on a "precautionary principle" (e.g., the European Union). Yet as I detail in chapter six, Argentina opts for a third approach, adding an assessment of the compatibility of new GMOs with the standards of trading partners. This additional regulatory step is intended to avoid even the possibility of cross-contamination of conventional exports with GMOs, meaning that a new GMO might be rejected if it has not been approved by foreign regulators. Though this policy is intended to protect the revenue generated by Argentina's agricultural exports, it had the seemingly counter-intuitive effect of significantly delaying the approval of GM wheat developed by an Argentine firm, thus limiting the returns reaped from domestic innovation (Jeon 2022).

The approval process of pharmaceuticals (especially that of biosimilars) varies significantly by country – much more so than regulations concerning GMOs, as drugs like biosimilars are a relatively recent innovation that states are just beginning to incorporate into their health systems. South Korean biosimilars producers were able to obtain regulatory approval when the European Medicines Agency (EMA) was still establishing its biosimilars standards. As a result, their products were thereafter used as sample guidelines by the EMA. South Korea was thus able to capitalize on the uncertain regulatory environment in promoting biosimilars, whereas approval of Argentina's agri-biotechnology innovation was delayed for many years.

Different as the agribiotechnology and pharmaceuticals sectors may be, there are a surprising number of overlaps beyond the basic fact that both rely heavily on biotechnology. First, for both industries, most patents are owned by firms in the U.S. and the EU. In some cases, the same multinational companies—Bayer for instance—produce both pharmaceuticals and GMOs. Second, although copied versions of a drug are a central fact of the biopharmaceutical industry, but not of the agribiotech field, there are comparable techniques

that agri-biotech producers use. For instance, some companies deliberately choose to create GM seeds using advanced biotech tools like "molecular marker assisted breeding" instead of genetic engineering with the aim of bypassing the significant costs in time and money that the biosafety regulatory approval process and the patents filings for the latter entail (Marín et al. 2014). Third, and most importantly, while the U.S. and EU regulatory guidelines for agribiotechnology and biopharmaceuticals have been imposed as global "model" frameworks, in both sectors the two regulatory systems diverge in a host of ways, including in their treatment of patent litigation and interchangeability of reference drugs with follow-on medicines.

Where South Korean pharmaceuticals firms were able to overcome applicable regulatory hurdles and successfully launch new chemical drugs and biosimilars in the U.S. and the EU, the approval of Argentine GMOs for commercialization in foreign markets, notably Brazil, was a far rockier process, and one that held the product back for years. Research on the experiences of Korean firms in the global pharmaceutical market therefore could partly explain the challenges Argentine agribiotech companies currently face and the opportunity structures that may be available to them. In any event, a chapter devoted to Argentina's GMO case will help illuminate some of these overlapping concerns shaping the innovation trajectories of latecomer countries.

1.4 Methods

To implement a study of the relevant regulatory chains, I conducted interviews in both South Korea and Argentina over the course of 2019 and 2022. Existing studies on the knowledge economy and a country's innovation status normally rely on such measurable indicators as utilization rates (as measured by the proportion of the population using the technology in question), expenditure on R&D, number of patents or scientific publications, and the availability of knowledge workers (Chorev and Ball 2022; McGranahan and Beale 2002;

Cader 2008). Similarly, studies on regulation often use statistical or network analyses to find variables or nodes that facilitate approval processes (Carpenter 2002; Kim 2006).

Nevertheless, participation in frontier technology GVCs, like that for pharmaceuticals and agri-biotech, entails an asymmetrical relationship between lead firms and suppliers, given the dominance of the former in global trade (Bair 2009). To thoroughly understand the power dynamics among states, between states and firms, and also between firms belonging to different global contexts, I combine multiple qualitative methods—interviews, short-term observations at a government office and expos, and secondary data analysis—to triangulate data and enhance the validity of my findings.

To describe the specificities of the field sites, the methods section is divided into two parts: data collected in Korea and data collected in Argentina.

1.4.1 The Korean Data

I use a mixed-methods qualitative analysis combining interviews, archival data analysis, and short-term observations. The data for this study were collected between summer 2021 and fall 2022. I conducted sixty-six semi-structured, in-depth interviews with key actors involved with the pharmaceuticals industry. My informants included industry actors in the Korean domestic pharmaceuticals sector; representatives of global pharmaceuticals companies located in Korea or partnering with Korean firms; public officials, including regulators and representatives of bureaucratic organizations that provide support for pharmaceuticals R&D; patent lawyers; and scientists working with biological products. For the full list of interviewees, categorized by occupation, see Table 1.4.1.

Table 1.4.1 List of Informants (Sorted by Occupation)

Government Officials	Government bureaucrats	8
	Regulators (Korean & foreign)	6
Industry Representatives	Large domestic firms	18
	Small and medium domestic firms (including start-ups)	16
	Foreign companies (including "Big Pharma")	10
Patent Lawyers		4
Scientists		4
Total		**66**

I supplement this data with an analysis of annual industry reports, legal and regulatory documents, videos of the 2021 and 2022 national assembly audit[5], applications for R&D support, information on clinical and non-clinical trials, price data, and news reports on the pharmaceuticals industry. I used newspaper articles chiefly for fact-checking, to verify names and other information.

Informants were sampled purposively to secure responses from people versed in trends in the pharmaceuticals industry and related regulatory frameworks. I attended the Bio Korea International Convention in both 2021 and 2022, an annual expo/conference for the global health biotech industry. Sponsored by the Ministry of Health and Welfare and other government organizations, this three-day event enabled me to meet with all the aforementioned kinds of experts in a single setting. I began constructing my initial pool of interviewees using contacts established at this event. New interviewees were subsequently gathered through snowball sampling.

Most interviews were conducted in person, but some were also done via Zoom or phone due to the Covid-19 pandemic in Korea. Interviews lasted 1-2 hours and were recorded either

[5] Known as the National Assembly Inspection, this is an annual hearing where selected members of the Korean Congress question government officials (e.g., the Commissioner of Food and Drugs), possibly leading to changes in the policies of relevant organizations. The whole process is broadcast on live TV, and also online, thus ensuring public oversight and a degree of transparency.

at the informants' offices or other locations convenient for them. They were conducted in Korean or English, depending on the language with which each informant was most comfortable. Interviews were transcribed shortly after they were conducted and coded in NVivo. To protect informants' privacy, I identify them by interview chronology and occupation (e.g., 'government official 1'), obviating the need for pseudonyms.

1.4.2 The Argentine Data

The Argentine portion of the data was collected primarily during the summer of 2019 in Buenos Aires and Santa Fe, Argentina. I conducted thirty-two semi-structured, in-depth interviews with key actors[6] in GMO regulatory policymaking. Follow-up phone and Zoom interviews were also conducted in the fall of 2020, 2021, and 2022 to learn about any newer developments regarding the approval and commercialization process in both Argentina and Brazil.

My informants comprise former and current regulators[7] from CONABIA, SENASA, and DNMA; representatives of biotech companies; academics [8] specializing in agri-biotechnology; activists; and other industry stakeholders. I reached out to activist organizations opposing GMOs to ensure a variety of views on GMOs. For the full list of the interviewees, categorized by occupation, see Table 1.4.2.

[6] 'Key actors' means people directly or indirectly involved in the regulatory approval of GM events.
[7] Regulators differ from government officials in that most regulators are molecular biologists or agronomists; this is because regulators are responsible for scientifically assessing proposed new GM events. Having evaluated them for safety, they report to the government officials, who decide whether to approve them or not.
[8] Academics include scientists, agronomists, economists and political scientists. Some of the scientists or agronomists I interviewed were also regulators; in those cases, I categorized them as 'regulators'. Those I classify as academics work in the area of gene manipulation, assessment of the socioeconomic and environmental impact of GMOs, etc.

Table 1.4.2 List of Informants (Sorted by Occupation)

Academics	7
Activists	3
Biotech Company Representatives	2
Farmers	3
Government Officials	6
Lobbyists	4
Regulators	4
Scientists	3
Total	**32**

In addition to in-depth interviews, I also analyzed policy documents on export taxes, government expenditures, OECD reports on Argentina's economy, and news reports[9] in major Argentine media outlets. I used newspapers chiefly for fact-checking, to verify names and other information.

As in the Korean context, informants were sampled purposively to provide responses from those experts most familiar with GMO regulatory policy. I attended ExpoAgro, the largest annual agricultural expo in Argentina, held in San Nicolas de los Arroyos in March 2019. This three-day event gathers people from across Argentina's agricultural sector, including the biotech industry, germplasm companies, distributors, farmers' associations, members of futures and options exchanges, and the media. Activists and academics who were not at the Expo were contacted via email. Following an initial round of interviews, additional interviewees were added to the study via snowball sampling.

Interviews from 2019 were conducted in person, with the exception of three held via Zoom due to scheduling issues. Interviews lasted between 1.5 and 2 hours and were recorded,

[9] I consulted four newspapers: Clarín and La Nación, the most widely circulated newspapers in Argentina; Página/12, which is known to cover protest events and social movements; and, Buenos Aires Times, Argentina's only English-language newspaper.

either at the informants' offices or other locations convenient for them (coffee shops, conference rooms, etc.). They were held in English, excepting two, where language was an issue; for these, I engaged a Buenos Aires-based interpreter, since my Spanish is proficient but not fluent. She also reviewed my transcriptions of the Spanish language interviews to ensure I understood each conversation correctly. For transcription and analysis, I followed the same procedure used for the Korean data.

1.5 Dissertation Overview

The dissertation is organized as follows. Chapter Two begins with a literature review, opening with a consideration of developmental state theory and pinpointing how changing global dynamics challenge the kind of state support systems that used to be central to development in East Asia. The rest of the chapter, using the Global Value Chain approach and literature on regulation and governance, describes how states instead facilitate knowledge-intensive sectors through regulatory means, seeking to ease the entry of domestic firms into participation in GVCs and the global market as a whole. Chapter Three dives deeper into the definition of the global regulatory chain by providing background information on the dynamics of the global pharmaceuticals industry, as well as how the regulatory landscape we see today came to be.

In the next two chapters, I begin my study of how latecomer economies navigate the global regulatory chain. In Chapter Four, I describe the role of latecomer *states* in supporting domestic firms by various regulatory means, the method depending on the relevant phase of the value chain. At the R&D stage, the state may seek to facilitate trade and innovation of domestic firms by gaining international recognition and acceptance through participation in the drafting of global regulatory rules. At the manufacturing phase, the state modifies domestic regulation to increase stringency and safety of drug production, preparing firms for international markets. While quality control has been a strategy the developmental state applied

to help prevent exported products being recalled (Wade 1990; Haggard 2018), today the primary purpose of more stringent regulation is to build international reputation and to facilitate regulatory process in other domains in the future. Lastly, at the distribution stage, it provides indirect subsidies to help domestic firms better negotiate prices at the global level. Likewise, the state's primary role —whether as facilitator, regulator, or buyer—will also differ depending on the particular chain it is attempting to influence. Overall, the most prominent way states intervene today is through regulatory support.

Chapter Five, in a related vein, examines how latecomer *firms* overcome barriers arising at different stages of the global regulatory chain and, at times, how they may even influence decisions made by foreign regulatory bodies. The strategies that companies apply, and the markets they target, vary by type of medicine. For new drugs, latecomers prioritize the U.S. market, as it is the largest in the world; for biosimilars, firms prefer the EU, because the EU seeks to extend the use of follow-on drugs (e.g., any drugs, whether biological or chemical, that are legally recognized as substitutes for pre-existing, legally-protected drugs) in order to reduce healthcare expenditure by using equivalent but cheaper versions of brand medications. Hence, firms use regulatory arbitrage, and attempt to avail themselves of a "first-mover advantage" when they can, as potential strategies to enter the most competitive markets.

To generalize our view of how the global regulatory chain impacts knowledge-intensive industries to other latecomer economies, Chapter Six focuses on the agri-biotech industry in Argentina and compares state-firm relations there to what we find in the South Korean pharmaceuticals sector. By analyzing the approaches these two countries take with respect to the regulatory issues that emerge at various stages of their respective value chains, the chapter describes state-firm relations in Argentina, as well as what alternate approaches domestic firms employ to overcome regulatory barriers. At the same time, however, it lays out the challenges

countries like Argentina (but not South Korea) tend to face—countries that rely heavily on agro-exports and endure a chronically unstable macroeconomic situation.

The dissertation concludes with reflections upon how the global regulatory chain framework helps us better understand broader intertwined issues surrounding latecomer innovation and market barriers, and also provides a nuanced way to understand global inequalities in the contemporary era. Thus, the conclusion aims not only to re-evaluate what development means today, but also to emphasize the need to reconceptualize the core/semi-periphery/periphery divides, or the global North/global South dichotomy, that have long been our default means of categorizing economies.

Overall, this dissertation demonstrates how the nature of the developmental state has changed over time, and what viable new strategies are available to latecomer firms in the global knowledge economy. In particular, the analysis brings out the importance of the global regulatory chain as an emergent structure that latecomers navigate as they seek to shape their developmental trajectories.

Chapter Two
What Does the Developmental State Look Like Today?

The developmental state literature has been the dominant approach to analyzing how countries, particularly in East Asia, were able to effectively develop selected industries and promote economic growth. Today, the leading economic sectors worldwide are no longer driven by manufacturing, but rather by production via sophisticated forms of knowledge-intensive technologies, the overwhelming majority of which are owned by firms and governments in the countries that are home to most MNCs (Arrighi et al. 2003; Barrientos et al. 2011; Gera and Mang 1998; Gibbon and Ponte 2005; OECD 1996; Powell and Snellman 2004). With changing global dynamics, development scholars from various disciplines began to argue concurrently that the traditional developmental state model, with such policies as sectoral targeting and the nurturing of "national champions", could no longer adequately explain the trajectories of latecomer economies (Chu 2021; Whittaker et al. 2020; Wong 2011; Yeung 2016).

Some scholars see the "ex-developmental states" (Pirie 2018) as having incorporated the spirit of the neoliberal turn, so that these governments now play only a "supervisory and regulatory role", as opposed to a role that involves more direct forms of economic oversight (Hundt 2005). They contend that a market-driven model that prescribes a narrower governance role for the state has become the dominant state of affairs in East Asia. As a result, states have now largely withdrawn from direct intervention in labor-capital relations (e.g., negotiating wages and working conditions), and from allocating credits (Kim 1999; Pirie 2018; Schwak 2020).

Others, however, argue that, while the landscape has changed in such a way that the developmental model established in the post-War period may no longer hold, the role of states

has not been eliminated or drastically rolled back as neoliberal scholars (and critics of neoliberalism) suggest, but merely reconfigured (Kalinowski 2020; Whittaker et al. 2020).

To what extent is the East Asian model of developmentalism still valid in the knowledge economy era? What new challenges do latecomer states face? Do we now see some form of convergence, or greater divergence, between East Asian countries and latecomers in other regions (e.g., Latin America)?

This chapter will walk the reader through the changes the developmental state model has undergone since its inception and how it has evolved in the contemporary world economy, where participation in global value chains has a definitive impact on a country's development trajectory. In particular, the chapter will highlight the regulatory arena as a locus where the state continues to play a coordinating role in promoting development. However, it also emphasizes how regulating for development typically involves a global, as opposed to a purely domestic perspective. One of the primary insights to emerge from this dissertation is that a state's regulatory activities both shape and are shaped by an interconnected global regulatory chain.

2.1 The East Asian Developmental State [1960s-1990s]

Since the end of World War II, a variety of "development" strategies emerged to facilitate growth in newly liberated societies. Cold War geopolitics loomed large at that time, and by helping less well-off countries to develop, the U.S. and its allies hoped to contain the spread of communism across the world. Often known as the liberal approach to development, modernization theory thus sought to identify the conditions that led to the rise of the western advanced economies and, thereby, to learn how to replicate that chain of events elsewhere. Viewing the divide between the developed and developing world in terms of the latter's disadvantage in economic productivity and technical processes, some of these scholars thought

that the solution was the adoption by underdeveloped countries of the Western political and economic system (Lewis 1959; Rostow 1959).

Seeing that the "economically backward" countries, in particular Russia and Germany, had needs and also opportunities that did not seem to match the more or less linear pathway to growth envisioned by modernization theorists, Alexander Gerschenkron (1962) argued that state intervention in a country is correlated with backwardness. According to Gerschenkron, since late developers have examples to emulate, they may able to "catch up" with other developed nations by taking "shortcuts" as opposed to replicating the Western trajectory as prescribed by traditional modernization theory a la Rostow. Industrial growth and technology transfer, however, require centralized planning and the development of institutional capacity. Gerschenkron thus argues that the state must be actively involved in organizing financial markets (since late developers tend to lack capital) and take on the functions of capitalists and private institutions, as Germany and Russia did.[10] In his view, this entrepreneurial aspect of a state's activity enables it to remain relatively independent of class interests and, eventually, to implement more effective policies.

Building on Gerschenkron's classic literature on late developers, the scholarship on the developmental state holds that the rapid economic growth of East Asia can be explained as the result of the active engagement of a centralized yet cohesive state apparatus, enabling the government to allocate resources to specific sectors and selectively, but aggressively, promote industrial upgrading (Haggard 2018; Wade 2003; Weiss 2006; Woo-Cumings 1999). Coined by Johnson (1982) in his study of Japan's economic expansion in the latter half of the 20th century, the term "developmental state" applied to a group of East Asian countries, whose economic system differed in key ways both from the Western market economies and the

[10] Germany experienced rapid growth in the 19th century, with the emergence of banks and large firms. By the time Russia developed, the state was directly involved in both economic planning and production.

communist economies. The developmental state model centered on achieved a high rate of economic growth through targeted industrial policies. The Ministry of International Trade and Industry (MITI), the single most powerful governmental organization in Japan at that time, selectively promoted specific industries and effectively controlled foreign exchange; at the same time, it provided preferential financing, tax breaks, and protection from foreign competition to selected domestic industries. Such bureaucratic leadership continued to play an important role even as Japan moved on into more technology-intensive industries in the 1980s. Johnson argued, therefore, that what led to Japan's economic success after 1960s was state dirigisme and cooperative state-firm relationships.

This type of state-driven economic development was soon being emulated by other East Asian countries. Among the four East Asian newly industrialized countries (NICs)[11], South Korea has often been presented as a paradigmatic case of a third-generation (after Russia and Germany, as first generation, and then Japan as second) developmental state. Following the lead of Japan's MITI, the Korean government cherry-picked the "winners" among industries and established stringent conditions that firms in the selected industries had to follow in order to receive government aid. In his comparison of South Korea's and India's divergent development outcomes, Chibber (2003) pinpoints the strength of the coordinated state apparatus in Korea as the key factor that distinguished it from India. Korea's so-called nodal agency, the Economic Planning Board (EPB), not only facilitated development projects, but was also empowered to "discipline" other bureaucratic organizations, so that its recommendations could not be easily blocked or overridden (2003:958).

Amsden (2001) posits that strong state intervention via export promotion policies undertaken by East Asian governments was what distinguished their outcomes from the less

[11] The four NICs were South Korea, Taiwan, Singapore and Hong Kong (before it was reunited with China in 1997).

successful efforts of late developers from other regions. According to Amsden, one reason Korean firms were so export-oriented was that the protection and subsidies offered by the state were contingent on meeting specified export targets. Comparing the East Asian economies to a set of developing countries—Argentina, Mexico, Brazil, and Turkey—Amsden pinpoints the pattern of government policies that established price controls and arranged "reciprocal control mechanisms." The states allocated subsidies to make the manufacturing industry profitable, but those funds were closely monitored and their recipients subjected to various performance standards (e.g., export targets, local content requirements, investment in R&D). In other words, the East Asian economies were able to develop rapidly by coordinated application of the "visible hand of the state," which intervened in significant ways in the private sector, including by intentionally "getting prices wrong". These government policies amount to protective mechanisms that enabled developmental states to compete in a competitive world market without being subverted by the existing industrial economies.

Like Johnson, Amsden argues that this active state engagement in Asia made possible investment in knowledge-based assets, something not widely replicated in Latin America (or, for example, Turkey), which remained heavily reliant upon foreign know-how. The acquisition of national proprietary skills, therefore, indicates the strategy East Asian countries used to survive in a constantly changing global environment, in which, as they had predicted, reliance on lower-wage manufacturing could be detrimental to sustained growth.

The extent to which export-led industrialization (ELI) was the key determinant in East Asia's rapid growth is debatable, as some scholars assert a combination of ELI and import-substitution industrialization (ISI)[12] as the basis of their success (Gereffi and Wyman 1991);

[12] EOI and ISI are economic policies states implemented throughout the 20th century. ISI's primary aim is to nurture domestic infant industry. Through tariff barriers and/or quantitative restrictions on imports, governments protect domestic firms from foreign competition. At the same time, they funnel public funds to local firms via subsidies, credits, and other financial incentives. EOI policies, in contrast, encourage more openness but allow for domestic content requirements and other incentives to prepare local firms to be competitive in international markets (Wade 1991; Chibber 2003).

this claim will be further elaborated below. Nevertheless, traditional developmental state scholarship singles out strong state intervention, or a top-down approach, as the crucial feature that enabled countries like South Korea to catch up to the advanced economies.

Another body of research, the neo-developmental state scholarship, includes a diversity of views as to the most desirable level of state intervention. If the traditional developmental state stressed the role of the bureaucracy and specific industrial policies, neo-developmental statists emphasize the seemingly contradictory combination of state autonomy and strong state-firm relations, also known as "embedded autonomy", as a key factor for successful development (Evans 1995). For instance, the Electronics and Telecommunications Research Institute (or ETRI), a government-funded research institution in Korea that functioned as the peak organization in the intercommunication and technology (ICT) sector, incentivized companies to upgrade by requiring that they publicly share their accomplishments during monthly meetings. The ETRI monitored and dispensed loans based on these progress reports. The result of this cooperative yet competitive setting among *chaebols* led them to not only upgrade themselves, but also eventually to become lead firms in the global electronics market. Simultaneously, the Korean state's strategic insulation from its ties to the private sector is what enabled Korea to be more economically successful than other latecomer countries of that era (Evans 1989 1995).

Others, however, have characterized the state-society relation in Korea as a kind of "mutual hostage" situation, reminiscent of the prisoner's dilemma, where the government and chaebols are reciprocally vulnerable to each other. The result is that they impose constraints respectively, keeping each other in check. In other words, it is not cooperation, but rather a sense of caution issuing from mutual vulnerability binding the two sides together, leading to lower transaction costs and making it harder for either side to take advantage of the other (Evans and Rauch 1999; Haggard 2004; Kang 2002).

2.2 The East Asian Developmental State [mid-1990s through the present]

In the mid-1990s, along with a deepening of democracy and as part of a government restructuring project, the Korean Economic Planning Board (EPB), the nodal agency that directed domestic industrial economic activities for many decades, was merged into the Ministry of Finance and Economy. This was followed by the Asian financial crisis of 1997-1998, which not only uncovered the dark side of "misguided state intervention" (Haggard 2018), but also shifted state policy closer to neoliberal, market-oriented values than it had previously been, as such a shift was necessary for accessing the rescue monies borrowed from the International Monetary Fund (IMF). Some studies explain that the phase-out of the EPB and market liberalization due to structural reform, together with a political shift towards democratization, generated a dearth of institutional leadership within the Korean state apparatus (Lim 2010). In consequence, power and authority grew increasingly decentralized, or even "progressively horizontalized", as having a single strong agency had "proven to be no longer sustainable in the era of science-based industrialization" (Wong 2011:22).

Given the complexity of emerging technology and the rapidity with which it evolves, bureaucratic capability has been outpaced by the technological innovation it was designed to monitor and stimulate via relevant policies. As a result, in the knowledge-intensive era, the government can no longer lead industry development, but will rather provide more general forms of support (Nobel 1998). Building on the neo-developmental state perspective, some scholars have begun referring to the traditional East Asian developmental states as "innovative states" (Wang et al. 2012) or "developmental network states" (O'Rian 2004; Chu 2021). This scholarship identifies the primary role of the state in knowledge-intensive sectors as the creation of environments (e.g., science parks) where innovative actors (firms, universities, research and development (R&D) institutes, venture capitalists) can collaborate (Breznitz 2007; McNamara 2016). In the case of the Korean ICT sector, for aforementioned reasons and

because of the growing importance of the ICT sector for the national economy, the government tried to recruit U.S.-trained PhDs and professionals into the Ministry of Information and Communication (MIC)[13], transforming its primary role from top-down coordination of the industry to providing network contexts for firms (Larson and Park 2014). Yet a focus on institutional arrangements affords only a partial view of the ways in which states facilitate the development of frontier technology sectors at home, paying insufficient attention to how domestic innovation is impacted by global market forces.

One of the factors behind the successful outcomes in Korea during the developmental state era may have been the aligned goals of firms and the state; today, the leading chaebols' firm-specific interests often diverge from national development goals. In their analysis of the intelligence robotics industry in Korea, for instance, Thurborn and Weiss (2021) demonstrate how the chaebols were initially reluctant to participate because there was no viable market for the innovation. Only when rising political economic tensions among Korea, Japan, and China became a pressing issue did they join the government's effort to innovate the sector, investing in constructing digitized-robotized factories.

To some extent, chaebols have become relatively leery of government support. Building on network theory, Siegel (2007) illuminates what he sees as the "dark side of embeddedness" in Korea, where a tie to the "wrong" political network could potentially lead even to unwanted consequences, including harsher enforcement of taxes, antitrust laws, and other policies when the next president assumes power. The situation was exacerbated by President Park Geun-Hye's impeachment in 2017, which exposed "ugly features of state capture" (You 2021) even in the democratic post-developmental era, culminating in the

[13] The MIC is now the Ministry of Science and ICT (MOST), which will be discussed in greater depth in subsequent chapters.

convictions of both the then-President of Korea and the current Chairman of Samsung (Lee Jae-yong), who was pardoned in 2022 after almost two years in prison.

Others with more critical views even argue that state intervention at the technological frontier is problematic because it can lead to stronger patron-client ties between government and R&D institutes that tend to have closer ties to state elites. These well-connected groups (e.g., public R&D labs or companies) are more likely to learn about investment and/or research opportunities in advance, and thus can have a greater chance of gaining access to them, excluding as a result other, less well-connected yet potentially more innovative actors (Kennedy 2016; Mahmood and Rufin 2005).

Appropriate and sufficient forms of state support depend upon the situation in a frontier technology sector and the specific stage(s) in the relevant value chain the state seeks to support. Some sectors, such as the intelligent robot market or the aerospace industry, consist largely either of start-ups or university labs or chaebols, with no notable players in the middle ground between those poles. Moreover, public access to these innovations tends to be limited even today, as they have yet to be commercialized. The kind of state support and the forms of state-firm relations that the robotic and aerospace industries need may be unlike what will help in more mature industries, as both are relatively young and are engaged mostly in research. The pharmaceuticals industry, on the other hand, is an established sector in Korea, long characterized by the coexistence of chaebols and small and medium enterprises (SMEs), with most of the domestic companies in the mid-sized range (Wang et al. 2012). The industry has also become known as an arena where even the richest of chaebol can be easily forced out unless it is willing to risk a very substantial investment and has sufficient scientific knowledge and the requisite understanding of industry norms (Cheon 2022).[14] What role, then, can the

[14] Multinational conglomerates such as Hanwha, Lotte, CJ, Amorepacific, etc. exited the pharmaceutical market between 2015 and 2020 with unsuccessful outcomes.

state play in an industry that has traditionally consisted of SMEs, and where the chaebols have failed to achieve any notable success?

