

**Louvain School of Management
and Nova School of Business & Economics**

**To what extent has the
Pharmaceutical Strategy for Europe
(European Commission, 2020)
achieved its objectives of
attractiveness, competitiveness,
access, and innovation?**

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Abstract

This thesis evaluates the impact of the European Commission's Pharmaceutical Strategy for Europe (2020-2024) across its four pillars: attractiveness, competitiveness, access to medicines, and innovation. Using a mixed-methods approach combining quantitative analysis and qualitative interviews with industry professionals and policymakers, the study assesses whether the Strategy's measures have delivered on their stated objectives.

The quantitative analysis tests four hypotheses using public data from the European Medicines Agency, the European Federation of Pharmaceutical Industries and Associations, Eurostat, and the World Health Organization. Results show that the Clinical Trials Regulation and CTIS portal have not reversed Europe's declining clinical trial market share, which fell from 27% to 20% between 2015 and 2024. The SPC Manufacturing Waiver's impact on pharmaceutical exports could not be isolated due to COVID-19 vaccine effects masking the policy signal. However, the HTA Regulation demonstrated statistically significant convergence in patient access delays across member states, and the PRIME scheme successfully reduced approval times by 4.7 months.

Qualitative interviews reveal that administrative simplification alone cannot overcome Europe's structural fragmentation and the competitive pull of United States industrial policy. The Strategy's objectives are coherent, but implementation suffers from insufficient political commitment, limited resources, and the persistent division of competences between the European Union and member states.

The thesis concludes that the Pharmaceutical Strategy for Europe represents a necessary but insufficient response to the sector's challenges. Recommendations include redesigning the CTIS portal around a product-centered model, finalizing the SPC Waiver with clear parameters, deepening HTA coordination between European and national levels, and elevating pharmaceutical policy to strategic priority status alongside energy and defense.

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Introduction

Context

The pharmaceutical industry stands as a cornerstone of Europe's strategic autonomy, public health, and economic stability. Understanding whether the strategy delivers on its promises has direct consequences for patients waiting longer in some countries than others, for companies deciding where to invest, and for Europe's ability to remain competitive in a sector that is increasingly contested by the United States and China. However, in recent years, the sector has faced mounting challenges, including intensified global competition from the United States and China, as well as internal disparities in patient access to medicines. In response to these pressing issues, the European Commission adopted the "Pharmaceutical Strategy for Europe" in 2020.

The European pharmaceutical sector is currently operating in a volatile geopolitical environment. Although the European Union and the United States reached a trade agreement in July 2025 to stabilize transatlantic relations, pressure remains high. On February 20, 2026, President Trump signed a proclamation imposing a 10% import duty on all foreign goods, targeting the U.S. trade deficit. This measure is particularly significant, given that bilateral trade between the two regions exceeded €1.6 trillion in 2024 (EU-US Trade Deal Explained, 2025). In this context, the potential for trade barriers and global volatility directly affects the stability of European exports. Such external shocks are a backdrop for the Pharmaceutical Strategy for Europe, because they demonstrate the importance of the European Union's objectives regarding strategic autonomy and industrial competitiveness.

This strategy acts as a comprehensive public policy framework, and is built upon four fundamental pillars designed to revitalize the ecosystem: The first pillar aims at enhancing the attractiveness of the European industry for R&D and investment, ensuring that Europe remains a competitive hub for clinical research and innovation. Secondly, supporting the competitiveness, innovation, and sustainability of the EU pharmaceutical industry, and the development of effective, safe, high-quality, and more environmentally friendly medicines. Thirdly, ensuring access to affordable medicines for patients and addressing unmet medical needs, while reducing disparities between member states. Lastly, fostering innovation by accelerating the development of breakthrough therapies, particularly in areas where medical needs remain unmet.

Research problem & objectives

This thesis focuses on evaluating this strategy implemented in 2020. Its aim is to determine whether the European Commission's ambitions have had a positive impact on the pharmaceutical sector. This thesis was written at a particularly relevant moment: five years after the strategy's adoption, enough time has passed to observe first measurable outcomes, yet the reform process is still ongoing. Evaluating the strategy at this stage is useful not only academically, but also for policymakers and industry stakeholders who need evidence-based feedback to adjust the framework before its next revision cycle. To this end, the research addresses the following question:

“To what extent does the European Commission’s policy achieve its objectives of attractiveness, innovation, access, and competitiveness in the European pharmaceutical sector?”

The primary objective of this thesis is therefore to evaluate the effectiveness of this EU initiative as a public policy framework. This evaluation is twofold: Firstly, quantify the outcomes; the aim is to measure the concrete changes that can be observed in the industry's performance following the implementation of this strategy. Secondly, explain the results; behind the figures, the aim is to understand why certain objectives may have been achieved, while others have not, by identifying, for example, the gaps between political intent and practical implementation.

Methodology

To answer this research question, a combination of quantitative and qualitative approach will be used.

The quantitative approach assesses the strategy's impact by analyzing European Commission measures across the four pillars: attractiveness, competitiveness, access, and innovation. The objective is to provide an evidence-based assessment using inferential statistics performed on R. This quantitative analysis is based on publicly available data. While various reports and online archives were consulted, the data were primarily consolidated from the European Medicines Agency (EMA) public databases, the European Federation of Pharmaceutical Industries and Associations (EFPIA), Eurostat, and the European Commission's public sources.

The qualitative approach will consist of interviews and will be used to interpret the quantitative results. Perspectives from two different groups will be gathered: players in the pharmaceutical

industry to understand market obstacles and perceived changes, and members of the European Commission to gain insight into the internal intentions and constraints of the policy.

This research encountered several practical limitations. On the quantitative side, pharmaceutical export data falls under a single customs category (SITC 54) that does not distinguish between generic and patented medicines. This makes it difficult to isolate the precise impact of measures such as the SPC Manufacturing Waiver. Additionally, some indicators, such as the W.A.I.T. data, are published annually by industry associations rather than public institutions, which introduces potential reporting biases. On the qualitative side, access to certain institutional profiles was limited, and several interviewees requested full anonymity, which restricts the ability to fully attribute some of the insights gathered.

1. Literature review

1.1 Structure of the Pharmaceutical Industry

The pharmaceutical ecosystem is characterized by great complexity and a large number of different players operating at the intersection of science, business, and public policy. While the industry has several different segments, the main dynamics of innovation and market access are driven by two categories of players: “Big Pharma” and biotechnology startups.

1.1.1 Big Pharma

“Big Pharma” refers to the world's largest pharmaceutical companies, generally multinationals generating billions of dollars in annual revenue. Pfizer, Roche, Novartis, Johnson & Johnson, and Sanofi are examples. These companies are characterized by their vertical integration and giant size. They have the resources to conduct global clinical trials, market drugs worldwide, and navigate complex regulatory and market access environments (Umbrex, 2025).

Despite their size, these companies are under intense pressure to maintain growth. They invest heavily in innovation, often 15-20% of their revenues, but are increasingly reliant on external sources to renew their pipelines. As a result, many of these companies have become “network orchestrators,” focusing on business strategy while partnering with or acquiring smaller companies or biotech startups to gain access to innovative technologies.

For illustration, the top 10 Big Pharma companies by revenue, market capitalization, and R&D expenditure are listed in Appendix A (Umbrex, 2025).

1.1.2 Biotechs

Biotechs are the other category of players in the pharmaceutical sector. These firms are research-oriented firms that often emerge from academic science, focusing on cutting-edge biological or genetic approaches to treating disease. They range from small startups (with a handful of scientists working on one experimental drug) to mid-size companies with a few marketed products.

Unlike Big Pharma, these companies are generally not fully integrated. They excel at discovery and early-stage clinical development, but they lack the capital and infrastructure for large-scale manufacturing or global commercialization. Biotechs are often characterized by high risk and high reward: many will fail to produce a viable drug, but a few achieve breakthroughs (e.g. pioneering new classes of therapy for previously untreatable diseases). Investors pay close attention to biotech pipelines, clinical trial results, and partnership news, as these can lead to significant value creation (Umbrex, 2025).

1.1.3 Relationship between Big Pharma and Biotechs

The relationship between these two groups of players is fundamental to the structure of the industry. Innovation often comes from startups, which is then integrated into the portfolios of Big Pharma through licensing deals, partnerships, or mergers and acquisitions (M&A).

This dynamic intensifies during "patent cliffs," when large companies lose exclusivity on major products and aggressively acquire Biotechs to fill revenue gaps. For this thesis, analyzing the European pharmaceutical sector requires examining the conditions of these two players: the ability of Biotechs to innovate and grow, and the ability of Big Pharma to retain their headquarters, R&D centers, and production facilities within Europe.

1.2 The European Regulatory Framework

The pharmaceutical sector in Europe is governed by a particular duality. Unlike in the United States, where the FDA is a single, central authority for both approval and market access, the European system operates on a division of powers between the European Union and its member states. This structure means that science is harmonized within the EU, but the economic aspect of market access is fragmented across different states.

1.2.1 EU Competence

At the supranational level, the European Union is responsible for ensuring the quality, safety, and efficacy of medicines entering the Single Market. This mandate is carried out by the European Medicines Agency (EMA) through the “Centralized Procedure.” There are three things to consider when discussing the EU's competence:

- **Scope and Mandate:** Under Regulation (EC) No 726/2004, the Centralized Procedure is mandatory for biotechnological products, orphan medicines, and new active substances treating cancer, HIV, diabetes, neurodegenerative disorders, and viral diseases.
- **The Assessment Process:** The scientific evaluation is conducted by the Committee for Medicinal Products for Human Use (CHMP). This rigorous process is legally bound to a timeframe of 210 active days to assess the risk-benefit balance of a new medicine.
- **The Single License:** Following a positive opinion from the CHMP, the European Commission has 67 days to grant a Marketing Authorisation (MA). This single authorization is valid simultaneously in all EU Member States, as well as in Iceland, Liechtenstein, and Norway.

This system ensures that European patients have access to new therapies at the same time as the license is granted. However, possession of a license does not guarantee that a drug will be available or reimbursed in a particular country.

1.2.2 Member State Competence

Once a drug is authorized by the EU, it is exclusively the responsibility of the member state to include the drug commercially in its national health systems. According to Article 168(7) of the Treaty on the Functioning of the European Union (TFEU), the definition of health policy and the organization of health services are national responsibilities. Consequently, manufacturers must navigate through several Pricing and Reimbursement (P&R) systems:

- **Reimbursement decisions:** National authorities evaluate whether to cover the cost of a drug based on local Health Technology Assessments (HTA). These assessments consider clinical benefit, cost-effectiveness, and the specific budget constraints of the national health system.
- **Pricing mechanisms:** Countries employ various mechanisms to control costs. A dominant method is External Reference Pricing (ERP), where a country sets the price of a drug by

benchmarking it against the price of the same drug in a "basket" of other European countries.

- Patient Co-payment: Member States also independently determine the level of patient contribution (co-payment), which can vary based on the severity of the illness or the patient's socio-economic status.

1.2.3 The regulatory intersection: The Transparency Directive

To mitigate the risk that national pricing measures might act as non-tariff barriers to trade, the EU introduced Council Directive 89/105/EEC, known as the Transparency Directive.

This directive aims to reduce the gap between EU authorization and national market access by imposing procedural rules on member states:

- Time limits: It mandates that national pricing and reimbursement decisions must be made within 90 days each (or 180 days for a combined process) following the application by the marketing authorization holder.
- Objective criteria: Any decision to freeze prices or exclude a drug from reimbursement must be justified by objective and verifiable criteria.

Despite these regulations, the “time to patient,” the delay between the EMA's centralized approval and the actual reimbursement in a Member State, remains a critical point of disparity within the EU, which has a significant influence on access and competitiveness, which are pillars analyzed in this thesis.

1.3 The Pharmaceutical Strategy for Europe (2020)

Adopted by the European Commission on November 25, 2020, the Pharmaceutical Strategy for Europe is a cornerstone of the European Health Union. It serves as a policy framework designed to safeguard the future of the European pharmaceutical sector. Unlike previous adjustments to the strategy, this latest version proposes a reform covering the entire life cycle of a drug, from R&D and manufacturing to authorization and patient access.

1.3.1 Objectives: the four pillars

The objectives of this strategy are structured around four main pillars:

1. Enhancing resilience: this pillar of the strategy aims to diversify supply chains and ensure the availability of medicines in order to avoid shortages. This pillar is linked to

“attractiveness,” which is essential for this research; to achieve resilience, Europe must be an attractive place for investment and manufacturing, thereby reducing its significant dependence on third countries for essential ingredients.

2. Ensuring competitiveness: the strategy recognizes that, although Europe is a major global player, its leadership is being challenged by the United States and China. To counter this decline and preserve Europe's attractiveness, the strategy proposes simplifying regulatory procedures and reducing administrative burdens in order to promote a globally competitive environment for industrial investment.
3. Ensuring access and affordability: the main objective is to ensure that patients across member states have timely and equitable access to medicines. The commission would like to address the significant disparities between countries in terms of time to market. It would also like to ensure that healthcare systems can bear the cost of innovative treatments.
4. Supporting innovation: the strategy aims to promote competitiveness and innovation, particularly in areas where medical needs are unmet (such as neurodegenerative diseases and rare cancers) and antimicrobial resistance (AMR).

1.3.2 Political logic: why a new strategy?

The creation of this strategy by the European Commission was motivated by several structural challenges and crises, which led to the adoption of a more assertive industrial policy. Firstly, the COVID-19 pandemic served as a wake-up call, revealing the fragility of global supply chains and the lack of coordination between member states. Another factor that prompted this strategy was market failures in innovation. The commission found that investments were not being made in areas where patients needed them most (e.g., the lack of new antibiotics), but in areas with commercial potential. The goal is therefore to move from a system focused purely on commercial potential to one focused on public health needs. Finally, global competition was also a factor that drove this strategy. With the US and China actively supporting their biopharmaceutical sectors, the EU risked losing its historical advantage in R&D. The strategy is therefore an attempt to reverse this trend by modernizing a regulatory framework that had not been updated for nearly two decades. Indeed, the EU's general pharmaceutical legislation is based mainly on two texts: Directive 2001/83/EC (dating from 2001) and Regulation 726/2004 (dating from 2004). Between 2004 and 2020, science exploded (gene therapies, personalized medicine, artificial intelligence), while these texts were written when these technologies did not exist. The regulatory framework had therefore

become unsuited to modern innovations, slowing down the arrival of medicines and making Europe less attractive.

1.3.3 Proposed reforms: from policy objectives to measurable actions

To turn these objectives and ambitions into reality, the European Commission has put in place a wide range of measures, all of which are mentioned and detailed in the official Communication (COM/2020/761). The strategy sets out a roadmap of more than 50 measures, legislative and non-legislative, to be implemented between 2021 and 2025.

Several flagship legislative reforms flow from this revision. First, the Clinical Trials Regulation (CTR 536/2014) and its implementation tool, the CTIS portal, aim to replace 27 national submission procedures with a single European application, directly targeting Europe's declining attractiveness for clinical research. Second, the SPC Manufacturing Waiver (Regulation 2019/933), adopted just before the strategy, removes a legal barrier preventing EU-based generic and biosimilar manufacturers from competing on global markets during the SPC period. Third, the HTA Regulation (adopted in 2021) aims to harmonize clinical assessments across member states and reduce the fragmentation that delays patient access to new medicines. Finally, the strategy formally integrates the PRIME scheme (Priority Medicines) into the regulatory framework, providing enhanced early support from the EMA to accelerate the development and approval of medicines targeting unmet medical needs.

Beyond legislative measures, the strategy also introduced non-legislative actions, including a structured dialogue on supply chain vulnerabilities, the creation of HERA (the Health Emergency Preparedness and Response Authority), and new incentives to address antimicrobial resistance, an area where market forces alone have proven insufficient to stimulate the required investment.

The four measures introduced above, the CTR/CTIS portal, the SPC Manufacturing Waiver, the HTA Regulation, and the PRIME scheme, constitute the analytical backbone of this thesis. These measures were chosen because of their representativeness (they constitute the EU's response to the major problem for the pillar in question), their materiality (they are concrete actions, not declarations of intent), and their measurability (they make it possible to define specific quantifiable performance indicators for the period 2015–2024).

Each measure is evaluated as the primary EU response to its respective pillar's challenge, and each gives rise to a central hypothesis tested in the impact assessment:

1. **H1 (Attractiveness):** The implementation of the CTR and the CTIS portal has successfully reversed the structural decline of Europe's global market share in clinical research by simplifying administrative procedures.
2. **H2 (Competitiveness):** The SPC Manufacturing Waiver has created a statistically significant jump in the volume of extra-EU pharmaceutical exports by allowing EU-based generic and biosimilar manufacturers to compete on equal terms.
3. **H3 (Access):** The preparation and adoption of the HTA Regulation have led to a convergence of access delays among Member States, reducing the variance of patient waiting times across the Union.
4. **H4 (Innovation):** The PRIME scheme effectively accelerates market entry for breakthrough therapies by reducing the Marketing Authorization delay compared to standard regulatory pathways, even when accounting for product complexity.

By testing these hypotheses, an accurate statistical assessment to determine whether the Commission's main objectives are translating into concrete results in the European pharmaceutical ecosystem will be obtained.

1.4 Conditions for a successful Pharmaceutical Strategy

To assess the effectiveness of this pharmaceutical strategy for Europe, we must first define the determinants of a successful pharmaceutical ecosystem. The literature and industry data provide us with further information on the four pillars of the strategy: attractiveness, competitiveness, market access, and innovation.

1.4.1 Attractiveness

Attractiveness is defined by a region's ability to attract Foreign Direct Investment (FDI) and host clinical research. The literature reveals a worrying trend for Europe compared to the United States and China. The United States has overtaken Europe as the main hub for pharmaceutical R&D. Between 2002 and 2022, the gap between R&D investment in the United States and Europe widened significantly. While the United States increased its R&D spending much more rapidly, Europe's share of global new drug launches declined. (EFPIA,2022).

Clinical trials are also a key indicator, as the ability to host clinical trials is essential to the success of the strategy. Europe is facing a decline in its share of commercial clinical trials, which fell from 25% in 2013 to 19% in 2023 (EFPIA, 2024). The speed of trials is also important. The United States and China are faster at setting up trials. For example, oncology trial starts have fallen consistently in Europe since 2021 while increasing in the US, partly due to the dispersion of regulatory requirements and the slowness of contract negotiations (EFPIA, 2024). The United States has a single market and a unified regulatory framework, while Europe has fragmentation that acts as a deterrent. Empirical evidence of CTIS's shortcomings has been documented in academic literature. Patrick-Brown et al. (2024) report that approval times improved slightly but remain unacceptably slow. The administrative burden has increased dramatically: a single protocol amendment now requires over 800 documents compared to fewer than 200 under the previous system. The authors also confirm that national requirements remain fragmented and conflicting despite CTIS's stated harmonization objective.

1.4.2 Competitiveness

A successful strategy must ensure that the region remains an industrial powerhouse to support economic resilience and trade balance. The pharmaceutical industry is the sector with the highest trade surplus in the EU, with €221 billion in 2025 (Eurostat, 2026). To maintain this surplus, competitive energy costs and favorable policies are needed. The literature highlights the importance of modernizing production to reduce dependence on Asia. The transition from batch processing to continuous manufacturing is the key innovation for improving the efficiency, quality, and flexibility of the supply chain (QbD Group, 2025).

1.4.3 Market access

The strategy fails if innovation does not reach the patient. Market access is measured by the time between regulatory approval and actual availability (reimbursement). The European Federation of Pharmaceutical Industries and Associations (EFPIA) uses the W.A.I.T. indicator to measure these delays. The data show huge disparities within the EU: patients in Germany wait an average of 128 days, while those in Romania wait 828 days (2020-2023) (IQVIA, 2025).