As will be discussed below, one of the reasons why it is more difficult for states to guide domestic industries today is that global industries in general have become far more complex (Coe et al. 2008; Yeung 2022). Lead firms, often multinational companies (MNCs), not only coordinate production networks that span national boundaries, but also dominate the regulatory realm, particularly in innovative sectors. This impacts the upgrading prospects for downstream actors and new competitors within industries, *inter alia* through monopoly ownership of intellectual property rights (Kinchy 2012; Kloppenburg 2005; Rikap 2018). It is thus important to determine which links in a global value chain (GVC) the state has the ability to affect.

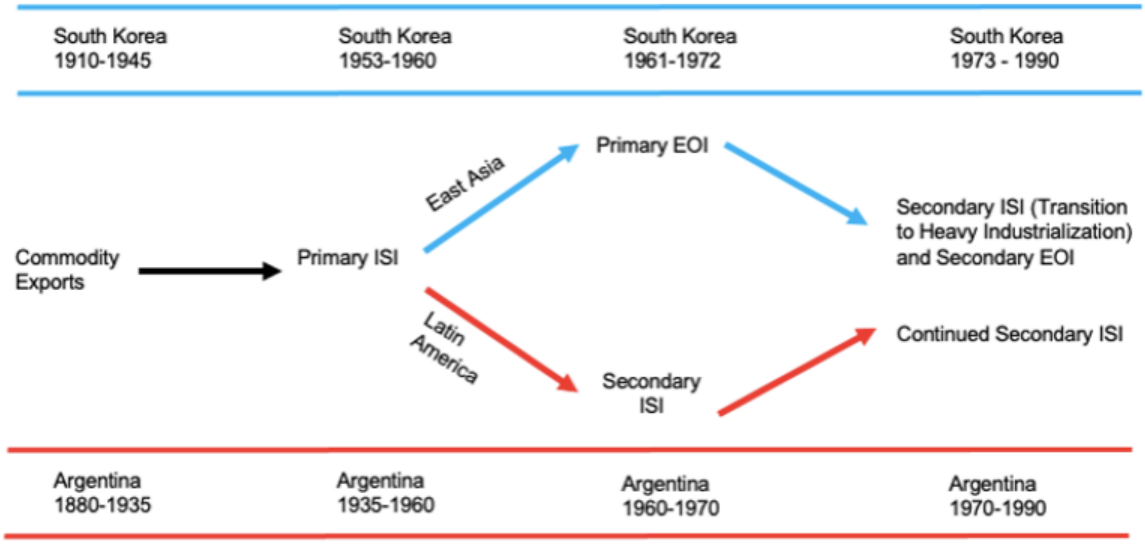
2.3 The Role of the Developmental State in Global Value Chains

Although studies on the East Asian developmental state have identified government-directed policy mechanisms and other institutional factors unique to East Asia as the key factors facilitating rapid growth and successful upgrading, the emphasis on domestic conditions in these studies meant that they largely downplayed the effect of globalization on local and national economic activities (Hamilton and Gereffi 2009; Yeung 2014).

Arguing for an examination of how economic growth is shaped by international market forces, the GVC literature and related work on global production networks (GPN) analyze the interorganizational linkages among multiple actors in both domestic and international contexts (Coe and Yeung 2015; Gereffi 1999; Yeung 2014). By taking firm-centric approaches, these scholars illuminate the "global-local nexus" (Bair 2005), at which the influence of global lead firms, typically MNCs, shapes international trade and the upgrading trajectories of local companies, especially in developing country contexts.

Compared to developmental state theory, which contrasts East Asia's export-oriented strategies and with regions' import-substitution industrialization approaches, the GVC literature points out that this distinction tends to oversimplify what really happened; in fact, in different ways and at different times, late developers from many regions, including East Asia, tried to apply a combination of the two strategic approaches (Gereffi and Wyman 1991). As we can see from Figure 2.3, East Asia started out in the 1960s with ISI, aiming to nurture light labor-intensive manufacturing industries (such as textiles, garments, and consumer non-durables), and then moved on to EOI thereafter. In the subsequent phase (in the 1970s and 1980s), East Asia pursued secondary ISI briefly, only to shift to heavy industry (steel, petrochemicals, shipbuilding, automobiles, computers, etc.) to lay the groundwork for more diversified future exports. Thus, as we can see, the industrial policies employed by East Asian countries were not as clear-cut as developmental state theorists may suggest (Whittaker et al. 2020).

Figure 2.3 Paths of Industrialization in East Asia and Latin America



Source: Author's compilation based on Gereffi and Wyman (1991)

Part of what happened was that the East Asian countries positioned themselves differently vis-à-vis global value chain than did other regions, such as Latin America. By stressing ISI, Latin America was largely trying either to develop its own domestic

manufacturing capacity to compete as a lead firm, or to continue exporting agricultural or primary commodities. The East Asian countries were much savvier, in contrast, in part because of early commercial linkages between local firms and U.S.- based importers during the 1970s and 1980s; East Asian producers changed their manufacturing capacities based on what their clients wanted (Feenstra and Hamilton 2006).

By the 1990s, however, the ability of the South Korean, Taiwanese, and Singaporean states to orchestrate economic development had lessened, firms having "disembedded" themselves from states and "re-embedded" themselves into GPNs (Yeung 2014, 2018). Thus, the dynamics of the value chain increasingly came to trump state-led policy initiatives. In this sense, the role of the state is best described as being primarily a catalyst for public-private interaction, rather than an industry leader, as described earlier.

GVC/GPN analysis has primarily focused on interfirm relations, and especially how MNCs coordinate and control various nodes within a particular chain. With the rise of China and south-south trade, led by developing states' important contribution to connecting domestic firms to GVCs, a growing body of work on GVCs is re-centering the role of state, but in a new way. Scholars in this line are exploring how the state in various latecomer countries manages and upgrades domestic knowledge-driven sectors to help them participate successfully in GVCs.

Specifically, Horner and Alford (2019) propose that one way to understand the role of the state in a GVC world is to recognize that at different times and in different industry contexts, the state may act as facilitator, regulator, producer, or buyer (see also Alford and Phillips 2018; Mayer and Phillips 2017; Morris and Staritz 2019). They distinguish "facilitator" from "regulator", where the primary task of the former is to selectively assist firms in GVCs via economic incentives or inter-state lobbying, while a regulator uses regulatory mechanisms

(tariffs and quotas, price controls, restrictions on foreign investment, quality control, etc.) to influence firm activities.

As we enter a new era of intensified scientific and technology innovation, shortened product life cycles, and greater global interdependency between developing and developed countries (Best 2001; Dodgson et al. 2005), the question Horner and Alford and other development scholars are trying to answer is what opportunities exist for states to support economic development. Whittaker et al. (2020) describe the contemporary era as one of "compressed development", by which they mean that there is now an accelerated pathway for late development, where innovation and production develop simultaneously, rather than in consecutive steps, as was the case in the industrialization era. These GVC scholars argue that contemporary developmental states should be expected to take an "adaptive approach" to their strategic support for domestic firms, given that the historically received model is no longer adequate.

In a highly knowledge-intensive field like pharmaceuticals, where innovation is accompanied by a high risk of failure, this kind of state adaptability is ever more necessary. The two roles most often played by the state in pharmaceuticals are those of facilitator, supporting innovative activities, and regulator, ensuring quality control and safety.[15] While many development studies have focused on the facilitative role of the state (Horner 2022), far fewer consider how the regulatory environment impacts firm prospects for upgrading and value creation. Even within the GVC literature, the state's role as a regulator is often conceived of solely as *constraining* the activities of global lead firms or local suppliers (Morris and Staritz 2019).

[15] In most East Asian countries, perhaps excluding China, the state is rarely a producer in frontier technology sectors. Global emergencies like COVID-19 and the procurement of vaccines constitute notable exceptions.

In a knowledge-intensive field like pharmaceuticals, however, the regulatory landscape establishes barriers that have to be overcome at every stage. Without sorting out regulatory and legal issues that emerge at a given point in a value chain or without obtaining the relevant government approvals, companies cannot move up the value chain—in GVC terminology, they cannot upgrade. As we will see, the state provides various forms of regulatory support, depending upon the node of the value chain it is attempting to influence.

More often than not, developmental state theory and the GVC approach have posited alternative accounts of the central driving force behind economic development. While GVC analysis has focused on firm-level issues, the developmental state's unit of analysis has been the state and/or state-society relations. Nevertheless, these literatures have similar understandings of upgrading; developmental state theory sees it as a process of shifting an economy away from labor-intensive and towards knowledge-based assets (Amsden 2001), while for GVC scholars it is the process whereby an economy moves up the value chain ladder (Gereffi 2019). In fact, efforts to understand the state-GVC nexus extend as far back as the early 1980s, when Gereffi and Evans (1981), prominent sociologists in GVC and developmental state theory, respectively, collaborated to establish an analytical framework that posited development as a process wherein states work with domestic industries, coordinating their activities to help them engage relevant niches in the global economy. Since then, the developmental state scholarship and GVC literatures have largely diverged, but as we will see in this dissertation, we are starting to see a kind of reconvergence, especially around latecomer state-firm efforts to navigate the global regulatory landscape.

2.4 Intellectual Monopoly Capitalism in the Era of Compressed Development

One of the defining characteristics of the knowledge economy is that the use of intangible assets has become a major driver of economic development and a new source of market power within GVCs (Buckley et al. 2022; Durand and Milberg 2020). To explain this

new dynamic, a branch of GVC scholarship has incorporated the innovation system (IS) framework to explore how latecomer firms and industries upgrade along a value chain and innovate proactively, rather than as passive learners (Choi et al. 2020; Lema et al. 2019; Lee et al. 2017).

Emerging from evolutionary economics and science and technology studies (STS), the national innovation system (NIS) framework explores how innovation is produced and distributed via relationships among firms, government, and research institutions (e.g., universities) (Freeman 1987; Lundvall 1992 2016; Nelson 1993). Focusing on the institutional contexts, NIS scholars try to articulate what can be done at the domestic level to increase the prospects for successful upgrading. According to them, innovation patterns differ by country due to structural particularities, as well as institutional settings (Anderson and Lundvall 1997). For instance, inter-firm and intra-firm relations, the role of bureaucratic organizations, R&D intensity, etc., can be factors contributing to divergences in innovative capacity cross-nationally.

In explaining how Korean firms entered the global biosimilars market, Hwang (2017) identifies the scientific research capability gained from experience producing vaccines and stem cell therapies, the expansion of infrastructure, the process of regularly updating domestic regulatory frameworks in connection with clinical trials, and an increased number of researchers as the primary contributing factors. Critics, however, argue that the conditions on which the NIS approach concentrates are restricted to the national level (Lane 2008), and that the approach consequently neglects broader power relations among organizations and actors (Rikap 2019).

As a result, GVC scholas have begun to explore the interactions between innovation systems and GVCs, with an eye towards assessing the limitations of knowledge transfers between MNCs and local firms in the developing world (De Marchi et al. 2018; Saliola and

Zanfei 2009). Lee and Malerba (2017) use a "catch-up cycle" theory to describe the logic whereby, although firms in developing countries usually learn from global lead firms initially, they may end up becoming leaders in their respective sectors, establishing new value chains. Lee et al. (2018) extend this idea, proposing that latecomer firms in Korea and Brazil used an "in-out-in again" strategy. They argue that once firms in developing countries learn from global lead firms, they separate themselves from the value chain to engage in "functional upgrading", adopting more sophisticated technologies and implementing in-house R&D (Humphrey and Schmitz 2000). Later, they reintegrate themselves in the global value chain as innovators to expand their market share.

The current movement toward a GVC-IS approach, then, indicates that opportunity structures for firms to upgrade are shaped not only by global market forces, but also by the local contexts in which firms are embedded. In this sense, the GVC-IS model shows us that an analysis of contemporary development needs a synthesis of globalization and domestic conditions, something the GPN literature refers to as "coupling", and something which NIS sees as facilitating successful upgrading within existing global niches.

While late developing states desire to expand the national innovation system and increase the number of domestic firms that function as the head of a value chain, the more intangible assets became crucial, the higher the barriers to entry for firms became. According to Pagano (2014), the contemporary era is characterized by "intellectual monopoly capitalism", where the protection of IPRs has not only concentrated market and legal power in the hands of the "owners of innovation", but also has led to locking out others from the use of knowledge in multiple jurisdictions.

The expansion of IPRs has also been promoted through various international agreements. In the 1980s, the U.S. government and its IP-based industries convinced business associations in Europe and Japan, two other key regions where knowledge-based assets are

generated and held, to join them in threatening to impose trade sanctions on developing countries unless they reinforced their IP protection (Sell and Prakash 2004). Since the mid-1990s, through the adoption of Trade-Related Aspects of Intellectual Property Rights (TRIPS) under the World Trade Organization (WTO), and the inclusion of IP provisions in bilateral and regional preferential trade agreements, as well as investment treaties, the central role of knowledge in production has been officially institutionalized (Abbott 2006; Shadlen 2008). Clearly, the knowledge-intensive sector has enabled MNCs and the home countries of these lead firms to capture a disproportionate share of GVC production value.

This focus on IP protection at the global level has negatively impacted latecomer states' power and the strategies available for upgrading along the relevant value chains (Durand and Milberg 2020; Wade 2003). First, late developers that used to upgrade in the industrial era by means of reverse-engineering or otherwise emulating lead-firm technologies find it more difficult to do so as they face exorbitant licensing fees. Second, the options available to governments seeking to support their national innovation systems are significantly reduced by globally protected IPRs. Nonetheless, as we will see in later chapters, latecomer countries and their innovative firms are beginning to navigate these constraining aspects of the globally interconnected regulatory landscape.

2.5 The Impact of the Regulatory Landscape on Late Developers

As explained in the preceding section, the impact of the global regulatory landscape on late developers' attempts to innovate has become increasingly pronounced in recent decades. Since IP-related regulatory barriers were implemented for the benefit of lead firms from advanced economies with the purpose of fending off competition, countries lacking proprietary rights tend to be "regulation-takers" – at least at first. This is, in fact, the situation for many developing countries, in which innovation is still at a nascent stage and which have insufficient

global market power to impact relevant established regulatory schemes at the international level.

Describing how foreign aid influenced upgrading in the pharmaceuticals industry in Kenya, Tanzania, and Uganda, Chorev (2019) discusses how adherence to international manufacturing standards (especially those of the European Union, which is the primary target market for the East Africa) more stringent than those originally required by domestic law eventually enabled local firms to produce higher quality generic drugs. Until the 2010s, East African states generally performed downstream activities in the pharmaceuticals value chain, such as bottling or filling tablets with imported chemical substances. East African producers were incentivized to meet standards for improved quality that were made conditions for access to a guaranteed market in Europe. Although here it was foreign aid, rather than domestic state initiative that led to the upgrading, the example indicates how important the ability to navigate the global regulatory landscape is for sustainable development.

Where countries have the requisite state capacity, production know-how, and involvement in relatively complex R&D activities, they may opt for "regulatory innovation", establishing unique regulatory frameworks that work to support industry in their particular domestic circumstances (Samford 2015), or even attempt to influence regulatory frameworks at the global level. In her analysis of food safety issues in China and India in connection with products imported from the U.S., Quark (2021) demonstrates how firms and the state in these two rising powers were able to challenge established global standards. Both countries saw potential health risks in imports—an imbalanced whey and casein ratio in baby formula for China, and a high pesticide residue concentration in soft drinks for India—which were produced and traded by MNCs. When a U.S.-based standard-setting body, the Association of Analytical Communities (AOAC) International, tried to settle food safety issues by proposing changes to each country's domestic food safety regulations, China not only rejected the offer,

but even turned the tables on the organization by inviting AOAC representatives to a standard-setting process directed by the Chinese government. While India eventually accepted the AOAC's offered settlement, the Indian state did at least manage to gain a seat at the AOAC's standard-setting table in the process. These two countries were thus able to navigate their disputes in a way that clarified their intent to be more than passive takers of standards originating in the global North.

China and India, however, are atypical late developers, since their large domestic markets may give them more clout than other countries enjoy. What options, then, aside from remaining passive "regulation-takers", are feasible for countries without the power to directly challenge international standards-setting bodies? Also, since the regulatory context in Quark's piece generally suggests a demand-side view, another question is: what happens on the *supply* side, where late developers are lead exporters rather than importers? How do latecomer countries trying to establish a presence for domestic producers in the global market negotiate their position at the international level and simultaneously prepare their domestic regulatory frameworks?

The understanding of how states use regulation and how regulation impacts development has undergone a dramatic change over the past three decades. In the 1980s, developmental state theorists began to discuss the "regulatory state" and juxtapose it with the developmental state, describing how the former bears the hallmark characteristics of neoliberalism, with states concerned primarily with maintaining effective competition, freedom of movement, and eschewing welfare state policies. This definition of the regulatory state has its roots in the late nineteenth century, after the industrial revolution era, when, according to Johnson (1982), the state "had little to do with the new forms of economic activity."

As a result, the regulatory state was largely seen as one that prioritized "market-rational" policies, where the United States was cited as a prime example (Haggard 2018). Johnson thus

held that a regulatory state like the U.S. takes a laissez-faire approach, acting through a restrained application of regulation compared to interventionist developmental states liken Japan, for instance. Along similar lines, studies on the regulatory state expanded in Europe in the early 1990s, seeking to describe how EU member states voluntarily ceded regulatory powers to a separate supranational authority, the Single European Market (Majone 1997; Moran 2011; Phillips 2006; Yeung 2010).

A new stream of regulatory state scholarship, however, proposes that we reorient our understanding of regulation and governance. Studies of the regulatory state in a contemporary context emphasize a "growing reliance on regulation" (Levi-Faur 2012), and often even expanded regulation, with increased global interdependence through outsourcing, joint ventures, and other collaborative activities, rather than the retrenched or deregulating state associated with neoliberalism (Vogel 1996). In this sense, regulation is the primary means by which governments continue to exert power and influence, particularly when the ability to use more interventionist measures are limited by international institutions. These scholars thus hold that states today are both developmental and regulatory (Križić 2021; Lavenex et al. 2021; Levi-Faur 2012).

Likewise, to better capture how latecomer states navigate a preexisting regulatory landscape designed, in essence, by the global North, we need to view this process through a GVC lens.

2.6 The Global Regulatory Chain in the Knowledge Economy Era

As described in this chapter, the role of the state has evolved significantly over the course of the 20th century and on into the 21st. Where the state once famously functioned as a top-down organizing authority, it has now come to act as an "enabler and supporter," or "facilitator", largely providing subsidies, tax credits, and other financial benefits to strengthen and encourage innovation and collaboration (Behuria 2018; Breznitz 2007; Gereffi and

Sturgeon 2013; Mazzucato 2013; Wong 2011). Simultaneously, states also act as "regulatory gatekeepers" (Wong 2011:151), helping firms by preparing them for the approval processes that will eventually be required for export (Curran et al. 2019; Mayer and Phillips 2017; Ponte et al. 2014). While such regulatory support is not new, a key difference today is the that the contemporary developmental state strategically employs an adaptive approach to regulatory decision-making, depending on the links or segments in the relevant GVC the state has the practical ability to affect.

Much like how value is realized through "interdependent stages of a production process" (Buckley et al. 2022) such as product development, manufacturing, logistics, and marketing, the global regulatory landscape affects one stage of a value chain after another, reflecting the importance of sorting out the intersected regulatory issues in order for a product to eventually reach the intended market. And as described in this chapter, the regulatory barriers, such as the IP-related issues, have been created by the actors who dominate knowledge-intensive sectors, for the purpose of self-protection. In the following chapter, we will explore the dynamics of the global pharmaceuticals industry and identify what factors, specifically, have prevented latecomers from moving more rapidly up the ladder, as they once did so dramatically in manufacturing industries.

Chapter Three

How Does the Regulation-Innovation Nexus in the Global Pharmaceuticals Industry Operate?

What regulatory hurdles do late developers face when seeking entry to knowledge-intensive global industries? Prior to explaining how latecomers navigate the global regulatory chain, this chapter will provide some background information on various upgrading processes in the pharmaceuticals industry, the overall regulatory landscape that firms must navigate to develop and market drugs, and different types of patents that create added complications for latecomers. The chapter will also discuss how state support for the pharmaceuticals industry has evolved over time and why financial incentives and other forms of support that were sufficient to support domestic industries historically are not sufficient to make a meaningful difference in developing knowledge-intensive sectors.

3.1 Overview of the Global Pharmaceuticals Industry: Where Does South Korea Stand?

The global pharmaceuticals sector is heavily influenced by American and European MNCs, whose domination of intellectual property rights, together with market exclusivity[16], radically increases the likelihood of a "winner-takes-all" situation (Chorev and Shadlen 2015). In fact, the pharmaceuticals market is probably more concentrated than any other frontier technology industry, including information technology, electronics and automobiles (Mucchielli 2020; Sunder Rajan 2017). It is also highly fragmented, because the MNCs choose to focus on upstream activities, outsourcing manufacturing and marketing to locations abroad. Even in the upstream links in the value chain, Big Pharma firms now outsource basic research to less powerful stakeholders – public research organizations, universities, and start-ups – in order to collateralize the risks of potential drug failure (i.e., distribute it among a greater

[16] Market exclusivity and patents are distinct forms of protection given to IPR holders. Patents are a property right granted by a patent office (e.g., US PTO) whereas exclusivity is provided by a regulatory body (e.g., US FDA) to offer delays and prohibitions on approval of competitor drugs.

number of actors) (Lane 2007; Rikap 2018). Consequently, the pharmaceuticals value chain is increasingly characterized by contract manufacturing, joint ventures, and other forms of inter-firm collaboration (Rikap 2019; Song and Shin 2019).

In the highly oligopolistic global pharmaceuticals sector, Korean firms occupy a middle ground between Big Pharma MNCs based in the U.S. and the EU, on the one hand, and strong generics producers from emerging markets like China and India, on the other (Pudelko and Büechl 2012). As latecomers to the industry (relative to the US, EU, and Japan), Korean firms are typically small or mid-sized. They also lack both a domestic market large enough to absorb a substantial percentage of their production, and entrenched footholds in alternative markets in the global South. Moreover, government-run R&D institutes devoted to drug commercialization are of limited number and scale (Song and Shin 2019).

The Korean pharmaceuticals industry emerged, together with other manufacturing sectors, during the period of rapid growth in the 1960s, and it was one of the candidate industries that received government support in the form of protection (via import-substitution) and promotion (export-led industrialization) (Shin 2015). It never scaled up to rival its traditional "Big Pharma" counterparts, however, unlike other frontier technology sectors, such as information and communications technology or automobiles, where Korean firms are counted among the industry leaders. In contrast, as we can see from Table 3.1.1 and Table 3.1.2 below, the Korean pharmaceuticals industry has remained in the proverbial middle of the pack, ranked 12th or 13th in the global market over the past several years (KPBMA 2022).

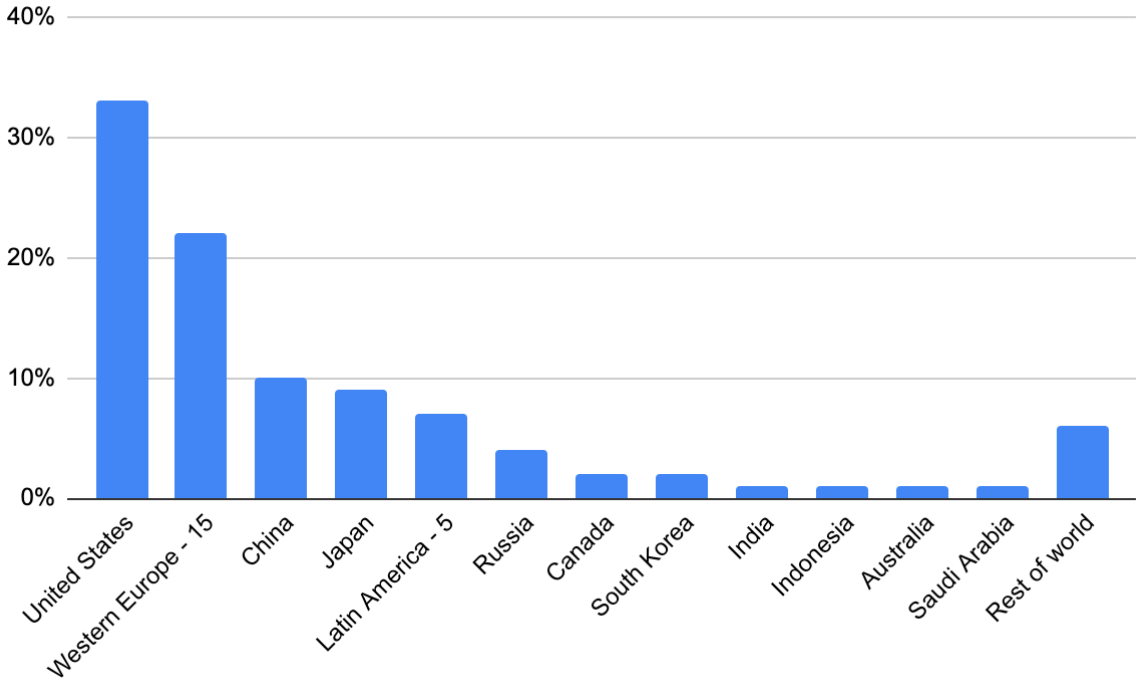
Table 3.1.1 Top Pharmaceutical-Producing Countries By Sales in $ million (2018-2021)[17]

Ranking	Country	2018	2019	2020	2021
1	United States	492,750	521,170	544,653	586,093
2	China	136,710	150,516	147,947	170,121
3	Japan	84,793	88,229	87,702	86,981
4	Germany	51,462	51,995	57,084	63,491
5	France	36,255	35,865	37,788	42,453
6	Italy	33,787	33,129	33,894	37,279
7	Great Britain	27,761	28,802	30,960	36,887
8	Brazil	34,853	36,108	30,207	32,706
9	Spain	24,585	24,647	26,539	30,921
10	Canada	22,174	23,357	24,225	27,491
11	India	17,837	19,152	19,053	22,507
12	Russia	15,524	17,071	17,262	19,412
13	South Korea	15,721	16,125	16,353	17,946
14	Australia	12,829	12,268	12,575	14,449
15	Mexico	8,344	8,922	8,985	10,808
16	Argentina	7,903	7,810	7,926	9,940
17	Poland	8,051	8,221	8,304	9,026
18	Saudi Arabia	8,210	8,548	8,200	8,701
19	Turkey	7,289	8,160	7,920	8,082
20	Belgium	6,388	6,698	7,194	7,962

Source: Author's compilation based on KPBMA (2022)

[17] This list was compiled based on the volume of drugs and drug-related products each country produces.

Table 3.1.2 The Share of Pharmaceutical Revenue Worldwide by Country (2017)



Source: www.statistica.com

South Korea's initial primary goal, as for many East Asian countries, was to develop innovative drugs and increase market share in the most competitive and rigorously regulated settings, such as the U.S. and Europe (Hwang 2017). To that end, South Korean firms have been partnering with global pharmaceutical firms at various points in the value chain since the early 2000s. These partnerships feature contract manufacturing, joint ventures, technology transfer arrangements, marketing and distribution, etc. (Kim et al. 2022). Participation in both upstream and downstream GVCs eventually led to some Korean firms (e.g., Celltrion, Samsung Bioepis, and SK Biopharm) becoming "the head of GVCs" (Gereffi 2019), independently moving into more sophisticated markets, such as the U.S. and EU, and creating their own backward and forward linkages (Gereffi and Fernandez-Stark 2016).

Since the 2010s, the government has spoken publicly of its intention to develop the *bio*pharmaceuticals industry to make it "the next semiconductor industry". Recently, in fact, the Korean pharmaceuticals industry has become known for biosimilars, which are biologically

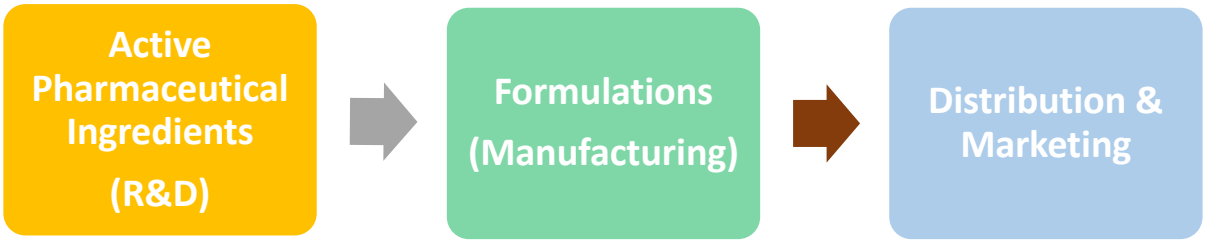
generated reproductions of patented biopharmaceutical products. Unlike generics, which are exact copies of brand-name originals, biosimilars are merely "highly similar" to the biologics ("reference drugs") they substitute for in terms of quality, safety, and efficacy. Biosimilars are sometimes seen as a form of "imitative innovation," a middle ground between replication and invention (Hwang 2017; Niosi 2017). Among the forty biosimilars approved by the FDA and the ninety-three approved by the EMA as of May 2023, ten and thirteen, respectively, are produced by South Korea, making South Korea the second most prolific producer of biosimilars, after the United States, in both the U.S. and the EU markets (See Appendix I &II)[18]

In the following section, I will provide background on how upgrading works in the pharmaceuticals industry and explain why traditional government support, including financial incentives and building infrastructure, is insufficient to make a game-changing difference in a knowledge-driven sector.

3.2 Upgrading in the Pharmaceuticals Industry

South Korea, typical for a latecomer country, entered the pharmaceuticals value chain in the formulations stage, as contract manufacturers assembling final products from imported active pharmaceutical ingredients (APIs)[19], together with non-APIs, such as fillers, flavorings, coatings and preservatives (see Graph 3.2.1).

Graph 3.2.1. A Simplified Pharmaceutical Value Chain

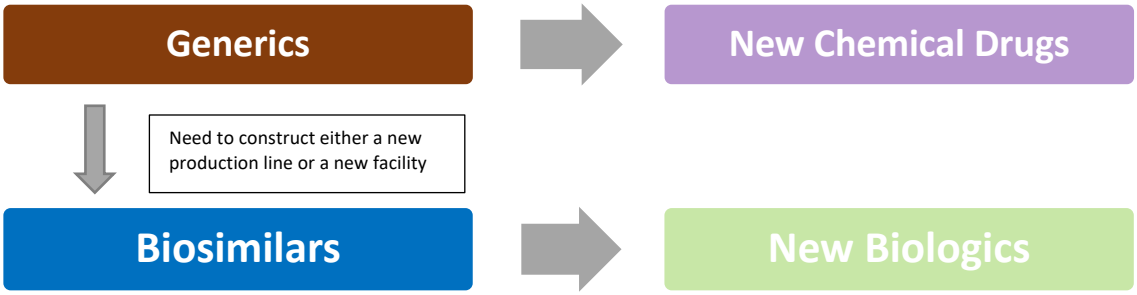


[18] In December 2022, Biocon, an Indian pharmaceuticals company, acquired Viatris, a biosimilars-producing subsidiary of the American-based MNC Mylan. Because of this acquisition, India suddenly became a country with four FDA-approved biosimilars.

[19] An "active pharmaceutical ingredient" is a component of a medicine that causes the desired medical effect. The APIs that have been described in extant social science studies are generally chemical APIs, which are different from biopharmaceutical APIs. In the case of biologics, an active ingredient is sometimes called a "bulk process intermediate" (BPI).

From there, some companies then upgrade to producing their own APIs by experimenting with various chemical components. Others also conduct biotechnology research. If a firm that has primarily been producing chemical drugs chooses to expand into biopharmaceuticals (including biosimilars), it will have to install new production lines (or even construct entirely new facilities), because the production process is completely different than the process for chemical drugs (See Graph 3.2.2).

Graph 3.2.2. General Upgrading Processes in the Pharmaceutical Value Chain



Many studies on the industry by social scientists fail to distinguish between chemically synthesized and biopharmaceutical drugs, even though they are entirely different. These products are manufactured using entirely distinct processes and prescribed for different treatment purposes. Since one of the aims of this dissertation is to explain how governments employ different strategies to facilitate upgrading of the different pharmaceuticals value chains, depending on the type of drug in question, we must clarify the distinctions between them.

Broadly, a drug can be synthesized either chemically or biologically. Until recently, most medicines, including over-the-counter drugs, were chemically-created substances comprised of small molecular structures. With advances in biotechnology since the mid-1980s, we now have biopharmaceutical drugs ("biologics"), consisting of significantly larger, more complex molecules' these molecules are less stable than chemically-synthesized drugs, which have a fixed and reproducible structure. Biologics, moreover, require involved production processes, as manufacturing means growing living cells into proteins, followed by isolation of the protein molecules, a highly delicate and challenging process (see Table 3.2). Biologics are

always available via prescription only, as they are often advanced treatments for rare diseases, immunological disorders, or cancers (Diependaele et al. 2018). Examples of biologics are vaccines, gene therapy, blood and blood components, and allergenics (Niazi 2020).[20]

Table 3.2 Overview of the main differences between chemical and biological drugs

	Chemical (including Generics)	**Biological (including Biosimilars)**
Production method	Produced by chemical synthesis	Produced by living cell cultures
Size of molecules/structure	Small molecules/well-defined structure	Large molecules/complex, heterogeneous structure
Stability	Stable	Unstable, sensitive to external conditions
Routes of administration	Typically orally and via injection	Typically via injection
Cost of development and production	Relatively low	Relatively high

Biosimilars production, additionally, requires a significant investment in terms of R&D, time, and manufacturing expertise. Since the cell lines and nutrients that produce a given target protein will vary, the processes of creating biosimilars will also differ from those by which their reference medicines are created (Moorkens et al. 2020). Thus, there is no guarantee that separate batches of a biopharmaceutical will be identical, and separate doses of a biologic are likely to have slight variations. This is one reason why some people may experience side effects from a Covid vaccine, whereas others do not, despite receiving doses from the same batch; there is always variation in biologics, even between two vials of a vaccine (Yu et al. 2021).

In the mid-2000s, the first patents and market exclusivity periods held by or granted to the creators of blockbuster biologics[21] (understood in the industry as drugs with more than $1 billion in annual sales) began to expire[22], providing a window of opportunity for pharmaceutical

[20] The term "pharmaceuticals" encompasses both chemically synthesized pharmaceutical drugs and biopharmaceutical drugs. Although pharmaceuticals are often referred to in the social sciences as chemical products, the term will be used in this paper in the broader meaning, which is also the sense in which it is generally understood in the pharmaceuticals industry.

[21] Types of these blockbuster biologics are monoclonal antibodies, human growth hormone, insulin, and tumor necrosis factor F(TNF)-inhibitors (see Niazi 2020 and Rathore and Bhargava 2020 for more detail).

[22] The patents of the top eight blockbuster medicines are set to expire by 2025.

companies and biotech institutes around the globe to produce biosimilars. The first biosimilar, Sandoz's Omnitrope, was approved in 2006 in Europe.[23] The U.S. opened its biosimilars market much later than the EU, with the first approval coming in 2015.[24]

Scholars have noted that, although generics are often considered analogous to biosimilars, the analogy "is not applicable and incorrect" (Agbogbo et al. 2019). Although both generic drugs and biosimilars are designed to produce the same clinical effects as their patented counterparts, they are entirely distinct types of products: generics are exact chemical reproductions of their brand-name counterparts, whereas biosimilars are produced in an entirely different way and thus cannot be more than "highly similar" to the biologics they substitute for.

Despite all this, biosimilars are not always considered "fully innovative" because, unlike innovative biologics, they are produced using "marketed molecules with known product attributes" (Agbogbo et al. 2019). Biosimilars companies can take advantage of the mature market the reference producers have already paid to create. In addition, compared to branded biologics, biosimilars involve a shortened development timeline and reduced costs issuing from a streamlined regulatory process. A typical new biologic development takes approximately twelve years and require three clinical trials, costing at least one to two billion dollars. In contrast, biosimilars development takes 8-10 years, needs only two clinical trials, and costs from one to two hundred million dollars, or about 20% of the cost of developing a biologic (Jacoby et al. 2016).

In fact, some of the public officials (including regulators) I interviewed in Korea clearly distinguished between biosimilars and new drugs:

[23] Although India started producing "biosimilars" in the early 2000s, the global market fails to recognize them as biosimilars, arguing that they do not meet global standards associated with that term. Moreover, India's biosimilars are primarily sold domestically, where annual sales amount to $250 million, a number that is growing at a compound annual rate of 14%. Export of Indian biosimilars has been mostly to emerging markets, with annual sales stumbling along at around $51 million (see Meher 2019 for more detail).
[24] The first biosimilar approved by FDA was Zarxio, also produced by Sandoz.

> Even if the production of biologics (including biosimilars) always involves a new method, biosimilars are not innovations *per se*, but rather involve upgrading in the production method…there is a major difference between a *discovery* and an *engineering.* (Regulator 1)

This inadequate acknowledgement of the innovative aspects of biosimilars helps explain why, for many years, there has been so little support for the biosimilars industry. Some development scholars have argued for the need to differentiate upgrading and innovation, since upgrading is "about following a path already taken by others" (Chorev and Ball 2022), which is not the case for true innovation (Lema et al. 2019; Ponte and Ewert 2009). While there is a blueprint to follow when producing biosimilars, as described above, they also require sophisticated technological capabilities to ensure that batches of biosimilars are effectively comparable, as the consistency of batches is difficult to control for due to the unstable nature of large molecules. In addition, if the manufacturing of biosimilars were as simple as some regulators seem to presume, there would be far more of them on the market, as we see in the generics market.[25]

Some biosimilars can also apply for recognition of "interchangeability"; once the regulatory body gives a biosimilar this kind of approval, a pharmacist can freely substitute it for a prescribed original biologic without the need to consult with the prescribing physician (as is commonly done for generics with respect to the branded chemical drugs they reproduce). Consequently, biosimilars can significantly help to reduce national healthcare costs spent on *bio*pharmaceuticals drugs; on average, biosimilars cost 15% to 35% less than their reference (original) biologics. In fact, biosimilar drugs saved nearly $8 billion in 2020 alone for end-users in the United States (Becker 2022). Notwithstanding these advantages, bar for follow-on drugs to gain interchangeability status in the existing U.S. regulatory landscape is set significantly higher. As a result, significantly fewer biosimilars have been approved and launched to date in the U.S. than in the EU. For this reason, even though all US states legally

[25] On average, the FDA approves at least 32,000 generics per year, whereas the corresponding number for biosimilars is only 6 (see 2022 FDA Generic Drugs Annual Report).

allow interchangeability, only three out of forty approved biosimilars are eligible for interchangeability as of June 2023.

Likewise, the approval process for biosimilars has complicating factors of its own, as will be elaborated below; getting a biosimilar through the regulatory process is far more challenging than it may at first appear.

3.3 The Regulatory Thicket in the Global Pharmaceuticals Regulatory Chain

The regulatory process firms must undergo in order to market their products depends on the type of medicine (e.g., whether it is an innovator or a follow-on drug) and the regulatory body in question. However, all must navigate regulatory hurdles posed at both the pre-market (both pre-clinical and clinical stages) and market phases. Broadly conceived, there is a regulatory approval phase, in which regulatory bodies assess health-related risks, and another, separate phase, where the relevant firms are expected to sort out any issues related to intellectual property rights. Although firms complete these steps independently, they are part of a single regulatory chain that must be negotiated before a product can reach the market.

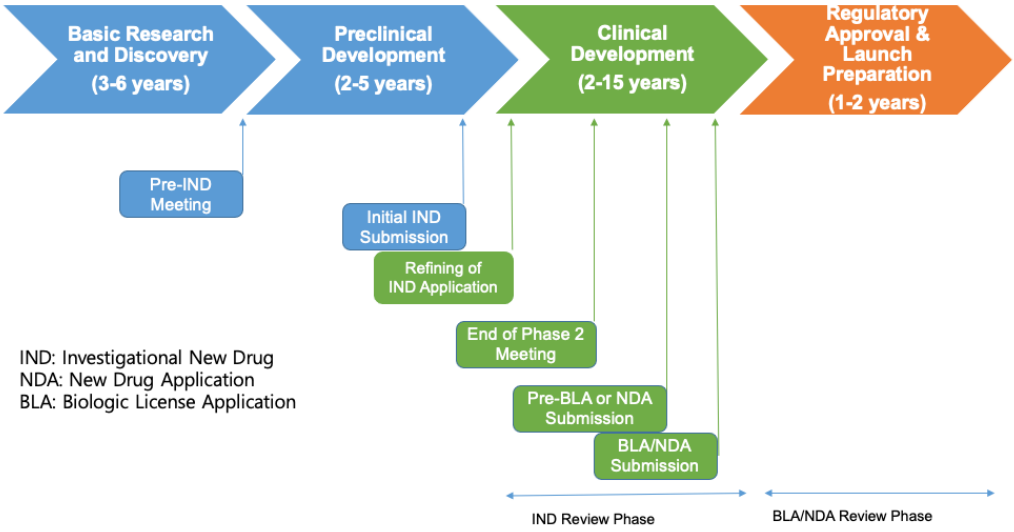
At the preclinical stage, researchers are called upon to test the therapeutic effectiveness and possible toxicity of a candidate molecule using animal (in vivo) and test tube subjects (in vitro). During this process, the drug developer determines dosing regimens, formulations, and delivery routes for the medicine in preparation for conducting human clinical trials. In the U.S., an investigational new drug application (IND)[26] is a developer's first interaction with the regulatory body. Before drugs can be tested on humans, the developer must make three submissions to the regulatory body: pharmacology and toxicology studies, demonstrating the candidate molecule's effectiveness; information on methods of manufacturing and how impurities will be handled; and a proposed clinical trial protocol, including the number and

[26] In the EU, IND is called Investigational Medicinal Product Dossier (IMPD).

demographics of test subjects, as well as identities and credentials of those administering the clinical trials.

Once the regulatory body approves the IND, the firm can move on to conducting clinical trials. In the U.S., the developer of an innovative chemical drug would file a new drug application (NDA), where the developer of a new biologic submits a biologics license application (BLA). For Biosimilars, a different route has been created, called an "abbreviated BLA" (aBLA). This second pre-market phase is "an interactive process between the FDA and the drug sponsor" (Morrison 2020), where the drug maker meets repeatedly with the regulatory body to explain the effectiveness of the drug in question, how the benefits of the new drug outweigh any potential risks that may be associated with it, and whether the manufacturing facilities they own or have contracted strictly follow GMP guidelines to ensure safe production. Based on these meetings, the regulatory body evaluates the drug; such determinations are made on a case-by-case basis (as we will see in Chapter Five, in some cases a drug may gain conditional approval in the second clinical trial stage, rather than having to wait for the third to be completed). Figure 3.3 provides a sample timeline for IND and NDA/BLA filing and when drug producers typically hold meetings with regulatory bodies.

Figure 3.3 Sample Timeline for Drug Approval



When asked whether there were any special challenges that latecomer firms from foreign countries may face, a representative from the FDA advanced the language barrier and lack of experience as two potential hindrances:

> I think if you're a foreign company that just doesn't know the process, it's going to be a disadvantage, because you're going to tend to just throw a bunch of documentation… [which is] going to gum up the whole process… they don't have the expertise or the in-house knowledge to just navigate the process. Because part of it is just knowing how to present the information in a way that is going to fit the regulations and the statutory criteria for, say, an approval (Government Official 7).

The regulatory body is "on a very strict review schedule in pre-market", with either a 30-day or a 60-day review window in which regulators must make a decision; thus, if the submitted documents fail to meet basic criteria, or if the drug maker is unable to communicate smoothly with the regulatory body, a submission may well get a disapproval. Regulators sometimes even recommend that latecomers hire consulting or law firms to represent them in this process. As we will see in Chapter Five, working interactively with the regulatory body is an important strategy, especially for latecomers, to overcome regulatory barriers.

Any new drug is provided, upon approval, with market exclusivity by the relevant regulatory body; these exclusivities function independently of whether the drug producer holds an active patent or not, because they are granted by the regulatory body, unlike intellectual property rights, which are registered with the national patent office (e.g., USPTO). As a result, an exclusivity can run concurrently with a patent, or sometimes even outlast the relevant patents, depending on what the innovator prefers. A new chemical drug is typically given five years of market exclusivity; the period for biologics is even longer – up to twelve years of protection. Even for follow-on drugs, the first company to apply for an abbreviated NDA (ANDA) or an aBLA gets a 180-day exclusive right to market their drug as sole producer. What all that means is that once a medicine is approved, the FDA must wait for the exclusivity period to end before it can approve follow-on drugs (either biosimilar or generic) (Morrison 2020). In addition, new drugs approved for one indication can, using the §505(b)(2) pathway, get

approval for a new indication as well, which can have the effect of extending the exclusivity period.

Patents are another form of protection for new drugs, and one which be an impediment for follow-on drug producers. Although whether a party can file a patent, and what patents can be filed, is a matter of domestic law, the following norms are applied in most patent-granting countries. Patents are generally registered when a product meets four criteria: it must be patent-eligible, useful, new, and nonobvious. Within broad categories of patent eligibility, a drug can typically have patent(s) for: product, process, formulation, and method of use. A product patent applies to the tangible product created by the inventor. This is often referred to as the "primary", "basic", or "parent" patent, because it covers the core active ingredient or protein sequence that is essential to making a pharmaceutical drug (Krishtel, 2019). A primary patent, therefore, provides the strongest protection for a drug product.

Other types of patents are referred to as "secondary" or "continuation" patents, which grant additional protection for derivatives of the primary patent. Examples include a new method of use, a new indication, a new composition, a change in dosage, a combination with other drugs, or a new manufacturing procedure. A process patent is granted for a unique manufacturing method for creating the product; a formulation consists of a novel dosage form, while a method of use is a new delivery method to treat particular illnesses (see Table 3.3). Overall, a patent is a kind of "negative right" (Morrison 2020), in that it is a property right issued to an inventor whose effect is "to exclude others from making, using, offering for sale, or selling the invention" (FDA/CDER 2015).

Table 3.3 Examples of Strategies for Avoiding Patent Litigation

Patent Types	Possible Strategies (Examples)
Product	Nearly impossible to avoid
Product-by-process	Use single purification step instead of three (e.g., Zarxio)
Use	Change from intravenous (IV) therapy to subcutaneous (SC) therapy (e.g., Remsima SC)
Formulation	Change salt, make citrate-free (e.g., Citrate-free Humira)

Studies have shown that, despite an alleged surge in investment in pharmaceutical R&D, the number of new breakthrough medicines worldwide has been decreasing (Light and Lexchin 2012; Pammolli et al. 2011; Pearl 2023; Scannell et al. 2012). This is because companies have been focusing on making incremental innovations, as even slight modifications in manufacturing or formulation are eligible for secondary patent protection. This is often referred to as "strategic patenting" as the secondary patents "piggyback" on the existing patents already protecting an invention; patent holders, moreover, typically file secondary patents shortly before the expiry of a parent patent, when competition from follow-on drugs is about to begin (Bansal et al. 2009; Gurgula 2020).

Given this, secondary patents have the effect of merely extending the scope and the length of protection of an innovation without encouraging genuine innovation, and those provide little or no therapeutic benefit to users. In fact, according to a report by the European Commission (EC), the ratio of secondary to primary patents tends to be 7:1. That ratio is even higher in the U.S., where the patent system enables and favors more extensive protection for patent owners (Goode and Chao 2022; Van de Wiele et al. 2022). Generics and biosimilars producers, therefore, have to learn how to navigate this "patent minefield" (European Commission 2009), since it is impossible for them to know for certain which patent(s) their products may infringe, when they may find themselves subject to an interim injunction, and thus whether and for how long they may be prevented from launching their drug.

3.4 How State Support for the Pharmaceuticals Industry Has Evolved in Korea

In Korea, the three government bodies that work most closely with (or, at a bare minimum, are connected with) the pharmaceuticals industry include: the Ministry of Health and Welfare (MOHW), the Ministry of Science and Technology (MOST), and the Ministry of Trade, Industry and Energy (MOTIE). All provide government funding and other forms of support, but in different contexts: MOST generally funds public R&D (including government-run institutes and universities), MOTIE funds emerging biotech venture capitals (and start-ups), while MOHW is responsible for the functioning of the national health system.

The Korea Health Industry Development Institute (KHIDI) was established in 1999 under MOHW to disburse funds for drug R&D projects, to facilitate overseas expansion of domestic firms, and to expand the pharmaceuticals industry, among others. As in several other latecomer countries, the Korean pharmaceuticals industry was initially focused on producing generics. Given that, KHIDI's support was also geared toward firms with a "production base for cheap and high-quality generic drugs", something that could lower government spending on prescription drugs and medical expenditures, since Korea has a universal healthcare system (Hwang 2015). Today, aside from financial support, KHIDI also provides consulting services for regulatory approval processes (for both domestic and foreign countries), patent filing, technology transfer, locating overseas partners, and more.

To help a firm carve out a niche for itself in the global pharmaceuticals market, both MOST and MOTIE have been trying to encourage Korean firms to be more involved in upstream research (Lee and Schrank 2010). In 2012, the Korean government enacted the "Special Act on Fostering and Support of the Pharmaceutical Industry" to increase R&D for new drug development, create jobs in the sector, and help establish relevant infrastructure. Also of interest is a program of state-led networking meetings among the so-called "pharmerging countries"– Mexico, Peru, Vietnam, and others – which eventually led to a lowering of

regulatory barriers (e.g., the GMP inspection exemption) in some of these countries (KHIDI 2020). In 2016, a new law was adopted under the Special Act on the Promotion and Support of the Pharmaceutical Industry, whereby MOST and MOTIE select "innovative pharmaceutical companies" to receive tax breaks, subsidies, loan opportunities, etc. The companies chosen enjoy these benefits for at least two years before their progress is reviewed again. Moreover, in early March 2021, the Ministry of Land, Infrastructure, and Transport, which coordinates transportation-related matters, including customs, amended its Aviation and Transportation Security Regulation[27] to simplify the export process for biosimilars by expediting security checks (Kang 2021).

When asked for their assessment of the quality of government support for the pharmaceuticals industry in recent years, however, many interviewees (including even those from the government, surprisingly) expressed ambivalence:

> Despite the government's ambitious goals for expanding the pharmaceuticals market, when you look at the support mechanisms closely, it is far from what it aims to achieve. In the past, the government could cherry-pick companies and invested in them heavily to develop the overall industry, but it can no longer do that. The government has limited options. Yes, it can expand the R&D budget within limits or ease the bureaucratic burden on applicants seeking to obtain funding. But can this kind of support practically help companies to really settle down and find their niches in the market? I highly doubt it (Government official 1)

Others have argued that government-funded projects tend to be short-term and that to receive continued funding a project needs to meet its stated project goals within five years – i.e., before the end of the current Presidential term (as a President can serve only one term in Korea). Thus, many lamented that the pressure to produce results within a limited time-frame and budget drives many R&D projects out of the funding competition and even leads to a kind of "brain drain", with experts moving to the U.S. or other more "business-friendly environments" in search of better research opportunities. Given this, even with the sustained, incremental

[27] Kang, Sehoon. "Simplified biopharmaceutical airline search process to strengthen export competitiveness." Newsis. March 09, 2021.
<https://newsis.com/view/?id=NISX20210309_0001363710&cID=10401&pID=10400>

increase in the annual government budget for investment in R&D in Korea (described in Chapter Two) and also a growing number of filed pharmaceuticals-related patents, the commercial rewards have yet to be reaped from domestic innovation.

There were two particularly notorious cases that may well have helped spur the retreat of the Korean state from its management role in the pharmaceuticals field. In the first, it was discovered that a famous South Korean scientist, Dr. Woosuk Hwang of the Seoul National University, had fabricated evidence and breached ethical regulations in obtaining donor eggs for his team's embryonic stem cell research in the early 2000s (Gottweis and Triendl 2006). Although scientific fraud rarely rises to the level of national political crisis (Bonetta 2006), this scandal received attention well beyond Korea's borders, because Hwang's prominence was essentially "manufactured" by the government (and accepted enthusiastically by society as a whole) with the aim of "rapidly upgrading" the Korean biotech industry (Wong 2011). Thus, he was not only supported financially by a range of bureaucratic organizations and chaebols, but also became part of then-President Roh Mu Hyun's close network, advising him on science and technology-related policy matters (Gottweis and Kim 2010).

Another, more recent scandal involved Kolon Life Science, a subsidiary of Kolon, a chaebol group, which claimed to have developed the world's first gene therapy for degenerative arthritis. The therapy, Invossa-K, was approved by the Korean FDA in 2017. In 2019, however, in clinical trials in the U.S., it turned out that, rather than using cartilage-derived cells as the company had claimed, kidney cells (inappropriate for an arthritis medicine) had been used. The Ministry of Food and Drug Safety, the Korean FDA, immediately revoked its approval and the company's CEO was indicted for violating the Pharmaceutical Affairs Act.[28]

[28] "Revived hope for new drug." Korea Times. April 15, 2020. <http://www.koreatimes.co.kr/www/opinon/2020/04/202_287922.html>

Both cases reflect the problem of "crony capitalism" in the relationship between the Korean government and the biotech industry, whether in the form of a state-sponsored celebrity industry scientist or chaebols (Kang 2002; Ha and Lee 2007). More importantly, however, these scandals are part and parcel of the evolution of the role of the state, and not only in biotechnology, but in its general approach to facilitating development. When the Hwang scandal occurred, the Korean biotech industry was still in its early stages, and the government was just beginning to retreat from its management role, selecting the industry as one it intended to actively support. In fact, a strain of literature from science and technology studies (STS) pinpoints "bionationalism" as the underlying basis for the powerful impetus to enhance national competitiveness through new biomedicine (Bak 2014; Gottweis and Kim 2010). The very notion of bionationalism reflects a culture that attaches national pride to achievement in a particular economic sector. And yet the form that bionationalism took in this case—i.e., the government investing in and promoting the public image of a scientist – was already a far cry from the kind of more interventionist role that the state had earlier exercised when seeking to support a specific industry. The corporate scandal involving Invossa-K was clearly the sole responsibility of the company; the regulatory body's approval of this questionable product (even if immediately rescinded when the scandal arose), however, indicates a knowledge deficit on the part of bureaucratic organizations vis-à-vis new and disruptive technologies.

Due to the complexity of the technology concerned, the uncertainty of R&D outcomes, the extended time frames, and the scope of funding required for pharmaceuticals innovation, the conventional types of government support are clearly insufficient to stimulate growth in the pharmaceuticals industry (Wang et al. 2012; Wield 2013; Wong 2011). Instead, as we will see, the state has targeted the regulatory environment as key means to achieving that goal. This includes thoroughly studying foreign regulatory frameworks and sharing regulatory

information about the global market with domestic firms, implementing necessary changes at home, and participating in the establishment of global regulatory guidelines.