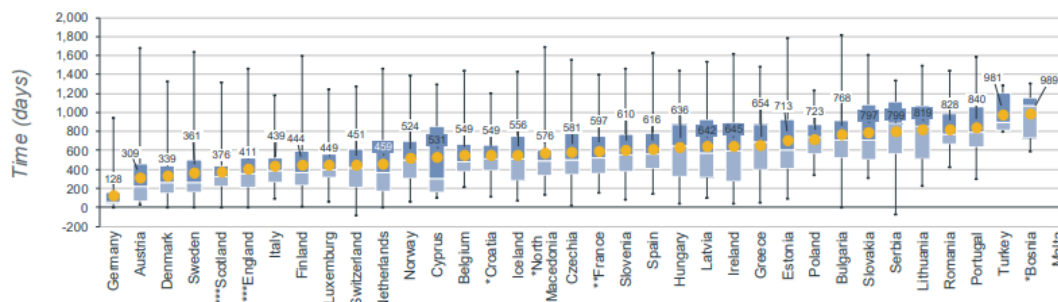


Figure 1: Time from central approval to availability (2020-2023) (IQVIA, 2025).

The literature suggests that these delays are not due to the EMA, but to national pricing and reimbursement processes. A successful strategy must address the gap between EU licensing and member state budget control. Beyond speed, availability is also an issue. In many southern and eastern European countries, less than 30% of centrally approved drugs are actually available to patients, compared to more than 90% in Germany (2019-2022) (IQVIA, 2024).

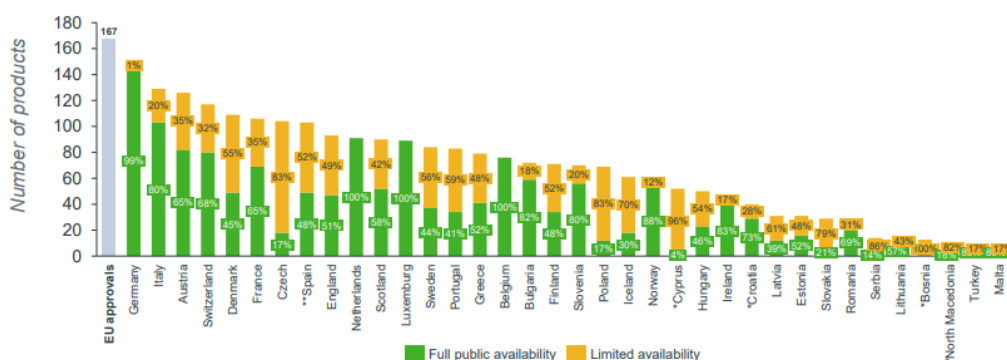


Figure 2: Rate of full availability (%; 2019-2022) (IQVIA, 2024).

1.4.4 Innovation

The literature and data on innovation in the pharmaceutical sector show that developing a new drug is a long, risky, and costly process. According to estimates, the cost of developing a new drug, including the cost of failures, can be as high as \$2.6 billion (DiMasi et al., 2016, p. 22). This significant investment requires a policy framework that can offer predictable returns in order to justify the risk.

Another factor to consider is the increasing complexity within the sector. The industry is shifting from traditional small molecules to complex biologic therapies, gene therapies, and “next-generation biotherapies.” A successful strategy must therefore support this technological evolution.

In 2024, the industry invested heavily in innovation, with global R&D funding reaching \$102 billion (IQVIA, 2025), a significant increase over the previous year.

It should also be noted that intellectual property (IP) protection is essential for innovation. It provides the necessary “incentive function” to attract venture capital and support R&D efforts during the 10 to 15 years it takes to bring a drug to market.

1.4.5 Lessons from the past

By analyzing certain European initiatives from the past, we can identify reasons why a pharmaceutical strategy succeeds or fails, and the key factors for success or failure. Literature highlights four important factors.

1. A major factor in failure in terms of access and competitiveness is the manipulation of a product's lifecycle. The Sector Inquiry (2009) shows that market forces alone cannot guarantee a smooth transition to cheaper generic drugs when patents expire. The report reveals that innovative companies all use a toolbox of strategies to delay competition. For example, they file multiple patents for the same drug (“patent clusters”) and launch second-generation products with minor modifications just before losing their exclusivity. A successful strategy must therefore clearly distinguish between protecting genuine innovation and combating abusive practices that prevent access to cheaper medicines.
2. The Pharmaceutical Forum (2008) and the Sector Inquiry (2009) both identify national pricing systems as a major obstacle. Although the EU has the Transparency Directive, which sets strict deadlines (90 or 180 days) for decisions, the Inquiry showed that these deadlines are often not met by Member States. The result is significant delays for patients and uncertainty for companies. Therefore, a strategy that focuses solely on regulatory approval at the EU level, without addressing administrative delays in each country at the national level, will not improve access.
3. For a strategy to truly reward innovation, it must define what “value” means. The Pharmaceutical Forum (2008) emphasized the need for a common method for assessing “relative effectiveness.” In concrete terms, this means scientifically determining whether a new drug is truly better than existing treatments. Without a common definition, different countries arrive at different conclusions about the same drug. This fragments the market

and confuses investors. To be successful, a policy must harmonize data requirements between regulators (EMA) and national payers.

4. Finally, a strategy can only succeed if the rules are applied in the same way throughout Europe in order to secure the market. The Report on Falsified Medicines (2024) shows that even if there are strict laws (such as the Falsified Medicines Directive), there will still be weaknesses if Member States do not apply these laws uniformly. In particular, the report highlights delays in applying these laws in countries such as Greece and Italy. Confidence in the European system, which is essential to its attractiveness, depends on the elimination of these weaknesses in the supply chain.

2. Impact Assessment: Quantitative Analysis of the Pharmaceutical Strategy's Measures

Having analyzed the strategy's context and objectives, this section evaluates its effectiveness empirically. By testing the hypotheses mentioned in section 1.3.3., the impact of measures taken by the European Commission to support the four pillars of the strategy will be assessed.

The table below summarizes the assessment of the pillars in this section.

Pillar	Identified Issue	Concrete Measure evaluated	Outcome Indicator	Evaluation Method
Attractiveness	Decline of R&D in Europe compared to the US/ Asia	Clinical Trials Regulation (CTR) & CTIS Portal	Global market share of clinical trials (%)	Trend Break Analysis & Multiple Linear Regression
Competitiveness	Relocation of industrial production	SPC Manufacturing Waiver (linked to IP Action Plan)	Volume of extra-EU pharmaceutical exports	Linear Regression (with dummy variable)
Access	Inequalities in access delays between Member States	HTA Harmonization (EU HTA Regulation)	Variance of access delays (W.A.I.T Indicator)	F-Test (variance comparison) & Sigma-convergence regression
Innovation	Slow market entry for breakthrough therapies	PRIME Scheme (EMA Priority Medicines)	Approval times and success rates	Multiple Linear Regression

Table 2: Methodological framework: assessment of Pharmaceutical Strategy pillars

2.1 Analysis of Pillar 1: Attractiveness

Assessing the pillar of attractiveness involves evaluating the effectiveness of the Clinical Trials Regulation (CTR 536/2014) and its implementation tool, the CTIS (Clinical Trials Information System) portal, which became mandatory on January 31, 2023. The European Commission's aim with this regulation was to modernize clinical research by simplifying administrative procedures. The main objective was to replace all national applications with a single submission via a European portal (the CTIS), to harmonize dossiers and increase the efficiency of multi-state trials.

To assess EU attractiveness, absolute trial volumes were excluded as they may be biased by natural global research growth. Instead, the analysis was based on relative market share (%). The data were extracted from the WHO International Clinical Trials Registry Platform, which aggregates data from primary global registries (EudraCT for Europe, ClinicalTrials.gov for the USA, etc.). For the statistical analysis, a panel covering the period 2015 to 2024 was constructed. For each year, the following ratio was calculated :

$$\text{Regional Market Share}_i = \frac{\text{Number of trials in Region}_i}{\text{Total global trials}} \times 100$$

This methodological choice allows us to isolate Europe's competitive performance relative to its strategic rivals (the United States and Asia), independently of the sector's expansion cycles. The results obtained are the following:

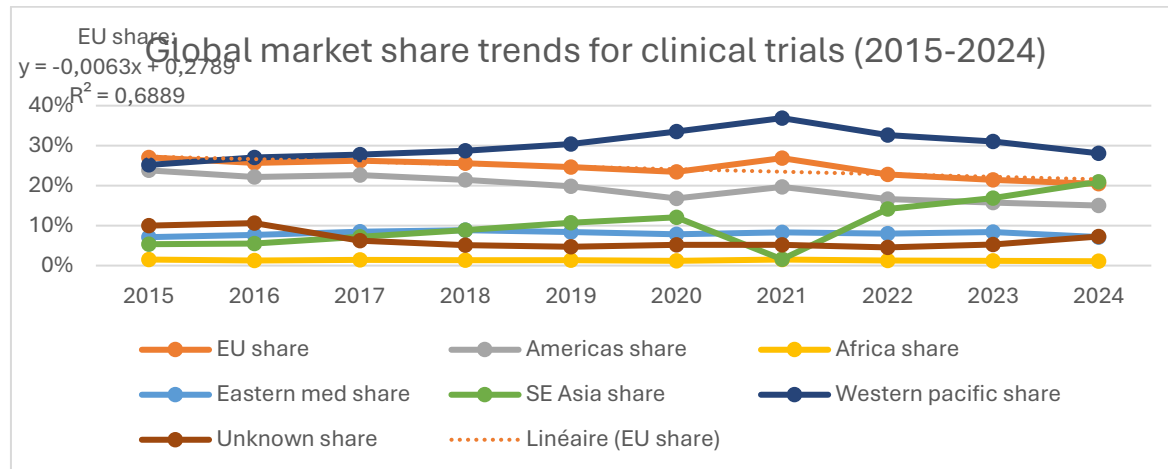


Figure 3: Global market share trends for clinical trials (2015-2024). Author's calculations based on World Health Organization (WHO) data.

The graphical analysis of market share trends over the decade 2015-2024 highlights three key points:

1. Structural erosion of the European position: The European Union curve (orange line) shows a continuous downward trend. While Europe captured approximately 27% of global clinical trials in 2015, this share fell to 20% in 2024. This loss of 7 percentage points in market share confirms the Commission's 2020 diagnosis: Europe suffers from a comparative attractiveness deficit.
2. The emergence of Asian competition: the graph reveals the rise of the South-East Asia region (green line). According to the WHO, this region includes India, Thailand, Indonesia, Bangladesh, Sri Lanka, Nepal, etc. Starting from a position around 5% in 2015, this region has experienced exponential growth.
3. The “crossover” of 2024: 2024 marks a geopolitical turning point in clinical research. For the first time, Southeast Asia’s market share (21%) has surpassed that of Europe (20%). This confirms the shift in the center of gravity of pharmaceutical R&D towards the East.

With this graph, we sought to observe whether the entry into force of the CTR regulation (2022) and the mandatory use of the CTIS portal (January 2023) had triggered a positive “trend break” (a recovery in the curve). The data for 2023-2024 show that the downward trend has not been reversed. The slope of the European curve remains negative after implementation, indicating that administrative simplification has not had an immediate “shock” effect on attractiveness.

To provide scientific validation of these observations, a multiple linear regression using an interrupted time series design was performed. The objective is to determine whether the 2022 Clinical Trials Regulation had a statistically significant impact on the EU's market share, while controlling global trends. The model has the following variables:

- Time: to measure the natural downward trend since 2015.
- CTR_Effect & Time_Since_CTR: to identify any immediate shock or change in the speed of decline after the 2022 reform.
- Americas share: used as a control variable to see if the decline is specific to Europe or part of a global Western trend.

$$EU_Share_t = \beta_0 + \beta_1 \cdot Time_t + \beta_2 \cdot CTR_Effect_t + \beta_3 \cdot Time_Since_CTR_t + \beta_4 \cdot Americas_Share_t + \epsilon_t$$

The results of the regression are the following:

```
Call:
lm(formula = "EU share" ~ Time + CTR_Effect + Time_Since_CTR +
  "Americas share", data = data_p1)

Residuals:
    1      2      3      4      5      6      7
0.0059014 0.0009275 -0.0035974 -0.0052764 -0.0059089 0.0019904 0.0059633
    8      9     10
0.0004026 -0.0008051 0.0004026

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  0.051778   0.046272   1.119  0.31400
Time         0.005715   0.002030   2.816  0.03730 *
CTR_Effect   -0.004551   0.009303  -0.489  0.64542
Time_Since_CTR -0.010358  0.004040  -2.564  0.05043 .
"Americas share" 0.870031  0.186881   4.656  0.00555 **
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 0.005511 on 5 degrees of freedom
Multiple R-squared:  0.9681,    Adjusted R-squared:  0.9427
F-statistic: 37.99 on 4 and 5 DF,  p-value: 0.0006196
```

Figure 4: Statistical analysis on the CTR.
Author's calculations using R software based
on World Health Organization (WHO) data.

The regression results validate the trends observed in the clinical trial data. With an adjusted R-squared of 0.94, the model explains almost 94% of the variations in the European Union's market share. One important result is the Americas share ($p = 0.0055$). The strong and positive correlation (coefficient of 0.87) shows that Europe's decline is not an isolated local failure. Instead, it proves that Europe is following a broader macroeconomic shift affecting Western markets as the global center of gravity for R&D moves towards Southeast Asia. Regarding the Clinical Trials Regulation (CTR), the model indicates that the reform has not yet had a shock effect. The CTR_Effect variable is not significant, which means that there was no immediate jump in attractiveness in 2022. Furthermore, the Time_Since_CTR ($p = 0.05043$) variable shows that the downward slope even accelerated slightly during the transition period. Based on these results, the first hypothesis H1 is being rejected. These findings are consistent with empirical evidence from Patrick-Brown et al. (2024), who document that CTIS has increased rather than reduced the administrative burden on sponsors in practice, with approval timelines still far exceeding those of competing regions. According to EFPIA (2025), average EU clinical trial approval times still exceed 100 days, compared with 30 to 60 days in other global regions, a gap that confirms the structural nature of Europe's attractiveness deficit.

In conclusion, while the CTR and CTIS portal simplification was necessary, the data suggests it has not decoupled Europe from the general Western decline. The loss of attractiveness appears to

be driven more by global competition and lower costs in Asian regions than simply by internal administrative barriers within Europe.

2.2 Analysis of pillar 2: Competitiveness

Analysis of the first pillar has shown a decline in the attractiveness of the European Union for clinical trials. However, to truly understand Europe's strategic autonomy, it is also necessary to look at its manufacturing industry.

The Supplementary Protection Certificate (SPC) was originally created to extend patent protection and compensate for the long approval process for medicines. But this system created a problem: it put European manufacturers of generic and biosimilar medicines at a disadvantage. Manufacturers outside Europe could start producing these drugs earlier because their intellectual property rules were less strict. To solve this problem and stop factories from moving abroad, the EU introduced the SPC Manufacturing Waiver in 2019 through Regulation (EU) 2019/933.

This waiver allows EU-based companies to manufacture generic or biosimilar versions of SPC-protected drugs under two conditions. First, they can produce these medicines for export to non-EU markets where protection has already expired. Second, during the final six months of the SPC, they can produce and stockpile these medicines in Europe to ensure they are ready for the EU market the day the certificate ends. This mechanism allows European factories to remain operational and competitive without waiting for the full legal expiration, conditional that they notify the authorities and use a specific logo on their packaging.

The analysis of the second pillar of the pharmaceutical strategy for Europe aims to measure the impact of this new law on Europe's industrial competitiveness. To do this, Eurostat data on pharmaceutical exports leaving the EU (SITC 54 category) from 2011 to 2025 was analyzed. Using Ordinary Least Squares (OLS) linear regression, the hypothesis that the SPC Waiver caused a significant jump in European exports was tested. To perform this regression, three main variables were created in R:

- The Dependent Variable (Y): The value of EU exports each year.
- The Waiver Dummy Variable: This is a statistical method used to measure the impact of a new policy. A value of "0" is assigned to all the years before the regulation (2011 to 2018), representing the period when European factories were restricted. A value of "1" is assigned

to the years from 2019 to 2025, representing the period when the SPC Waiver was fully active.

- The Time Trend Variable: By looking at the historical data, it was clear that European exports were already growing before 2019. To be scientifically accurate, a "time trend" variable (counting the years as 1, 2, 3, etc.) was added. It allows the model to separate the natural, continuous growth of the global market from the specific impact of the new European law.

$$Exports_i = \beta_0 + \beta_1 \cdot Time_Trend_i + \beta_2 \cdot Waiver_Active_i + \epsilon_i$$

After running the regression in R, the following results were given:

```
Call:
lm(formula = exports ~ time_trend + waiver_active, data = data_pillar2)

Residuals:
    Min       1Q   Median       3Q      Max
-23.353 -16.723  -1.066   13.135   44.833

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)    60.80      13.84   4.393 0.000876 ***
time_trend     16.70       2.57   6.498 2.94e-05 ***
waiver_active   10.34      22.26   0.465 0.650478
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 21.5 on 12 degrees of freedom
Multiple R-squared:  0.9408,    Adjusted R-squared:  0.9309
F-statistic: 95.34 on 2 and 12 DF,  p-value: 4.307e-08
```

Figure 5: Statistical analysis on EU exports. Author's calculations using R software based on Eurostat data.

These results can be interpreted as follows:

- The Specific Waiver Effect (Coefficient = +10.3, p-value = 0.650): When the natural progression of time is being controlled, the specific coefficient for the Waiver shows a positive addition of 10.3 billion euros. However, its p-value is 0.650 (which is higher than the 0.05 threshold). It means the SPC Waiver did not cause a sudden, isolated "jump" out of nowhere. Instead, it shows that the massive growth in exports was primarily driven by a strong, pre-existing time trend (and later accelerated by global events like the COVID-19 pandemic). The SPC Waiver acted as a necessary legal facilitator that allowed the European industry to fully participate in this natural market growth.
- The overall model P-value (P-value = 4.31e-08): This extremely low p-value ($p < 0.001$) proves that our overall statistical model is highly significant and perfectly captures the reality of the market.

- The R-squared ($R^2 = 0.94$): This is a high score. It means that the model (the combination of the time trend and the SPC Waiver) explains 94% of the real-world variation in European pharmaceutical exports.

An Interrupted Time Series (ITS) graph was also generated so that these results can be visualized:

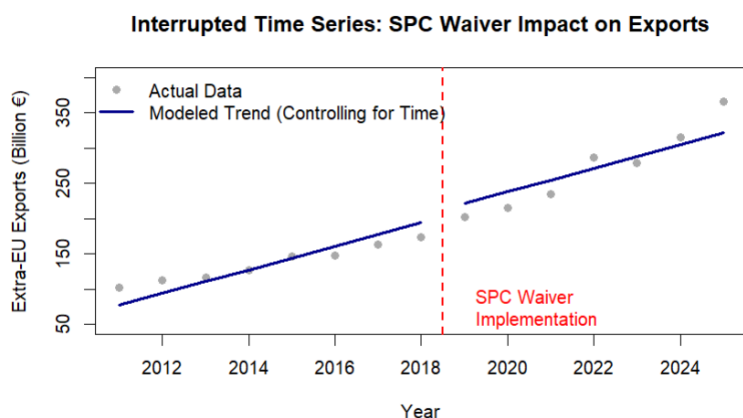


Figure 6: Interrupted time series: SPC Waiver impact on exports. Author's calculations using R software based on Eurostat data.

This graph plots the actual export values year by year. A dashed red vertical line was added in 2019 to mark the exact moment when the SPC Manufacturing Waiver came into force. Visually, the graph shows an acceleration after this red line. However, the statistical model tells us to be careful. Since the “time trend” variable was included in our calculations, the Waiver variable itself is not statistically significant. This means that it cannot be concluded that the law alone caused the acceleration. Instead, the graph shows a global demand that was already growing and then exploded due to external events such as the COVID-19 pandemic.

To understand this result, a major limitation in international trade data is noted. In global customs systems, there is no specific code that separates “generic medicines” from “patented medicines.” Every drug, from a basic generic pill to a highly expensive patented cancer treatment, is recorded in the exact same category: SITC 54. As there is no other option, this broad category as a macroeconomic proxy to measure the health of the European industry had to be used.

However, as the SITC 54 category is so broad, it captures massive global shocks. During the 2022-2024 period¹, Europe exported €37.14 billion worth of mRNA COVID-19 vaccines (specifically

¹ The vaccine-specific analysis is restricted to the 2022-2024 period as the dedicated customs code (CN 3002 41 10) was only systematically implemented by European authorities starting in 2022. Prior to this, COVID-19 vaccines

under CN code 3002 41 10). When compared to the total exports of the SITC 54 category, which reached €881.82 billion over the same timeframe, these vaccines represent approximately 4.21% of the total trade volume. The SPC Waiver is a targeted microeconomic law that only applies to specific generic and biosimilar factories. Therefore, the exact financial impact of the Waiver is statistically drowned out by the massive noise of the pandemic and the natural growth of the global market (which explains our high R-squared of 0.94). Based on the results of this model, hypothesis H2 is being rejected.

In conclusion, analysis of the second pillar shows that Europe's pharmaceutical manufacturing base remains very strong. While global trade makes it difficult to measure the exact financial footprint of the SPC Waiver, its strategic value is clear. By removing an outdated legal barrier, the Waiver has acted as a shield for European factories. It has enabled the generic and biosimilar industry to remain in the EU and participate fully in global demand. As a result, Europe has successfully defended its industrial competitiveness and maintained its role as a global manufacturing leader.

2.3 Analysis of pillar 3: Access

The measure being analyzed to evaluate the access pillar is called the HTA regulation. This regulation makes cooperation between Member States mandatory through Joint Clinical Assessments (JCA). Although the law was adopted in 2021, it only became fully applicable on January 12, 2025. From that date onwards, new medicines will no longer have to be evaluated 27 times by 27 different national agencies. Instead, they will receive a single scientific evaluation at the EU level.

This law is very recent, but it will be analyzed because even though it became fully applicable in early 2025, it was adopted in 2021. By looking at 2018-2024, it can be observed if the transition period has already started to work. To analyze this regulation, this study examines the variance of waiting times, as variance measures inequality: the higher the variance, the greater the gap between countries. The data used for this analysis are W.A.I.T indicators (time from central approval to availability) found in the EFPIA annual reports. 24 countries instead of the 27 countries of the European Union will be considered. Malta, Cyprus, and Luxembourg have been removed because

were aggregated within broader SITC 54 categories, making them statistically indistinguishable from other pharmaceutical exports.

these small countries often do not have data in their annual reports, making it difficult to compare them fairly over several years.

To assess the impact of the HTA cooperation, the variance of access delays between the 2020 cohort and the 2024 cohort will be compared, using a Fischer's F-Test. The results are the following:

Variance 2020 : 38891.22 Variance 2024 : 33218.63

```
F test to compare two variances

data: data$Delay2024 and data$Delay2020
F = 0.85414, num df = 23, denom df = 23, p-value = 0.3543
alternative hypothesis: true ratio of variances is less than 1
95 percent confidence interval:
 0.000000 1.720605
sample estimates:
ratio of variances
 0.8541422
```

Figure 7: Fischer's F-test of W.A.I.T. indicators variances. Author's calculations using R software based on EFPIA data.

The data and results show that variance (inequality) decreased by about 14.6% between 2020 and 2024. However, the p-value is 0.3543, which is higher than the standard 0.05 threshold for statistical significance. This means that while a clear drop in inequality can be observed, we cannot prove with 95% certainty that this change is solely due to the reform rather than annual variations, when looking at this Fischer's F-test. This result can be explained probably because structural changes in healthcare systems are slow, and the mandatory regulation only officially started in January 2025.

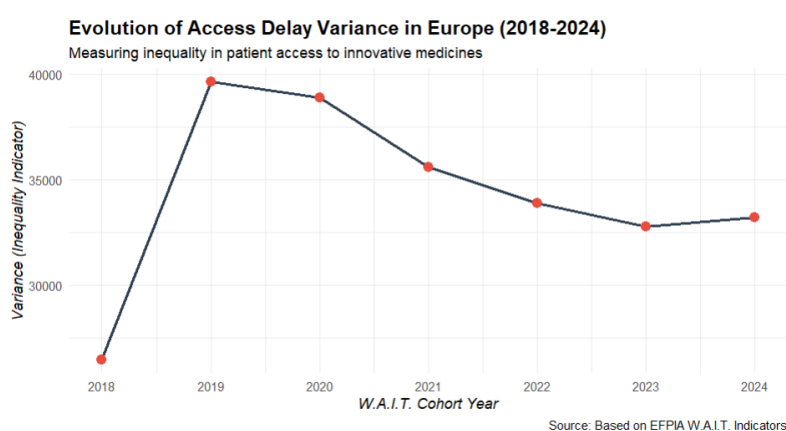


Figure 8: Evolution of access delay variance in Europe (2018-2024). Author's calculations using R software based on EFPIA data.

This graph shows the evolution of the European landscape over the past seven years:

- The 2019 peak: The graph shows a major spike in variance in 2019, reaching nearly 40,000. This represents the greatest peak of inequality in drug access across Europe since 2018.

- The convergence trend (2020–2023): Following the peak, the curve shows a steady decline. This suggests that the preparation for the HTA Regulation (adopted in 2021) created an "anticipation effect" where countries began to align their scientific evaluation processes.
- The 2024 stabilization: In 2024, the variance slightly stabilized around 33.000. This illustrates the limits of voluntary cooperation. It proves that while countries have moved closer together, they have reached a point where voluntary efforts are no longer enough to further reduce the gap.

Although the F-test shows a decrease in variance between 2020 and 2024, it does not confirm a stable trend. Therefore, to provide a more robust and longitudinal validation, a sigma convergence regression over the period 2020-2024 was performed.

$$\sigma_t = \beta_0 + \beta_1 \cdot Year_t + \epsilon_t$$

This model measures the evolution of the standard deviation (Sigma) of access delays over time. The results of the regression are the following:

```
Call:
lm(formula = Sigma ~ Year, data = df_convergence)

Residuals:
Delay2020 Delay2021 Delay2022 Delay2023 Delay2024
  3.053    -1.738    -2.558    -1.882     3.125

Coefficients:
              Estimate Std. Error t value Pr(>|t|)
(Intercept)  7779.578   2094.816   3.714   0.0340 *
Year         -3.755     1.036   -3.625   0.0361 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 3.276 on 3 degrees of freedom
(2 observations effacées parce que manquantes)
Multiple R-squared:  0.8141,    Adjusted R-squared:  0.7521
F-statistic: 13.14 on 1 and 3 DF,  p-value: 0.03613
```

Figure 9: statistical analysis on W.A.I.T. indicators. Author's calculations using R software based on EFPIA data.

The results, notably the p-value of 0.036, demonstrate a statistically significant trend of convergence. The model shows that the health gap between member states has narrowed by 3.75 days per year. With an adjusted R-squared of 75%, the passage of time since the launch of the Pharmaceutical Strategy (2020) explains 75% of the reduction in disparities. These significant results show that, even before the HTA Regulation became mandatory in 2025, there was already an anticipation effect. This movement toward alignment, probably driven by national agencies preparing for the new EU framework, proves that the Strategy's objective of equitable access is

being met. The 2025 regulation acts as the final legislative anchor to stabilize and complete this convergence process. Based on these results, hypothesis H3 is accepted.

Beyond legislative reforms like the HTA Regulation, professional bodies such as the *French National Chamber of Pharmacists* emphasize the role of digitalization. They argue that tools like the ISO IDMP standards and digital health records are crucial to manage medicine shortages and secure supply chains. This highlights that improving patient access depends not only on faster clinical assessments but also on a strong digital infrastructure across Europe.

2.4 Analysis of pillar 4: Innovation

To analyze the innovation pillar, this section measures the impact of the PRIME scheme on the speed of drug approval. The unit of measurement evaluated is the Marketing Authorization (MA) delay. This delay is defined as the total time between the formal application submission to the EMA and the final decision of the European Commission. This timeframe is critical because it represents the waiting time for patients to access a new therapy. While the EMA provides scientific advice to speed up development, the objective of the PRIME program is to reduce this specific administrative and scientific review period. The PRIME label is reserved for drugs that offer a major therapeutic benefit for diseases that have no satisfactory treatment, while standard (non-PRIME) drugs are for conditions for which alternatives already exist or for which the innovation is incremental rather than a solution where there was none before. By comparing the timelines for PRIME drugs with standard drugs, we can quantify the effectiveness of the program.

The data was collected manually using the European Public Assessment Reports (EPARs) available on the official website of the European Medicines Agency. For each existing PRIME drug (up to date in January 2026), we extracted²:

- The submission date (start of the procedure)
- The authorization date (final decision)
- Specific characteristics used as control variables: orphan drug status and ATMP (Advanced Therapy Medicinal Products) classification

² See Appendix B for the complete list of 66 medicines analyzed (33 PRIME and 33 standard authorization medicines).

For each PRIME drug, a standard drug was selected as a control, targeting the same therapeutic area (oncology, endocrinology, vaccines, etc.). For these drugs, the same data were extracted.

Since PRIME drugs are often complex drugs (many are ATMPs or treat rare diseases), a simple comparison of averages would be biased. Therefore, we used a multiple linear regression model. This method allows us to isolate the “PRIME effect” by neutralizing other factors that usually slow down the process, such as the technical complexity of a product or the rarity of a disease. This ensures that PRIME and standard drugs are compared on equal terms.

$$Delay_Months_i = \beta_0 + \beta_1 \cdot Is_PRIME_i + \beta_2 \cdot ATMP_i + \beta_3 \cdot Orphan_i + \epsilon_i$$

The regression results are as follows:

```
Call:
lm(formula = Delay_Months ~ Is_PRIME + ATMP + Orphan, data = final_data)

Residuals:
    Min       1Q   Median       3Q      Max
-7.3592 -2.5558 -0.7934  1.9045  9.5052

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  15.3634    0.7437   20.657  < 2e-16 ***
Is_PRIME     -4.6933    1.1396   -4.118  0.000115 ***
ATMP          3.7164    1.4646    2.537  0.013695 *
Orphan        0.2744    1.1009    0.249  0.804023
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 3.909 on 62 degrees of freedom
Multiple R-squared:  0.2304,    Adjusted R-squared:  0.1931
F-statistic: 6.186 on 3 and 62 DF,  p-value: 0.0009561
```

Figure 10: Statistical analysis on PRIME medicines. Author’s calculations using R software based on EMA data.

According to the model, the PRIME label reduces the approval delay by approximately 4.7 months (estimate = -4.69), compared to standard procedures, ceteris paribus. This represents a significant acceleration in the regulatory process, allowing breakthrough therapies to reach European patients much faster. The p-value for the PRIME variable is 0.000115, which is highly significant. This means that there is less than a 0.01% probability that this speed advantage is due to chance.

The regression also highlights the impact of technical complexity. A drug that is classified as an ATMP significantly increases the review time by approximately 3.7 months ($p = 0.013$). This means that PRIME drugs are naturally slower to evaluate because they are more complex. However, the PRIME program successfully compensates for this complexity. Without PRIME support, these innovative therapies would face much longer delays due to their technical nature.

The “orphan drug” status does not show a significant impact on the approval delay in this model ($p = 0.80$). This suggests that for this sample, the speed of the process is driven more by the support of the PRIME scheme and the technical complexity (ATMP) than by the rarity of the disease itself.

The adjusted R-squared is 0.193, indicating that the model explains almost 20% of the total variation in approval delays. This is an expected result, as unpredictable factors can influence timelines (such as company responsiveness or specific clinical issues). This result confirms that the PRIME program is a significant driver of faster market entry, and that hypothesis H4 is accepted.

3. Impact assessment: Qualitative Analysis of the Pharmaceutical Strategy's Measures

Having analyzed the effectiveness of the Pharmaceutical Strategy for Europe using quantitative methods in the previous section, this section turns to a qualitative analysis in order to interpret, contextualize, and, where necessary, challenge the results obtained so far. While regression models and hypothesis tests provide an evidence-based picture of measurable outcomes, they cannot capture the lived experience of the Strategy, that is, the institutional frictions, operational realities, and competitive dynamics that shape how the Strategy's measures translate into practice. The qualitative analysis addresses this gap.

The data for this section was collected through interviews with professionals representing a range of perspectives on the European pharmaceutical ecosystem. The interviewees include a former member of the European Medicines Agency (EMA) with expertise in medicine availability and shortage management; three regulatory and policy professionals from Big Pharma companies, anonymized at their request; a representative of GSK with prior experience at the FDA; a former FDA director involved in ICH harmonization and data standards; a partner at a life sciences consultancy specializing in regulatory strategy; a co-founder and CEO of a biotechnology firm operating in Belgium; the head of the medicines section at CEPS, the body responsible for negotiating medicine prices in France; a competition law official from the European Commission's Directorate-General for Competition (DG COMP); and the director of ICH, a former policy officer in DG SANTE at the European Commission. This diversity of profiles ensures that the qualitative results reflect different interests and viewpoints, rather than the perspective of a single sector.

3.1 Analysis of pillar 1: Attractiveness

The quantitative analysis in Section 2.1 showed that Europe's share of global clinical trials declined steadily between 2015 and 2024, falling from 27% to 20%, and that the implementation of the Clinical Trials Regulation (CTR) and the CTIS portal did not produce the reversal predicted by Hypothesis 1. Interviews with industry professionals and regulatory experts provide a clear picture

of why this is the case and point to structural barriers that administrative reform alone cannot overcome.

The CTIS portal, the central tool of this pillar, was described by respondents as failing to achieve its goal of simplification. Frits, a regulatory consultant (personal communication, 2026), described the portal's development cycle as "*catastrophic*". Upon launch, "*nobody liked it*" and most users preferred workarounds over integration. A regulatory affairs professional from a major pharmaceutical company (Participant B, personal communication, 2026), highlighted a specific technical shortcoming: the CTIS lacks an API, meaning that companies cannot connect their internal systems to the portal and are therefore forced to upload documents manually. In contrast, the United States and Canada use the eCTD format for clinical trial submissions, which allows sponsors to reuse existing automated tools. This forces European teams to maintain a parallel set of processes, thereby doubling the administrative burden for multi-regional trials. Participant B concluded that, while the CTR's intention to centralize was correct, its implementation retained too many national specificities, which undermined the goal of harmonization. Frits added that a "*CTIS optimization*" project had since been launched to address usability issues, suggesting that the tool might eventually deliver on its promises, but had not yet done so. Participant E, a regulatory policy professional at Roche (personal communication, 2026), gave a concrete example of how CTIS actively worsens operations: the system only allows one substantial amendment per trial at a time, making it impossible to run the agile, evolving protocols that modern clinical research requires. They also noted that EFPIA is now pushing for a product-centered "core dossier" model similar to the US IND system, and that the Commission is becoming open to it, though resistance from member states over IT budgets and national systems remains a real obstacle.

Beyond the portal's shortcomings, the respondents agreed on a more fundamental observation: Europe's lack of appeal stems less from administrative complexity than from a structural fragmentation that no single regulation can resolve on its own. Thibault (personal communication, 2026), who works in preclinical research for two Belgian biotech companies, puts it honestly: although it is the world's second-largest market in terms of purchasing power, Europe is in practice divided into as many submarkets as there are member states, each with its own regulatory authorities, pricing systems, and national interpretations of European rules. Even intellectual property protection remains fragmented: a patent must be defended country by country, whereas in

the United States, a single federal market means a single legal process. Ben, a former FDA official now at GSK (personal communication, 2026), explained why this matters. The EMA works in collaboration with the competent national authorities rather than acting as their superior, which means that guidelines developed at the European level may not align with what sponsors encounter on the ground in certain countries when they submit applications for clinical trial authorization. He described the appointment of rapporteurs from different Member States as a “*matter of chance*”, with some countries being significantly more rigorous than others in certain areas, which introduces an element of unpredictability into the review process. At the FDA, by contrast, official guidelines are authoritative across the entire country. Norman (personal communication, 2026), a former FDA director involved in ICH harmonization, confirmed this, noting that the diversity of national regulations governing clinical trials in Europe has long made the environment “more confusing” for the industry compared to the United States. Participant E reinforced this point, highlighting that ethics committees remain entirely uncoordinated across member states despite the CTR, a concrete barrier that no portal can fix. They also noted that Europe now competes with China, not just the US, for clinical trial volumes.

Several interviewees noted that the decline observed in the quantitative analysis is not only a result of internal European failures but is also due to external forces on a different scale. Thibault described the “*Trump effect*” as a major turning point: following U.S. trade measures that effectively made market access contingent on domestic production, many pharmaceutical companies redirected significant investments toward the United States rather than Europe. He summarized the contrast: “*When a strong voice says ‘this is how it will be’ and it is implemented the very next day, that is powerful. In Europe, you have many countries with their own regulations; even with the best intentions, it is less effective*”. Participant C (personal communication, 2026), who took part in the original 2020 strategy consultation, noted that manufacturing investment data for Europe looked positive until 2024, but that the trend had since reversed sharply. This timing suggests that any positive effects of the CTR on attractiveness may have been offset by the pull of U.S. industrial policy. Participant F, (personal communication, 2026), who heads the ICH, confirmed this, describing attractiveness as the strategy's most critical weakness. She pointed to the fact that Switzerland alone hosts more major pharmaceutical laboratories than the entire EU, a telling sign of Europe's failure to build a competitive investment environment and noted that aggressive US tariff policies are pushing companies to relocate activities away from Europe to

reduce commercial risk. This dynamic is consistent with the results obtained in the quantitative analysis, which showed that Europe's decline in clinical trial market share is strongly correlated with that of the Americas, reflecting a broader westward shift in R&D gravity toward Southeast Asia rather than a purely European failure.

A final theme emerging from the interviews is whether regulatory instruments are simply the right tool for the job. According to Frits, the Strategy did not pursue the far-reaching reform that Europe needed, and in his view, the document's political architecture, built on consensus among member states with divergent interests, structurally limits the pace and ambition of change. Participant B described the outcome of the strategy consultation process as *“an evolution of the existing rather than a radical transformation”* and stressed that the framework adopted will likely govern the sector for ten to twenty years, raising the stakes of its current limitations. Participant E noted that from a US perspective, the strategy is not perceived as a serious geopolitical signal, it is seen as affecting European operations without challenging the global competitive balance. Both Participant E and Participant F agreed that the strategy's priorities are coherent, but that without stronger political commitment and dedicated funding, it risks remaining aspirational rather than transformative. The former EMA staff member (Participant A, personal communication, 2026), added an institutional note: the strategy placed significant new demands on the agency without a proportional increase in resources, creating internal tensions and a perception within the EMA that the Commission's ambitions exceeded what the agency could realistically deliver.

Overall, the qualitative data confirms and contextualizes the rejection of hypothesis H1. The CTR and CTIS constitute a necessary but insufficient response to Europe's lack of attractiveness. The launch of the portal has introduced new frictions rather than eliminating the old ones, and the underlying factors driving the decline, regulatory fragmentation, the absence of a truly unified research market, and growing competitive pressure from the United States and Asia, require responses that go beyond mere administrative simplification.