3.5 Implications

There is no linear pathway to upgrading in frontier technology sectors like pharmaceuticals, because some companies may enter as downstream producers for chemical drugs, whereas others, such as biotech start-ups, whose primary tasks are drug discovery and nonclinical studies, may be at the very first link in the chain. As mentioned above, however, the various activities within the value chain are all subject to global regulations that have been established and reinforced by Big Pharma and the advanced economies with their dominant holdings of intellectual property rights. Thus, in a situation where multiple paths to upgrading are possible, one way for today's developmental state to support firms (assuming the state cannot challenge or meaningfully alter the existing global regulatory landscape) is to identify a particular segment(s) of a value chain where it can have a significant practical effect through selected forms of regulatory support (Lee et al. 2018; Whittaker et al. 2020). As we will see, even the state's role as facilitator involves regulatory innovation or adaptation, fields which have expanded and become much more complex in recent years.

Chapter Four
Latecomer States in the Global Regulatory Chain

Because regulation is an important determinant of whether an innovation can reach the market in the knowledge economy era, the regulatory landscape has naturally become a key domain for government action. But how, where, and to what extent can states use regulation to shape prospects for upgrading in knowledge-intensive industries? And what does this imply for a state's ability to influence global value chains?

As discussed in the previous chapter, the three government bodies that work most closely with the pharmaceuticals industry are the Ministry of Health and Welfare (MOHW), the Ministry of Science and Technology (MOST), and the Ministry of Trade, Industry and Energy (MOTIE). All support the industry via government funding, but with different aims: MOST generally funds R&D, MOTIE focuses on supporting emerging biotech start-ups, and MOHW is the ministry responsible for the national health system as a whole. The Korea Health Industry Development Institute (KHIDI), a division of MOHW, carries out most ministry projects aimed at fostering and expanding the domestic pharmaceuticals industry.

There is also the Ministry of Food and Drug Safety (MFDS), a Korean version of the U.S. FDA, which was first established as an agency subordinate to the MOHW in late 1990s. In March 2013, through the restructuring of the government agencies, the MFDS was upgraded to the status of ministry, becoming an independent body. Since then, the role of the MFDS has expanded to include much more than regulatory approval, as will be described in the following sections.

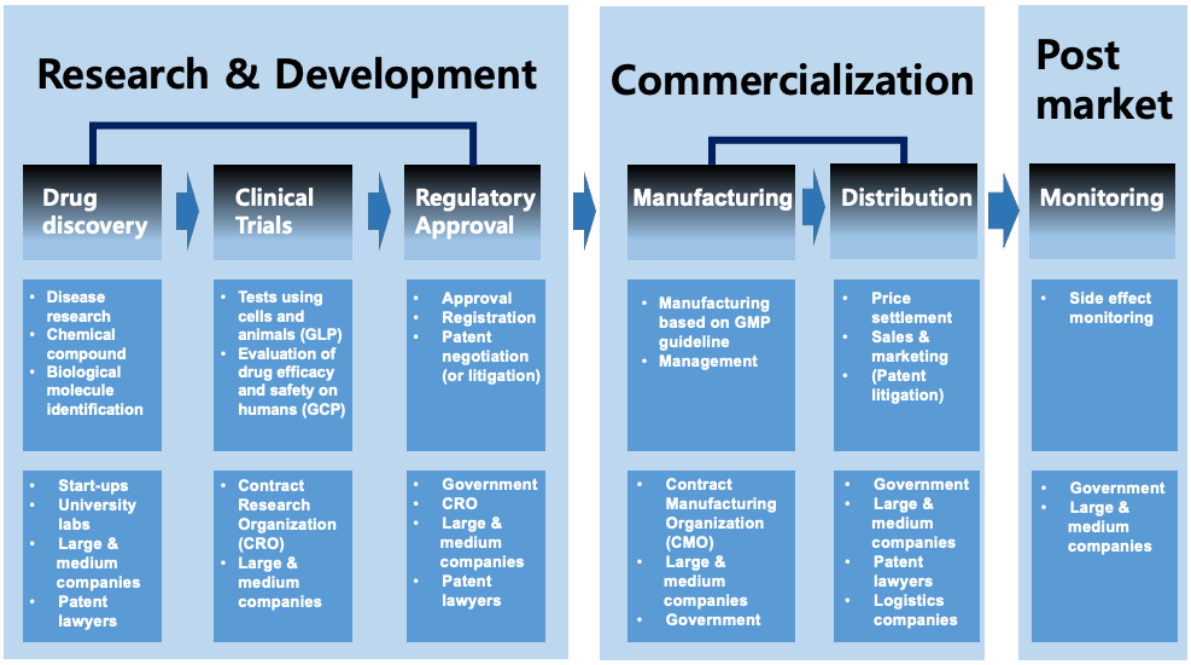
Divided into three stages—R&D, manufacturing, and distribution—this chapter walks the reader through the ways in which the design of regulatory systems depends on those links in the relevant global value chains that the state has the practical ability to affect. As we will see, the roles played by MFDS and KHIDI are crucial in R&D and manufacturing phases. In

distribution stage, despite the aligned efforts of the two ministries to expand the domestic pharmaceuticals industry, there is sometimes a degree of tension between MOHW and MOST, issuing from their different priorities. Overall, we will show how the state uses regulatory measures as tools to support this knowledge-intensive industry, in place of or in addition to such traditional methods as financial incentives or providing network opportunities.

4.1 Navigating the Global Regulatory Landscape

The process of bringing a drug to market runs through a number of stages in the relevant GVC. Within each of the three "umbrella" steps—R&D, manufacturing, and distribution—there are a set of substages, and the Korean state actively targets the ones upon which it sees a means of exerting a real practical influence (See Figure 4.1).

Figure 4.1 Example of Pharmaceuticals Value Chain



Source: Author's compilation based on Tewari (2017)

The R&D stage, for instance, includes a range of actions and events, including the finding of a candidate molecule, the conduct of preclinical research[29], the sorting out of any patent-related issues, the testing of the drug's effectiveness and safety via clinical trials, and

[29] Preclinical research is a required regulatory step intended to assess the safety of a potential drug (to evaluate its toxicity). This stage begins prior to actual clinical testing (on humans), typically in laboratories, and is governed by guidelines laid out in good laboratory practices (GLP) (FDA 2023).

the obtaining of regulatory approval from a government regulatory body. Options available to a state here include actively participating in global regulatory fora, such as the relevant World Health Organization (WHO) working group, or the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), and particularly in the drafting of relevant drug guidelines for international standards-setting bodies, as well as aiding firms in networking with relevant regulatory experts in foreign markets. The global guidelines are what most regulatory bodies around the world use as a basis for decision-making, so influencing this segment in the value chain is an obvious choice.

The manufacturing stage is where the actual production occurs, which can be blending APIs with non-APIs, milling, bottling, etc. Here, the state has prioritized quality control, implementing relevant regulatory changes to better facilitate exporting firms. This has the effect of simultaneously restructuring the domestic market to push out firms that have failed to properly follow manufacturing guidelines, and also those lacking the capacity to innovate in production.

As for the distribution stage, where we generally see the marketing, delivery and procurement of drugs, the state is employing price control mechanisms to create a basis for local firms to negotiate their stance at the global level. In the following sub-sections, I will further explain several distinct types of regulatory support the Korean government has provided for firms at different stages of the value chain.

4.1.1 The Research & Development Stage

Pharmaceuticals production typically begins with drug discovery. The R&D stage is a crucial link in the chain, a process of unpredictable duration and cost when the destiny of a potential drug is determined. Generally put, R&D includes all upstream activities prior to entering the manufacturing stage.

While firms are responsible for the majority of the aforementioned tasks, the state can indirectly support firms to facilitate the drug development process. One way a state can do this is through international cooperation. Since participation in the drafting of global regulatory frameworks can help a country establish a reputation as having a strong pharmaceuticals industry, which can then, in turn, help ease the commercialization and export of Korean pharmaceuticals at the distribution stage, the state has expanded its industry-related activities at the global level by regularly interacting with international regulatory standard-setting bodies. For instance, the Ministry of Food and Drug Safety (MFDS)[30] is part of the World Health Organization Collaboration Center Forum, where member states collectively deliberate to create relevant pharmaceuticals industry regulations. As a part of the Biosimilars Working Group of the International Pharmaceutical Regulators Forum, the MFDS and regulatory bodies from eight other countries home to advanced pharmaceuticals industries, including the U.S., EU, and Japan, have published guidelines on biosimilars. The goal is to enhance transparency, to harmonize regulations across member countries, and to promote the interchangeability between biosimilars and their patented biologics (Kang et al. 2020). Particularly, the MFDS played a leading role in drafting the Guidelines for Production and Quality Control of Monoclonal Antibodies (MABs) for Human Administration and Guidelines for Evaluation of Biosimilars (MFDS 2022; Noh 2022). This is partly because MABs are one type of biosimilars that several Korean firms, including Celltrion and Samsung Bioepis, have successfully developed and launched in the EU and U.S. markets. Thus, experience in evaluating these products led the MFDS to participate in crafting the relevant global regulatory guidelines. As will be elaborated in the next chapter, the innovative capacity of Korean firms in the biosimilars field also provided the MFDS a first-mover advantage in the form of influence on the emerging

[30] The MFDS is the Korean version of the Food and Drug Administration. It used to be referred to as the KFDA, but since 2013, the organization was restructured and upgraded to the ministry level.

biosimilars regulatory arena. Here we have an example of how domestic regulatory experience can make it possible to influence regulation on the international level.

Since 2018, the MFDS has also been a member of the *management committee* of the ICH, meaning that it oversees the overall administrative and financial operations of the ICH, as well as of all existing ICH working groups. Originally formed in 1990 as a partnership among the U.S., EU, and Japan aimed at harmonizing regulatory standards for clinical trials and new drug approval (thereby facilitating trade among member countries), the ICH expanded to include several other pharmaceuticals-producing countries in 2015 (see Lourenco et al. 2016).[31] Korea's MFDS first joined the ICH as its sixth *regulatory member* in 2016*,* and that membership status provides voting rights on the adoption, amendment or withdrawal of ICH guidelines. When asked about the implications of becoming first a regulatory member, and then part of the management committee of the ICH, one interviewee from MFDS said:

> Becoming a regulatory member at the ICH is similar to being admitted to a version of the OECD for the pharmaceuticals industry. So the MFDS became part of what they call the "P6 (the Pharmaceutical 6)", the way people refer to powerful states as "the G6". After the MFDS's status was elevated, drug approval procedures were simplified in countries in the Middle East and Taiwan…this would also eventually empower Korean exporters in foreign markets. In the past, they [firms] had to sign MOUs with overseas governments independently, but now the Korean government can do the job on their behalf (Regulator 3).

For many years, Big Pharma companies and their home countries have used harmonization as a tool to maintain global hegemony in the pharmaceuticals market (Applbaum 2006; Davis and Abraham 2013; Sunder Rajan 2017). This amounted, in essence, to a monopoly in the global regulatory setting that persists even today.

With new entrants to the global pharmaceuticals market, however, we have also seen changing dynamics. Since late 1990s, some East Asian countries have asserted the need to change the ICH guidelines to incorporate ethnic sensitivity analysis into the evaluation criteria

[31] Until 2015, the ICH included regulatory bodies on only five countries: the U.S., the EU, Japan, Canada, and Switzerland.

for conducting clinical trials. Spearheaded by Japan, these Asian countries argued there may be interindividual variability in drug responses across different races and ethnicities (Yasuda et al. 2008). Regulatory authorities from Korea, Japan, and China have also entered into tripartite cooperation to study ethnic group-related factors (KFDA 2008). The issue has been formally instituted into the ICH framework under the name of "E5 ethnic factors", and if necessary, the regulatory authorities in some regions may request a "bridge study" to extrapolate from existing clinical trial data to verify a suspected relationship between sensitivity to a drug and ethnic factors (see Kuo 2008). Hence, greater presence at the global level indicates, to some extent, a "window of opportunity" (Gereffi 2019) for latecomer countries not only to share their insights, but also "to change or to influence one another" (Kuo 2012).

To support Korean firms navigating the complicated U.S. regulatory landscape with the aim of ultimately launching Korean drugs (particularly biosimilars) in the U.S. market, KHIDI has also been arranging meetings with relevant stakeholders and experts in the U.S. health system. Through networks at the Korean American Society in Biotech and Pharmaceuticals, the Korean-American Professional Association in Life Sciences, and other U.S. health organizations and in universities, it helps to seek ways that Korean biosimilars producers can overcome the regulatory hurdles encountered in the course of the "patent dance" and market exclusivity (Lee and Kwon 2019). In addition, KHIDI also carefully monitors and analyzes regulatory and legal reforms in the U.S. health system, such as the law establishing the interchangeability of biosimilars and their reference drugs, or the Guidance for Competitive Generic Therapies, a recent executive order issued by the Biden Administration, which encourages biotech production and research in the U.S. By analyzing these regulatory frameworks in foreign domains and publishing them at least biweekly on the KHIDI website, it identifies potential growth opportunities for Korean firms.

According to my interviewees, through its active participation in these international fora, the Korean state seeks to "establish trust in the expertise of the MFDS on the part of other regulatory bodies" and to "expand its influence at the global level". In fact, the Korean approach, alongside those developed by the U.S., the EU and Japan, has become a model for many countries that have only now begun to implement biosimilars regulations of their own (Kang et al. 2021).

As discussed in Chapter Three, the Korean government, however, has not always perceived biosimilars as a truly innovative technology, a view which for many years meant only limited support for the industry. With an increasing number of Korean biosimilars receiving FDA and EMA approval, however, we are seeing a shift in this perspective, as evidenced by the Korean state taking on a facilitative role at the R&D stage for the industry. For instance, on April 9, 2020, the MFDS initiated the Support Group for the Commercialization of Biosimilars to provide consulting services for firms seeking advice on regulatory applications in foreign domains and, more broadly, on exports. Overall, the efforts of the state at the R&D stage have been relatively successful, as it has been able to participate in and influence the conversation about the global regulatory landscape in international fora, and also identify strategies in which its domestic firms can stake out their claims in the global market.

4.1.2 The Manufacturing Stage

The manufacturing stage of a medicine may start immediately after a firm gains approval from the relevant regulatory bodies. This is also the beginning of drug commercialization. One way the government can intervene to upgrade an industry is via implementing regulatory frameworks to ensure safety through elevated quality control. Quality control in pharmaceuticals includes an examination not only of the end product (to assess the possibility of contamination), but also of the manufacturing process. Good manufacturing

practices (GMP) guidelines are a common strategy adopted by most exporting countries, but it also creates a new problem, as those practices are inconsistent across countries.

Two international instruments, the Pharmaceutical Inspection Convention and the Pharmaceutical Inspection Co-operation Scheme (PIC/S)[32], have been established precisely to resolve this issue through harmonized GMP standards across participating countries. One strategy the Korean state chose to facilitate exports is to actively implement changes at the domestic level to harmonize local regulations with global standards. In Korea, all pharmaceutical drugs are required to be produced in a facility with GMP certification. At least in part, that is because failure to have an adequate GMP standard may result in lost product credibility and can eventually act, in effect, as a nontariff barrier to trade (Balsiger Betts and Jariwala 2023).

Latecomer countries may pursue PIC/S membership to effectuate access to new markets (Chorev 2019), as belonging to this group is seen as validating the manufacturing capacity of a pharmaceuticals-producing country. The adoption of PIC/S guidelines would facilitate cooperation among PIC countries, and inspections performed in any of those countries would be recognized by all member states.

South Korea joined the PIC/S in 2014, its application process beginning around 2011, when Celltrion's application for EMA approval of the world's first antibody biosimilar was still under review. On average, it takes roughly 4 to 5 years from filing an application to becoming a member; the assessment involves rigorous multi-tier inspections. But the Korean MFDS was able to achieve membership in less than 3 years, which turned out to be perfect timing, as Celltrion launched its first biosimilar, *Remsima*, in 12 European countries in February 2015.

[32] The PIC was founded by the European Free Trade Association in 1970 to harmonize GMP schemes across European countries. In 2004, the PIC was formally established as an international organization under the Swiss Civil Code; since that time, the PIC was transformed to the PIC/S and membership has been expanded to include a number of non-European countries.

One of the factors that helped Korea pass through the process so quickly was Korea's decision to change various manufacturing regulations within the existing Korean GMP (KGMP) frameworks to harmonize them with the PIC/S guidelines prior to the application and during the review. By comparing the KGMP and EU-GMP guidelines, along with the c-GMP (the US FDA's version) and PIC/S GMP guidelines, and after analyzing the similarities and differences among them, the MFDS updated its norms for the pre-GMP evaluation, validation, automation and safety tests, all with the goal of upgrading its manufacturing quality control requirements (MFDS 2012 2013). According to an interviewee at the MFDS:

> By joining PIC/S, KGMP guidelines have become almost identical to global standards. To be honest, it may even be more "global" than EU-GMP or cGMP, because these GMPs are locally-based. Whereas for KGMP, since we restructured our regulations so much to harmonize with the international standards, it is considered more "global" (Regulator 4).

PIC/S membership can, in some cases, lead to a signed mutual recognition agreement (MRA) relating to pharmaceutical GMP between member countries. Without an MRA, manufacturing facilities for medicinal products are inspected not only by the domestic regulatory body, but also by a regulatory representative from an import country. Having an MRA waives this inspection requirement. In fact, the Korean government has had an MRA with the Swiss Federal Council since 2019, which has not only facilitated trade, but also reduced the workload of regulators authorizing and inspecting medical products (Brennan 2020). In May 2019, Korea also became the EU's 7th "whitelisted" country – exporters from Korea are exempt from submitting a GMP written confirmation, which is typically required as a validation of compliance with GMP standards equivalent to the rules applied in the EU. An interviewee who works as a regulatory affairs specialist in a Korean firm explained that, given all these factors, PIC/S membership has become a "necessary condition" for a country to export a pharmaceuticals product.

One of the major drawbacks to this active harmonization is that, since the MFDS's framework is a mixture of the U.S., EU, and Japanese regulatory guidelines, it has become much more "stringent" than was originally intended. This rigorous framework can help domestic firms to achieve success when they enter export markets; simultaneously, however, it has made import into the domestic market more difficult, restricting Korean patients' access to various imported drugs. The same regulatory specialist related an anecdote about how some of her clients from German companies even complained that "the MFDS tends to require far more data than the EMA in order to file for approval."

Beyond upgrading its manufacturing guidelines, the South Korean government has also restructured its generics approval process to reorganize the structure of the domestic market, previously a hindrance to quality control. As already mentioned, South Korean firms initially entered the pharmaceuticals value chain as generics producers. Learning from their experience as contract manufacturers of reference drugs, owned largely by MNCs, many Korean companies developed the skills necessary to produce quality generics more effectively and efficiently than companies elsewhere. From the 2000s to the mid-2010s, the Korean government implemented various strategies to support generics production, as these cheaper alternatives to reference drugs promised to ease the financial burden of operating Korea's universal health care system (Wong and Quach 2009). When it provided financial and regulatory support to generics producers, the state initially expected that the companies accruing assets through generics sales would move on to developing original drugs of their own:

> The South Korean government's aim has always been to nurture pharmaceutical firms that are able to come up with new drugs. The government expected that generics producers would naturally reinvest their profits in R&D, so as to upgrade to producing innovative medicines. Yet this was a mistake on the government's part. We never foresaw that the firms would "settle" for producing generics only (Government official 1).

As it turned out, producers were generally satisfied with selling generics and accumulating cash without investing these profits in the kind of innovation the government expected them to undertake. However, with the massive worldwide recall of a high blood pressure medicine called Valsartan in July 2018[33], the government began acting to constrain the Korean generics market.

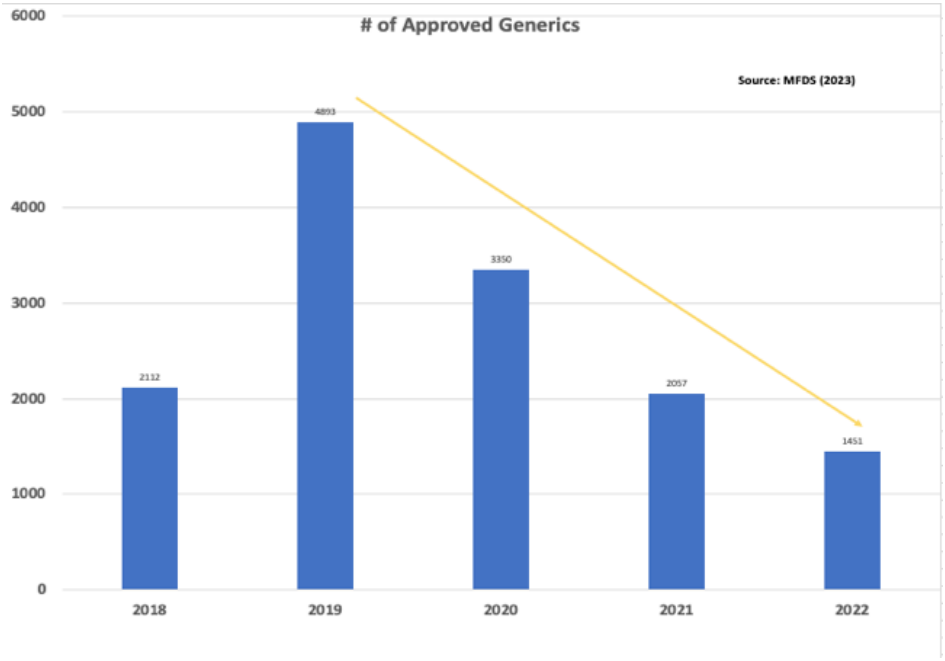
To obtain regulatory approval for a generic drug, a producer needs to demonstrate bioequivalence between the reference drug and the "copy" they produce. For many years, because a bioequivalence test for a drug costs somewhere between US$3.4 million and US$4.2 million, many small and medium generic producers in Korea obtained test results collectively from other contract manufacturers (e.g., those with facilities capable of mass production) to reduce expenditures, rather than conducting new tests of their own. And these outside contract manufacturers tend to receive multiple production requests for the same type of drug from various companies. As a result of this situation, when the Valsartan recall occurred, over 115 generics were recalled in Korea, as opposed to a mere 10, 5, and 21 in the U.S., the UK, and Canada, respectively (Jackevicius et al. 2020; Sohn 2018).

Both the FDA and EMA investigations showed that the primary issue in the Valsartan case was the use of contaminated APIs imported from several facilities in emerging markets that failed to comply with international GMP guidelines.[34] However, this case revealed a deep-seated problem within the domestic generics market: excessive flexibility in testing procedures. The fact that multiple companies were relying on the same testing facility caused the Valsartan recall to have an outsize impact on Korean generic producers. While this was a particularly extreme example, the underlying problem of lax testing regulations has been a continuing hindrance to effective quality control of manufactured products.

[33] In 2018, the EMA issued a massive recall of valsartan, which was found to be contaminated with a carcinogen called N-Nitrosodimethylamine.
[34] https://www.drugwatch.com/valsartan/recalls/

In June 2021, to avoid similar problems in the future and to eventually restructure an "overcrowded" generics market, the Korean government instituted a new regulation called the "1+3 restriction," an addendum to the Pharmaceutical Affairs Act. Under this new regulation, the number of generics that can be approved with a single bioequivalence test result is limited to a maximum of four. Aside from clearing up the "mess" the generics market had become, some informants maintained that one of the underlying reasons for having such stringent regulation was to overhaul and "upgrade" the activities of small and medium enterprises producing chemically synthesized medicines, encouraging new R&D over a continued reliance on manufacturing copied drugs. Since the implementation of more stringent regulations, the number of generics approved decreased to 1,451, the smallest number approved over the past 5 years, with the numbers for 2018-2021 being 2,112, 4,893, 3,350, and 2,057 respectively. According to the 2023 MFDS report, this number is projected to decline still further in future years. Simultaneously, between 2019 and 2021, the number of approved new drugs has increased more than twofold (See Graphs 4.1.1 & 4.1.2). While that number decreased slightly in 2022, this was because fewer foreign innovative drugs were approved in that span; in fact, the same number of new drugs were developed by Korean companies in 2022 as in 2021 (See Table 4.1). Although the sample size is rather limited, the number of new medicines coming on the market is growing, unlike the trend for regulatory approval of generics (MFDS 2023).

Graph 4.1.1 The Implementation of the "1+3 Restriction" Regulation and the Aftermath: Changes in the Number of Generics Approved



Graph 4.1.2 The Implementation of the "1+3 Restriction" Regulation and the Aftermath: Changes in the Number of New Drugs Approved

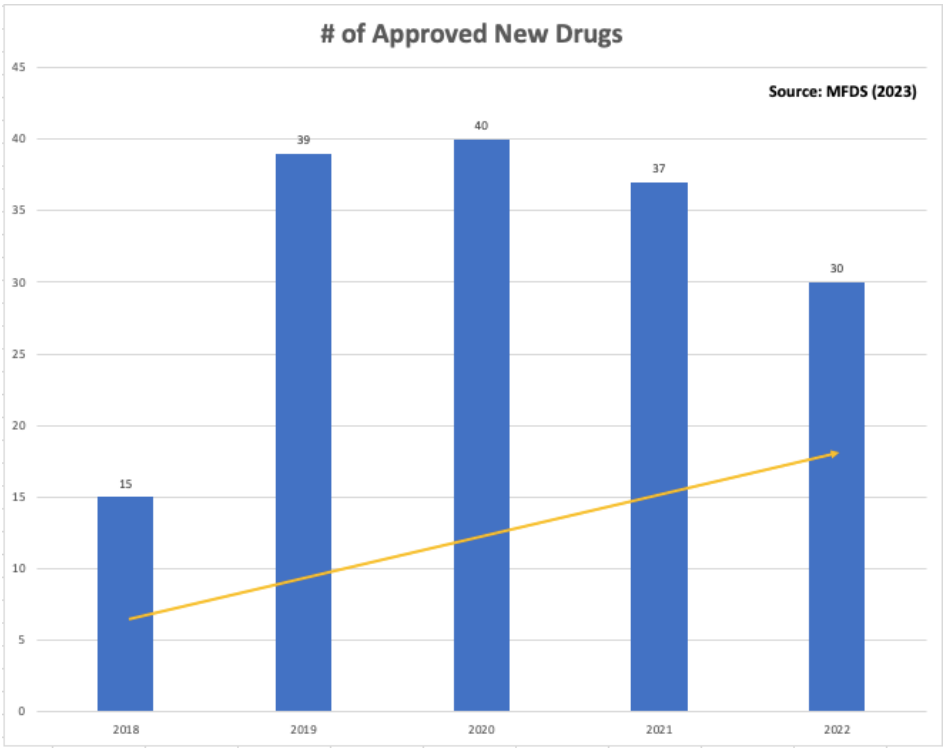


Table 4.1 The Number of New Drugs Developed by Korean Firms at the MFDS by Year

Type of Drug	2018	2019	2020	2021	2022
Chemical Drugs	2	0	0	2	1
Biologics	0	0	0	2	1

Likewise, by playing the role of regulator—tweaking its regulatory policies to promote quality control—the government has sought to encourage overall upgrading of the industry (see Table 10). It is too early to know whether this regulatory effort will eventually pay off. In the case of the Japanese pharmaceutical industry, however, government efforts to curb the size of generics producers between 1980s and 1990s eventually led to Japan's pharmaceutical sector becoming the third largest in the world (Kim 2014). The Korean government's posture may even be an effort to replicate Japan's trajectory.