3.2 Analysis of pillar 2: Competitiveness

The quantitative analysis presented in Section 2.2 assessed the supplementary protection certificate (SPC) derogation (Regulation 2019/933), and the results revealed that, although EU pharmaceutical exports experienced significant growth during the period studied, this growth could not be statistically attributed to the derogation itself; it was primarily driven by a pre-existing time-

series trend and amplified by external shocks such as the COVID-19 pandemic. Hypothesis 2 was therefore rejected. Qualitative interviews help explain why this result is both predictable and, to some extent, misleading, while identifying the broader competitive challenges that the derogation was intended to address.

The most pertinent message from the interviewees regarding the SPC Manufacturing Waiver was straightforward: it is simply too early to evaluate its impact. Participant C (personal communication, 2026), a CMC and policy professional from a Big Pharma company who has been closely involved in monitoring the strategy, argued that manufacturing investment decisions are inherently long-term. Pharmaceutical manufacturing sites cost tens of billions of dollars and require years of planning; *“it is the proverbial oil tanker”*, they noted, *“it takes time to turn around”*. Companies are paying attention to the Waiver, but no major site decision would have been made and executed within the short timeframe of the analysis. This observation directly supports the quantitative finding: the absence of a statistically significant jump in exports is not evidence that the Waiver has failed, but rather that its effects operate on a different timescale than the available data can capture. Participant C also highlighted that the Waiver's final scope has not yet been fully settled, which further explains why companies have not yet acted on it. Ben (personal communication, 2026), drawing on his experience at both the FDA and GSK, reached a similar conclusion: *“A new manufacturing site costs tens of billions and takes years of investment, a few months of extra exclusivity is a drop in the bucket compared to those macro decisions”*.

While interviewees did not dismiss the Waiver as irrelevant, several questioned whether extended exclusivity is the most effective mechanism to keep pharmaceutical manufacturing in Europe. Both Participant C and Ben pointed to two alternative models that have proven more impactful in other regions. The first is taxation: Singapore has attracted large-scale pharmaceutical manufacturing primarily through near-zero tax on manufactured goods, a model that is highly effective but politically unavailable in Europe, where tax policy remains a national prerogative and no member state has shown desire for the reductions that would be required. The second is reimbursement pricing: the United States pays significantly more for its medicines, which gives the American government considerable leverage when it tells companies to produce domestically if they want continued market access. Europe, with its tradition of price control and national health budget constraints, cannot easily replicate this dynamic. Jean-Gonzague (personal communication, 2026),

a senior figure at GSK, captured the underlying tension well: *"You cannot demand low prices and at the same time ultra-secure supply chains. Rebuilding a chemical factory does not happen in six months, it requires massive subsidies and a change in how we value medicines"*. This points to a structural contradiction at the heart of the competitiveness pillar: Europe wants to attract manufacturing investment while simultaneously keeping medicine prices low, and the SPC Waiver, however useful as a legal instrument, does not resolve this contradiction. Participant C summarized the hierarchy of incentives: *"Low tax and higher prices are better models. The Waiver is a 'nice to have', but it is not going to reverse the trend of offshoring"*. Participant E (personal communication, 2026), added that the new EU pharmaceutical legislation was perceived by the industry as more punitive than stimulating, with hopes now largely shifting toward the EU Biotech Act as the next real lever. They also flagged that the FDA recently announced real-time review of ongoing clinical trial data to accelerate approvals, a move Europe currently has no equivalent response to.

Across multiple interviews, the emergence of aggressive US industrial policy was described as a competitive force of an entirely different scale from anything the 2020 strategy had anticipated. Thibault (personal communication, 2026), noted that following US trade measures effectively requiring domestic production as a condition of market access, numerous clients of his biotechnology firm, including both large pharmaceutical groups and smaller biotech companies, had announced major investment redirections toward the United States rather than Europe. Participant C confirmed this trajectory, noting that while EU pharmaceutical manufacturing data looked strong through 2024, the direction had since reversed, with most major recent investment announcements pointing toward the United States. Participant F (personal communication, 2026), added a striking illustration: Switzerland alone hosts more major pharmaceutical laboratories than the entire EU combined, a sign that Europe has long struggled to build the investment environment needed to retain high-value industrial activity. This external pressure also helps explain why the quantitative analysis found strong export growth driven primarily by the time trend and the COVID shock rather than by the Waiver specifically.

One dimension of competitiveness that goes beyond the Waiver itself was raised by Participant D (personal communication, 2026), a competition law official at the European Commission's DG COMP. They noted that effective competition in the pharmaceutical sector requires not only incentives for manufacturing, but also mechanisms to ensure that patent exclusivity periods are not

artificially extended by incumbent companies. They described ongoing enforcement actions against pay-for-delay agreements and abuses of dominant position, practices that, as the literature review noted, were already documented in the 2009 Sector Inquiry and remain prevalent today. Participant D specifically noted that patent "*divisionals*", where companies split parent patents into multiple derivative applications to create extended zones of legal uncertainty, continue to be a tool used to delay generic entry, and that the European Patent Office's attempts to limit this practice had not been effective. The CEPS representative (personal communication, 2026), confirmed this concern from a national pricing perspective, observing that the practice of filing thousands of patents around a single blockbuster product, combined with the launch of new formulations (such as subcutaneous versions of intravenous drugs) just before the expiry of exclusivity, was not only still common but had in their view become more sophisticated over time. They noted that the pharmaceutical strategy had not yet provided a concrete response to these lifecycle management practices. This finding is significant for the competitiveness pillar: if the strategy strengthens manufacturing incentives through the Waiver while failing to curb exclusivity extension practices, the competitive gains at the production level may be partially offset by continued delays in generic market entry.

The qualitative evidence confirms the quantitative rejection of H2, while adding important nuance. The absence of a measurable statistical impact from the SPC Manufacturing Waiver is explained by three converging factors: the long investment cycles of pharmaceutical manufacturing, the unresolved parameters of the Waiver's final design, and the overwhelming scale of external competitive pressures, particularly from the United States, that have redirected investment flows in a way that no European regulation could plausibly counteract in the short term. The Waiver represents a necessary legal correction that removes a historical disadvantage for European generic and biosimilar manufacturers, and its strategic value should not be dismissed. However, the interviews make clear that it is one component of a much larger competitiveness challenge, and that more powerful levers, fiscal policy, pricing reform, and rigorous enforcement against exclusivity abuse, remain either politically unavailable or insufficiently developed within the current strategy, and, as Participant E noted, this will not change as long as pharmaceutical and biotech industries are not treated as strategic priorities by the EU, on a par with energy or defense.

3.3 Analysis of pillar 3: Access

The quantitative analysis in Section 2.3 revealed a statistically significant narrowing of access delays across member states, at approximately 3.75 days per year. Hypothesis 3 was therefore accepted, with the limitation that the HTA Regulation only became fully mandatory in January 2025, and that the trend likely reflects an anticipation effect rather than the full impact of the reform. The interviews help explain both why this progress is real and why it remains fragile.

Across interviews, professionals consistently identified national pricing and reimbursement decisions, not the EMA's approval process, as the main obstacle to equitable patient access. Jean-Gonzague (GSK) (personal communication, 2026), summarized it plainly: *"You have a European strategy for innovation, but 27 different strategies for access and prices. This fragmentation is the biggest obstacle to any coherent European pharmaceutical policy"*. The CEPS representative (personal communication, 2026), provided the most detailed account of how this plays out in practice. In France, a medicine must first obtain a clinical benefit opinion from the HAS before the CEPS can open price negotiations with the manufacturer, a sequential process whose duration depends as much on the manufacturer's pricing position as on the institution itself. They also stressed that cross-country comparisons of waiting times must be read carefully: Germany grants patient access immediately upon EU marketing authorization and negotiates price afterwards, which produces shorter headline delays without necessarily reflecting a more efficient system overall. Participant B (personal communication, 2026), from a Big Pharma company, captured the practical consequence for the whole strategy: *"You gain time on the initial approval, but you lose it again in country-by-country reimbursement negotiations"*. This observation directly connects the access pillar to the innovation pillar, the time saved through PRIME or faster EMA review is often absorbed downstream by fragmented national processes.

The CEPS representative explained how External Reference Pricing, a mechanism where countries set medicine prices by benchmarking against a basket of other EU countries, creates perverse dynamics that ultimately reduce access. Because a low price in one country can pull down prices elsewhere, manufacturers sometimes choose not to launch a product in lower-price markets at all, to protect their pricing position in larger Western markets. Participant D (DG COMP) (personal communication, 2026), confirmed having seen this as an actual commercial consideration. The result is that patients in lower-income member states are double penalized: their health systems cannot afford high prices, yet manufacturers avoid those markets precisely because of their low

price levels. Participant D also mentioned parallel trade as a related problem. When price gaps between member states are large, wholesalers buy medicines cheaply in Southern or Eastern Europe and resell them in the West, creating local shortages in the original procurement countries. Participant F (personal communication, 2026), who heads the ICH secretariat, gave a personal illustration of this fragmentation: her daughter was on an immunosuppressant treatment that was regularly out of stock in Belgium, while the same medicine was consistently available in France on a simple prescription.

Interviewees acknowledged the logic of the HTA Regulation while managing expectations about its reach. Frits (personal communication, 2026), noted that even with harmonized clinical assessments, pricing and reimbursement decisions remain under national sovereignty, meaning that a perfectly harmonized EU-level evaluation will not automatically produce equal access if member states continue to apply divergent economic criteria. The CEPS representative made the same point from the French perspective: the European clinical assessment does not replace the HAS opinion, because it does not account for national-specific comparators or reimbursement criteria. The European layer therefore adds a potentially useful preparatory step but does not eliminate the fundamental sequential process that creates delays. Participant F argued that Europe is actually a genuine leader in terms of patient interest, the EMA and European institutions bring a level of coordination and political oversight that has no equivalent in most other regions. However, she noted that Europe has become hesitant to assert this leadership, partly because of the political pressures it has faced in other domains such as defense, which has created a broader institutional timidity that spills over into health policy.

The qualitative evidence supports the acceptance of H3, while making clear that the convergence observed is still fragile and partial. The narrowing of access delays reflects a real anticipation effect driven by the approach of the HTA Regulation, but the structural barriers, fragmented national pricing systems, the distortions of external reference pricing, and the disconnect between EU-level approval and national reimbursement, remain largely intact. Real progress on this pillar will require not just harmonized clinical assessments, but deeper coordination on the economic decisions that ultimately determine whether a medicine actually reaches patients.

3.4 Analysis of pillar 4: Innovation

The quantitative analysis in Section 2.4 evaluated the PRIME scheme, the EMA's priority medicines program designed to accelerate approval for therapies targeting unmet medical needs. The multiple linear regression showed that PRIME-labelled medicines reach approval approximately 4.7 months faster than standard medicines, even after controlling product complexity. Hypothesis 4 was therefore accepted. The interviews help explain the mechanisms behind this result, while also identifying the limits of what an accelerated approval pathway can achieve on its own.

The former EMA staff member (Participant A, personal communication, 2026), offered a straightforward explanation for the speed gain: PRIME is essentially a prioritization exercise. Medical assessors carry a heavy workload, and giving formal priority to a specific product means it moves to the front of the queue. No new scientific capacity is created, the gain comes from better scheduling and faster turnaround at each step of the review. They described PRIME as *"a well-circulated success story"* within the agency, comparing it to the COVID vaccine review: when something is made the absolute priority, the process moves as fast as it possibly can without compromising quality. This explains why the effect is real and statistically significant, but also why it has a ceiling, the gain is largely organizational rather than structural. Participant B (personal communication, 2026), from a Big Pharma company, confirmed the financial stakes that make even a few months meaningful for industry: every month gained on the market translates into millions of euros, particularly for products targeting smaller or less commercially attractive patient populations. This makes PRIME a strong motivator for companies to invest in therapies for unmet needs, which is precisely the innovation objective the strategy was designed to serve.

While PRIME clearly accelerates individual products, several interviewees noted that Europe remains slower than its main competitors at a systemic level. Frits (personal communication, 2026), pointed out that average approval times in Europe run around 430 days, approximately 100 days longer than in other major regions. At a recent industry conference, he noted, the dominant question was simply: *"Is Europe competitive?"*. The general feeling in the room was that the world was moving faster. He identified the main bottleneck as the interaction between national agencies and the EMA: the review clock stops every time a question is sent, nothing happens in parallel, and the back-and-forth is entirely sequential. By contrast, the FDA is moving toward a cloud-based environment where multiple reviewers can work simultaneously and respond to questions in real

time, a fundamentally different operating model. Participant E (personal communication, 2026), at Roche, flagged a recent development that illustrates how quickly this gap can widen: the FDA has just announced that it will begin accepting ongoing clinical trial data in real time, allowing earlier and faster approvals. Europe currently has no equivalent initiative, meaning the speed advantage of the US regulatory system is likely to grow further in the near term.

Participant C (personal communication, 2026), a CMC and policy professional at a Big Pharma company, offered an important nuance. For complex products, the bottleneck is often not the EMA's review time but the earlier stage of generating the evidence needed to support the submission. The critical path is producing the data package, not waiting for the regulator to assess it. This means that even a perfectly efficient PRIME process cannot compensate for the time required to develop and manufacture complex therapies. On ATMPs specifically, which the regression showed add approximately 3.7 months to review time, Participant C argued that the EMA's focus on this category may be somewhat disproportionate, given that the most impactful emerging modalities are not ATMPs but rather antibody-drug conjugates, complex oligonucleotides, and advanced vaccine platforms. They also highlighted a genuine area of European leadership: the CMC flexibility toolbox introduced by the EMA in 2021, which allowed manufacturers to submit alternative forms of evidence during the COVID crisis and was instrumental in getting vaccines approved at unprecedented speed. This toolbox, based on benefit-risk reasoning rather than rigid data requirements, represents world-class regulatory thinking, though Participant C noted that the EMA has become somewhat more conservative since the pandemic and has partially stepped back from this approach.

A recurring theme across interviews was the fundamental tension between rewarding innovation and ensuring affordability. Jean-Gonzague (GSK) (personal communication, 2026), described it as a structural dilemma: strong IP protection and high returns are necessary to attract the R&D investment that produces breakthrough therapies, but they directly conflict with the access and affordability objectives of the same strategy. Participant D (DG COMP) (personal communication, 2026), approached this from a competition law angle, arguing that the innovation cycle only functions properly when exclusivity periods are not artificially extended, because if companies can delay generic entry indefinitely, their incentive to invest in genuinely new products weakens. The CEPS representative (personal communication, 2026), confirmed that the PRIME-driven reduction

in approval delays is a positive development but noted that many of the gains are absorbed downstream in national reimbursement negotiations, limiting the real-world impact on patients.

The qualitative evidence supports the acceptance of H4 and confirms that PRIME is a genuine and effective tool for accelerating approval of breakthrough therapies. The mechanism is clear, the industry recognizes its value, and the EMA has demonstrated with COVID vaccines that it can move with real speed when the conditions are right. However, the interviews make clear that PRIME operates at the end of a long chain, and that its benefits are partially offset by slower upstream development timelines for complex products, a broader systemic lag compared to the FDA, and the familiar problem of fragmented national reimbursement processes that delay access even after fast approval. Innovation in Europe is alive, but the regulatory and economic environment around it still needs to move faster to keep pace with global competition.

3.5 Synthesis of findings

Pillar	Measure evaluated	Quantitative outcome	Qualitative outcome	Objective status
Attractiveness	Clinical Trials Regulation (CTR 536/2014) & CTIS portal	27%→20% market share no trend reversal post-CTR H1 rejected	CTIS increased burden No API Ethics committees uncoordinated US investment pull	Not achieved
Competitiveness	SPC Manufacturing Waiver (Reg. 2019/933)	Export growth pre-existing ($p=0.65$) COVID masks effect H2 rejected	Too early to assess 10-15 years investment cycles Taxation more effective Removes real legal disadvantage but parameters unsettled	Not yet achieved

Pillar	Measure evaluated	Quantitative outcome	Qualitative outcome	Objective status
Access	HTA Regulation (EU) 2021/2282	-3.75 days/year (p=0.036) Anticipation effect H3 accepted	National P&R main barrier ERP distortions persist 128 vs 828 days gap remains	Partially achieved
Innovation	PRIME scheme (EMA Priority Medicines)	-4.7 months vs standard (p<0.001) ATMP +3.7 months H4 accepted	Organizational gain only EU still 100 days behind Benefits lost in national P&R	Achieved

Table 4: Synthesis of findings: quantitative and qualitative assessment across four pillars

4. Recommendations, limitations and future research

4.1 Recommendations

The findings of both the quantitative and qualitative analysis point to four concrete recommendations for EU pharmaceutical policy.

First, the CTIS portal needs to be fundamentally redesigned rather than incrementally patched. The current "CTIS optimization" project is unlikely to solve the core problems identified by industry professionals, namely the absence of an API, the restriction to one amendment at a time, and the retention of country-specific dossier sections. Europe should move toward a product-centered model similar to the US IND system, where all studies related to a single product are managed under one unified application. EFPIA is already advocating for this, and the Commission is reportedly open to it, the political will now needs to translate into concrete action.

Second, the SPC Manufacturing Waiver needs to be finalized with a broader product scope, a longer duration than the current 12-month proposal, and clear geographic criteria. As long as its parameters remain unsettled, companies cannot factor it into long-term investment decisions. More

broadly, the EU should acknowledge that extended exclusivity alone is not sufficient to retain manufacturing, fiscal incentives and a more coordinated approach to medicine pricing are stronger levers that deserve serious political discussion at the European level.

Third, the HTA Regulation's full potential will only be realized if it is accompanied by deeper coordination on national pricing and reimbursement processes. Harmonizing clinical assessments is a useful first step, but it does not address the economic decisions that ultimately determine patient access. The EU should consider establishing a structured dialogue between the EMA, national HTA bodies, and pricing authorities to reduce the sequential delays that currently occur between EU approval and national reimbursement.

Fourth, and most fundamentally, the pharmaceutical and biotech sectors need to be explicitly recognized as strategic priorities by the European Union, on a par with energy and defense. This means dedicating real financial resources, political attention, and coordinated industrial policy to the sector, rather than relying solely on regulatory reform to solve what are, at their core, economic and geopolitical challenges.

4.2 Limitations

This thesis has several limitations that affect the strength of its conclusions. On the quantitative side, the analyses are constrained by data granularity and sample size. The export data relies on the broad SITC 54 category, which aggregates all pharmaceutical products without distinguishing between generic and patented medicines. This prevented isolating the SPC Waiver's specific effect, as the €37 billion COVID vaccine exports masked any targeted policy impact. Similarly, the clinical trial market share data reflects registered trials rather than actual research investment volumes, potentially underestimating Europe's competitive position.

The interrupted time series model for Pillar 1 includes four explanatory variables over only ten annual observations, raising overfitting concerns. While the adjusted R-squared is high, replication over a longer horizon would strengthen confidence. For Pillar 3, the W.A.I.T. indicator measures time to reimbursement but not affordability or availability rates, a medicine approved by the EMA may reach patients quickly in Germany yet remain unavailable in Bulgaria. The sigma-convergence regression relies on only five data points (2020-2024), making the trend indicative rather than conclusive.

On the qualitative side, the interview sample, while diverse, underrepresents Southern and Eastern European perspectives, the member states facing the greatest access challenges. Several interviewees requested anonymity, limiting full attribution and contextualization of certain claims. Finally, the evaluation horizon ending in 2024 is relatively short for policy reforms whose effects operate over years or decades, particularly for manufacturing investment decisions driven by the SPC Waiver.

4.3 Future research

Several avenues for future research emerge from this thesis. First, a re-evaluation of the CTR and CTIS portal in three to five years, once the CTIS optimization project has been implemented and adoption has stabilized, would allow a more definitive assessment of whether administrative harmonization can meaningfully reverse Europe's declining clinical trial market share. Second, a study specifically focused on the SPC Manufacturing Waiver's impact on generic and biosimilar manufacturing investment decisions, using firm-level data rather than aggregate trade statistics, would provide a much more precise measure of its actual effect. Third, a comparative analysis of patient access in Eastern versus Western Europe, examining the interaction between HTA harmonization and national pricing systems after the HTA Regulation's full entry into force in 2025, would be highly valuable for evaluating whether the convergence trend observed in this thesis holds over time. Finally, future research could examine the relationship between pharmaceutical industrial policy and broader EU strategic autonomy objectives, particularly considering the geopolitical developments since 2024 and the emergence of new instruments such as the Biotech Act and the Critical Medicines Act.

5. Conclusion

This thesis sets out to evaluate the extent to which the Pharmaceutical Strategy for Europe, adopted by the European Commission in 2020, has achieved its objectives of attractiveness, competitiveness, access, and innovation. To answer this question, it combined a quantitative impact assessment based on public data with a qualitative analysis drawn from interviews with professionals across the sector. The results are mixed, two of the four hypotheses were accepted and two were rejected, a finding that reflects the uneven nature of the strategy's early impact rather than a simple success or failure.

The results of this evaluation across the four pillars are synthesized in section 3.5, which consolidates quantitative outcomes, qualitative findings, and overall objective status for each measure analyzed. Taken together, these findings suggest that the Pharmaceutical Strategy for Europe is better described as a necessary but insufficient response to the challenges facing the European pharmaceutical ecosystem. Its objectives are the right ones, and some of its instruments are working. But the strategy consistently runs into the same set of structural obstacles: the fragmentation of the European internal market, the division of competences between the EU and its member states, and the absence of the economic levers, fiscal policy, pricing coordination, strategic investment, that would be needed to truly compete with the United States and China on a level playing field.

Reflecting on the findings of this thesis, it is striking how consistently the same obstacle appears across all four pillars: the structural fragmentation of Europe. Whether the question is about clinical trials, manufacturing, patient access, or innovation pathways, the answer always comes back to the same tension between European ambition and national sovereignty. In my view, this is not simply a technical or regulatory problem, it is a political one. The strategy is well designed on paper, but it asks European institutions to achieve results in areas where they do not have full authority. What surprised me most in conducting this research was not that some hypotheses were rejected, but how much the external environment, particularly the industrial policy of the United States under the Trump administration, had shifted the competitive landscape in a way that no European regulation could realistically counteract in the short term. This raises a question that goes beyond the scope of this thesis but that I believe is worth asking: is a regulatory strategy, however well-crafted, the right tool to respond to what is ultimately a geopolitical challenge?

The most fundamental insight emerging from this research is perhaps the simplest one. Regulatory reform can reduce friction and improve processes, but it cannot substitute for political ambition. As long as the pharmaceutical and biotech industries are not treated as strategic priorities by the European Union, the gap between the strategy's aspirations and its real-world impact is unlikely to close. The 2020 strategy was a good start. What comes next will need to go further.

Glossary

<u>Word or Abbreviation</u>	<u>Explanation</u>
ATMP (Advanced Therapy Medicinal Products)	Category of highly technical medicines including gene therapies, cell therapies and tissue-engineered products. Subject to the EMA's mandatory centralized procedure and requiring longer evaluation times due to their technical complexity.
Big Pharma	Refers to the world's largest pharmaceutical multinationals (e.g. Pfizer, Roche, Sanofi) generating billions in annual revenues, characterized by vertical integration.
Biotechs	Research-oriented firms, often emerging from academia, specializing in biological or genetic therapies. Unlike Big Pharma, they excel at discovery but lack capital for large-scale manufacturing. High risk, high reward: their relationship with Big Pharma is central to European attractiveness and competitiveness.
Biotech Act	A proposed EU legislative initiative aimed at strengthening the competitiveness of the European biotechnology sector. It is seen by industry as a potential complement to the 2020 Pharmaceutical Strategy, with a broader scope covering incentives for investment, manufacturing, and innovation.
Centralized Procedure (CP)	Mandatory EMA procedure granting a single marketing authorization valid in all EU Member States, Iceland, Liechtenstein and Norway. Compulsory for biotech medicines, orphan drugs and treatments for specific serious diseases such as cancer, HIV and diabetes.
CEPS (Comité Économique des Produits de Santé)	The French committee responsible for negotiating the reimbursement price of medicines and medical devices with manufacturers. It intervenes after the HAS has issued its clinical benefit opinion.
Clinical trials	Studies conducted on human patients to evaluate a medicine's efficacy and safety prior to authorization.

<u>Word or Abbreviation</u>	<u>Explanation</u>
Clinical Trials Regulation (CTR)	European regulation (CTR 536/2014) harmonizing the submission and assessment of clinical trials through a single portal (CTIS), replacing 27 national procedures.
CMC (Chemistry, Manufacturing, and Controls)	The section of a regulatory dossier covering everything related to how a medicine is manufactured, tested, and quality-controlled. A critical area of review for both the EMA and the FDA, particularly for complex biological products.
Co-payment	The portion of a medicine's cost paid by the patient. Set independently by each Member State, it can vary based on the severity of the illness or the patient's socio-economic status.
Committee for Medicinal Products for Human Use (CHMP)	EMA's scientific committee responsible for evaluating the benefit-risk balance of new medicines under the centralized procedure.
CTIS portal	Clinical Trials Information System: the single European portal allowing sponsors to submit one clinical trial application for the entire EU, replacing fragmented national procedures.
eCTD (Electronic Common Technical Document)	A standardized electronic format used in the United States and Canada for regulatory submissions, including clinical trial applications. It allows companies to reuse existing digital tools and automate submissions, making the process more efficient than the European CTIS format.
EFPIA (European Federation of Pharmaceutical Industries and Associations)	Represents the innovative pharmaceutical industry in Europe. Publishes the W.A.I.T. indicator measuring patient access delays to innovative medicines across Member States.
Emergency Preparedness and Response Authority (HERA)	EU health emergency preparedness and response authority created as part of the Pharmaceutical Strategy for Europe, representing one of more than 50 concrete actions to strengthen EU resilience against health crises.

<u>Word or Abbreviation</u>	<u>Explanation</u>
European Medicines Agency (EMA)	The EU body responsible for the scientific evaluation, supervision and safety of medicines. Conducts the centralized procedure via the CHMP and manages the PRIME scheme for medicines addressing unmet medical needs.
External Reference Pricing (ERP)	Pricing mechanism used by Member States whereby a country sets the price of a medicine by benchmarking it against prices in a basket of other European countries. The dominant method of national cost control.
FDA	Food and Drug Administration: the US federal agency acting as a single authority for both drug approval and market access, unlike the EU system where these powers are split between the EMA and Member States.
Generic medicines	Medicines whose patent or supplementary protection certificate (SPC) have expired, allowing other manufacturers to produce them at lower cost.
HAS (Haute Autorité de Santé)	The French national authority responsible for assessing the clinical benefit of medicines before the CEPS can negotiate a reimbursement price. Its opinion determines whether and at what level a medicine will be reimbursed in France.
HTA regulation	Regulation (EU) 2021/2282 on health technology assessment. Makes cooperation between Member States mandatory through Joint Clinical Assessments (JCA), avoiding duplication and reducing inequalities in access.
ICH (International Council for Harmonisation)	An international body that brings together regulators and the pharmaceutical industry from Europe, the United States, and Japan to develop common technical guidelines for medicine development and approval. Its standards are widely adopted globally.
IND (Investigational New Drug)	The US regulatory model for clinical trial submissions, managed by the FDA. All studies related to a single product are grouped under one application, making it

<u>Word or Abbreviation</u>	<u>Explanation</u>
	easier to manage multiple trials simultaneously. Often cited as a more flexible alternative to the European CTIS model.
Intellectual property (IP)	The set of rights protecting pharmaceutical innovations (patents, supplementary protection certificates).
ISO IDMP standards	International standards for the identification of medicinal products. Considered essential digital tools for managing medicine shortages, securing supply chains and improving patient access across Europe.
Joint Clinical Assessments (JCA)	EU-level joint clinical evaluations carried out under the HTA Regulation, allowing a new medicine to receive one common scientific assessment rather than 27 separate national ones, reducing duplication and harmonizing access criteria.
Marketing Authorisation (MA)	Market authorization granted by the European Commission following a positive CHMP opinion. Valid simultaneously in all EU Member States. However, obtaining it does not guarantee availability or reimbursement in each country.
Orphan drug	Medicine intended to treat rare diseases. Benefits from specific regulatory incentives (extended market exclusivity, enhanced scientific support).
Parallel trade	A practice where medicines are purchased in a low-price EU member state and resold in a higher-price member state by wholesalers seeking to profit from price differences.
Patent	Intellectual property right granting its holder exclusive exploitation of an invention for a set period.
Patent cliffs	Moments when a blockbuster medicine loses its patent protection, exposing its manufacturer to generic competition and causing a sharp revenue decline.

<u>Word or Abbreviation</u>	<u>Explanation</u>
Patent clusters	Strategy used by innovator companies of filing multiple patents on a single medicine to artificially extend protection and delay generic market entry.
Patented medicines	Medicines still under patent or SPC protection, for which the manufacturer holds commercial exclusivity.
Pay-for-delay	An agreement where an originator pharmaceutical company pays a generic manufacturer to delay entering the market after patent expiry. Considered a violation of EU competition law as it artificially prolongs exclusivity and delays access to cheaper medicines.
Pricing & Reimbursement (P&R)	National process by which each Member State decides on the price and reimbursement level of an authorized medicine.
PRIME program	PRiority MEDicines scheme: EMA program offering enhanced early scientific support for medicines targeting unmet medical needs.
R&D	Research & Development: all activities from basic research to clinical development leading to a new medicine reaching the market.
SITC 54 category	International customs category grouping all pharmaceutical products in international trade statistics.
SPC Manufacturing Waiver	Derogation to the Supplementary Protection Certificate (Regulation EU 2019/933) allowing EU-based generic and biosimilar manufacturers to produce during the SPC period for export to non-EU markets where protection has expired, and to stockpile products ahead of the EU launch date.
The Single Market	The EU's integrated economic area in which medicines with a centralized authorization can be marketed simultaneously in all Member States.

<u>Word or Abbreviation</u>	<u>Explanation</u>
Time-to-patient delay	The delay between the EMA's centralized approval and the effective availability of a medicine for patients in a given Member State (including reimbursement).
Transparency Directive	Council Directive 89/105/EEC imposing procedural rules on Member States for pricing and reimbursement decisions: 90-day (or 180-day for combined procedures) deadlines, and an obligation to justify any refusal on objective and verifiable criteria.
Treaty on the Functioning of the European Union (TFEU)	Founding EU treaty. Article 168(7) reserves health policy and the organization of health services as national responsibilities, explaining why pricing and reimbursement decisions remain at Member State level despite EU-level authorization.
W.A.I.T. (Waiting to Access Innovative Therapies) indicators	Indicators published annually by EFPIA. Measure the delay between centralized authorization and effective patient availability in each Member State

Bibliography

AbbVie. (2025). AbbVie reports full year and fourth quarter 2024 financial results. AbbVie Investor Relations. <https://investors.abbvie.com/news-releases/news-release-details/abbvie-reports-full-year-and-fourth-quarter-2024-financial>, consulted on 13 March 2026.

Alhena Consult. (2025, November 4). Understanding the differences between the FDA and the EMA: Strategic implications for market access. <https://alhena-consult.com/differences-between-fda-and-ema-market-access/>, consulted on 4 February 2026.

#AlwaysInnovating: Pharmaceutical Industry Facts & Figures | IFPMA. (2024, December 9). IFPMA. <https://www.ifpma.org/initiatives/alwaysinnovating-pharmaceutical-industry-facts-figures/>, consulted on 12 April 2026.

All for Health Health for All. (n.d.). https://media-sinopharm.todayir.com/2025042516400161711641458_en.pdf, consulted on 13 march 2026.

An agency of the European Union. (n.d.). https://www.ema.europa.eu/en/documents/annual-report/2024-annual-report-european-medicines-agency_en.pdf, consulted on 3 February 2026.

Assessing the clinical trial ecosystem in Europe. (2024). <https://www.efpia.eu/media/0ipkatpg/efpia-ct-report-embargoed-221024-final.pdf>, consulted on 18 January 2026.

Attracting Life Science Investments in Europe. (n.d.). <https://www.europabio.org/wp-content/uploads/2023/10/Life-Science-Attractiveness-2023-October-22-Final.pdf>, consulted on 20 January 2026.

Barfoed, C. (2016). *The attractiveness of the European pharmaceutical market and its explanatory factors* [Master's thesis, Copenhagen Business School], consulted on 17 march 2026.

Bayer. (2024). *Bayer's Integrated Annual Reports*. Bayer.com. <https://www.bayer.com/en/investors/integrated-annual-reports>, consulted on 13 march 2026.

Castellana, E., & Chiappetta, M. R. (2025). The Impact of U.S. Tariffs on the Pharmaceutical Industry and Medicine Access in Europe: Challenges, Opportunities, and Future Outlook. *Hospital Pharmacy*. <https://doi.org/10.1177/00185787251390781>, consulted on 2 April 2026.

Caporal, J. (2025). *Pharmaceutical tariffs: Which countries does the U.S. import the most from? | The Motley Fool*. The Motley Fool. <https://www.fool.com/research/pharmaceutical-tariffs-imports/>, consulted on 12 February 2026.

CEICdata.com. (2024). *United States Exports: Medicinal and Pharmaceutical Product*. Ceicdata.com; CEICdata.com. <https://www.ceicdata.com/en/indicator/united-states/exports-medicinal-and-pharmaceutical-product>, consulted on 14 January 2026.

Clinical trials: Swift EU reforms could make 2026 a turning point. (2026). Efpia.eu. <https://www.efpia.eu/news-events/the-efpia-view/blog-articles/clinical-trials-swift-eu-reforms-could-make-2026-a-turning-point/>, consulted on 2 February 2026.

Companies Market Cap. (n.d.). *Pharmaceutical companies ranked by market capitalization*. <https://companiesmarketcap.com/>, consulted on 3 April 2026.

Critical medicines Act. (2026, March 19). Public Health. https://health.ec.europa.eu/medicinal-products/critical-medicines-act_en, consulted on 21 April 2026.

DiMasi, J. A., Grabowski, H. G., & Hansen, R. A. (2016). Innovation in the pharmaceutical industry: New estimates of R&D costs. *Journal of Health Economics*, 47, 20-33.

Directive - 89/105 - EN - EUR-Lex. (2026). Europa.eu. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.1989.040.01.0008.01.ENG, consulted on 6 January 2026.

EFPIA. (2024). *The Pharmaceutical Industry in Figures*. <https://efpia.eu/media/2rxdkn43/the-pharmaceutical-industry-in-figures-2024.pdf>, consulted on 14 January 2026.

EMA. (2025, February 7). *PRIME: priority medicines | European Medicines Agency*. Ww.ema.europa.eu. <https://www.ema.europa.eu/en/human-regulatory-overview/research-development/prime-priority-medicines>, consulted on 24 February 2026.

EU-US trade deal explained. (2025). European Commission - European Commission. https://ec.europa.eu/commission/presscorner/detail/en/qanda_25_1930, consulted on 14 April 2026.

European Commission. (2008). *Safe, innovative and accessible medicines: A renewed vision for the pharmaceutical sector* (COM(2008) 666 final). Commission of the European Communities. <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=COM:2008:0666:FIN> , consulted on 9 January 2026.

European Parliament & Council of the European Union. (2014). *Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC*. Official Journal of the European Union, L 158, 1. <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32014R0536> , consulted on 8 January 2026.

EUR-Lex - 52020DC0761 - EN - EUR-Lex. (n.d.). Eur-Lex.europa.eu. <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52020DC0761>, consulted on 11 January 2026.

EUR-Lex - 32004R0726 - EN - EUR-Lex. (n.d.). Eur-Lex.europa.eu. <https://eur-lex.europa.eu/eli/reg/2004/726/oj/eng> , consulted on 11 January 2026.

European Commission. (n.d.). Eurostat data browser: Pharmaceutical sector statistics [Data set]. https://ec.europa.eu/eurostat/databrowser/view/ds-059331_custom_20116238/default/table , consulted on 19 February 2026.

European Commission. (2020). *Pharmaceutical strategy for Europe*. Public Health – European Commission. https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe_fr , consulted on 5 January 2026.

European Medicines Agency. (2024). *Le système européen de réglementation des médicaments : La mise sur le marché de nouveaux médicaments sûrs et efficaces pour les patients dans l'ensemble de l'Union européenne*. Publications Office of the European Union. <https://doi.org/10.2809/783758>, consulted on 30 March 2026.

European Medicines Agency. (n.d.). European Public Assessment Reports (EPARs). <https://www.ema.europa.eu/en/medicines> , consulted on 17 February 2026

EFPIA. (2022). *Europe's share of global medicines R&D shrinks by a quarter in 20 years - as sector's declining trends continue*. (n.d.). Wwww.efpia.eu. <https://www.efpia.eu/news-events/the-efpia-view/efpia-news/europe-s-share-of-global-medicines-rd-shrinks-by-a-quarter-in-20-years-as-sector-s-declining-trends-continue/> , consulted on 12 January 2026.

Eurostat. (2026, April 13). *Medicinal & pharma products: €221 billion trade surplus*. @EU_Eurostat; Eurostat. <https://ec.europa.eu/eurostat/web/products-eurostat-news/w/ddn-20260413-1> , consulted on 2 May 2026.

Eurostat. (n.d.). International trade in medicinal and pharmaceutical products (SITC 54). European Commission. <https://ec.europa.eu/eurostat/databrowser/view/ds-059331/default/table> , consulted on 3 March 2026

External reference pricing of medicinal products: simulation-based considerations for cross-country coordination. (2014, March 10). Public Health. https://health.ec.europa.eu/latest-updates/external-reference-pricing-medicinal-products-simulation-based-considerations-cross-country-2014-03-10_en , consulted on 15 March 2026.

Fact Sheet: President Donald J. Trump Imposes a Temporary Import Duty to Address Fundamental International Payment Problems. (2026, February 21). The White House.

<https://www.whitehouse.gov/fact-sheets/2026/02/fact-sheet-president-donald-j-trump-imposes-a-temporary-import-duty-to-address-fundamental-international-payment-problems/> , consulted on 3 April 2026.

Food and Drug Administration. (n.d.). Development & approval process (Drugs). U.S. Food and Drug Administration. <https://www.fda.gov/drugs/development-approval-process-drugs> , consulted on 22 February 2026.

FOSTERING INNOVATIVE THERAPIES AND TECHNOLOGIES IN EUROPE: A FORWARD LOOK 2021 A position paper on the Pharmaceutical Strategy for Europe. (n.d.). Retrieved May 2, 2026, from <https://www.eucope.org/wp-content/uploads/2021/10/eucope-pharmaceutical-strategy-position-paper.pdf> , consulted on 2 May 2026.

Full. (2025, February 6). *Full Year and Q4 2024 results.* Astrazeneca.com. <https://www.astrazeneca.com/media-centre/press-releases/2025/full-year-and-q4-2024-results.html> , consulted on 13 April 2026.