4.1.3 The Distribution Stage

Since as far back as the classic developmental state era, price regulation has been a common strategy that East Asian governments use to protect domestic industry (Amsden 1989 2001). The story is relevant for the Korean pharmaceuticals industry today, as both price floors and price ceilings are still applied to for pharmaceuticals in the domestic market. Originally, the price floor was established to protect domestic firms producing generics, and the price ceiling was imposed on innovative drugs, which, for the most part, were imported from Big Pharma firms, at least well into the mid-2000s (Wang and Quach 2009). What's missing from the developmental state theory is an answer to the question: why do we still see a similar type of indirect subsidy even today, when the pharmaceuticals industry has become more export-oriented and the number of domestic innovative drug producers has increased?

"Copy" drugs are typically reimbursed at around 80 percent of standard sales price of the original drug in Korea (Kwon 2005), and this applies to both generics and biosimilars. In October 2016, the government instituted the "Plan for Improving Insurance Prices for

Biopharmaceuticals and Global Innovative Drugs", aiming, in particular, to support the biosimilars industry. At first, the sales price of biosimilars was less than 70 percent of the price of the reference drug in the Korean market. However, with the implementation of this regulation, the price of biosimilars increased to 80 percent of the price of the original. Studies indicate that the price of biosimilars in Korea tends to be higher than in Japan, the EU or the United States. In Korea, for instance, *Herzuma,* a breast cancer biosimilar, is approximately 19.9% cheaper than its reference drug, *Herceptin*. In Japan, the same biosimilar costs approximately 31% less than the branded drug. Biosimilars companies could, theoretically, lower their prices in the Korean market, but setting lower targeted prices in the country of origin could negatively impact the price negotiation process in a foreign market (Lee 2021). Thus, through guaranteeing a relatively high price at home, the government provides indirect support for its domestic biosimilars industry.

This protective mechanism also applies to generics. In fact, the effect is even more pronounced for generics than biosimilars. According to a recent study, generics in Korea are priced at least 41 to 54 percent higher than in other OECD countries, holding exchange rates, health care premium, and other factors constant (Bae et al. 2021). A primary reason for such high pricing for imitative drugs (both generics and biosimilars) is that these are what most Korean firms produce. Even as we see a dramatic increase in the number of firms devoted to innovative drugs, the current strength of the Korean pharmaceuticals industry is in manufacturing generics and biosimilars.

More recently, the government introduced a number of measures[35] to cut drug prices, including the Price-Volume Agreement[36] and the "tiered pricing system"[37]. These regulations apply to drugs of all types, including generics, but MOHW's primary aim here is to reduce prices for innovative drugs, which can significantly impact the government budget and the national health care system overall.

A number of my interviewees discussed discrepancies between the aims of separate governmental organizations as one reason why we are seeing only a modest and generally disappointing rate of growth in the Korean pharmaceuticals industry. MOHW, for instance, which is responsible for the operation of Korea's health care system, focuses on purchasing drugs at the lowest possible cost. MOST (and MOTIE to some extent), on the other hand, as mentioned above, prioritizes innovation and wants innovative firms to recoup their R&D investments. Thus, they view the price ceiling on new drugs as "an obstacle to the growth of [the] biopharmaceuticals industry."[38]

By adopting a "reference-based pricing system" (Wong and Quach 2009), the MOHW (more specifically, its Health Insurance Review and Assessment Service (HIRA)) calculates the price of new drugs based on their average pricing in the Advanced 7 ("A7") countries – the US, UK, Germany, France, Italy, Switzerland, and Japan.[39] Of the 7 (now 8, since Canada joined) countries, HIRA will choose the cheapest among them as a reference. Even if a drug is

[35] It was designed to restructure the generics market. It does not necessarily apply to biosimilars, largely because there are only a few biosimilars on the Korean domestic market.
[36] Under the PVA in Korea, if a pharmaceutical company's sales of a particular drug exceed a threshold expectation (the volume negotiated between the drug producer and MOHW for sales over a particular period), its price is cut for the subsequent contract period. This rule is applied irrespective of whether the drugs were produced by Korean firms or by MNCs.
[37] In this recently instituted regulation, the price of generics is determined based on 1) whether the producing firm conducted its own bioequivalence test, and 2) whether the API used is registered in a drug master file kept by the MFDS. If the drug meets both, one, or neither of these conditions, for the first twenty drugs listed for the same medicine, the drug will be priced at 53.55%, 45.52%, and 38.69% of the original drug price, respectively. Beginning with the 21st listed drug, the price will decrease stepwise by 15%, according to the order of registration.
[38] Interview with a government official.
[39] Canada was added to the list on December 2022, making it the "A8".

not only new, but the first of its kind to be developed by a domestic firm, HIRA will still establish a reference, selecting a drug it determines to be closest to the medicine in question and reviewing how it is priced in other contexts. According to some of my interviewees:

> The government support system for the pharmaceuticals industry was never created to reward innovation; rather it was built with a view towards expanding generics production. Korean generics are unnecessarily expensive. Even compared to U.S. generics prices, any given drug costs probably 4 times more in Korea. And who is responsible for the deficient budget the MOHW currently has due to all these reimbursements? It's the patients, Korean citizens, through their payroll taxes. So when someone asks why Korea produces so few innovative drugs – it's the system that has led to this tragedy (Healthcare provider 1).

In fact, at first, the government attempted to provide protection measures for domestic innovative medicine, but the US-Korea Free Trade Agreement led to this indirect subsidy measure being abolished in 2018 (KPBMA 2022). From the MOHW's perspective, however, retaining the price ceiling mechanism and using a reference-based system was critical. Despite the increasing number of domestic innovators, incentivizing innovators via higher prices could easily drain the government budget for operating the national health care system, given how expensive biopharmaceutical drugs are to begin with. South Korea's role as a monopsonic "buyer" of healthcare has been well documented elsewhere (see Wong and Quach 2009 or Wong 2010). Even when the state plays the role of buyer—meaning, in this case, that it is focused chiefly on a drug's use in the domestic market—it remains sensitive to changing global market dynamics.

While medicine in the U.S. is expensive, chiefly a result of intellectual property protection, high prices in Korea are meant to stimulate domestic production. However, we can see that even domestic innovation is constrained by both the national health care system and the global market. Overall, the tension between the state as a buyer, seeking cheap medicine for the national health system, and the state as facilitator, promoting innovation, goes a long way towards explaining why the Korean pharmaceuticals industry has experienced only modest growth in the past few decades (See Table 4.1.3).

Table 4.1.3 Types of Feasible Regulatory Support for Knowledge-Intensive Sectors

Stages of the Value Chain	Types of Support	State's Primary Role	Level of the Effectiveness of the State Intervention
R&D	International recognition: Participation in the drafting of global regulatory rules	Facilitator	Moderately High
Manufacturing	Quality control: Modifying domestic regulation to increase stringency and safety	Regulator	Moderately high
Distribution	Indirect subsidies: Price controls imposed by regulation to help firms to better negotiate their prices at the global level	Buyer and Facilitator	Low

4.2 Patent Law and Industrial Upgrading: India and Korea Compared

So far in this chapter, I have been discussing the role of the state at each link in the chain. But there is an overarching regulatory framework—intellectual property law—that is of crucial importance for the industry as a whole, even if it may exert its most direct influence at the R&D stage. Recall how, in Chapter Three, we described the particular importance of patent law – specifically, that while it provides incentives to innovators, it can also block or delay innovative activities of competitors seeking entry to the pharmaceuticals field. Thus, how well a country or company navigates the global regulatory landscape can impact growth and upgrading for latecomers.

This is evidenced by the case of the Indian pharmaceuticals industry. Between the 1910s and late 1960s, the Indian pharmaceuticals sector was dominated by foreign companies, with only a handful of domestic firms participating (Chaudhuri 2005). In this period, under the Indian Patents and Design Act of 1911, both product and process (manufacturing) patents could be held. This patent law was changed in 1970, however, to recognize only process patents. In those years, many domestic Indian pharma companies took advantage of the opportunity to

reverse-engineer existing pharmaceuticals without having to pay royalties to the original patent holders, the majority of which are Big Pharma companies.

Due partly to this regulatory change, the number of domestic pharma companies rose from 2,000 in 1970 to 24,000 in 1995, a genuine boom in the generics industry, and there was also a corresponding exodus of foreign firms from India (Avhad 2020; Horner 2014). Between 1995 and 2005, there was an intensification of Indian generics exports. Since India joined the World Trade Organization (WTO) in 1995[40], and in particular since the 2005 Patents Act was implemented at the end of its 10-year phase-in to WTO rules, Indian firms can no longer produce copies of a generic while patent protection is still in force. This change in the regulatory landscape pressured domestic companies to either innovate their own molecules or enter into joint ventures with foreign companies, which eventually led to upgrading of the industry.

The modern form of the patent system in Korea was established shortly after it regained its independence from the Japanese in 1946, when the United States Army Military Government became the country's official ruling body.[41] By the time it began to industrialize in the 1960s, Korea, like India, excluded substance patents from available forms of protection, a decision that was part of a strategy aimed at helping domestic enterprises to learn from and catch-up to foreign firms. By the mid-1970s, however, as domestic firms needed imports of advanced technology to successfully shift from light to heavy (and chemical) industries, Korea began to harmonize its IP laws with those of its trade partners (primarily Japan and the United States). In 1979, Korea joined the World Intellectual Property Organization; in the early 1980s,

[40] Although India joined the WTO in 1995, the WTO granted a 10-year transition period for many countries in the global South, including India, to integrate TRIPS into its domestic patent system. Technically, then, between 1995 and 2005, Indian firms could continue to reverse engineer and produce generics and it was not considered as infringement of IPR.

[41] The very first written patent law in Korea was promulgated on August 12, 1908. It resembled Japanese industrial property laws of the time. Between 1910 and 1945, under Japanese occupation, the Japanese imposed its IP laws upon Korea.

it also acceded to both the Paris Convention and the Patent Cooperation Treaty. By the time it joined the WTO in 1995, many chaebol firms had already invested heavily in R&D and needed protection for their innovations; at the same time, Korean companies were involved in numerous IP litigations against several U.S. firms in connection with semiconductor patents. Naturally, then, the Korean patent system evolved to be even more similar to that of the U.S. than it might otherwise have been, since domestic firms began to register as many patents as possible, both in Korea and overseas, in order to secure maximally adequate protection (Lee and Kim 2010).

Both the Korean and the Indian cases with respect to IP law highlight how development in a knowledge-intensive industry is closely intertwined with the capacity to navigate global regulatory standards to one's benefit. In the early stages of learning and industrialization, flexible IP law can be beneficial to a country – for example, the Indian state's intentional delay in bringing domestic law into conformance with TRIPS requirements effectively extended the then-applicable grace period, enabling domestic firms to sell generics without infringing IP law and also upgrade their drug manufacturing capabilities. Conversely, as the Korean example shows, once they industrialize and shift to an attempt to move up the ladder to more knowledge-intensive fields, latecomer states eventually have to institute IP laws that can protect domestic innovation.

4.3 Implications

While existing research establishes that states can play multiple roles as they seek to upgrade an industry in the knowledge economy era, my study expands upon our understanding of this situation, showing that different state entities undertake various roles for this purpose, and that sometimes a tension may arise among those roles where they at least partially conflict.

Developmental state theorists have argued that it is states that ultimately create markets[42], especially where the state takes on such defining functions as setting prices, purchasing drugs through reimbursement policies, and establishing regulatory guidelines, as the Korean state does for its pharmaceutical industry. This viewpoint, however, is limited to the state's role in the *domestic* realm. As latecomers upgrade their capacity and become more export-oriented, the role of the state has also evolved and reconfigured. Given the significance of the regulatory landscape for the pharmaceuticals market, the state has also brought regulatory means to bear in support of the industry. Relative to the regulatory roles states once so obviously played, roles which often revolved around protecting domestic industry from MNCs and relaxing regulatory restrictions (Evans 1995), today's developmental states prioritize regulatory innovation, not only familiarizing themselves with global regulatory standards, but also implementing regulations designed to prepare domestic industries for evolving global market dynamics.

The global regulatory landscape for the pharmaceuticals field, however, was established well before the latecomers discussed here entered the market; unsurprisingly, then, it is designed in favor of the countries where most Big Pharma firms are located. Unless the newcomers can challenge and revamp the existing regulatory frameworks themselves, the most viable alternative for nontraditional competitors will be to increase their presence at the global level and to continually reorient their domestic regulatory policies to account for and leverage, where possible, ongoing changes at the global regulatory level.

The use by the state of regulation as a tool to bring about desired changes in the industry is not limited to the pharmaceuticals sector. To boost productivity in the semi-conductor industry, for instance, and to help it secure one of the top producer positions globally, the

[42] In some countries, like the U.S., it is the pharmaceuticals firms that set the prices and insurance companies are responsible for reimbursement. In many East Asian countries, in contrast, both roles are assumed by the state.

Korean government has not only offered new tax incentives and financial support to chipmakers, but has also selectively relaxed its national labor regulations. Whether this regulatory measure will have the desired outcome, of course, remains to be seen, but in any event, the government created an exemption by allowing employers in this specific sector to establish work weeks of up to 64 hours, instead of the 52 hours per week currently mandated by law for all other industries (Park and Lee 2022). Similarly, the Ministry of Science and ICT began to curb copyright infringement and digital piracy actively blocking illegal streaming sites, in order to support the Korean over-the-top (OTT) industry, including the Korean versions of Netflix and Disney+.[43]

Whether pharmaceuticals or semi-conductors, the global context has become a much more important factor of the state's capacity to effectively promote upgrading and innovation than was true in the heyday of the post-war developmental state. With the more limited choices now available to the state, government decisions have to be both subtle and precise. The Korean government's use of regulation to create changes in the pharmaceuticals industry, nevertheless, clearly demonstrates that the influence it exerts, now largely via regulatory policy, remains an important and effective part of its development strategy.

[43] https://www.koreatimes.co.kr/www/tech/2023/06/129_353178.html

Chapter Five
Latecomer States in the Global Regulatory Chain

As described in the preceding chapter, the role of the latecomer state in the pharmaceuticals industry centers on international reputation-making, elevating quality control, and providing indirect subsidies via price regulation. This chapter turns from a focus on states to a focus on firms to ask how do firms from latecomer countries navigate the complex global regulatory landscape? The existing literature on pharmaceuticals regulation underscores the problems of regulatory capture by the global pharmaceuticals industry and the "revolving door" between the regulators and the regulated in the U.S. and EU (Moynihan and Cassels 2005; Davis and Abraham 2013). It remains unclear, however, whether this kind of "revolving door" relationship extends to foreign pharmaceutical companies seeking entry to the EU and US markets, or whether, to the contrary, the latter may face heightened difficulties, precisely because they lack the kinds of ties that already bind regulatory bodies and pharmaceutical firms in the EU and in the U.S.

In this chapter, I discuss the experience of latecomer firms in sorting out regulatory issues in order to launch products in competitive foreign settings. Since many of these companies lack global reputations, networks, and familiarity with the regulatory environment, as well as the market power of Big Pharma, these foreign newcomers need to adopt additional strategies to overcome the regulatory hurdles they encounter. This chapter walks the reader through the process whereby latecomer firms attempt to cope with the regulatory thicket characterizing the pharmaceutical industry. Specifically, I address here the following questions: How do latecomer firms negotiate regulatory hurdles at each stage of the regulatory chain? To what extent have their attempts been successful? How similar (or different) are firm activities in the contemporary knowledge-intensive era to what they were in the manufacturing-driven period? On what stage(s) of the value chain do firms focus more or less attention today?

To better explain the situations faced by latecomer firms, I incorporate insights from economic and organizational sociology to demonstrate how pharmaceuticals firms navigate the complex global regulatory chain and what varied strategies they employ, depending on the structure of the relevant market and who their competitors are. Specifically, I show that when the market for a drug product is relatively new and there is no generally accepted regulatory model, firms try to take the "first mover advantage"—that is, they try to become the first, or at least the second, candidate to receive regulatory approval, as this guarantees at least some period of market exclusivity after they launch their products. Where the market is relatively settled and there are clear preexisting regulatory guidelines, firms will often opt for what we may term regulatory arbitrage. "Regulatory arbitrage" is described as a type of strategy private market actors employ to take advantage of divergences in regulatory approaches and gray areas in legal regimes in an attempt to bypass avoidable regulatory hurdles (Partnoy 1997; Jackson et al. 2014; Rao et al. 2011). In this same spirit, pharmaceuticals firms prioritize markets where they can accrue the greatest possible profit. But the regulatory arbitrage we are concerned with in this chapter expands that more familiar concept, considering how pharmaceuticals firms intentionally choose to apply for regulatory approval in more challenging settings in order to facilitate the launching of their products in other, less competitive markets thereafter. In other words, regulatory arbitrage in this case may mean pursuing a *more* stringent regulatory process in the pursuit of easier market access in the long run, as opposed to seeking to maximize profits in the short term.

As discussed in the previous chapter, since the regulatory barriers at various stages of a value chain are all intertwined, a product cannot move on the next stage of the value chain ("up the ladder") without sorting out a given regulatory issue at the previous stage. For instance, when scientists begin basic research in the lab, companies often check with patent lawyers to ensure that a particular molecule or protein a firm chooses to produce will not infringe existing

patents. Thus, sorting out patent issues begins at the R&D stage of a value chain (in connection with the regulatory process). However, patents are also directly implicated at the final stage of the chain, since patents are a key determinant of whether a product reaches the market or not. If patent owners and users fail to reach an agreement in the earlier phase, a new product can never be sold. Because the phase ultimately affected by unresolved patent conflicts is the distribution stage, since the consequence may be that a manufactured innovation is blocked from commercialization, patent-related issues will be assigned in this dissertation to the last phase of value chain.

An important difference between this chapter and the preceding one is that the activities of pharmaceuticals firms that we are interested in here are concentrated more in the R&D stage than further downstream, because manufacturing, marketing and distribution are often outsourced in this industry to other companies. Hence, the chapter delves more deeply into the R&D phase, where most upgrading is accomplished, bringing in limited descriptions of the manufacturing and distribution phases as needed.

5.1 The R&D Stage

As described in the previous chapter, the R&D stage runs from drug discovery all the way to the moment immediately preceding the beginning of actual manufacturing. It is not only the longest and the most uncertain phase in the pharmaceuticals value chain, but also one that involves a wide variety of actors (see Figure 4 in Chapter 4). To reach the manufacturing stage, firms must first identify a candidate molecule (or mixture of candidate molecules), test its safety and efficacy in both preclinical and clinical trials, and obtain regulatory approval from a relevant government body. While the timeline for the obtaining regulatory approval may vary, depending on whether a drug is new or whether it is a "follow-on" medicine (a category that includes biosimilars), and also on the regulatory agency in question, almost every approval process requires a drug's pharmacokinetics (PK) and pharmacodynamics (PD) results from

preclinical trials, as well as a maximum of three clinical trials.[44] And the entire process (including every substage of R&D) will be overseen by a regulatory body, as drug makers are typically required to submit the results of all required tests in documentation.

PK and PD analyses are done in both *in vivo* (via research on living organisms, e.g., animals) and *in vitro* (in a laboratory dish or test tube).[45] Essentially, the purpose of the preclinical stage is to establish safety margins for, and the efficacy characteristics of, the drug in question (Budha et al. 2009; Negus and Banks 2018). After successfully completing the preclinical phase, drug makers move on to conducting at three, and sometimes four, clinical trials on humans (See Table 5.1). Specifically, phase I of clinical testing determines the dosage level for a drug that will be safe and effective, while phase II evaluates whether a drug candidate works in the manner intended, and phase III is intended to clarify and confirm the benefits and risks of the candidate drug prior to approval. Often, there is a phase IV, called a post-approval study, where the drug maker continues to monitor the drug after patient intake (pharmacovigilance).[46] This phase can also be helpful because it allows a drug producer to seek permission to market a medicine for use in treating symptoms in addition to those it was approved for in the original application (Morrison 2020).

[44] Regulatory bodies typically require only two clinical trials (Phase I and Phase III) for biosimilars. For generics, neither animal study nor clinical trials on humans are necessary.
[45] PK traces the movement of drugs through the body and how it is concentrated on different body compartments. PD assesses the body's biological response to drugs.
[46] Pharmacovigilance (PV) is a process of monitoring to detect, assess, and try to understand in case any adverse effects of medicines arise. The purpose of this is to ensure that a medication is safe for patient use in the long run.

Table 5.1 Overview of the Phases of Clinical Trials

Phase I	Phase II	Phase III	Phase IV
• Aims to identify any side-effects of a drug and the maximum dose that can be administered to a human • Emphasis on safety • Typically involves less than 100 healthy subjects and takes less than a year	• Aims to establish preliminary data on whether the drug works on people with specified illnesses or conditions • Emphasis on effectiveness and safety • Typically involves several hundred patients • May involve consultation with regulatory agency before design of Phase 3 trial	• Aims to gather further information about safety and efficacy, studying different populations and dosages • May involve using the drug in combination with other drugs • Typically involves several hundred to about 3000 people	• Aims to gather additional information about a product's safety, efficacy, and optimal use • Permits drugmaker to test its approved drug on >1000s of patients over the course of years

Author's compilation from the US FDA, the EMA, the MFDS, and Morrison (2020)

Using two drugs as cases for consideration—a new chemical drug and a biosimilar—the following sections look at how latecomer firms navigate the three overall stages of the global value chain (R&D, manufacturing, and distribution) for the industry to eventually launch their products in chosen foreign markets. These companies have employed some form of regulatory arbitrage and, in the case of biosimilars, they also had a "first-mover advantage", which enabled them not only to overcome regulatory hurdles, but also to influence regulatory frameworks in foreign jurisdictions. The section also describes the social implications of such common firm-level strategies.

5.1.1 Regulatory Arbitrage: The Case of New and Innovative Drugs

From a firm perspective, regulatory variations across jurisdictions may be an element of a corporate opportunity structure (Rao et al. 2011). Sometimes firms shift from one geographic location to another specifically in order to exploit legal and/or regulatory variations, a process often referred to as "regulatory arbitrage" (Partnoy 1997). In the finance world, arbitrage means a situation where firms or individual market participants calculate value or expected profits of cash, stock, or bond holdings by comparing disparate markets so as to

purchase at lower cost and simultaneously sell at higher prices and, as a result, to make a riskless profit. Economic sociologists thus view arbitrage as an attempt to take advantage of differing contexts: market participants choose a particular interpretation of the value they want to maximize, which informs their choice of market strategy (Beunza and Stark 2003; Dequech 2011; Seabrooke 2014). Similarly, regulatory arbitrage can also be a way to take advantage of a grey area in the regulatory landscape to reduce taxes, avoid accounting disclosure, or skirt investment restrictions (Costa-Font 2016; Jackson et al. 2014).

While existing studies of regulatory arbitrage describe profit as one of a firm's primary driving motivations, there may be other long-term reasons for firms to opt for this kind of strategy. In the case of latecomer pharmaceutical firms, regulatory arbitrage can serve as a stepping stone, facilitate future regulatory process applications in other foreign markets, and possibly provide greater bargaining power when dealing with government agencies.

Consider the example of a new epilepsy medicine developed by a Korean biopharmaceutical company. In 2020, SK Biopharmaceuticals ("SK" hereafter) launched a new chemical drug called XCOPRI in the United States. A third-generation anti-epilepsy medicine, XCOPRI received its approval from the FDA in late 2019 after 18 years. SK Biopharm's experience stands out for several reasons. First, XCOPRI was the first case where a Korean company completed the entire R&D process, including regulatory approval, independently (that is, without technology transfer or even the help of contract research organizations, and so forth). Hence, SK Biopharm's approval was a milestone for the Korean pharmaceuticals industry. The company successfully established a precedent for future Korean firms' entry into the US drug market. Second, this outcome is based on SK's multiple rounds of trial-and-error approval process at the FDA after its initial failure to launch the medicine in the U.S. market back in 2008. Third, where drug producers ("sponsors") would typically file for regulatory approval in their domestic market prior to, or at least simultaneously with, an application in

foreign countries, SK Biopharm chose the U.S. as its primary target market. In fact, XCOPRI is still in the clinical trials process in Korea.

The question, then, is: why would a latecomer firm like SK Biopharm be so determined to obtain their new drug's first approval at the FDA? There are several reasons for this. First, from a latecomer's point of view, obtaining regulatory approval from the FDA, and eventually launching its products in the U.S market, has symbolic value: it is "the most successful path", an emblem of success. Even though various studies underscore the impact of neoliberalism on FDA regulations, showing how their leniency has led to corrosive effects on U.S. society (Davis and Abraham 2013; Moynihan 2005), the majority of my interviewees described FDA approval as the "most challenging" to obtain, a greater prize than even EMA approval.

After SK failed to get a green light from the FDA for its first innovative epilepsy medicine (called Carisbamate) back in 2008, the FDA became its "primary target". It thus devoted several years to preparation of a "comprehensive document" that would meet the expectations of the FDA as closely as possible, analyzing along the way more than 2000 synthetic compounds, together with preclinical and clinical data. SK ultimately submitted an application of more than 2.3 million pages.[47] Today, the therapy, XCOPRI, has a 23-member patent family spanning 19 national jurisdictions, a "patent family" being a set of patents associated with a single invention that can be registered in more than one country. When asked about specific regulatory strategies the company employed to get the approval, a representative from the firm explained:

> We were able to obtain the FDA approval shortly after completing phase 2B of the clinical trials. When we filed the new drug application (NDA), we compiled and submitted the results of 26 clinical tests, as well as of over 200 non-clinical trials. Clearly, we spent a great deal of time doing drug profiling and preparing to provide almost every kind of information that could be asked for by the regulatory agency. For instance, to enhance the efficacy of the drug, we designed a study to focus on patients who continue to experience symptoms even after trying more than 3 different types of epilepsy medicine. Moreover, unlike other firms, which have typically conducted

[47] https://www.pharmnews.com/news/articleView.html?idxno=211658

> adjunctive therapy and mono therapy sequentially, we initiated those tests simultaneously. As a result, by the time we finished the 2B phase of the clinical trial, the FDA acknowledged it as the "pivotal study".[48] And after that, we only had to show the safety of the medicine in the remaining phase, phase 3, of the clinical trial (Pharmaceutical representative 8).

In 2021, shortly after getting approval from the FDA, XCOPRI was approved by the EMA and then the company licensed its technology to Japan, China, and Canada.[49] A SK representative said that "after first establishing a foothold in the U.S. market, we plan to gradually expand to the EU, Latin America, and then eventually to Asia." This is because getting the regulatory approval in what was perceived to be the most competitive and challenging pharmaceuticals market, the U.S., had the potential to facilitate regulatory processes in other foreign agencies, since "dominant countries' regulations have transnational implications", being used as a "global benchmark" (Farrewell and Newman 2010; Rikap 2019).

Along similar lines, SK chose to market in the U.S. prior to doing so in its home market due to a regulation that set a price ceiling on new and innovative medicines in South Korea. Recall from Chapter 4 how, in Korea, the Health Insurance Review and Assessment Service (HIRA) establishes prices for all types of drugs. For new and innovative drugs, which are typically very expensive, HIRA takes the prices of the drug in question in the A8 countries as references. If a drug is not only new, but the first of its kind in the world (so that there is no precedent to use as a reference), HIRA will still establish a reference price, selecting the drug it determines to be closest to the medicine in question and reviewing how it is priced in other contexts. Likewise, even after getting regulatory approval, a launch in the Korean market takes far longer than in the U.S., and any kind of delay may be detrimental in a frontier technology

[48] A pivotal study is a clinical trial or set of trials that form the basis upon which a regulatory body can reach a conclusion as to whether the drug producer has provided "substantial evidence of effectiveness" or not. Based on this phase of clinical trials, regulatory bodies will determine whether to approve the drug or not (Lexchin et al. 2020).
[49] XCOPRI was approved by the EMA under the brand name "Ontozry".

like the pharmaceuticals sector, given that the timing of its introduction can greatly affect its subsequent market share.