Garattini, S., Natsis, Y., & Banzi, R. (2021). Pharmaceutical Strategy for Europe: Reflections on Public Health-Driven Drug Development, Regulation, and Policies. *Frontiers in Pharmacology*, 12. <https://doi.org/10.3389/fphar.2021.685604> , consulted on 14 February 2026.

Global Trends in R&D 2025. (2025). <https://www.iqvia.com/Insights/The-Iqvia-Institute/Reports-And-Publications/Reports/Global-Trends-In-r-And-d-2025>. <https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2025> , consulted on 17 January 2026.

G I O M E D I C I N E S - R E P O R T High Level Group on innovation and provision of medicines in the European Union recommendations for action. (2002). https://ec.europa.eu/health/ph_overview/Documents/key08_en.pdf , consulted on 8 January 2026.

High Level Pharmaceutical Forum High Level Pharmaceutical Forum. (2005). https://www.rees-france.com/en/IMG/pdf/2008_High_level_Pharma_forum_en_final_report.pdf , consulted on 7 January 2026.

IMMC.COM%282024%29274%20final.ENG.xhtml.1_EN_ACT_part1_v5.docx. (2024). Europa.eu. <https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:52024DC0274> , consulted on 14 January 2026.

International trade in medicinal and pharmaceutical products. (n.d.). Ec.europa.eu. https://ec.europa.eu/eurostat/statistics-explained/index.php?title=International_trade_in_medicinal_and_pharmaceutical_products , consulted on 22 February 2026.

IQVIA. (2019). *EFPIA patients W.A.I.T. indicator 2018 survey.* IQVIA Institute for Human Data Science. <https://www.efpia.eu/media/412747/efpia-patient-wait-indicator-study-2018-results-030419.pdf>, consulted on 11 February 2026

IQVIA. (2020). *EFPIA patients W.A.I.T. indicator 2019 survey*. IQVIA Institute for Human Data Science. <https://www.efpia.eu/publications/downloads/efpia/efpia-patients-wait-indicator-2019-survey/>, consulted on 11 February 2026.

IQVIA. (2021). *EFPIA patients W.A.I.T. indicator 2020 survey*. IQVIA Institute for Human Data Science. <https://www.efpia.eu/media/602652/efpia-patient-wait-indicator-final-250521.pdf>, consulted on 11 February 2026.

IQVIA. (2022). *EFPIA patients W.A.I.T. indicator 2021 survey*. IQVIA Institute for Human Data Science. https://www.efpia.eu/media/676539/efpia-patient-wait-indicator_update-july-2022_final.pdf, consulted on 11 February 2026.

IQVIA. (2023). *EFPIA patients W.A.I.T. indicator 2022 survey*. IQVIA Institute for Human Data Science. https://www.efpia.eu/media/s4qf1eqo/efpia_patient_wait_indicator_final_report.pdf, consulted on 11 February 2026.

IQVIA. (2024). *EFPIA patients W.A.I.T. indicator 2023 survey*. IQVIA Institute for Human Data Science. <https://www.efpia.eu/media/hosted-publications/efpia-patients-wait-indicator-2024-survey/>, consulted on 11 February 2026.

IQVIA. (2025, May). *EFPIA patients W.A.I.T. indicator 2024 survey*. IQVIA Institute for Human Data Science. <https://www.efpia.eu/media/hosted-publications/efpia-patients-wait-indicator-2024-survey/>, consulted on 11 February 2026.

Joint Clinical Assessments. (2024, November 19). Public Health. https://health.ec.europa.eu/health-technology-assessment/implementation-regulation-health-technology-assessment/joint-clinical-assessments_en, consulted on 21 January 2026.

L'accord commercial entre l'UE et les États-Unis expliqué. (2025, July 29). Représentation En France. https://france.representation.ec.europa.eu/informations/laccord-commercial-entre-lue-et-les-etats-unis-explique-2025-07-29_fr, consulted on 17 April 2026.

Lilly. (2025). Lilly reports full Q4 2024 financial results and provides 2025 guidance. Lilly Investor Relations. <https://investor.lilly.com/news-releases/news-release-details/lilly-reports-full-q4-2024-financial-results-and-provides-2025>, consulted on 4 April 2026.

Macrotrends. (n.d.). Pharmaceutical industry financial data and charts. <https://www.macrotrends.net/>, consulted on 6 January 2026.

MedTech Europe. (n.d.). Health technology assessment. <https://www.medtecheurope.org/access-to-medical-technology/health-technology-assessment/> consulted on 7 January 2026.

Merck. (2025). Merck announces fourth quarter and full year 2024 financial results. Merck News & Media. <https://www.merck.com/news/merck-announces-fourth-quarter-and-full-year-2024-financial-results/>, consulted on 4 March 2026.

National Academies of Sciences, E., Studies, D. on E. and L., Technology, B. on C. S. and, & Manufacturing, C. to I. I. T. to A. P. (2021). Summary. In *www.ncbi.nlm.nih.gov*. National Academies Press (US). <https://www.ncbi.nlm.nih.gov/books/NBK570306/>, consulted on 23 March 2026.

Novartis. (2024). *Novartis continues strong momentum of sales growth with margin expansion, reaches key innovation milestones in 2024*. Novartis. <https://www.novartis.com/news/media-releases/novartis-continues-strong-momentum-sales-growth-margin-expansion-reaches-key-innovation-milestones-2024> , consulted on 4 March 2026.

Number of clinical trials by year, country, region and income group. (n.d.). Wwww.who.int. <https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/number-of-clinical-trials-by-year-country-who-region-and-income-group> , consulted on 4 February 2026.

OECD Health Policy Studies Pharmaceutical Innovation and Access to Medicines. (n.d.). https://www.oecd.org/content/dam/oecd/en/publications/reports/2018/11/pharmaceutical-innovation-and-access-to-medicines_glg98d77/9789264307391-en.pdf , consulted on 12 February 2026.

Ordre national des pharmaciens. (2021, octobre). *Contribution de l'Ordre national des pharmaciens à la réflexion sur la stratégie pharmaceutique pour l'Europe*. Ordre national des pharmaciens. <https://www.ordre.pharmacien.fr/>, consulted on 25 April 2026.

Pfizer. (2024). Pfizer annual review. <https://annualreview.pfizer.com/> , consulted on 4 March 2026.

Pharmaceutical Sector Inquiry Final Report. (2009). https://competition-policy.ec.europa.eu/system/files/2022-05/pharmaceutical_sector_inquiry_staff_working_paper_part1.pdf , consulted on 6 January 2026.

Pharma sector: A changing US landscape will prove disruptive for the entire sector | Credendo. (2025, October 27). Credendo. <https://credendo.com/en/knowledge-hub/pharma-sector-changing-us-landscape-will-prove-disruptive-entire-sector> , consulted on 12 March 2026.

(2026). Pharmainfo.be. <https://pharmainfo.be/themes/combien-fois-je-payer-pour-mon-medicament-a-la-pharmacie> , consulted on 7 April 2026.

Plaza, L. (n.d.). *Fédération Européenne d'Associations et d'Industries Pharmaceutiques Principes for application of international reference pricing systems*. <https://www.efpia.eu/media/15406/efpia-position-paper-principles-for-application-of-international-reference-pricing-systems-june-2014.pdf> , consulted on 18 April 2026.

Prescrire Rédaction. (2022). Face à la stratégie de la Commission européenne (chaînes d'approvisionnement, accès à des médicaments abordables, innovation), une alliance d'associations de la société civile, dont Prescrire, demande notamment plus de transparence et de preuves pour l'évaluation et les décisions, la suppression d'incitations financières peu efficaces voire néfastes, le soutien aux besoins de santé publique et des patients. *La Revue Prescrire*, 42(468), 784–787. <https://www.prescrire.org/politiques-de-sante/468-changements-en-vue-de-la-reglementation-pharmaceutique-europeenne> , consulted on 4 April 2026.

Press corner. (n.d.). European Commission - European Commission. https://ec.europa.eu/commission/presscorner/detail/nl/IP_11_370 , consulted on 22 April 2026.

Press Release: Q4 sales growth of 10.3%, 2024 business EPS guidance exceeded, and strong business EPS rebound expected in 2025. (2024). Sanofi.com. <https://www.sanofi.com/en/media-room/press-releases/2025/2025-01-30-06-30-00-3017713> , consulted on 4 march 2026.

Proposal for a Regulation to establish measures to strengthen the Union's biotechnology and biomanufacturing sectors (European Biotech Act). (2025, December 16). Public Health. https://health.ec.europa.eu/publications/proposal-regulation-establish-measures-strengthen-unions-biotechnology-and-biomanufacturing-sectors_en , consulted on 22 April 2026.

QbD Group. (2025, February 5). Continuous manufacturing in the pharmaceutical industry. <https://www.qbdgroup.com/en/blog/continuous-manufacturing-in-the-pharmaceutical-industry> , consulted on 24 March 2026.

Reimbursement of pharmaceuticals in Europe requires a comprehensive strategy. (2024). Iges.com. https://healthecon.iges.com/reimbursement/index_eng.html , consulted on 18 January 2026.

Reglamento - 2019/933 - EN - EUR-Lex. (2019). Europa.eu. <https://eur-lex.europa.eu/legal-content/PT/ALL/?uri=CELEX:32019R0933> , consulted on 9 January 2026.

Regulation - 2021/2282 - EN - EUR-Lex. (2021). Europa.eu. <https://eur-lex.europa.eu/eli/reg/2021/2282/oj/eng> , consulted on 9 January 2026.

Review of the SPC Manufacturing Waiver: a 2024 Industry Report. (n.d.). <https://www.medicinesforeurope.com/wp-content/uploads/2024/06/Updated-2024-Industry-Report-on-SPC-Manufacturing-Waiver-Medicines-for-Europe-REV-CLEAN.docx.pdf> , consulted on 10 January 2026.

Révision pharmaceutique de l'UE : des médicaments plus accessibles et innovants en vue. (2024). IFIS. <https://www.ifis.fr/actualites/revision-pharmaceutique-de-lue-des-medicaments-plus-accessibles-et-innovants-en-vue> , consulted on 17 January 2026.

Roche. (2024). Roche | Roche's Annual Report 2024. Roche.com. <https://www.roche.com/investors/annualreport24> , consulted on 14 April 2026.

SciencePharma. (2025, July 4). SciencePharma. <https://www.sciencepharma.com/blog/centralised-procedure-the-european-union/> , consulted on 21 January 2026.

Statista. (n.d.). Pharmaceutical industry statistics and data. <https://www.statista.com/homepage> , consulted on 17 January 2026.

Supplementary protection certificates for pharmaceutical and plant protection products. (n.d.). Single-Market-Economy.ec.europa.eu. https://single-market-economy.ec.europa.eu/industry/strategy/intellectual-property/patent-protection-eu/supplementary-protection-certificates-pharmaceutical-and-plant-protection-products_en , consulted on 6 January 2026.

Thale, Bournier, J., Kali, S., Marius Trøseid, Yazdan Yazdanpanah, Piero Olliaro, & Inge Christoffer Olsen. (2024). Experiences and challenges with the new European Clinical Trials Regulation. *Trials*, 25(1). <https://doi.org/10.1186/s13063-023-07869-x> , consulted on 12 January 2026.

The decline of U.S. pharmaceutical production | FRED Blog. (n.d.).

<https://fredblog.stlouisfed.org/2020/06/the-decline-of-u-s-pharmaceutical-production/> , consulted on 18 January 2026.

Trading Economics. (2019, August 19). *United States Exports*. Tradingeconomics.com; TRADING ECONOMICS. <https://tradingeconomics.com/united-states/exports> , consulted on 17 March 2026.

Umbrex. (2025, April 7). *How the Pharmaceutical Industry Works*. Independent Management Consultants. <https://umbrex.com/resources/how-industries-work/healthcare-and-life-sciences/how-the-pharmaceutical-industry-works/> , consulted on 6 January 2026.

Appendix

Figures & Tables

Appendix A – Table 1: Top 10 Global Pharmaceutical Companies (2024)

Source: Umbrex (2025). Ranked by annual revenue.

Company	Country	Revenue (\$B)	Market Capital (\$B)	R&D Spend (\$B)
Johnson&Johnson	USA	88.82	349.22	17.232
Roche	Switzerland	66.42	225.59	17.384
Eli Lilly & Co.	USA	45.03	704.31	10.991
Merck & Co.	USA	64.17	225.20	17.938
Pfizer	USA	63.63	150.85	10.822
AbbVie	USA	56.33	314.56	12.791
AstraZeneca	Great Britain & Sweden	54.07	203.60	13.583
Bayer	Germany	51.07	19.75	6.719
Novartis	Switzerland	50.32	196.70	10.022
Sanofi	France	42.68	122.17	8.001

Appendix B – Table 3: List of medicines analyzed for PRIME assessment

PRIME Status	Medicine Name	Therapeutic Area	EMA Authorization Date
Yes	Autologous human T cells genetically modified ex-vivo with a lentiviral vector encoding a	Oncology	2022-05-25

	chimeric antigen receptor (CAR) for B-cell maturation antigen (BCMA) (JNJ-68284528) (CARVYKTI)		
Yes	Autologous peripheral blood T cells CD4 and CD8 selected, and CD3 and CD28 activated transduced with retroviral vector encoding an anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured (KTE-X19) (Tecartus)	Oncology	2020-12-14
Yes	Axicabtagene ciloleucel (Yescarta)	Oncology	2018-08-23
Yes	Brensocatib (Brinsupri)	Pneumology-allergology	2025-11-18
Yes	Bulevirtide (Hepcludex)	Infectious Diseases	2020-07-31
Yes	CTX001 (Autologous CD34+ hematopoietic stem cells with a CRISPR-edited erythroid enhancer region of the BCL11A gene) (Casgevy)	Haematology - Haemostaseology	2024-02-09
Yes	Chikungunya virus virus-like particle vaccine (PXVX0317) (Vimkunya)	Infectious Diseases	2025-02-28
Yes	Danicopan (Voydeya)	Haematology - Haemostaseology	2024-04-19
Yes	ECT-001-CB (Zemcelpro)	Oncology	2025-08-25
Yes	Entrectinib (Rozlytrek)	Oncology	2020-07-31
Yes	Etranacogene dezaparvovec (AMT-060, AMT-061) (Hemgenix)	Haematology - Haemostaseology	2023-02-20
Yes	Genetically modified replication-incompetent herpes simplex virus-1 expressing collagen VII (KB103) (Vyjuvek)	Dermatology	2025-04-23
Yes	Givosiran (Givlaari)	Endocrinology - Gynaecology - Fertility - Metabolism	2020-03-02
Yes	Idecabtagene vicleucel (bb2121) (Abecma)	Oncology	2021-08-18
Yes	Imlifidase (Idefixir)	Immunology - Rheumatology - Transplantation	2020-08-25
Yes	Iptacopan (Fabhalta)	Endocrinology - Gynaecology - Fertility - Metabolism	2024-05-17
Yes	Lumasiran (Oxlumo)	Uro-nephrology	2020-11-19
Yes	Nirsevimab (MEDI8897) (Beyfortus)	Infectious diseases	2022-10-31

Yes	Obecabtagene autoleucel/ AUTO1 (Aucatzyl)	Oncology	2025-07-17
Yes	Odevixibat (A4250) (Bylvay)	Gastroenterology - Hepatology	2021-07-16
Yes	Olipudase alfa (Xenpozyme)	Endocrinology - Gynaecology - Fertility - Metabolism	2022-06-24
Yes	Onasemnogene abeparvovec (Zolgensma)	Neurology	2020-05-18
Yes	PF-06863135 (Elrexio)	Oncology	2023-12-07
Yes	Polatuzumab vedotin (Polivy)	Oncology	2020-01-16
Yes	Recombinant Vesicular Stomatitis Virus with Envelope Glycoprotein replaced by Zaire ebolavirus (Kikwit Strain) Glycoprotein (Ervebo)	Vaccines	2019-11-11
Yes	Risdiplam (Evrysdi)	Neurology	2021-03-26
Yes	Setmelanotide (Imcivree)	Endocrinology - Gynaecology - Fertility - Metabolism	2021-07-16
Yes	Sotatercept (Winrevair)	Cardiovascular diseases	2024-08-22
Yes	Tabelecleucel (Allogeneic Epstein-Barr virus- specific cytotoxic T lymphocytes, ATA129) (Ebvallo)	Haematology - Haemostaseology	2022-12-16
Yes	Talquetamab (Talvey)	Oncology	2023-08-21
Yes	Teclistamab (Tecvayli)	Oncology	2022-08-23
Yes	Tisagenlecleucel (Kymriah)	Oncology	2018-08-23
Yes	VLA1553 (Ixchiq)	Vaccines	2024-06-28
No	Abrysvo	Vaccines	2023-08-23
No	Adtralza	Dermatology	2021-06-17
No	Arexvy	Vaccines	2023-06-06
No	Camzyos	Cardiovascular diseases	2023-06-26
No	Columvi	Oncology	2023-07-07
No	Enspryng	Immunology - Rheumatology - Transplantation	2021-06-24
No	Esperoct	Haematology - Haemostaseology	2019-06-20
No	Filsuvez	Endocrinology - Gynaecology - Fertility - Metabolism	2022-06-21
No	Fintepla	Neurology	2020-12-18
No	Furzaqla	Oncology	2024-06-20
No	Isturisa	Endocrinology - Gynaecology - Fertility - Metabolism	2020-01-09
No	Jaypirca	Oncology	2023-10-30
No	Jemperli (Dostarlimab)	Oncology	2021-04-21
No	Kerendia	Uro-nephrology	2022-02-16

No	Kimmtrak (Tebentafusp)	Oncology	2022-04-01
No	Lumykras (Sotorasib)	Oncology	2022-01-06
No	Ngenla	Haematology - Haemostaseology	2022-02-14
No	Obizur	Haematology - Haemostaseology	2015-11-11
No	Orserdu	Oncology	2023-09-15
No	Pemazyre (Pemigatinib)	Oncology	2021-03-26
No	Pombiliti	Neurology	2023-03-20
No	Quofenix	Infectious Diseases	2019-12-16
No	Retsevmo (Selpercatinib)	Oncology	2021-02-11
No	Rukobia	Infectious Diseases	2022-02-04
No	Sogroya	Endocrinology - Gynaecology - Fertility - Metabolism	2021-03-31
No	Sunlenca	Infectious Diseases	2022-08-17
No	Tepmetko (Tepotinib)	Oncology	2022-02-16
No	Tezspire	Pneumology-allergology	2022-09-19
No	Tibsovo (Ivosidenib)	Oncology	2023-05-04
No	Tukysa (Tucatinib)	Oncology	2021-02-11
No	Velsipity	Gastroenterology - Hepatology	2024-02-16
No	Veozza	Endocrinology - Gynaecology - Fertility - Metabolism	2023-12-07
No	Veyvondi	Haematology - Haemostaseology	2018-08-31

Note: All data extracted from European Medicines Agency European Public Assessment Reports (EPARs). PRIME = Priority Medicines scheme.

Interview Transcriptions

Participant A from the EMA

Maëlys: Hello! Thank you for taking the time to have this discussion.

Participant A: Of course! I'm more than happy to help with whatever I can. I'm not sure if it's a lot, but let's see.

Maëlys: No worries. For my master's thesis, I'm analyzing the Pharmaceutical Strategy for Europe based on four pillars: the attractiveness of Europe, access to medicines, competitiveness, and innovation. I've already done the quantitative analysis, but I think it's important to gather insights from what's happening inside the institutions and the pharmaceutical sector. Your insights from the EMA will be really valuable because you said it was a hot topic when you worked there ?