As mentioned in an earlier chapter, the U.S. is one of the few countries where the price of a medicine is set by the pharmaceutical companies themselves, rather than by the government. Thus, by first selling in the U.S., drug makers gain the freedom to *set* the price of a drug, instead of it *being set by* a government agency. And since other countries, including the South Korean government, then take the price of the drug in the U.S. into account when deciding its domestic price (since the U.S. is also an A8 country), Korean innovators will have greater bargaining power by launching in the U.S. than they would have had beginning their regulatory journey on the home front. Thus, if a firm has sufficient capital and the capacity to overcome the necessary regulatory hurdles, prioritizing regulatory approval at the FDA can improve its prospects for sufficient global market share and reputation building more than would any other available option.

Given the above, SK's targeting of the FDA can be considered a form of regulatory arbitrage, but not in a conventional sense, where firms capitalize on regulatory loopholes. On the contrary, SK intentionally chose to overcome the hurdles presented by one of the most rigorous regulatory environments for latecomers as an intentional strategy to ease regulatory obstacles in the long-run in other contexts. In fact, some interviewees noted that, the so-called "pharmerging countries'[50] can themselves be a challenging regulatory environment, but if we tell them that either the FDA or EMA was okay with a particular matter they problematize, then those regulatory agencies tend to be ok with it, too. In other words, getting a regulatory approval at the FDA or the EMA can create an opportunity to bypass complications that may arise in other contexts.

[50] "Pharmerging countries" are those where the pharmaceuticals industry occupies a lower tier in the global rankings, but are growing at a rapid rate. Examples include China, India, Brazil, Russia, South Africa, and Mexico.

However, because the current price of XCOPRI exceeds what the Ministry of Health in Korea expects to reimburse, and because epilepsy is not considered a rare disease, the launch of XCOPRI has been delayed in Korea, which was expected. As of May 2023, XCOPRI is still in phase 3 of its global clinical trials, which are being conducted in Korea, Japan, and China.[51] However, even after the company finishes the trials and files for approval in 2024, the earliest that XCOPRI can reach the domestic market will be 2025. Although patients who have participated in the early stages of clinical trials in Korea can be prescribed XCOPRI through an "extended program" approved by the MFDS, no other patients who are in need of or would like to try XCOPRI are similarly eligible.[52] For this reason, Korean patients suffering from epilepsy complain that SK Biopharm cares only about accruing profits; they are also critical of what they see as the inefficient and ineffective price negotiation process between SK Biopharm and the Korean government, as it is excluding them from access to the drug.[53] The situation thus not only implies misaligned state and firm development goals in the frontier technology sector (as described in the previous chapter); it also explains why latecomer firms' strategy for regulatory arbitrage may incur social costs to patients who are constrained by the regulatory system, even if the innovative medicines in question are available in other countries.

5.1.2 First-Mover Advantage, Regulatory Co-Creation and Arbitrage: The Case of Biosimilars

Even today, regulation of biosimilars varies significantly by country, as they are a relatively recent innovation that states are just beginning to incorporate into their health systems. A South Korean biosimilar producer was able to obtain regulatory approval back in 2013, when the European Medicines Agency (EMA) was still establishing its biosimilars

[51] FDA approval enabled SK Biopharm to fast-track its approval process elsewhere; instead of beginning back at phase 1 of clinical trial, SK Biopharm was allowed to jump right to phase 3 in applications for regulatory approval in East Asian countries.
[52] http://www.monews.co.kr/news/articleView.html?idxno=314175
[53] http://www.bizhankook.com/bk/article/22481

standards.[54] Celltrion's Remsima, the first monocolonal antibody (MAB) biosimilar ever approved in the world, is still one of the bestselling products of any Korean biopharmaceutical company.[55] The experience is noteworthy because Celltrion grew from a start-up founded in 2002 into a large-scale firm in only a decade. Some interviewees recollected that, when Celltrion first reached out to the EMA and the FDA for a pre-submission meeting, both agencies asked "what's Celltrion?" Since both Celltrion itself and biosimilars as a category of drug were new and unfamiliar to many, Celltrion prioritized building the credibility of both the firm and biosimilars as such through regular exchanges with regulatory bodies.

Celltrion chose to file for regulatory approval at the EMA prior to the FDA for several reasons. First, the EU has shown a more favorable attitude toward biosimilars than the U.S. Since the early 2010s, the EU has been seeking ways to cut its healthcare budget. Biosimilars, which can potentially be used as alternatives to patented biologics, were thus a desirable solution for the EU, especially as it closely regulates pharmaceutical prices, which the U.S. does not. Biosimilars can thus provide EU patients, and the EU pharmaceuticals sector, with wider and cheaper access to therapeutic biologics. In contrast, the FDA approved its first biosimilar in 2015, nine years after the EMA. Second, the patent for Remicade, Remsima's reference product, was set to expire in the EU (February 2015) earlier than in the U.S. (September 2018). Third, the EU tends to set higher bars for patent extension than the U.S., meaning it prevents the kind of evergreening and the creation of the denser patent thicket that patent owners can often achieve in the U.S. As a result, barriers to entry for biosimilars are lower in the EU than in the U.S. (Gherghescu and Delgado-Charro 2021; Van de Wiele et al.

[54] Although Omnitrope was the first biosimilar ever approved in the world, back in 2006, it is a different type of biopharmaceutical drug (a recombinant human growth hormone) than a monoclonal antibody.

[55] As mentioned in the previous chapter, South Korea is the only latecomer country with biosimilars approved by both the FDA and EMA (according to the most-up-to-date available data from both websites, which appeared in December 2022). Although in 2022 Biocon, an Indian company, acquired Viatris, the biosimilars subsidiary of the American Big Pharma firm Mylan, and thus suddenly gained exclusive ownership of four FDA-approved biosimilars, that process cannot reasonably be considered an example of latecomer innovation.

2022).[56] For all these reasons, Celltrion's choice constitutes a form of regulatory arbitrage, notwithstanding that its motive (issues related to patents) differed from that of new drug producers like SK Biopharm (price regulation).

When asked how Celltrion was able to navigate the regulatory hurdles of its target market, the EU, interviewees explained that Celltrion was fortunate in having the benefit of being a first-mover:

> We definitely had the first-mover advantage. When we began developing our first biosimilar, Remsima, in 2008, there were no detailed guidelines as to how to regulate either monoclonal antibody (MAB) or even biosimilars in general, because it was all pretty new. In the very first draft for a biosimilar guideline which EMA came up with in 2006, there was only a vague description of how to conduct a bioequivalence test, without a specific quantitative range that describes the extent to which a biosimilar could be considered "similar" to its reference product. So, we had numerous meetings with the EMA to figure everything out from scratch, including the extent and bases on which a MAB biosimilar could be considered "similar" to its reference product. What testable items did we need? Was the method appropriate? Moreover, there was not even a relevant animal model study on the infliximab[57] so we would ask: how should we test the toxicity level? We didn't even have guidelines as to what population we should conduct clinical trials on, the dose we should inject, or what the endpoint should be. So we decided to bring our own suggestions to the EMA. We conducted tests, brought raw data to the EMA, and asked them to comment on our results. Then, based on their advice, we would meet and consult with other experts, including physicians, scientists, and academics, to revise the documents and bring them back to the EMA. It was through this iterative process that Remsima was approved in 2013. … Remsima's approval process became the basis for the sample guidelines used thereafter by the EMA. In fact, the conversations we had were incorporated into the official MAB guidelines, which were published in 2016. This was definitely a unique experience in which we were able to draft regulatory guidelines together with the agency (Pharmaceutical representative 4).

By virtue of being first, and because biosimilars are a relatively new kind of therapeutics, Celltrion was able to not only exert a strong and targeted influence on the formation of the regulatory space, but its interaction also translated into a form of "regulatory co-creation" (Gao and McDonald 2022). In a nascent industry, companies may have more direct engagement with regulators, because they are engaged in filling a "regulatory void", in determining an unsettled

[56] As a reminder, the concept of patent thicket was introduced in Chapter Three. I will return to this concept in the section below on distribution.
[57] The scientific name of Remicade (or Remsima's reference product)'s active ingredient.

regulatory landscape. Since firms are knowledge creators, regulators may rely on their technical expertise when making regulatory decisions (Aldrich and Fiol 1994; Ramanna 2015). In the course of this mutual learning process, firms can leverage their experience to propose regulatory frameworks that work to their benefit (Kemmerling and Trampusch 2022). In doing so, first-movers may create a "competitive barrier" in which their cooperation with regulators becomes a form of experience or "intangible knowledge" which followers may not be able to imitate (Fligstein 2001; Rivkin 2000). Celltrion was thus able to capitalize on an uncertain regulatory environment to promote its own biosimilar.

Not all first movers will have these kinds of advantages in the frontier technology sector. Boyer (2022), for instance, describes how, in the digital platform market, first movers may be at risk of being less user-friendly, as consumers may not initially be familiar with the complicated technology. Others have noted that, in the biosimilars industry, there has been a first-mover *dis*advantage, because of the uncertain regulatory environment and the legal challenges that a first mover needs to sort out, efforts which followers are likely to take advantage of as "free riders" (Konara et al. 2016; Konara 2019).

While this may be true to some extent, there are also important first-mover benefits – for example, in terms of marketing and distribution. Hollis (2002) suggests that a first-mover advantage is especially important in the generics market, because not only does it guarantee a longer period of greater market share, but also patients (and pharmacists) tend to be "reluctant to switch" from one generic to another, since there is no notable difference among copied drugs. A similar situation adheres in the biosimilars industry, according to my interviewees. If a product cannot be launched either as the first, or at least as the second biosimilar of a given kind, firms are unlikely to accrue profits sufficient for survival. In addition, when biosimilars are introduced, the price of name-brand drugs naturally declines. In some cases, the producers of the original drug cut their price radically, effectively "dumping" their product on the market,

in an effort to bar biosimilars (or generics) rivals from gaining a market foothold. For all these reasons, in a competitive knowledge sector like pharmaceuticals, companies strive to be a first-mover, not only to minimize dealing with any regulatory barriers that can potentially be avoided, but also simply to remain in business.

5.2 The Manufacturing Stage

The pharmaceuticals industry is an R&D-intensive rather than a manufacturing driven sector. Given this, latecomer companies often follow the lead of many multinational lead firms in outsourcing the production phase to other domestic or overseas contract manufacturers, which is generally more cost-effective than manufacturing on their own. In fact, maintaining GMP certification requires constant management:

> There are frequent inspections, not only by domestic regulatory bodies, but also overseas agencies from where products are exported to, to ensure that the GMP-certified facility is keeping up with GMP guidelines. (Pharmaceutical company representative 3).

As described in Chapter 4, most latecomer pharmaceuticals firms enter the value chain as contract manufacturing organizations (CMOs). Even Celltrion began its business as a CMO for Big Pharma companies. Samsung Bioepis, another successful Korean biosimilars producer, was intentionally spun off from its parent company, Samsung Biologics, so that the former could focus on R&D, including regulatory approval work, while the latter is now responsible for downstream operations.

The primary task of a CMO is mass production of approved drugs, but it also manufactures samples for clinical trials. Technically, then, there is an element of manufacturing that overlaps with latter part of the R&D stage. Compared to chemical drugs, where the production process is relatively straightforward, so long as the "recipe" is provided, the manufacturing of biological products, including biosimilars, with minimal variability (since each biological product is inevitably unique, given the nature of large molecules) is a challenging and complex process. For this reason, biologics-producing CMOs stress how

"drastically different" they are from chemical drugs producers. Due to the unavoidable differences in batches of each biological product, manufacturers explain why following GMP guidelines is the most important yet the most challenging task they face:

> When it comes to the production of a biological product, the competency of a firm is determined by how closely it can follow the manufacturing guidelines laid out by regulatory bodies like the FDA or the EMA. Referred to as a "gmp-mindset", sticking to the regulatory frameworks is crucial, because, in the event a problem arises, manufacturers must be able to trace the entire process back to detect the issue area (Pharmaceutical representative 11).

Additionally, there is an important regulatory reason why CMOs are necessary in the pharmaceuticals industry; to avoid a supply chain bottleneck, regulatory agencies require "double sourcing" of medicines:

> According to the FDA guidelines (for the assessment of a third phase of clinical trial), drug makers are required to have "double sourcing" of manufacturing, meaning drugs must be produced in at least two different facilities. This is because should one of the factories shut down for some reason or other, the other facility would be able to maintain the production process, at least to some extent, minimizing any supply shortfall. This is because, after all, the drugs are produced to be available to patients. Evidence of double sourcing (e.g., contract information of CMO partners) must be incorporated into an application for filing with the FDA (Pharmaceutical representative 4).

Representatives from latecomer firms that have successfully transitioned from CMOs to head companies, however, explain that it is crucial to move to conducting R&D and thus to innovate one's way out in the CMO industry, because otherwise "a company's future is far too dependent on partners' orders." This is one reason why a number of CMOs have ventured into the field of biosimilars as an intermediary step to ultimately becoming innovative biopharmaceuticals companies. Overall, the manufacturing stage of the pharmaceuticals value chain serves as a supporting link, facilitating the innovative activities crucial to the value chain, and not as a key locus for upgrading.

5.3 The Distribution Stage

The distribution stage is the final phase in a pharmaceutical value chain, the one where profit is directly accrued from sales. Typically, the distribution phase for a drug includes

logistics and marketing. But one of the most critical aspects in this stage is the ability to actually commercialize the manufactured goods. Depending on the type of drug, though, firms may be faced with significant regulatory challenges that can prevent them from launching their products. In particular, makers of follow-on drugs like biosimilars are expected as part of the regulatory approval process to resolve patent-related issues with original producers, as described in Chapter 3. If biosimilars companies fail to negotiate successfully with patent owners, the issue may lead to litigation.

To avoid patent litigation, firms tend to employ a form of regulatory arbitrage at this stage too. And in that arbitrage there also exist first-mover benefits, which biosimilars makers seek to take advantage of. Alternatively, in some cases, biosimilars producers may upgrade to production of "biobetters", which are biosimilars that have improved properties relative to the corresponding branded biologics (for example, an easier method of use). And because these drugs have more advanced characteristics than existing biologics, they are treated as *new* drugs, and therefore do not need to engage in the patent dance. Beyond the regulatory issues, latecomers are also beginning to shift away from outsourcing certain aspects of distribution, bringing them back in house to gain autonomy in decision-making, as well to reduce costs. Likewise, since the commercialization of a drug is shaped by various regulatory and legal approvals, including the need to navigate the patent thicket, as described earlier, we will discuss issues connected with IPR at this stage.

5.3.1 Patent Negotiation and Litigation

As briefly mentioned in Section 5.1.2, Celltrion purposely chose to file for regulatory approval and to launch its product in the EU market prior to launch in the U.S., not only because the patent on Remicade expired earlier in the EU than in the U.S., but also because the patent thicket that biosimilars producers must navigate is less dense in the EU than in the U.S.

Among other things, the approval process for biosimilars requires producers to exchange information regarding patents that might potentially be infringed. This is the patent dance – a process whereby the parties jointly identify relevant patents and negotiate to see whether the originator may be willing to license any of the patents to the biosimilar producer. And even during this process there is a first-mover advantage. When asked about what strategies, if any, biosimilar producers typically use when negotiating with patent holders, an interviewee stressed the importance of timing:

> Patent issues differ, case by case, so it is difficult to generalize, but Big Pharma firms frequently stack up patents. The issue for latecomers is: how do you avoid these patent claims? If you cannot avoid them, how do you reach a settlement with the patent owners? The timing of the settlement is important. If your competitor [another biosimilar producer] starts settling with the original producer slightly earlier than your company does, then the patent owner will give them priority for launching their product. For instance, the patent owner will say: company A can launch in January, and then you, company B, can launch in July (Pharmaceutical Representative 3).

Based on these narratives, we can clearly see that the power of original producers extends beyond patent ownership and market access into such issues as market entry order. Despite biosimilars technically having their own, separate value chain, the existing regulatory landscape clearly puts biosimilars in a subordinate category, where even their marketing and distribution are subject to a level of control by patent owners.

All this is relevant only when the negotiation process goes smoothly. Recall from Chapter 3 that there are different kinds of patents. In addition to a "base" patent, which covers the core active ingredient in a medicine, there also are "secondary" patents, subsidiary to the base patent, covering such things as manufacturing, method of use, dosage and formulation. Original producers frequently employ strategic patenting, sometimes even more than a decade after obtaining regulatory approval, for the sole purpose of extending protection of their drugs (Van de Wiele et al. 2022). This stacking of patents creates the so-called "patent thicket" or "patent clusters" surrounding the base patent, ultimately helping patent holders to effectively delay the onset of competition from biosimilars (or generics) producers (Song and Han 2016).

Studies show that patent thicket problems are more frequently encountered in the U.S. than in other countries. The patent system in the U.S. enables inventors to acquire multiple subsidiary patents that collectively impede market entry for rivals (Konara et al. 2016; Krishtel, 2019). For instance, Goode and Chao (2022) show that, on average, there are nine to twelve times more patent claims asserted against biosimilars in the U.S. than in Canada or the United Kingdom. One blockbuster drug, Humira, has 63 patents filed in Japan, 76 in the EU, and 247 in the U.S. (Krishtel, 2019).

In the case of a new drug, a Korean firm might choose the U.S. market precisely because, despite the challenging regulatory approval process, once it is accepted by the FDA, the regulatory processes in *other* countries can be facilitated, as the drug's proven efficacy and safety will be considered to have been demonstrated. When it comes to biosimilars, however, Korean firms have an incentive to find the least stringent IPR regime available, because they will inevitably have to negotiate the patents that are relevant for the product in question. Clearly, then, the appropriate approach to regulatory arbitrage for biosimilars is to choose markets with less of a patent thicket.

Among these patents, however, the base patents are rarely litigated, as even biosimilars producers are aware that "it is nearly impossible to successfully challenge an API patent." Rather, the vast majority of allegedly infringed patents concern the "peripheral features" of drugs, such as methods of manufacturing, dosage form and new formulations (Van de Wiele et al. 2022). Critics claim that this kind of patent stacking, involving the use of subsidiary patents, contradicts the purposes of having IPRs, as they grant rights in the absence of such qualities as novelty or nonobviousness—all of which raises concerns over the excesses of the U.S. patent system (Rai and Price 2021).

Original drugmakers sometimes sue biosimilars solely for the purpose of delaying their market entry:

> Branded drug producers sometimes opt for litigation because, typically, during litigation, competitors [biosimilar producers] typically cannot sell their products. Meanwhile, the period over which the original drug enjoys market exclusivity is prolonged. So, the purpose [of the litigation] is really to delay the market launch of biosimilars, rather than to win [on any substantive issue] (Patent lawyer 2).

Johnson & Johnson (the original producer of Remicade) successfully delayed the market entry of Remsima in the EU, even after Remsima was granted market authorization (regulatory approval) by the EMA in 2013, when Johnson & Johnson obtained a pediatric extension for its patent. Eventually, in February, 2015 (two years later), the biosimilar was launched in 12 EU countries. At the same time, however, Remsima secured for itself a first-mover advantage:

> In the case of Remsima, because it was the first MAB biosimilar, there were only ten or twenty patents in Europe. Today, though, a typical biosimilar litigation case would involve more than a hundred patents (Pharmaceutical Representative 11).

More recently, to avoid patent issues, some biosimilars producers are beginning to produce "biobetters", which are therapeutic alternatives engineered to have improved properties (e.g., easier methods of use) than the related branded biologics (Beck 2011). Celltrion developed an upgraded version of Remicade (or Remsima) called "Remsima SC", which can be injected subcutaneously and is thus more convenient to use at home than earlier medicines of its kind (including both Remicade and Remsima), which are administered intravenously and only at clinics or hospitals.

Because a biobetter is superior in specific ways to a related original drug, it requires a new drug application, being ineligible for the abbreviated regulatory pathway available to biosimilars. At the same time, however, it may not be classified as an "innovative" drug, because it already has a target market in hand and the reference biologics are proven to be sufficiently effective (Sharma et al. 2019). In other words, it does not have the potential risk of failure one would expect from an innovative drug. According to interviewees, biobetters may reduce frequency of administration through higher dose concentration, provide more convenient methods of application, or have greater effectiveness than original biologics (e.g.,

pain-free formulations –citrate-free, for example). Since a biobetter has advantages similar to those associated with new biologics, including a longer exclusivity period and the potential for patent protection, latecomer biosimilar producers are working to venture more into this new field in upcoming years.

5.3.2 Market Exclusivity and Bringing the Distribution Stage Back In

In addition to litigation and the patent dance, latecomer firms must overcome hurdles posed by the market exclusivity obtained by original producers through their market dominance and existing ties with healthcare providers and insurance companies. Big Pharma companies tend to have a portfolio of drugs that can be "bundled", something most of the latecomer firms cannot offer. Through bundling, Big Pharma companies can enter into exclusionary contracts with healthcare providers. This was a charge that Pfizer, Celltrion's U.S. distribution partner, raised against Johnson & Johnson (J&J), accusing J&J of anticompetitive practices.

For the U.S. market, Celltrion partnered with Pfizer to distribute Remsima, a common strategy used by latecomer firms venturing into unfamiliar foreign terrain. Pfizer held exclusive commercialization rights to Celltrion's biosimilar, and it filed a lawsuit against J&J, claiming that J&J's "rebate trap" was preventing Pfizer and other biosimilars producers from competing against Remicade (Pfizer Inc. v. Johnson & Johnson, 2018). A "fail first" provision laid out in exclusionary contracts between Johnson & Johnson and commercial insurance companies, for instance, required a patient to first try Remicade with unsatisfactory results before the insurance company could reimburse purchases of Inflectra (the U.S. brand name of Remsima) or another biosimilar. According to Pfizer Inc. v. Johnson & Johnson, at least 70 percent of commercially insured patients in the U.S. are subject to such provisions. In addition, through an "all-or-nothing" multi-product bundled rebate program, Johnson & Johnson combined its other arthritis treatments (e.g., Simponi, Simponi Aria, Stelara) with Remicade to provide savings.

Pfizer claimed that to overcome the rebate trap, it had to follow Johnson & Johnson's lead and price Inflectra below its own average variable cost. The parties eventually settled the claim in 2021, although the terms have not been made public. One thing that can be deduced from this high-profile case is that it is significantly more difficult for latecomers than it is for U.S. or EU firms to overcome exclusionary contracts designed to block both insurers from reimbursing and hospitals and clinics from purchasing biosimilars, and also that these practices are, in fact, commonly employed by Big Pharma to foreclose rivals' access to the market.

A study by Caves and Singer (2011) showed that, even in the vaccines industry, incumbent vaccine makers (typically Big Pharma) regularly create barriers to entry through such bundling. For instance, companies like Sanofi, GSK, and Merck bundled essential vaccines, including treatments for IPV, HPV, and Rotavirus, in an attempt to ward off Novartis (which offered only one vaccine, Menveo). These firms also established a penalty price for drugs purchased outside the bundle, meant to make it even more difficult for other, equally efficient vaccines to enter the market. Critics thus argue that the emergence of bundling has eroded the ability of physicians to make individual product choices based on performance characteristics or clinical data, as they are financially penalized for doing so.

Despite these mounting difficulties, some latecomer companies are beginning to reintegrate previously outsourced aspects of the distribution stage. Since this is the phase where companies accrue profit from sales, even Big Pharma firms will distribute their own products, irrespective of whether they outsource elements of the manufacturing stage. One of the biggest challenges for latecomers in the distribution stage derives from differences in drug pricing and reimbursement structures across countries. Thus, latecomers intentionally turn to either Big Pharma or local pharmaceutical firms that already have strong footholds and networks to facilitate commercialization.

As the production life cycle theory predicts (Gereffi 2018; Yeung 1999), however, once firms gain a sufficient presence in the foreign market, they will want to internalize distribution activities, not only to reduce costs, but also to gain increased autonomy:

> The decision to opt for direct sales is not just about reducing costs. Working with distribution channels in foreign countries is challenging. One of the primary motivations [for bringing the distribution in-house again] is to make it possible to design marketing strategies the way we want to, instead of just having to follow what our partners do. Of course, our distribution channel is not as extensive or effective as that of our partners right now. And this is probably our biggest weakness. However, just as with CMOs, our success or failure is too dependent on a distribution partner. Since we have not been doing direct sales, there was not much we could do about this. For instance, even if we wanted to sell as much as possible, partners will seldom put in the kind of effort we would invest if we did it all ourselves, because they will make money no matter what (Pharmaceutical representative 7).

During the 1990s, as the East Asian NICs became successful original equipment manufacturers (OEM), they sought to move up the ladder. In the case of apparel manufacturing, the East Asian NICs undertook "forward integration" by shifting to retailing. As a result, almost all of the Hong Kong apparel manufacturers eventually launched their own brands and retail chains (Gereffi 2018). This production life cycle model shows that, as firms get involved in activities further along in the value chain, the incentives that motivate their decision-making change.

In a similar vein, early on, Korean biosimilars focused on finding a market where they could sell their products, and as a result, they partnered with local companies or MNCs in foreign domains. But as they began to gain experience and become more familiar with the relevant market dynamics, they no longer wanted to work with intermediaries. Since the majority of the latecomer firms that I interviewed described "becoming like a big pharma company" as one of their ultimate goals, it seems that they are working to restructure the value chain by mirroring what lead firms typically do, despite numerous challenges they may encounter along the way.

5.4 Implications

Existing studies have often noted the regulatory ties between Big Pharma companies and regulatory agencies. This chapter attempted to evaluate whether a similar relationship exists between latecomer firms and foreign regulatory bodies, and if not, what strategies latecomers may employ to overcome regulatory hurdles and market barriers they face in a foreign context.

As described in this chapter, latecomer firms will opt for regulatory arbitrage, regulatory co-creation, and efforts to take advantage of first-mover status, depending on the market context and their capacity. Yet these different strategies are intended not only to maximize short-term profit, but also to facilitate long-term regulatory and market launch processes in other foreign contexts.

Given the unpredictable nature of frontier technologies and the inevitable knowledge deficiency of the regulatory bodies, there is no single "right" way for latecomers to enter a foreign market. In the case of South Korean firms, they have opted to start with the most challenging and competitive market, in order to gain experience and then to use the U.S. or EU regulatory frameworks as their models when moving into other foreign countries. Thus, these latecomer firms tend to be faced with more upfront challenges.

However, this landscape is changing in ways that may decrease the obstacles and increase the opportunities for Korean biosimilars. In September 2022, the EMA established interchangeability for patented biologics and biosimilars (Eckford 2022). This means that, from now on, biosimilars approved in the EU will automatically be available at the pharmacist level, if patients so choose, with no requirement to consult first with the prescriber. As more and more countries adopt this new norm, Korean biosimilars producers can potentially take greater advantage of the situation for marketing their products.

Chapter Six

Divergent Paths Crossing? Argentina's Agri-Biotech Industry as a Comparative Case

Preceding chapters have focused on how South Korean pharmaceuticals firms navigate the global regulatory chain (chapter 5) and the role the government plays in facilitating their activities (chapter 4). The strategies used and the challenges faced by latecomers, however, are topics applicable far beyond just the pharmaceuticals industry. In this chapter, I will explore the agri-biotechnology industry in Argentina as a point of comparison to demonstrate how the state and firms in Argentina similarly (or differently) navigate their relevant global regulatory chains.

The divergence in the trajectories of Latin America and East Asia has been an enduring point of interest for development studies over the past several decades. The existing literatures argue that it is either institutional capacity (e.g., the advantages conferred by the developmental state), a greater ability on the part of East Asian states to mobilize opportunity structures in the global economy, or the persistent legacy of Latin America's import substitution industrialization model, as opposed to East Asia's early embrace of export-oriented industrialization, that is most central to explaining the divergence (Amsden, 2001; Gereffi and Wyman, 1991; Haggard, 2018; Hamilton and Feenstra, 2006). Despite the oft-noted differences between these two regions, most Latin American countries eventually did adopt more export-driven models in the wake of the so-called the "Third World debt crisis".

Among the frontier technology sectors in Latin America, Argentina's agri-biotech industry stands out. Notwithstanding the social and ecological controversies genetically modified (GM) crops may pose, Argentina's domestic agribiotech firms, like those in Korea, have pioneered multiple new strains of GM crop strains. Despite the fact that the current genetically modified organisms (GMOs) market is increasingly consolidated among the "Big

Four" multinational companies [58], perhaps even more concentrated than the global pharmaceuticals market, non-traditional competitors from Argentina are seeking entry to the field. While there is evidence that firms in Argentina (often in collaboration with public research labs) have the capacity to innovate, they regularly stumble at the regulatory approval stage. Moreover, even after completing the necessary approval processes, latecomers like Argentina have been experiencing additional difficulty with market launch that multinational firms do not necessarily undergo.

Apart from the differences in industry contexts, what factors can explain the divergent regulatory trajectories and outcomes of South Korea and Argentina in these cases? Using the regulatory approval processes for Argentine GMOs as a comparative case, this chapter will explore the impact of the global regulatory chain on both state decisions and firm activities in Argentina, and how these compare to the case of South Korea.

6.1 The Argentine Agricultural Sector: How Facilitative is the State?

Like many other latecomer countries, Argentina has been determined to expand the biotechnology sector via various forms of industrial policies. Through two Science, Technology and Innovation (STI) plans, the "Plan Estratégico Bicenternario" (2006-2010) and the "Plan Argentina Innovadora 2020", the government has aimed to foster and encourage public-private partnership by creating innovation platforms and science parks around Argentina, such as the Rosario Biotechnological Pole (el Polo Tecnológico Rosario). In addition, by way of Laws No. 26,270[59] and No. 27349[60], the government has contributed to the proliferation of biotech start-ups in recent years. As of May 2023, there were approximately

[58] As of May 2023, the "Big Four" are Bayer (which acquired Monsanto), Corteva (formerly DuPont), ChemChina (formerly Syngenta) and BASF.
[59] This law provides for tax incentives, accelerated amortization (to help with corporate tax reduction), and tax refunds to selected biotech companies.
[60] Through the creation of the National Fund for Entrepreneurial Capital (FONDCE), the state established the "co-investment system" where the Argentine government would provide subsidies of double the amount invested by domestic Argentine companies.

300 biotech companies in Argentina, with 65 of them emerging between 2019 and 2022. Over the last three decades, the number of biotech firms has grown eightfold; among them, the majority is engaged in developing pharmaceuticals products (38 percent), with a second substantial group belonging to the agricultural sector (22 percent) (MINCyT 2021; Stubrin 2022).

Despite all the government has done thus far, a majority of my Argentine informants, when asked about the feasibility and practicality of this support, reported that "it is not enough" – just as my respondents in Korea said, as discussed in Chapter Three. In fact, they argued, the agricultural sector as a whole has actually been receiving "negative support":

> Unlike farmers in the United States, we don't have safety nets. We have the futures market here in Argentina, where our farmers can hedge prices on their products, but we don't have any risk management plan, such as insurance policies, here in Argentina. For instance, in the past season, we experienced a severe drought. We lost 35% of total production in Argentina in just one season, but the industry was given nothing (Lobbyist 3).

A government official further confirmed that, despite the start-up fund available to agri-biotech firms, cumulatively speaking, the sector is "unprotected":

> PSE (Producer Support Estimates) is an indicator used by the OECD to analyze to what extent policies are helpful or unhelpful. In our [Argentina's] case, this indicator has been always negative, while in the US it has been 10-20%. For this reason, we couldn't make as much progress in innovation as you might see in Brazil or the U.S. And this is not only because of macroeconomic policies - the taxation policies, too, are virtually against the sector…And we need to compete with the majority of countries that have much a better economic environment and support system. This means that the adoption of biotechnology has not helped Argentina because…the relative price for product input in Argentina is worse than in most of the world (Government official 1).

Stakeholders also suggested that there tends to be a lack of available credit and high interest rates, which also function to hinder growth in the sector. As the above informant explained, however, the agricultural sector in Argentina faces a unique challenge that other agro-exporting countries (especially those in the global North) do not: export taxes.[61]

[61] Most agro-exporting countries have either eliminated or never had such export taxes. Even similarly positioned economies, like Brazil and Colombia[61], do not impose export taxes on grain products (Deese and Reeder 2007).

In Argentina, there is an export tax (*retenciones*) on agricultural commodities. Instituted in the 1970s, the export tax came to serve as an "emergency tax" in 2002-2003 to help cope with the large fiscal deficit after the debt crisis of 2001. Because then-President Eduardo Duhalde assured the agricultural sector that the export taxes were a necessary but temporary measure to compensate for collapsing tax income and fund urgent social assistance, agri-businesses accepted them (Barlow and Peña, 2022). They were never rescinded, however, and remain in effect even two decades later. The average export tax rates per year vary depending on the yield, exchange rate, inflation level, and more; in 2022, the tax on soybean, soybean oil, and soybean meal was 33%[62], while for wheat and corn it was 12%.[63]

The government's determination to maintain this high export tax rate is due to the deteriorating macroeconomic condition in Argentina, particularly since 2018. Argentina has been facing one of the highest inflation rates in the world – in 2023 it exceeded 100% per annum for the first time in three decades, a situation exacerbated by a lack of access to foreign capital and a negative fiscal balance (Gillespie 2023).[64] Since the agriculture industry is one of the few thriving sectors in Argentina, and therefore one of the few that that brings in foreign currency, the revenues generated from this sector have been used to support other, more disadvantaged sectors, such as footwear, machinery, and transportation (Brambilla et al. 2018; Fairfield 2011).

Another reason export taxes play so significant a role in the domestic economy is that they can be easily changed through Presidential "Emergency and Urgency" Decrees, which bypass legislative control (Barlow and Peña 2022), where other taxes (value-added tax, income

[62] There were additional hikes on soybean oil and soybean meal, raising tax rates from 31% to 33%, to collect more revenues to help the government fight inflation.
<https://www.reuters.com/article/grains-argentina/update-2-argentina-hikes-export-tax-on-soy-oil-meal-to-33-to-combat-inflation-idUKL2N2VM096>
[63] https://www.thepigsite.com/news/2022/02/argentina-farm-sectors-pushes-to-remove-tax-levied-on-grain-exports
[64] https://www.washingtonpost.com/business/2023/03/23/why-70-inflation-is-just-one-of-argentina-s-problems-quicktake/0e013ea4-c932-11ed-9cc5-a58a4f6d84cd_story.html

tax, etc.) require the approval of the legislature. In fact, President Kirchner extended export taxes without consulting the agricultural sector in 2007 under the 2002 Law of Economic Emergency (Cetrángolo and Gómez Sabaini 2010). Export taxes, on average, already constitute approximately 10% of government revenue; this proportion, moreover, can increase substantially, depending on the base rate. Moreover, where revenues from most taxes are shared by the federal and the provincial governments, export taxes are wholly at the discretion of the federal government (Ministerio de Hacienda 2018). Thus, they are a "readily available source of fiscal revenue for the government" (OECD 2019).

The extent to which export and other taxes on agriculture are indispensable to the country's fiscal budget may be debatable. The evidence, however, suggests that agro-exports have been the government's preferred option for raising revenue in times of economic difficulty. Some accounts suggest that the Argentine economy is "in [the] worst shape" it has known since the 2001 debt default, with just $5 billion in cash and gold reserves remaining and a looming national debt of $45 billion owed to the International Monetary Fund (IMF) (Dube 2021). In addition, almost half (42%) of the Argentine population is mired in poverty,[65] a 20% increase from 2019, and the situation is only expected to worsen as the country faces an inflation rate of 114% - the third highest in the world today.[66] Since government spending consistently exceeds government revenue, the export tax on agricultural sector will likely persist and may even increase.

As we can see, even if support for the agri-biotech industry has been increasing in Argentina, the facilitative role played by the Argentine government has generally been perceived as insufficient from the industry perspective, as the amounts the state collects from the agricultural sector in taxes outweighs the volume of aid it provides for innovation (this is

[65] Based on the statistical data published in Bloomberg on April 1, 2021.
[66] https://www.economist.com/the-americas/2023/06/22/annual-inflation-of-114-is-pushing-argentina-to-the-right

the notion of "negative" support). Moreover, much like what we have seen in the case of the Korean pharmaceuticals industry, the nature of biotechnology, which requires high up-front investment, in amounts beyond what the government can provide, makes government support relatively ineffective.

As will be laid out in the following sections, the regulatory arena in Argentina, much like the situation in our South Korea case, is where we see the state's impact on the agri-biotech industry most clearly. The extent to which it is effective in supporting the industry, however, is less clear.

6.2 How Does the Argentine State Navigate the Global Regulatory Chain?

Recall how we saw in Chapter 4 that, despite the fact that latecomer countries are generally supportive of domestic innovation, bureaucratic organizations may have divergent goals, which can hinder the expansion of a frontier technology sector. Where the Korean pharmaceuticals industry is concerned, there is a tension between the Ministry of Health (MOHW) and the Ministry of Science and Technology (MOST) over issues of price regulation. In the context of a single-payer health care system, MOHW implements a price ceiling on *new* drugs to reduce what could lead to medicine costing more than the government budget could bear. In contrast, MOST aims to boost innovation, and thus it argues for the need to provide incentives for firms devoted to R&D activities, helping to compensate for the substantial sums they are required to invest to develop innovative drugs.

A case comparable to this situation in Korea is found in the Argentine government and its attitudes towards GMO innovation. The Argentine Ministry of Science, Technology and Innovation (MINCyT) oversees R&D activities in various research organizations, including the National Scientific and Technical Research Council (CONICET) and the Instituto Nacional de Technología Agropecuaria (INTA), and disburses funding to finance R&D projects carried out in these public labs, as well as by start-up companies. The Ministry of Agriculture (MAGyP)

is in charge of the operation of the entire agricultural value chain, including the regulatory system and matters related to trade.

In 2019, an Argentine agri-biotech company called Bioceres filed for regulatory approval of the world's first genetically modified (GM) wheat, a drought-resistant GM wheat strain known as "HB4 wheat". Typically, for a GMO to be approved, it needs to undergo health and safety testing, as well as an environmental assessment, to ensure it does not negatively impact other organisms in the ecosystem. As a result of its interests as an agro-exporting country in the global South, and one with an extreme dependence on trade in agricultural commodities (of which GMOs comprise more than 63 percent)[67], Argentina has instituted a new, additional criterion of its own, called the "market evaluation" or "mirror policy" (Burachik 2020). The function of the market evaluation is to assess the compatibility of a new GMO with the standards of Argentina's trading partners. This additional regulatory step is intended to avoid even the possibility of cross-contamination of conventional exports with GMOs, meaning that a new GMO might be rejected domestically if it has not been approved by *foreign* regulators.

In GMO trade, only traits approved by the regulatory bodies of both exporting and importing countries can enter the destination market (Price and Cotter 2014). Yet there are often cases where an unapproved strain of GMO is discovered in a shipment, contaminating other products (e.g., approved GMOs or conventional food). Eventually, this could lead to an exporting country potentially losing trading partners, as was the case for Argentina, when unapproved GM events were found in its exports to South Korea, as well as to the EU (Jeon 2023).

In 2016, South Korea discovered an unapproved strain of GM wheat in a shipment of conventional feed wheat from Argentina. This was even prior to the development of HB4 wheat

[67] https://www.batimes.com.ar/news/argentina/wind-blows-in-favour-of-argentinas-gm-crops.phtml

and the filing for its approval with CONABIA. No one knew the origin of the contaminating GM wheat; nevertheless, the entire cargo was rejected and returned, and at Argentina's expense. According to the yearly import data published by the Korea Customs Service, South Korea imported more feed wheat from Argentina in 2016 than from any other country except Ukraine; since 2017, however, Argentina has vanished from the list (see Table 6.2).

Table 6.2 South Korea: Import of Feed Wheat (2016-2019)

2016		2017		2018		2019	
Country	**Amount (in Kg)**	**Country**	**Amount (in Kg)**	**Country**	**Amount (in Kg)**	**Country**	**Amount (in Kg)**
Ukraine	1,298,661,448	**Ukraine**	896,180,568	**Ukraine**	764,540,666	**Ukraine**	603,145,257
Argentina	455,626,601	**United States**	254,206,265	**Russia**	491,548,385	**Canada**	232,610,858
Russia	123,864,710	**Brazil**	250,250,542	**United States**	205,989,146	**Bulgaria**	193,688,052
Bulgaria	89,625,683	**Bulgaria**	141,129,010	**France**	182,000	**Romania**	151,986,741
Romania	75,851,180	**Russia**	115,196,691	**Australia**	62,360	**Russia**	8,335,710
France	68,111,656	**France**	71,209,945	**Pakistan**	5	**United States**	1,551,860

Source: Trade Statistics Service of South Korea

In short, contamination can and does happen. And the consequences of a contamination case are likely to be more harmful for countries in the global South than for more diversified and less export-dependent countries (Nicita and Rollo 2015). Understandably, then, it was to avoid just this kind of economic hit that the market evaluation phase of the Argentine GMO regulatory process was created. Nevertheless, this policy had the seemingly counter-intuitive effect of significantly delaying the approval of Argentina's own domestic innovation, HB4 wheat.

HB4 wheat passed both its environmental and health assessments, but it stumbled at the market evaluation stage. As the wheat was considered a groundbreaking opportunity for Argentina's agri-biotechnology sector, then-President Mauricio Macri himself invited representatives from different government bodies to hold periodic meetings and discuss the innovative prospects of HB4 wheat and whether Argentina should approve it or not. There was,

however, an escalating tension between the MINCYT and the MAGyP, a tension issuing from the agencies' divergent goals. While the MINCYT defended HB4 wheat as a significant step forward in domestic innovation and increased technological autonomy, the MAGyP expressed concerns over the possibility that the GM wheat might contaminate conventional wheat shipments, especially as wheat is Argentina's third most exported agricultural product:

> The Minister of Agriculture was saying: "No, all the markets will be closed because of the possibilities of contamination. We will not be able to export to Europe or China or other countries." The Minister of Science and Technology, on the other hand, was very happy. He was a biotechnologist himself, very excited about science, and he was happy with the fact that Argentina could have technological developments of its own. Even the President said: "Please talk with each other and make a decision before our next meeting." It was a huge dispute and it was in all the newspapers (Academic 3).

With the precedent of the aforementioned contamination case in mind, the MAGyP was cautious about this new GMO. Given that the MAGyP is the ultimate authority, the one that determines whether a new GMO can be commercialized or not, the GM wheat was initially disapproved in Argentina, despite the fact that government officials agreed that the HB4 wheat was "highly symbolic" for Argentina's national innovation system. As a result, Bioceres had to take an alternate route, seeking and obtaining approval of the wheat at the Brazilian regulatory agency prior to launching even in its native Argentine market, Brazil being Argentina's largest wheat importer. I will elaborate upon this further in the next section.

An additional ongoing regulatory tension associated with GMOs is related to Argentina's intellectual property rights (IPR) law. Multinational biotech companies like Monsanto (now Bayer) first entered Argentina to benefit from its relatively lax (for the Latin American context) regulatory regime in terms of health and environmental reviews (Newell 2009). They also saw growing possibilities in a changing global economic context. Like other Latin American countries, Argentina underwent waves of neoliberal reform in the 1980s and 1990s; spearheaded by structural adjustment policies, the country's ports and the energy sector were privatized, and the agricultural sector was reorganized, with multinational companies

acquiring national enterprises (Grimson and Kessler 2005). Seeing this as an opportunity, Monsanto began licensing the Round-up Ready (RR) gene in the mid-90s to a multinational germplasm firm, Nidera, which acquired the Argentine company Asgrow in the late 80s (Nidera is now a subsidiary of Syngenta).

Monsanto, however, failed to foresee, or underestimated, particular aspects of Argentina's IPR law. As Table 6.2 shows, IPR law in Argentina and most other Latin American countries adheres to the International Union for the Protection of New Varieties of Plants (UPOV) treaty, first enacted in 1978. This law allows farmers to save seed and replant it without paying royalties. As a result, there continues to be a massive black market, known as *bolsa blanca*, keeping the price of genetically engineered soybean seed (Monsanto's Roundup Ready) below global market prices (Newell 2009). Even though many foreign biotech companies, led by Monsanto, have pressured the Argentine government to sign the 1991 version of the UPOV (which prohibits seed saving), they have achieved no progress on this issue, and farmers continue to save and replant seeds. As a result, Monsanto and many other foreign biotech companies have stopped selling new GM soy seeds in Argentina.[68]

[68] Even after replanting, GM soy retains its genetically engineered characteristics; the same is not possible for maize or sunflower, which are hybrid seeds.

Table 6.2 Regulatory Policy Stance towards GMOs among GMO-Producing Latin American Countries

Country	Intellectual Property Rights - GMOs[69]	Biosafety Regulation	Domestic Consumption and Labeling	Trade Policy on GMOs
Argentina	UPOV 1978	No strict restriction on the release of GMOs into the environment	No labeling required; most food contains GMOs and public acceptance is high	GM crops promoted; no particular restrictions on imports of GM seeds/crops
Bolivia	UPOV 1978	Restriction on the cultivation of GM maize	Pending GM food labeling measure	Allows import of GM food/feed
Brazil	UPOV 1978	The Biosafety Law (2005) establishes safety standards and mechanisms for monitoring activities involving GMOs and their byproducts; takes *precautionary* measures for the protection of the environment	Labeling required for food/feed containing GMOs (though there is a lack of enforcement)	GM crops neither promoted nor prohibited; imported GMOs treated as substantially equivalent to non-GMOs
Chile	UPOV 1978	GMOs substantially *different* from non-GMOs	Prohibits in-country consumption of domestically produced GMOs; only imported GMOs are consumed; No labeling	GM crops neither promoted nor prevented; imported GMOs treated as substantially equivalent to non-GMOs
Colombia	UPOV 1978	Ratified the Cartagena Protocol; risk evaluation available for both GE crops and GE animal products	Pending GM food labeling	GMO import promoted
Costa Rica	UPOV 1991	Registration of new GM traits suspended since 2013 due to a court case involving Monsanto	Strong anti-GM campaigns aimed against corporate control of the food supply; No labeling requirements	No restriction on GM maize and soybean import
Honduras	N/A	First established a biotech committee in 2017 to monitor and approve new GM traits	N/A	Strong demand for imported GM maize
Mexico	UPOV 1978	GM soybean and maize prohibited due to court injunctions	Strong consumer & small-scale farmer backlash against GM maize to protect maize biodiversity; No labeling	GM crops promoted; no restrictions on import of GM seeds or crops
Paraguay	UPOV 1978	Ratified the Cartagena Protocol, but GM maize being produced illegally	No labeling requirements	Beginning to promote GM crops
Uruguay	UPOV 1978	Complicated application process limits GMO commercialization; three-years moratorium on corn currently in effect	GMOs treated as substantially equivalent to non-GMOs; labeling is voluntary	GM crops promoted; no restrictions on import of GM seeds or crops

[69] Both UPOV 78 and UPOV 91 protect seed intellectual property. Some fundamental changes were made from UPOV 78 to UPOV 91 – these include: 1) Farmers cannot freely save seeds from protected varieties for their own use; 2) Plant varieties can be patented; 3) Harvest belongs to the breeder; 4) Further breeding is restricted (APBREBES n.d.). Thus, the changes in UPOV 91 further restrict farmers' rights and their control of production systems, limits diversity via extended plant patenting, and more.

At the same time, though, just as relatively lenient IPR regulations facilitated upgrading in the Indian pharmaceuticals industry from the 1970s to the 1990s, as discussed in Chapter Four, the laxity of Argentina's regulatory system with respect to IPRs is what has enabled it to become the third largest GMO-exporting country over three decades since GMOs were first introduced to Argentina in the 1990s.[70] Since farmers do not need to pay additional license fees after purchasing GM seeds once (as described above), GM seeds were replanted and harvested, quickly scaling up the volume of GM soybean production. This situation also incentivized domestic agri-biotech firms and research labs to diversify into the development of GMOs other than soybeans, such as potato, wheat, alfalfa, maize and sugarcane (see Lewi and Vicién 2020). Yet when asked about the Argentine IPR law, those involved in the upstream activities of the GMO value chain generally view it as a kind of "double-edged sword," expressing concerns that this very flexibility may contribute to the evaporation of both domestic (and foreign) biotech firms in the long run, as many of them have begun to move their headquarters to foreign domains (e.g., the United States, the EU, Uruguay) and plan to operate more actively in overseas regions.[71] The effect of the state's insistence on retaining the lenient IPR law, then, has been of questionable value for the growth of the agri-biotech industry. The situation reminds us the "Goldlilocks principle", which says that the IPR law that is neither too stringent nor too soft, but rather "just right", is the one likely to induce the greatest volume of innovation.

6.3 How Do Latecomer Firms Navigate the GMO Regulatory Landscape?

As described in the preceding section, Bioceres' HB4 wheat was disapproved by domestic regulators at first. The firm decided to take an alternate route, filing a dossier in Brazil, the largest importer of Argentina's conventional wheat. To cope with the complex set of

[70] Argentina was the world's second largest GMO producer after the United States, until Brazil suddenly increased its GMO planting volume in the early 2010s. Argentina is also the third largest producer of soybeans in the world, after the U.S. and Brazil.

[71] Although there is a host of reasons why Argentine frontier technology companies are leaving Argentina and moving overseas, including continuing macroeconomic instability, there has been a general concern among scientists and other agri-biotech stakeholders (other than farmers) that the lax IPR law will eventually stall innovation in Argentina.

regulations relating to GMOs (both at the domestic and international level) and to eventually launch their products, agri-biotech firms in Argentina employ a variety of strategies. In the following subsections, I will describe how two Argentine firms that prioritize different stages of the agri-biotech value chain—Bioceres and Don Mario—navigate the global regulatory landscape.

6.3.1 Regulatory Arbitrage and First-Mover (Dis)Advantage

Just as Korean pharmaceuticals firms purposely prioritized approval in the most competitive foreign markets—for new drugs in the U.S. and for biosimilars in the EU—Bioceres employed regulatory arbitrage, targeting Brazil as its primary market. Notwithstanding their initial disapproval of HB4 wheat, the Argentine regulators suggested that if Bioceres were to successfully obtain regulatory approval in Brazil, they would reconsider that earlier decision. When asked about the dossier filing process in Brazil, a representative from Bioceres explained that it involves both "technical" and "political" strategies:

> I think the approval processes require a technical strategy, obviously, in terms of the information that needs to be presented, how you comply with what regulators would like to see. And then there is a political strategy, in the sense of making sure there are no incremental costs, politically speaking. In terms of moving forward with a clearance, you have to make it easy for the political authorities that oversee the regulatory process to deal with the potential conflicts that may arise from a particular approval (Biotech representative 1).

Once, back in the early 2000s, Monsanto attempted to launch a glyphosate-resistant wheat, an attempt which ultimately failed because of the concerns related to public opposition. Then, in the 2010s, on a farm in Oregon, farmers found a strain of Monsanto's unapproved glyphosate-resistant wheat. For this reason, the interviewee emphasized, Bioceres worked hard to convince the Brazilian regulators that the HB4 wheat had no such gene flow issues and that it was not likely to contaminate conventional wheat.

Yet the more challenging aspect of the regulatory process was, as my informant explained, the fact that the HB4 wheat was the first GM wheat in the world, a product with no precedent, and simultaneously that there was no approval by the Argentine government:

> For us, it was very important to get the first approval somewhere, because that creates a precedent that others [other regulatory bodies] can use themselves to come to their own judgment…It was very difficult for us to ask other countries to provide regulatory clearance when we were still not fully approved in the product's country of origin (Ibid).

Contrary to what most of the literature says about first-movers, and contrary even to the situation we saw with respect to the Korean pharmaceutical firms, Bioceres found itself with a first-mover *dis*advantage, as it was saddled with the burden of creating an entirely "new market" on its own. The regulatory experience in the case of HB4 wheat also differs from the situation for biosimilars, and even new drugs, because for these there is typically guaranteed demand (patients requiring treatment for particular diseases), whereas in the case of new GMOs there tends to be a significant degree of public skepticism. In addition, because the HB4 wheat was a new type of product within an existing GMO world where the regulatory landscape was relatively settled, it had no opportunity to seek the kind of regulatory co-creation that may be available to biosimilars producers.

After more than three years of persuasion and deliberation, HB4 wheat was finally approved for consumption in Brazil in 2021, which led to subsequent approvals in Argentina, Australia, New Zealand, and Nigeria. As of May 2023, it also received a green light from the U.S. FDA, and it is currently awaiting decision from the United States Department of Agriculture (USDA), which would make possible exports to the U.S. market as well.[72]

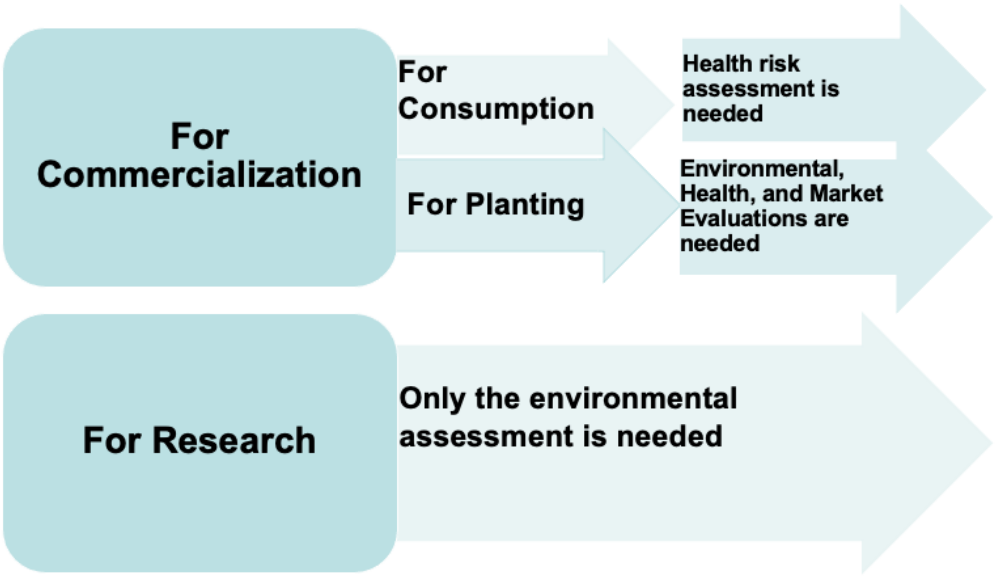
HB4 wheat is not the first case in which Bioceres had to resort to regulatory arbitrage to overcome a "first-mover disadvantage". For a drought-resistant soybean (the "HB4 soybean"), the gatekeeper country was China, currently the largest importer of Argentine

[72] https://www.reuters.com/markets/commodities/argentinas-bioceres-says-its-gmo-wheat-gets-key-ok-us-fda-2022-06-27/

soybeans (Silva 2021). With the help of a local firm, Beijing Da Bei Nong Science and Technology Group Co. Ltd., Bioceres was granted approval after about two years (in April 2022), much faster than the process for HB4 wheat in Brazil. Some observers noted that the endorsement from China, now the world's largest consumer of soybeans, could potentially bring broader acceptance for drought-resistant seeds globally (Millan and Veloso Ribeiro 2022).