Participant A: It was, yes. That was just the time when medical devices were introduced into the scope of our team, and then a dedicated department was created. When it came to availability, if you separate availability, affordability, and accessibility, we were five months into the pandemic. Supply chains were being disrupted all over the world. An ad hoc group had been set up to deal with the implications of that when it came to having the medicines be available. We were doing all kinds of experimental things and trying to model what the needs, the supply and demand bits, were in quite a few therapeutic areas. We were

basically one of the hottest departments because, apart from getting the vaccine, that was the second biggest concern: that the rest of the healthcare system could function "normally" by having the medicines there.

Maëlys: Especially for the shortage department, it was a big issue. Did you feel like the EMA and the European Commission were well-coordinated on the pharmaceutical strategy, or were there some tensions in between?

Participant A: There were some tensions. I think there was, on the EMA side, the very technical aspect of approaching the problem. Of course, the Commission had to take into consideration the political aspect of it. Sometimes the two collided. Even the "little politics" that the EMA as an organization was interested in was a bit conflicting with what the Commission wanted. Ultimately, it was the Commission's role to decide. I think everyone knew what the power play was.

Maëlys: So, in general, the pharmaceutical strategy was really present in the daily work of the EMA? It was not like a far political document?

Participant A: No, adaptations were being made. I'm not sure I can talk about all the departments, but maybe the core business, medicine evaluation, didn't change so much. What did change was how the administration and the other departments tackled what they had to be looking at. I remember there was this reshuffle in mid-2021, where the horizon scanning team got a lot more serious. They started having to really deal with a lot more and expand their framework of operation to adapt.

Maëlys: In general, did you feel like the EMA had the financial and human resources to handle the pharmaceutical strategy, or were they a bit overstretched?

Participant A: That's a tricky question. The EMA is a huge organization. I think the human capacity at the EMA was not being made use of efficiently. A lot more could have been outputted. But what was being asked with the pharma strategy clearly required a lot more than what the EMA realized they had. The European Commission was asking too much, or at least that was the perception from the inside.

Maëlys: In the shortage department, how would you detect and manage a shortage? Were European tools adequate for that?

Participant A: There are a lot of problems with that. First of all, no one knows what a shortage is. The EMA and the Heads of Medicines Agencies had adopted a definition where supply doesn't meet demand, but that's too vague. If the shortage was being reported by the Member States, that was one thing; by the wholesalers, that was another; or if it was being anticipated by the marketing authorization holder. Is it a shortage if it didn't impact the patients? And what does "impact" mean? Is substitution okay? There's a lot of conceptual variables. Then there's the reporting system, which was not homogeneous at all. Every Member State had their own, their own timings, and their own responsiveness. It was basically us, with close to no tools other than Microsoft Excel, trying to make the most out of what the Member States or the companies would tell us.

Maëlys: And did you feel like they were handling those shortages well?

Participant A: It's super subjective. What "handling well" on a regional scope might mean is not the same as on a national or European-wide scope. I think the companies were cooperating, but I'm not sure they would be disclosing everything they knew about inventory in other Member States. First, because in some situations they weren't legally allowed to. In other situations, it wasn't in their best interest to reveal that

some parallel export was being done. I think the whole information system had to be reformed and set up in a way that could leave no doubt about inventory or Member State-to-Member State deltas of availability.

Maëlys: For the "innovation" pillar, I analyzed the PRIME scheme from the EMA. In my regression, it comes out that medicines with this label are approved 4.7 months faster on average. Why is it actually going faster?

Participant A: It wasn't my department, but that was actually a well-circulated success story around the agency. From what I remember, it was a mix of trimming the calendar wherever possible, shortening the times, and mostly giving priority to that. Medical assessors have quite a load, so prioritizing one thing over another does make a difference. It was really just a scheduling and prioritizing issue; it was not that we needed new capacity or a new skill. It was managing the logistics. Take the vaccine: that was the priority, and it went as fast as it could without compromising quality.

Maëlys: From your EMA experience, what would be your takeaway about the Europe's capacity to manage its pharmaceutical strategy?

Participant A: The thing that everyone knows, both in the Commission and the EMA, is that it's really about the Member States. When you get into a political process or the implementation level, it's about working with the Member States and the national competent authorities. They have to be sold on the idea, otherwise, cooperation won't work. I also think those tensions I mentioned resulted from a lack of exposure of both parties to what the other party's day-to-day or reality looked like. It was really about coming to a negotiation table with a lot of positions but with little context on why the other party brought those positions.

Maëlys: Thank you so much for your time. Your insights are really valuable for my thesis. I'll send you the final work!

Participant A: That would be great. Good luck!

Jean-Gonzague from GSK

Monsieur Fontaine (sur l'attractivité et l'innovation) : « Le problème de fond de la stratégie pharmaceutique européenne, et plus particulièrement du pilier sur l'attractivité, c'est l'équilibre entre l'innovation et l'accessibilité financière. Si vous regardez où circulent les capitaux, ils vont souvent vers les États-Unis ou même la Chine aujourd'hui. L'Europe possède une base académique incroyable, mais nous avons du mal à passer à l'échelle supérieure. La stratégie vise à corriger cela, mais l'industrie craint que les réglementations sur les prix et le raccourcissement des périodes de protection intellectuelle, discutés pour améliorer l'accès, ne finissent par éloigner encore plus la R&D du continent. »

Monsieur Fontaine (sur les pénuries et la chaîne d'approvisionnement) : « Quand on parle de pénuries, ce n'est pas seulement un problème de fabrication, c'est un problème géographique. Pendant des années, nous avons externalisé la production de principes actifs (API) vers l'Inde et la Chine pour des raisons de coûts. Aujourd'hui, la stratégie tente de ramener une partie de cette "autonomie stratégique" en Europe. Mais on ne reconstruit pas une usine chimique en six mois. Cela nécessite des subventions massives et un changement dans la manière dont nous valorisons les médicaments. On ne peut pas exiger des prix bas et, en même temps, des chaînes d'approvisionnement ultra-sécurisées. »

Monsieur Fontaine (sur le rôle de l'EMA et la coordination) : « L'EMA fait beaucoup avec les mandats qui lui ont été confiés après le COVID, notamment sur la surveillance des pénuries. Cependant, le véritable pouvoir reste entre les mains des agences nationales de tarification et de remboursement. Vous avez une stratégie européenne pour l'innovation, mais 27 stratégies différentes pour l'accès et les prix. Cette fragmentation est le plus grand obstacle à toute politique pharmaceutique européenne cohérente. »

Maëlys : C'est très intéressant. Pensez-vous donc que le pilier « accès » entre en contradiction avec celui de la « compétitivité » ?

Monsieur Fontaine : « À bien des égards, oui. C'est une tension classique. Si vous voulez plus d'accès, vous voulez des prix plus bas et plus de génériques. Si vous voulez de la compétitivité et de l'innovation, il faut de fortes récompenses pour les nouveaux médicaments. La Commission européenne essaie de trouver un juste milieu, mais le chemin est très étroit. »

Thibault from Catalya

Thibault: Salut Maëlys! Donc tu avais quelques questions pour moi, comment ça marche ? J'étais assez impressionné par ton sujet de mémoire, qu'il soit si spécifique.

Maëlys : Ah oui ? Oui, je ne sais plus si je t'avais déjà expliqué le sujet précisément.

Thibault : Tu m'as envoyé le sujet, je ne connaissais pas du tout. J'ai regardé deux secondes dans ChatGPT qui m'a donné un peu le contexte. C'est étonnant, c'est dans mon secteur donc je devrais connaître, mais je n'en avais jamais entendu parler.

Maëlys : Oui, parce qu'on est d'accord, si je ne me trompe pas, tu travailles dans une entreprise de biotechnologie ?

Thibault : Oui, je travaille pour l'instant dans deux entreprises de biotech : une à Anvers et une à Liège. Mais c'est vrai que le cadre qu'ils décrivent est plutôt un cadre réglementaire et d'accord général pour les médicaments qui sont déjà approuvés. Alors que moi, je suis vraiment très en amont dans la recherche. Je suis plutôt dans les phases, ça te parle certainement, quand tu regardes les phases de développement clinique, tu as le préclinique, puis les phases 1, 2, 3 et enfin le commercial. Moi, je suis plutôt dans tout ce qui est préclinique. Donc voilà, c'est un monde à part.

Maëlys : Oui, c'est ça. Mais en général, si j'ai bien compris, les entreprises de biotech sont surtout dans l'innovation, et tout ce qui est commercialisation et industrialisation, c'est plutôt les "Big Pharma".

Thibault : C'est un peu comme l'exemple des grands groupes tels que Google ou Facebook. En fait, eux-mêmes n'arrivent plus à innover parce que c'est devenu d'énormes machines de guerre, un peu comme les grands groupes pharma. Du coup, typiquement, Instagram ou Snapchat ont été créés par des plus petites structures, puis des Facebook les rachètent parce qu'ils ont le réseau, les utilisateurs, et ils savent industrialiser et développer un produit. Mais ils ne savent plus faire de l'innovation. Ça ne veut pas dire que le pharma ne fait pas de R&D, mais souvent, le bon exemple, c'est Ablynx, qui était une biotech en Belgique rachetée par Sanofi parce qu'ils étaient intéressés par leurs médicaments.

Maëlys : Oui, c'est souvent comme ça que ça se passe. Mais du coup, ce cadre réglementaire que la Commission Européenne a mis en place, mon but était d'évaluer s'il avait fonctionné ou s'il y avait déjà des résultats. J'ai trouvé des chiffres en faisant des régressions, mais je trouvais ça important d'avoir le point de

vue du terrain et de l'intérieur du secteur. Comme tu travailles dans une biotech, c'était intéressant d'avoir ce point de vue plutôt à côté de celui d'une Big Pharma. Est-ce que chez Catalya vous avez déjà envisagé, ou envisagez-vous de développer hors Europe ?

Thibault : Aujourd'hui, nos principaux clients sont en Europe. Mais en général, le monde biotech et pharma est réparti ainsi : 50 % aux États-Unis, 30 % en Europe et 20 % en Asie. C'est un peu la règle d'or. Il y a toute une partie du marché qui est aux États-Unis et avec qui on se retrouve finalement à faire des deals, alors que notre secteur naturel est plutôt l'Europe. Mais le terrain de jeu reste le monde, et principalement l'axe États-Unis/Europe. Pour revenir sur l'étude, je crois que "l'effet Trump" a vraiment accéléré les choses. Plein d'entreprises, à cause des mesures prises par Trump, sont en train de relocaliser une partie de leur production et de leurs activités aux États-Unis. Les États-Unis ont mis un gros coup de pression : "si vous voulez continuer à commercialiser chez nous, il faut produire ici". Les mesures européennes pour contrer cet effet, enclenché dès le COVID, ont un effet très léger face à des politiques aussi agressives.

Maëlys : Donc tu le ressens vraiment dans le secteur ?

Thibault : Oui, c'est gigantesque. Tous nos clients chez Catalya, qui sont des biotechs et des grands groupes pharma, sont nombreux à avoir relocalisé des activités ou annoncé des investissements massifs aux États-Unis plutôt que dans leurs usines en Europe.

Maëlys : C'est bon à savoir, car c'est exactement ce que la stratégie européenne cherche à contrer, mais ce sont des effets externes difficiles à prévoir.

Thibault : Quand tu as une voix très forte comme celle de Trump qui dit "on va faire comme ça" et que c'est appliqué dès le lendemain, c'est puissant. Au niveau européen, on a plein de pays avec leurs propres réglementations, c'est très fragmenté. On a beau avoir la meilleure volonté du monde, c'est moins efficace.

Maëlys : Par rapport aux parts de marché, mon analyse montre une perte continue des parts européennes pour les essais cliniques. D'après toi, quels sont les vrais freins à l'attractivité européenne pour la recherche ?

Thibault : Les initiatives de l'acte européen étaient pas mal : harmoniser, simplifier... Mais pour moi, le plus gros problème du marché européen est sa fragmentation. En termes de population et de pouvoir d'achat, le marché intérieur européen est le deuxième mondial, juste derrière les États-Unis. Mais en réalité, il est divisé par X pays qui ont leurs propres autorités réglementaires. Même s'il y a l'EMA (European Medicines Agency) censée coordonner, c'est pareil au niveau de l'IP (propriété intellectuelle) et des brevets : quand tu déposes un brevet, tu dois quand même aller le défendre dans chaque pays. Aux États-Unis, tu te bats sur un seul marché. Et même si le remboursement y est négocié par État, ils ont réussi à créer des synergies et une simplification bien plus poussée. L'Europe est toujours trop timide là-dessus. La difficulté réside dans la mise en œuvre de l'harmonisation et de l'intégration.

Maëlys : On n'est pas encore assez harmonisés pour que ce soit attractif.

Thibault : Non. Et je ne sais pas comment tu as analysé l'atteinte des objectifs par rapport au pacte annoncé, mais je pense qu'on ne les a pas tous réalisés.

Maëlys : Certains oui, d'autres non. Pour l'attractivité, il n'y a pas eu d'évolution. J'ai aussi analysé l'innovation, notamment le programme "Priority Medicines" de l'EMA. C'est un label spécial pour les

médicaments couvrant des besoins non satisfaits. Mon analyse montre que ça a accéléré le processus. Est-ce que vous avez déjà utilisé ou envisagez d'utiliser ce programme ?

Thibault : Nous, on ne l'utilise pas en tant que tel. Mais c'était une très bonne initiative car c'était une de nos faiblesses. Aux États-Unis, quand ils décident de rembourser un médicament et d'en faire une priorité, ça représente une manne financière énorme pour les entreprises. Ici, il faut se battre pays par pays. En Belgique, on a eu le problème avec les nouveaux traitements contre le cancer : on parlait d'un budget de 20 millions, alors qu'aux États-Unis, ils mettent 2 milliards sur la table. C'est dérisoire. C'est David contre Goliath, on ne se bat pas avec les mêmes moyens.

Maëlys : Donc la fragmentation reste le problème principal. S'il y avait une chose à améliorer, ce serait l'harmonisation ?

Thibault : Oui. Et après, c'est mon avis personnel : le modèle actuel est de développer des médicaments pour guérir des maladies. Je pense qu'il doit y avoir un vrai changement de paradigme. Le plus longtemps possible, en mettant le paquet sur la médecine préventive. Aujourd'hui, ce n'est pas assez fait. Des études démontrent que si on investissait plus en prévention, on éviterait des maladies et tous les coûts associés (perte de travail, remboursement de médicaments chers). Ce serait un beau pari pour l'Europe de se distinguer ainsi. Il faut continuer à soigner les malades, mais essayons d'abord de rester en bonne santé. Arrêtons la "malbouffe", par exemple. Notre génération va vivre jusqu'à 90 ou 100 ans. On voit nos grands-parents avec Alzheimer, Parkinson, le diabète... Aujourd'hui, qu'est-ce qui cartonne en bourse ? Eli Lilly et Novo Nordisk, parce qu'ils ont développé des médicaments pour perdre du poids. C'est génial quand on a un vrai problème de surcharge pondérale, mais en vrai, il faut juste surveiller son alimentation et faire du sport. L'accent devrait être mis sur la prévention plutôt que sur la solution après-coup.

Maëlys : Ton point de vue m'aide beaucoup. Si ça ne te dérange pas, je vais intégrer tout ça dans mon mémoire.

Thibault : Évidemment, avec grand plaisir ! N'hésite pas si tu veux que je relise ou si tu veux une confirmation "secteur".

Maëlys : Trop bien, merci ! Je te tiens au courant ! Salut Thibault !

Thibault : Avec plaisir, à bientôt Maëlys !

Ben from GSK & FDA

Ben: Hi Maëlys! How are you?

Maëlys: Good, thanks. Thanks for taking the time. Nice to meet you. You are based in the United States?

Ben: Yeah. We have a research and development site in the town I live in, in Pennsylvania, so it's right down the street for me. You're interested in regulatory work ?

Maëlys: Yes. I'm doing my research right now for my thesis during my last semester. My thesis is evaluating the impact that the European Pharmaceutical Strategy has had since it was implemented. To conduct this research, I analyzed the four pillars: attractiveness of the European market, competitiveness, access to medical care, and innovation. For each of them, I analyzed one regulation. I looked at data to see the actual

impact, but I thought it was also important to gather insights from people working in the market. You worked at the FDA ?

Ben: I did. Both my wife and I did. I was primarily in the Chemistry, Manufacturing, and Controls (CMC) area on the new drug side. I worked a lot with new product submissions for investigational products under the IND (Investigational New Drug) path and commercial products submitted for NDAs (New Drug Applications).

Maëlys: From your FDA point of view, what is the most fundamental difference in structure between the FDA and the European Medicines Agency (EMA) that affects how Europe competes in clinical research and investment?

Ben: It's interesting timing because this is being talked about a lot right now, specifically regarding how other countries like Australia and China are competing. Regarding Europe, the most obvious challenge is that it's a much more complicated setup. You aren't just dealing with the EMA as the top regulator; you are dealing with the EMA plus all the competent authorities within the various member states.

When you're talking about clinical trials or pathways to innovate, they have a lot more of a challenge dealing with all the different countries involved. The European Union has to delegate certain final authorities to the actual member states. I've observed that this creates complexity when you go from getting feedback from the EMA to going country-by-country, particularly on the clinical development side. You see disconnects between what they tell you at the EMA versus what you see on the ground in specific states when you file for trials.

In the US, we have the "Pre-NDA" or "Pre-BLA" meeting with the FDA right before you submit your marketing application. In Europe, they have something similar with the EMA, but you are also dealing with the other competent authorities. When you work on a marketing application, they pull from certain countries to assign a rapporteur and co-rapporteur. It can be a bit of a "luck of the draw." Some countries are much more particular about certain areas of review; for example, Germany has a very strong biologics agency (Paul-Ehrlich-Institut) with a lot of expertise. If you wind up with a different country, it can be an unexpected twist that makes things complicated.

Maëlys: So, the main issue is that there are too many competent authorities in Europe and it should be more harmonized, while in the US, the administration is easier for companies?

Ben: Yes, but I should say, and I tell you this as someone who used to work at the FDA, I find the EMA folks much more outgoing and able to engage industry on specific topics. For example, the Quality Innovation Group (QIG) the EMA stood up a couple of years ago focuses specifically on innovation in manufacturing for pharmaceuticals. They do a great job facilitating discussions.

The problem is simply the nature of the regulations in Europe and how the EMA's authority is structured. They will always have limited authority over what each individual country is able to finally say "yes" or "no" to. You can feel really good about a conversation with the EMA, but then get surprised by a disconnect at the clinical trial stage in a specific region. The FDA, however, has total authority over whatever goes on in the US. If the FDA says it in official meeting minutes, you can take it to the bank. It's a very big agency and bureaucracy can be a challenge, but the authority is centralized.

Maëlys: Beyond cost, what are the decisive factors for a company when deciding to run a trial in the US versus Europe?

Ben: One challenge in Europe is the lack of harmonization regarding Institutional Review Boards (IRBs). In the US, it is much more harmonized across the country. The FDA doesn't really touch the IRB process much; it's carried out by institutions. From what I understand, it is much more complicated across Europe because local laws differ and the way regulators carry out the assessment of that process is different. Some regulators will carry out their own review process in parallel with the CTA (Clinical Trial Authorization) application. In the US, that's all taken care of before you even submit an IND; the sites are essentially ready to go.

Maëlys: How do you perceive the European Pharmaceutical Strategy? Was it more of a political document, or did it make genuine shifts in how companies like GSK operate?

Ben: For a big company like GSK, it often doesn't change things too much because they develop products with an eye on global marketing from the start. They try to get a footprint in trials very early on.