Yet even after gaining regulatory approvals for consumption in all these countries, HB4 wheat has yet to be commercialized. In light of GMO regulation, there is a separate approach firms are compelled to take for consumption and planting (See Figure 6.3.1).

Figure 6.3.1 Regulatory Approval Process for GMOs (by Purpose)



Source: Author's compilation based on Burachik (2020)

As we can see from Figure 6.3.1, with regard to planting, there are two different kinds of regulatory approval for which firms can apply, depending on the purpose of the planting: for actual harvesting or solely for research. This is why, despite the fact that a majority of countries in the European Union prohibit production of GMOs, they still consume (not always without continuing controversy) GM food obtained via import.[73] Because Bioceres seeks to

[73] While most of the countries in the world (including the EU, which is consistently resisting GMOs) admit processed GMOs, cultivation is an extremely sensitive issue, because of gene flow and other possible forms of environmental

sell not just processed flour, but also HB4 wheat seeds, to agro-exporting countries like Brazil, it needs to pass an additional regulatory process. In the meanwhile, due to public unfamiliarity with the new trait, there has been escalated consumer anxiety and resistance to the HB4 wheat in Brazil. In March 2023, however, after a national survey result indicating that more than 70% of Brazilians would consume transgenic wheat (Samora 2022), the Brazilian regulatory body finally approved planting of GM wheat, which is expected to ease the beginning of commercialization of the strain in Argentina, as well (Heath and Mano 2023). To obtain this additional approval, Biceres followed the broad lines of the approach it took in China and partnered with a local plant genetics company, Tropical melhoramento e Genetica.

The HB4 strain's road to regulatory approval highlights yet again the importance of regulatory arbitrage. In this case, however, the Argentine company was faced with a first-mover *dis*advantage, which delayed market launch for years even after the granting of regulatory approval for consumption. The additional approval required for the cultivation of HB4 wheat may then, potentially, contribute to the wheat finally being commercialized in both the Argentine and Brazilian markets.

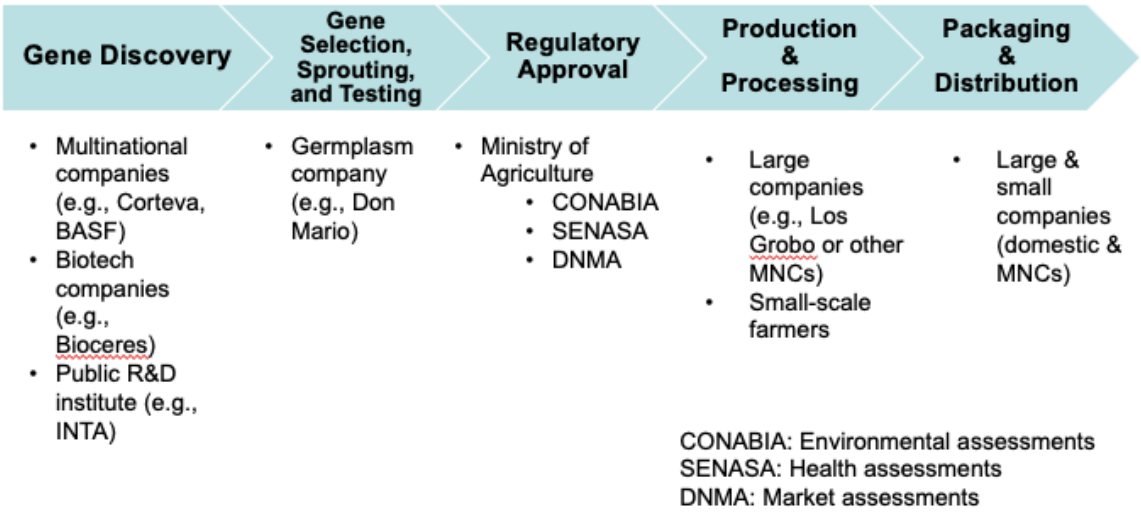
6.3.2 Lax IPR Law: Opportunity to Upgrade?

In a typical agri-biotech value chain, unless the inventor is a vertically integrated enterprise, genetically engineered genes, after they undergo testing, field trials, and regulatory approval, are often licensed out to plant breeders (also known as germplasm companies) (see Figure 6.3.2). At a later stage of the value chain, germplasm companies incorporate those genes into their own varieties to create seeds with enhanced characteristics (e.g., rust-resistant soybean), organisms that are more adaptable to a particular climate. GM events are transgenics, meaning they are created via a form of gene editing where genes with a desired trait are copied

contamination. This is why, thus far, only 67 out of 195 countries have started growing biotech crops, with only about 10 countries actively producing GMOs (ISAAA 2023).

from one species to another. While transgenics have dominated the agri-biotech industry, there are newer forms of genetic engineering that companies have been incorporating, where a particular gene within the same species is manipulated using clustered regularly interspaced short palindromic repeats (CRISPR) scissors or molecular marker. These types of gene editing, quite unlike the technology usually used to produce GMOs thus far, have been less controversial, because they allow for non-random gene editing and as a result, are known to have a reduced danger of producing unintended consequences.

Figure 6.3.2 A Sample GMO GVC



Source: Author's compilation based on croplife.org

An Argentine germplasm company called Don Mario, which currently supplies 20 percent of the soybean varieties used in the world, uses this kind of non-transgenics technology and conventional cross-breeding (Marin et al. 2022). According to informants, Don Mario intentionally avoids developing transgenics – "not for the lack of technological capabilities", but motivated by the prohibitively expensive costs (in research, field trials, and regulatory approval) GMOs require. On average, the R&D phase (including the obtaining of regulatory authorization) for GMOs costs US$115 million, and it takes about 16.5 years to commercialize one product (AgbioInvestor 2022). The regulatory process alone may cost between US$33 and 35 million (Kalaitzandonakes and Zahringer 2018).

Instead, to "survive" in an increasingly concentrated agri-biotech market, Don Mario tries to create as many new varieties as possible, all tailored to the agroecological conditions of particular regions. For instance, for areas with a longer ripening time (e.g., Southern Brazil), it creates soybean seeds with a shortened life cycle, so that the plant will be less exposed to diseases. In this process, representatives of Don Mario also stress the importance of timing and trying to be "the first one to supply to the market" (also see Marin et al. 2022).

The regulatory landscape creates complicated problems for germplasm companies to solve. As mentioned in the previous section, most Latin American countries conform to UPOV 78, which prohibits patenting of gene edited plants and provides protection only for the modified gene itself. Because of this, since Monsanto stopped selling new GM seeds, Don Mario has been experimenting with previously purchased GM events to create new varieties. As a result, some of my informants argue that this lax IPR law has prompted an upgrading of germplasm companies.

At the same time though, because Don Mario uses genes developed by other biotech companies, it does not have patents of its own, even where it develops new crop varieties (since plants cannot be patented in Argentina). As described above, farmers purchase soybean seeds just once, and then reuse them in the years that follow. Thus, germplasm companies like Don Mario are sandwiched between patent owners and large-scale farmers, unable to reap adequate benefits from the innovative activities they undertake.

6.4 Implications

This chapter discusses the extent to which the experiences of latecomers to a knowledge-intensive sector in Latin America are similar or different to what we have seen in the Korean pharmaceuticals industry. As in Korea, the Argentine state has been working to expand a frontier technology sector by providing funding for start-ups and creating platforms

for public-private partnership. In fact, Bioceres was a recipient of government-sponsored funding when it was itself a biotech start-up.

Government subsidies may be necessary, of course, to facilitate the growth of a frontier technology sector. But even in the case of Argentina today, the role the state most clearly plays is that of regulator. The step that Argentina added to its GMO regulation does not necessarily support the agri-biotech industry; rather, it aims to protect agricultural trade crucial to the state budgets. And it is precisely because of this domestic regulatory barrier that Argentine firms are more incentivized to obtain regulatory approval overseas and venture out into foreign markets. For GMO developers, regulatory arbitrage is one way to find a "path of least resistance"; by overcoming regulatory hurdles in its selected target market, it opens up greater windows of opportunity in other, subsequent contexts.

The delayed market launch of the Argentine GM wheat, however, also raises a potential hypothetical question: given that the wheat constitutes a new GM event, what might have happened had Argentina opted to apply for its first regulatory approval in the U.S., the most challenging regulatory market, rather than in Brazil? Might this have led to any change in either the process or the results? Additionally, notwithstanding industry-specific differences, Argentina's experience demonstrates that obtaining first-mover advantages (opportunities for regulatory co-creation, or influencing the existing global standards) is more difficult for latecomers from the global South, where innovative activities tend to be limited. Recently, there has been a major intensification of South-South trade, with China playing a leading role, particularly in South America and Africa (De Medeiros and Mazat 2019). In fact, as described in this chapter and Chapter Three, China is the largest importer of Argentina's soybeans today, where in earlier decades the EU was Argentina's main market. This shift in geopolitical situations and trade pattern may eventually have an impact on the global regulatory chain, and

that may also result in an opportunity (or the reverse) for the expansion of Latin American agri-biotech industries.

Chapter Seven
Conclusion

This dissertation has explored the meaning of the term "development" in the knowledge economy era and analyzed the roles and strategies latecomer states and firms have come to employ in this new context. Specifically, it aimed to answer such questions as: how has the developmental state evolved since its heyday? How can the state best support innovation and upgrading? Despite several decades of increasing expenditures on R&D, what factors continue to make it difficult for latecomer firms to "catch up" to the innovative activities of the United States and the European Union?

I argue that, in the contemporary era, an *interconnected global regulatory chain* is a central factor in development, one that drives and determines the extent to which latecomer states and firms can successfully achieve developmental goals. In essence, this is a chain of regulation that spans the globe and impacts various stages of production processes. It was established by MNCs and the countries that are home to them. If dismantling these preexisting regulatory barriers is not an option, then late developers need to discover how to navigate them via state-firm cooperation.

Scholars and global policymakers alike are interested in the mechanisms behind the rapid industrialization of East Asian economies. But since many of these nations "graduated" to the status of core economies, there has been limited research on their role and place in knowledge-intensive industries.

As described in the course of the dissertation, the extent to which firms and the state can overcome regulatory hurdles imposed on every stage of a value chain in frontier technology sectors such as pharmaceuticals and agri-biotechnology is a key determinant of their developmental trajectories. In other words, development today means developing the

capability to navigate global regulatory hurdles so as to integrate domestic firms into global value chains.

The main theoretical contribution of this dissertation, the global regulatory chain framework, can be understood in two intertwined ways. First, the regulatory context at each link affects all the others across a particular chain. The global aspect of the framework refers to how regulatory contexts overlap and intersect one another in ways that make what happens in any particular country relevant for what happens in others. And the influence of the regulatory landscape on countries that are not home to traditionally dominant pharmaceuticals MNCs is significantly more pronounced. The challenges latecomer economies face, in fact, amount to their lacking the advantages conferred by the traditionally dominant MNCs – the capacity to maintain their positions via patent protection and market exclusivities in the already competitive and challenging setting. In other words, even successful non-traditional core countries may be at a certain disadvantage, due to the dominance of incumbent firms and the countries in which they are based. In some sense, the legacy of being a latecomer persists even as economies graduate to the status of a high-income country.

At the same time, despite a situation where power in frontier technology industries is increasingly concentrated in the hands of fewer companies, latecomer firms have managed to carve out a niche for themselves. In the pharmaceuticals value chain, South Korea has been able to shape the regulatory rules for biosimilars to a certain extent by using its first-mover advantage. For new drugs, an area where Big Pharma firms continue to be the dominant players, South Korean firms use such techniques as regulatory arbitrage to navigate the existing regulatory challenges. Firms in the Argentine agri-biotechnology field also employ regulatory arbitrage, but there we tend to see a first-mover *dis*advantage issuing from the characteristics of the established GMO regulatory landscape. Likewise, depending on the type of product in

question, firms opt for different strategies, and they target those markets where the relevant regulatory landscape appears to be most favorable for their activities.

The role of states, too, has evolved, and they now seek to support domestic firms and integrate them into their GVCs. Not long ago, states obviously played a particular kind of regulatory role, relaxing relevant regulations to promote a more competitive playing field and protecting domestic industries from multinational companies (Evans 1995). Today's developmental states take on facilitative and regulatory roles, applying selected regulatory tools at each stage of the relevant value chain. In the R&D phase, states attempt to build international reputation and help to shape global regulatory standards by participating in the drafting of regulatory guidelines for emerging technologies. In the manufacturing stage, they focus on improving quality control, even if it means implementing more stringent regulations and restructuring their domestic industry. Finally in the distribution phase, states continue to use price subsidies (for follow-on drugs, but not for new medicines) for the purpose of helping domestic firms to better negotiate their prices in foreign markets.

At the same time, however, we found greater tensions among various bureaucratic organizations involved in development than were common in the industrialization period. In line with ideas in the development literature, which explores the effect of decentralization and the rise of competition among bureaucratic organizations among latecomers (Ang 2017; Wang 2021), we have seen that the differing aims of those organizations come into conflict with one another in the regulatory process and in the disbursement of financial support. What we learn from these changing dynamics within state bureaucracies is that the role of developmental states evolves based on the "temporal and spatial transformation of international and domestic settings" (Whittaker et al. 2020).

Specifically, the dissertation aimed to explain how a late developer like the South Korean pharmaceutical industry managed to navigate existing regulatory barriers and the

"patent dance" so as, ultimately, to successfully launch domestically-developed products in the global market.

7.1 Intellectual Property Rights (IPR): To What Extent Do They Stimulate or Stifle Innovation?

This dissertation also addresses long-standing questions relating to IPR issues, and the degree to which IPRs hinder innovation activities in many parts of the world. Among frontier technologies, a majority of IPRs around the world are owned by a small number of patent holders (primarily from the advanced economies) and many studies indicate that this has stifled innovation in the biotech industry, including biopharmaceuticals and agribiotech, outside of the U.S., EU and Japan (Acemoglu and Akcigit 2012; Chang 2002; Kinchy 2012).

As discussed in Chapter Five, the U.S. government has enabled the creation of a plethora of fragmented IPRs in the upstream part of the value chain, enabling patent owners to stack up licenses. In fact, studies show that approximately 40 percent of patents filed worldwide remain unused and about 67 percent of patents are filed for the purpose of blocking other patents (Torrisi et al. 2016). While such patenting strategies are lawful in principle, artificially preventing competition through "evergreening" (Bansal et al. 2009) and extending market monopolies has inhibited discoveries by competitors, leading to "the tragedy of anticommons" (Heller and Eisenberg 1998).

Regulatory hurdles like this are what late developers hope to avoid wherever possible because both patent negotiation and litigation are expensive and time-consuming processes. Given this, the market for follow-on drugs tends to be especially competitive and complex. Only firms that are able to challenge the existing patent system, and that can successfully negotiate the "patent dance", can enter the biosimilars market, a situation that deters many small and medium producers with limited financial assets and experience from attempting to enter the field. The question is the degree to which the contemporary intellectual property

system undermines innovation, rather than stimulating it, becoming in effect a deterrent to competition (Chorev and Shadlen 2015).

As discussed above, both latecomer states and individual firms from those states can try to overcome the patent thicket by finding a niche for themselves. Firms can either try to avoid patent litigation by choosing to pursue *incremental* upgrading, such as modifying the content of a product (e.g., changing the salt in a chemical compound) or the use of a product (e.g., modifying the size of an auto-injector needle). States can support domestic firms at the R&D stage by providing information about patents (currently obtained primarily by law firms) that may form the basis of a potential dispute.

In fact, recently, the Korean Intellectual Property Office (KIPO) cooperated with a domestic semiconductor SME to create a titanium nitride atomic layer deposition (TiN-ALD) equipment, which is an essential device in the manufacturing process for semiconductors.[74] To date, most Korean semiconductor companies have relied on foreign-produced equipment; however, beginning at the R&D stage, KIPO analyzed worldwide patents related to the device and helped the firm to create the prototype design of the machine in a way that would avoid any potential IP issues. Upon successfully creating the TiN-ALD, the company also filed and obtained 10 patents. This demonstrates how the global regulatory chain can be successfully navigated jointly, by a state-firm collaboration at the R&D and distribution stages.

7.2 Shifting Global Dynamism?

As discussed at the end of Chapter Six, China has increasingly become an important and influential global economic actor, particularly in the Southern Cone. Since China joined the World Trade Organization (WTO) in 2001, trade between Latin America and China has

[74] Within each semiconductor dynamic random-access memory (DRAM), there is a transistor and capacitor. A capacitor is comprised of insulator films and electrode films. The ALD equipment helps to deposit these films at an atomic level by functioning as a metal barrier across capacitors, oxide films, and other materials. < https://www.yonhapnewstv.co.kr/news/MYH20230526001900641?input=1825m>

grown more than twenty-fold, from $14.6 billion to $315 billion in two decades (Wintgents 2023). As of May 2022, seven South American countries—Venezuela, Ecuador, Peru, Bolivia, Chile, Argentina, and Uruguay—are participants in China's "Belt and Road Initiative (BRI)," a massive China-led development project, which includes investment in the construction of physical infrastructure worldwide as a means to facilitate trade with China and increase its geopolitical presence.[75] What is important for this research is the question of how the rise of China may impact the global regulatory landscape, which has essentially been created by traditional dominant players in the U.S. and the EU (Ciccantell and Bunker 2004).

In the case of the agri-biotech industry, the recent acquisition of Syngenta by ChemChina, a Chinese state-owned enterprise, has suddenly made China home to one of the Big Four GMO firms. As evidenced by the Argentine case, which has long seen the EU as its main target market, there is a possibility that China may become the de facto standard market (Quark 2013), so that Argentine firms may now prioritize getting initial regulatory approval there.

Even with new trading partners such as China, however, the kind of "dependent development" (Evans 1979; Stallings 1990) traditionally associated with Latin America remains a reality for the region today. The top four Latin American states in terms of volume of trade with China between 2017 and 2021 are Argentina, Brazil, Chile, and Peru. Table 7.2, though, shows that China's imports from these countries were largely in raw materials and agricultural commodities. In Argentina's case, more than 70 percent of its export to China are soybeans and their derivatives (Haro Sly 2017).

[75] Launched in 2013, the BRI envisions the construction of roads, rail, airports, ports, pipelines, and communications to link China with countries in Southeast Asia, Central Asia, and Europe eventually. China's investment in South America and Africa are also part of this project. The infrastructure building is, however, only the first step for the meta project China aims to achieve (see Foreign Affairs Committee 2022 for detail).

Table 7.2 Four Latin American Countries – Exports to China (Top 3 Products / Country)

Brazil

Exports from Brazil to China

	Top 1	Top 2	Top 3
2021	Iron Ore 32.7%	Soybeans 30.9%	Crude Petroleum 6.1%
2020	Soybeans 30.8%	Iron Ore 27.3%	Crude Petroleum 16.7%
2019	Soybeans 32.2%	Crude Petroleum 24.4%	Iron Ore 21.4%
2018	Soybeans 42.5%	Crude Petroleum 22.5%	Iron Ore 17.1%
2017	Soybeans 42.3%	Iron Ore 21.7%	Crude Petroleum 15.3%

Chile

Exports from Chile to China

	Top 1	Top 2	Top 3
2021	Copper Ore 54.7%	Refined Copper 18.0%	Iron Ore 6.16%
2020	Copper Ore 45.5%	Refined Copper 24.5%	Pitted Fruit 5.58%
2019	Copper Ore 41.9%	Refined Copper 26.6%	Pitted Fruit 7.31%
2018	Copper Ore 38.6%	Refined Copper 31.3%	Sulfate wood pulp 8.03%
2017	Copper Ore 34.5%	Refined Copper 33.0%	Raw Copper 7.24%

Argentina

Exports from Argentina to China

	Top 1	Top 2	Top 3
2021	Soybeans 30.0%	Frozen Bovine Meats 28.3%	Sorghum 8.29%
2020	Soybeans 34.5%	Frozen Bovine Meats 31.8%	Soybean Oil 5.47%
2019	Soybeans 43.5%	Frozen Bovine Meats 29.8%	Crustaceans 3.91%
2018	Soybeans 30.2%	Frozen Bovine Meats 19.8%	Crude Petroleum 14.0%
2017	Soybeans 55.2%	Crude Petroleum 10.9%	Frozen Bovine Meats 9.31%

Peru

Exports from Peru to China

	Top 1	Top 2	Top 3
2021	Copper Ore 61.0%	Iron Ore 9.67%	Animal Feed 8.19%
2020	Copper Ore 52.0%	Refined Copper 10.1%	Iron Ore 9.25%
2019	Copper Ore 60.2%	Animal Feed 8.1%	Refined Copper 6.9%
2018	Copper Ore 61.3%	Animal Feed 9.22%	Refined Copper 8.44%
2017	Copper Ore 61.3%	Animal Feed 10.1%	Refined Copper 9.08%

Source: Author's compilation based on the Observatory of Economic Complexity (https://oec.world)

Some are concerned by the prospect of China's increasing demand for agricultural commodities potentially encouraging the practice of genetically modified (GM) soy monoculture and land grabbing (Giancola et al. 2009; Svampa 2013); others argue that because the increased trade with China is confined primarily to exports of primary products, it may lead to deindustrialization and a loss to China of both domestic and foreign markets for manufacturing goods produced in Latin America. Expanded GMO production and the region's declining share of industrial production in recent years are interpreted by some as evidence that such fears are warranted (Medeiros and Mazat 2019; TELAM 2014).

Whether the trade between China and Latin America is a reflection of a stratified world system or a relationship that can yield mutually beneficial outcomes is open to debate (Jenkins and Dussel 2009; Lopes et al. 2021). However, as discussed in Chapter Six, this evolving trade

pattern, together with China's growing influence—especially given China's potentially important role in the global agri-biotech regulatory chain—in a region that has traditionally had stronger ties with the United States and European Union, clearly impact innovation prospects for latecomers in Latin America.

Compared to its dominance in the agri-biotech industry, Chinese firms account for a relatively small fraction of the global pharmaceuticals market today. The fact that it has the second largest market in the world (see Table 3.1.1 and Table 3.1.2 in Chapter 3), together with its over twenty-fold growth in expenditure on R&D for the pharmaceuticals industry (from $162.6 million in 2000 to $3249.2 million in 2011) (Ni et al. 2017), however, suggests that the Chinese pharmaceuticals sector is destined for continued growth in the coming decades. And this, in turn, suggests that China's trade power may be expected increasingly to impact the prospects of other latecomer economies. The Korean pharmaceuticals industry, too, then, may have its fortunes shaped by decisions made in China in the upcoming years.

The rise of China also raises a question about how we can think about global hierarchies and development trajectories today. This dissertation illustrates using indicators such as GDP per capita, innovative capacity, numbers of patent, or the human development index many not necessarily capture the developmental trajectory of a given country in the knowledge economy era. For instance, developmental studies continue to categorize China as a semi-peripheral country, despite its economic achievements. But does China really belong to the semi-periphery zone, alongside countries with small economies like Costa Rica? We need to take more industry-specific characteristics into account if we are to formulate more effective policies for promoting development. And the global regulatory chain model provides new insights into what accounts for development today – the extent to which a country can navigate, challenge, and overcome regulatory hurdles encountered at the global level will determine the developmental trajectory of a country in the knowledge economy era.

In conclusion, this dissertation aims to update the sociological understanding of developmental states, addressing in addition to issues related to the kind of autonomy in pharmaceuticals production, which many non-Western countries aim to achieve, even more intently since the outbreak of COVID-19.

Appendix I. FDA Approval Status of Korean Pharmaceuticals

	Year Approved	Company Name	Drug Name	Treatment Type	Type of Drug
1	2003	LG Chem	Factive	Antibiotic	New chemical drug
2	2007	LG Chem	Valtropin	HGH[76]	Biosimilar
3	2013	Hanmi	Esomezol	GERD	IMD[77]
4	2014	Dong-ah ST	Sivextro	Antibiotic	New chemical drug
5	2015	Daewoong	Meropenem	Antibiotic	Generic
6	2016	Celltrion	Inflectra	MAB	Biosimilar
7	2016	SK Chem	Afstyla	Antihemophilic	New Biologic
8	2017	Samsung Bioepis	Renflexis	MAB	Biosimilar
9	2017	Huons	0.9% Sodium Chloride Solution	Injection	Generic
10	2018	Celltrion	Truxima	Oncology	Biosimilar
11	2018	Celltrion	Temixys	HIV	IMD
12	2018	Celltrion	Herzuma	Oncology	Biosimilar
13	2018	Huons	Lidocaine	Injection	Generic
14	2018	Samsung Bioepis	Ontruzant	Oncology	Biosimilar
15	2019	Daewoong	Jubo	Botox	New Biologic
16	2019	SK Biopharm	Sunosi	Wake-promoting agent	New Chemical Drug
17	2019	Celltrion	Linezolid	Antibiotic	Generic
18	2019	Samsung Bioepis	Eticovo	MAB	Biosimilar
19	2019	Samsung Bioepis	Hadlima	MAB	Biosimilar
20	2019	SK Biopharm	XCOPRI	Anti-Seizure	New Chemical Drug
21	2019	SK Chem	SID710	Alzheimer's (patch-type)	Generic
22	2019	Huons	Bupivacaine	Anesthetic injection	Generic
23	2021	Samsung Bioepis	Byooviz	Anti-VEGF[78]	Biosimilar

[76] HGH stands for a human growth hormone.
[77] IID stands for incrementally improved drug.
[78] Anti-VEGF is a vascular endothelial growth factor therapy that can treat retinal vascular disorders. Samsung Bioepis created this biosimilar in a joint venture with Biogen.

Appendix II. EMA Approval Status of Korean Pharmaceuticals

	Year Approved	Company Name	Drug Name	Treatment Type	Type of Drug
1	2006	LG Chem	Valtropin	HGH	Biosimilar
2	2013	SK Chem	SID710	Alzheimer's	Generic
3	2013	Celltrion	Remsima	MAB	Biosimilar
4	2015	Dongah-ST	Sivextro	Antibiotic	New Chemical Drug
5	2015	Shinpoong	Pyramax	Malaria	New Chemical Drug
6	2016	Samsung Bioepis	Benepali	MAB	Biosimilar
7	2016	Samsung Bioepis	Flixabi	MAB	Biosimilar
8	2017	SK Chem	Afstyla	Antihemophilic	New Biologic
9	2017	Samsung Bioepis	Lusuduna	Diabetes	Biosimilar
10	2017	Celltrion	Truxima	Oncology	Biosimilar
11	2017	Samsung Bioepis	Imraldi	MAB	Biosimilar
12	2017	Samsung Bioepis	Ontruzant	Oncology	Biosimilar
13	2018	Celltrion	Herzuma	Oncology	Biosimilar
14	2019	Daewoong	Nuceiva	Botox	New Biologic
15	2019	Celltrion	Remsima SC	MAB	Biobetter
16	2020	Sk Biopharm	Sunosi	Wake-promoting agent	New Chemical Drug
17	2020	Samsung Bioepis	Avincio	Oncology	Biosimilar
18	2021	Celltrion	Regkirona	Covid-19	New Biologic
19	2021	Samsung Bioepis	Byooviz	Anti-VEGF	Biosimilar
20	2021	Celltrion	Yuflyma	MAB	Biosimilar
21	2022	Celltrion	Vegzelma	Oncology	Biosimilar
22	2023	Samsung Bioepis	Epysqli	PNH[79]	Biosimilar

[79] PNH stands for paroxysmal nocturnal hemoglobinuria, which is a rare, life-threatening disease of the blood.

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