For a smaller biotech, it can definitely make a difference. I've seen smaller companies stop running Phase I studies in both the US and Europe and move them to Australia or China. Australia is quite appealing because it hits a nice middle ground, they do things fast, but you can be confident in the quality. They also propagate a lot of the same practices used in Europe, so if you do it in Australia, you're pretty sure you can go back to Europe and things will be okay.

Generally, companies will go where they think they can do things faster and for lower cost. But quality and the ability to find reputable investigators matter too. In Europe and the US, if you find an investigator and get set up, you can "take it to the bank."

Maëlys: For the competitiveness pillar, I analyzed the SPC (Supplementary Protection Certificate) Manufacturing Waiver. It allows manufacturers of generics and biosimilars to export outside of Europe while the patent has not expired, provided it's to countries where the patent has expired. It also allows them to stock products so they can commercialize them immediately once the patent expires. Do you think this was the right tool for competitiveness?

Ben: My personal read on it, without looking at specific data, is that it's probably not going to make that much of a difference. It seems this is mainly to cover the time lost during regulatory review by extending the patent. In Europe, those timelines are usually pretty well-defined.

It might be part of a broader combination of incentives that would make you stay, but by itself, it makes a very small dent in a manufacturer's decision. A new manufacturing site costs tens of billions of dollars and years of investment; a few months of extra exclusivity for a blockbuster product is a drop in the bucket compared to those macro decisions. A lot of it comes down to taxation, I hear it all the time from people making site decisions; they are always looking for tax incentives. It's a "nice to have," but it's not going to reverse the trend of offshoring.

Maëlys: According to you, what is the one thing the EU is getting right with its strategy, and what is one thing that is unlikely to be fixed by regulation alone?

Ben: One thing they are getting right is being proactive about harmonization and coordination with other global regulators. They have been leaders in creating new paths that work across different regions. For

example, "Reliance" models where Europe serves as an initial point of review and other countries rely on those findings. They are very proactive there.

On the other hand, I'm seeing issues emerge regarding AI, particularly in manufacturing. They are trying to be proactive with rules, but nobody really knows how this stuff is going to play out yet. If they are too aggressive about regulating things strictly "out of the box," they might inadvertently limit the innovation that would benefit them. It's often best to focus on broader principles rather than nitty-gritty rules when technology is emerging. They are trying hard, but I would keep an eye on that one.

Maëlys: Thank you so much for your insights! They will be very helpful for my thesis.

Ben: Happy to help! Take care, and nice to meet you.

Maëlys: Nice to meet you too. Bye!

Norman from FDA

Maëlys: Hello! Nice to meet you. Thank you for taking the time.

Norman: Nice to meet you too. I was wondering, since you are looking at the EU compared to the FDA, if you had a chance to see that webinar link I sent you related to Orphan Drugs?

Maëlys: Yes, I read it. It was quite interesting because there was someone speaking about the EU and someone speaking about the FDA, so I got a direct comparison of what was going on.

As I mentioned, I'm writing my master's thesis on the impact of the European Pharmaceutical Strategy since 2020. I'm looking at the four pillars: attractiveness, competitiveness, access, and innovation. I've analyzed the data, but now I'm gathering insights from professionals to complement the quantitative analysis. I thought your insights from the FDA would be very interesting.

Norman: Well, I'll give you my short summary. At the FDA compared to the EMA, and of course, I am primarily involved in data standards and CMC (Chemistry, Manufacturing, and Controls) quality aspects, the expectations are actually quite similar. I don't really see that there are very many differences in those requirements.

Maëlys: From your experience at the FDA, at what point did the agency start to perceive Europe as losing ground on pharma R&D and clinical research?

Norman: I didn't really perceive them as losing ground. I just understood that in past years, there were diverse regulations about clinical trials in Europe which made it somewhat confusing for industry. In subsequent years, the EMA has clarified some clinical trial information, but to me, it still seems more confusing because there are various country regulations that make complying with clinical trials a complex task for industry. Here at the FDA, it is more straightforward.

Our current Commissioner actually recently wrote an article talking about some innovations in Chinese clinical trials that maybe we should think about here in the US. It gives you an idea of what we're looking at now.

Maëlys: How did the FDA view the EMA as a peer? Was it a competitive relationship or more about coordination?

Norman: I would say they are our colleagues. We have numerous groups that have regular collaboration with the EMA. I was involved in the Drug Shortage Group at the FDA, and we had regular meetings with the EMA Drug Shortage Group.

I've also been involved in a lot of data standards activities. We actually hosted the head of the SPOR project (Substances, Products, Organisations, and Referentials), which is essentially an implementation of ISO data standards for the exchange of medicinal product information. Isabelle Cludts came to the FDA for a few weeks, and I was one of her hosts. We have also done a couple of visits over to the EMA, including when they were located at Canary Wharf in London. The feeling is really that these are our colleagues and we can learn from them. Typically, there is an "embedded" person from the FDA who is at the EMA, and likewise, an embedded EMA person at the FDA.

Maëlys: You were involved in building the ICH (International Council for Harmonisation) framework. Looking back now, what did it achieve in terms of harmonizing the US, Japan, and EU environments, and where did it fall short?

Norman: One major achievement was the agreement to organize the dossier for Quality in the way the US had done it, separating drug substance from drug product. That was a great thing because we could then take dossiers compiled for the EU and use them at the FDA without a lot of change. That is largely a result of the CTD (Common Technical Document) and the eCTD (Electronic Common Technical Document).

One of the disappointing things was a group called Q4, which was Pharmacopeial Harmonization. It probably should have been called "pharmacopeial disharmonization." It was very contentious. We could harmonize certain monographs and practices among the Japanese, European, and US pharmacopeias, but there were always exceptions. It would be a "harmonized monograph" except for points A, B, C, and D. I had to wonder what the point was of spending all that time if, in the end, we didn't really harmonize everything.

Regarding quality submissions, I believe those are more common across regions than other sections. One difference used to be that the EMA did not require individual patient data in clinical trials, whereas that was a major focus of the FDA. We would look at individual patient data and do our own subgroup analysis. I understand now that the EMA is moving more towards this, getting individual patient safety data.

For safety, that is very important. In clinical trials, you may be looking at averages for efficacy, but for safety, what is really important are the outliers. I recall one drug we approved that had thousands of people in the trial, but once it hit the market, a few people died from liver failure. That product was eventually withdrawn. In clinical trials, you just can't possibly account for everyone once a drug reaches a huge population that isn't subject to strict selection criteria, like the elderly or people with organ failure.

Maëlys: Looking at the European Pharmaceutical Strategy today, does it read like something that could reposition Europe, or is it trying to use regulatory tools to solve economic and geopolitical problems?

Norman: It is a global market now. Big pharma firms prefer to manufacture at one site and distribute globally. Therefore, it's important to get that facility approved in both Europe and the US. We have mutual recognition agreements on inspections now, and we share detailed information with the EMA.

However, for generic drugs, those are frequently small national companies. There isn't as much collaboration there. In the US, there are very small margins on generic products. Frequently, we see a

number of initial approvals for a drug, like Ciprofloxacin, but eventually, nearly all those firms withdraw from the market because they just cannot compete with one another. The economics of generics is much different for companies.

Maëlys: So there is a problem where, for those big companies, the strategy might not work the same way. Thank you so much, Norman! This was very interesting.

Norman: You're welcome. Good luck with the thesis!

Frits from Implement Consulting Group (Partner Life Sciences)

Maëlys: Good morning. Thank you for taking the time to meet with me. Peter told me about you because he said you would have valuable insights for my thesis, which is on the EU Pharmaceutical Strategy.

Frits: It might be. I hope so, yes.

Maëlys: My thesis evaluates the EU Pharmaceutical Strategy and its impact since it was implemented in 2020. I analyze the four main pillars: attractiveness of the market, competitiveness, access to medical care, and innovation. For each pillar, I analyze one specific regulation implemented to support it. I've gathered data, but it is important to get insights from what is happening inside the market.

For the attractiveness pillar, I analyzed the Clinical Trials Regulation, which implemented the CTIS portal, a harmonized portal for clinical trial applications across Europe instead of doing it in each member state. When this portal became mandatory, how did pharma companies experience that transition? Was it a simplification or did it add complexity?

Frits: Do you want a bit of background as well on why, or have you looked into that already?

Maëlys: I have looked into it, but it's still interesting to have your background.

Frits: I studied chemistry, worked in the industry for ten years, then moved to consultancy. I've always been involved with life sciences, and over the last 15 years, I've been heavily involved with regulatory topics. Let me tell you this, so you understand the "skeleton" of the issue.

The European Medicines Agency (EMA) is a key concept of European governance, but in all countries, there is a national agency that plays a key role in the approval and management of medicines. The EMA was never intended to replace them. Sometimes the consequences at a national level are still felt; national agencies and the European agency are not always friends. They have to defend their territories.

Your question around CTIS is a direct consequence of the Clinical Trials Regulation (CTR). The EMA was tasked to set up a system to allow for harmonized approval of clinical trials across Europe. Before, it was country-by-country, which was intensive and variable. This should open the market more. However, the CTR also had more stringent requirements, which didn't necessarily make Europe a more attractive market, because the rules are even stricter to protect the patient.

CTIS has had a terrible development life cycle. It took a very long time to develop, and a lot of tax money was spent. The result was a system that went live about two years ago, and I think it was appreciated by no one. Most people said, "I cannot work with this." Many companies found workarounds because it was not easy.

Maëlys: So, did it make Europe more attractive?

Frits: It should have, and it may eventually, but so far it has been cumbersome. There is now a "CTIS optimization" project to streamline it. If you streamline CTIS properly, then it should have an effect on the competitiveness of Europe.

Maëlys: That confirms my results. Until now, I could not confirm that it helped Europe be a more attractive market. It didn't make the numbers go up.

Frits: That is a fair conclusion. The data supporting my statement that "it will work" is also not there yet. It has to prove itself in practice.

I just did research for the Dutch environment asking: "Are we attractive for clinical research?" The Dutch government took a lot of inspiration from Denmark and Spain. The Spanish have been really good at attracting clinical research. The Danish have traditionally been very good at defending economic interests alongside scientific interests. They are not afraid to fight for the fact that it will benefit their country.

In the Netherlands, despite being a small country, we have many academic centers. But at a practical level, there is a lot of harmonization still needed. For example, a Clinical Research Organization (CRO) might contact doctors to execute trials, and one center might ask 100 questions while another asks only two. There is no standardized level. If you harmonize those things, which is why the Netherlands is thinking about a National Trial Bureau, it can have a big effect on attractiveness.

Europe should realize that if we keep playing as independent players and not as a joint soccer team, we're never going to win the match. If we make sure there are six or seven countries in Europe that are really good at clinical research, then you might be a competitor to India, China, or even the US.

Maëlys: Regarding national agencies, do you think the EU regulatory infrastructure is fit for purpose? Is the data architecture set up so the EMA and national agencies operate as a competitive asset, or is there a structural liability compared to the US?

Frits: We have not optimized it. If you look at the USA, they are united by a federal government. Food and drug is a federal thing. You don't approve a drug in one state and not in another. In Europe, nobody gave up their government to be part of Europe. You still have "local kingdoms" that manage their own processes and are not always happy with Brussels stepping in.

The EMA has been working on a directory of all medicines in Europe (ISO IDMP standards). This initiative has been ongoing for 10 years. When they said, "What if we organize this properly at the EMA and everyone uses it?", everyone either went quiet or said, "I think it's going to be shit." There were fights. "I don't trust your data; our data is way better."

For newer products, approvals are done at the EMA level, so the data is held centrally and it's easier. But for older products (some up to 150 years old), there is a lot of legacy data. If we were able to align our data and processes better and reduce the politics, we would be way more competitive.

Maëlys: When pharma companies decide where to locate clinical operations, manufacturing, or R&D in Europe, how much does the regulatory environment play a role compared to, for example, fiscal incentives?

Frits: What do you think is the answer?

Maëlys: I think the regulatory environment plays a role, but it is too complex to be the biggest part of the decision. Other factors like fiscal incentives probably have a bigger role.

Frits: I tend to agree. The regulatory conditions are quite similar across Europe now because of the CTR. What does play a big role is the reimbursement process and Health Technology Assessment (HTA). You have to agree on the pricing and reimbursement of the product, and that varies a lot.

The Netherlands is famously known for bargaining the lowest price. Recently, some manufacturers have decided not to introduce a medicine in a country (like Denmark) because the price was too low and it would have a huge effect on their American pricing. So, other incentives like fiscal, pricing, and general economic factors play a bigger role than regulatory conditions in deciding where to establish operations.

Maëlys: For the innovation pillar, I analyzed the EMA's Priority Medicines (PRIME) program. My data shows that PRIME-labeled medicines have an approval time reduced by about 4.7 months. Is the bottleneck at the EMA review stage, or is it earlier in how companies prepare submissions?

Frits: It is clear that Europe has the longest approval times, around 430 days, which is 100 days more than other regions. At the recent DIA Europe conference, the theme was "Are we competitive as Europe?" The general feeling is that the world is passing us by.

The bottleneck is often the interaction between national agencies and the EMA. Also, the "clock" stops when questions are asked, and nothing happens in parallel. It's very old-fashioned. The FDA is moving toward a cloud-based environment where multiple regulators can work together and react to questions in real-time. Europe's process of "I send something, someone looks at it, sends a question back" is ancient and needs improvement.

Maëlys: Is the EU Pharmaceutical Strategy fundamentally changing the ecosystem, or is it just an incremental adjustment to a system that needs radical reform?

Frits: My feeling is that it did not take the drastic reform that it could have, and maybe that Europe needed. On the other hand, Europe can't deal with changes that big, so you always have to do incremental changes.

We need to become more agile. Right now, we talk for a long time about a change, we prepare it, it comes in, and we take 10 years to digest it. That's too slow. China has a much higher speed of adoption. So, for the moment, I don't think the strategy is fundamentally changing the whole ecosystem.

Maëlys: That was all my questions. Thank you so much for your help and your time.

Frits: Good luck with your thesis.

Maëlys: Thank you! Bye.

Representative of the CEPS – Ministère de la Santé Française

Maëlys : Bonjour. Merci beaucoup pour le temps que tu prends pour répondre à mes questions !

Représentant CEPS : Bonjour, Maëlys ! Je te laisse préciser un peu ton mémoire et évidemment si tu as des questions précises. Je t'expliquerai en deux mots ce qu'on fait au CEPS à la suite de ta présentation rapide.

Maëlys : Mon mémoire évalue la stratégie pharmaceutique pour l'Europe implémentée en 2020. J'essaie d'évaluer l'impact qu'elle a eu en analysant les quatre piliers principaux : l'attractivité du marché, l'accès aux médicaments, l'innovation et la compétitivité du marché. Pour chaque pilier, j'évalue une régulation ou une mesure mise en place. Sur la base de données publiques, j'ai obtenu des résultats quantitatifs, mais il est important pour moi de comprendre comment c'est vécu sur le terrain par les professionnels du secteur. C'est pour cela que ton expertise au CEPS m'intéresse, surtout par rapport à l'accès aux médicaments.

Représentant CEPS : Pas de souci. Je suis le responsable de la section médicament du CEPS. Le CEPS est l'entité chargée de négocier le prix des produits de santé (médicaments et dispositifs médicaux). Ma section contient 11 personnes, en partie des cadres évaluateurs qui sont en lien direct avec les industriels. Le CEPS est un comité composé de 10 voix : des représentants des directions de l'administration centrale (Santé, Sécurité Sociale), des payeurs (Assurance Maladie, mutuelles), ainsi que la Direction Générale de l'Entreprise à Bercy, sous une présidence et une vice-présidence. Nous intervenons en bout de course de l'accès au marché. Une fois qu'un produit a son AMM (Autorisation de Mise sur le Marché), pour avoir un remboursement en France, il doit passer par la Commission de la Transparence (HAS) qui donne un avis médico-technique sur la plus-value comparative du produit. Ensuite, nous négocions le prix de remboursement avec l'industriel sur la base de cet avis.

Maëlys : Justement, par rapport à la fixation des prix, je parle dans mon mémoire de la pratique du prix de référence externe par rapport aux autres pays. Cela crée un effet cascade : un prix bas en Pologne peut tirer les prix vers le bas en France. Comment le CEPS gère cet arbitrage ?

Représentant CEPS : Déjà, il faut savoir que dans nos discussions, il y a environ 7 % des produits pour lesquels on fait une décorrélation entre le prix facial (rendu public) et le prix net (négocié avec l'industriel). Ce prix facial est le prix le plus bas pratiqué par nos voisins européens (Espagne, Italie, Allemagne et Angleterre). Nous négocions la valeur thérapeutique au travers du prix net. Le prix facial ne représente absolument pas la valeur réelle du produit. En termes de dépenses, cela représente environ 8 milliards d'euros de remises sur un chiffre d'affaires remboursé brut de l'ordre de 30 milliards. Ce sont majoritairement des produits innovants. Nous négocions sur la base de piliers législatifs et d'un accord-cadre négocié avec le LEEM (Les Entreprises du Médicament). Seuls les médicaments vraiment innovants (ASMR 1 à 3 et certains ASMR 4) ont droit à ce système de prix facial.

Maëlys : Concernant l'accès au marché, mon analyse montre une convergence entre les États membres depuis 2020, mais les inégalités structurelles restent fortes (128 jours en Allemagne contre 828 jours en Roumanie). Comment interprètes-tu cette convergence ?

Représentant CEPS : Le délai d'accès au marché est public dans les rapports d'activité du CEPS. Notre "T0" commence dès que l'industriel nous donne un dossier complet (avis HAS et proposition tarifaire). S'ensuit un "ping-pong" avec les industriels jusqu'à l'accord, puis une phase administrative pour la publication au Journal Officiel. Pour les comparaisons, il faut garder en tête qu'en Allemagne, le produit est accessible dès l'AMM (phase AMNOG), et le prix est négocié ensuite. En France, dans le cadre du droit commun, il faut l'avis de la HAS puis la fin des discussions de prix avant l'accès, sauf pour les dispositifs dérogatoires comme l'accès précoce ou l'accès direct. Ces derniers permettent aux patients d'avoir le produit dès l'AMM ou l'avis HAS. Comparer les chiffres bruts de délais entre pays revient parfois à comparer des pommes avec des poires car les procédures diffèrent. De plus, une négociation se fait à deux ; si l'industriel rejoignait plus vite une position tarifaire raisonnable pour l'État, on irait plus vite.

Maëlys : J'ai aussi évalué l'évaluation clinique commune (procédure centralisée européenne). Comment le CEPS vit l'arrivée de ce niveau européen pour ce qui était auparavant une compétence nationale ?

Représentant CEPS : Il faut distinguer la partie HTA (évaluation des technologies de santé) et la partie pricing. L'HTA n'est pas mon champ d'expertise directe, mais de ce que j'en comprends, l'évaluation clinique commune européenne ne se substitue pas à l'avis de la HAS. Il nous faudra toujours la base de l'avis de la HAS pour juger du bénéfice clinique car l'évaluation européenne ne tiendra pas forcément compte des spécificités nationales de remboursement ou des comparateurs cliniques pertinents en France. Cet élément comparatif est crucial dans la discussion tarifaire.

Maëlys : Sur les essais cliniques, il semble y avoir une séparation entre les compétences européennes et celles des États membres. Est-ce un obstacle à la stratégie pharmaceutique ou une garantie nécessaire ?

Représentant CEPS : Il y a eu des modifications récentes. L'Allemagne a intégré une appréciation des patients européens ou allemands dans ses critères de fixation de prix. L'Espagne a modifié l'accès aux essais pour que ce soit plus rapide. En France, des réflexions sont en cours pour éventuellement intégrer cela dans les discussions de l'accord-cadre, ou via des simplifications administratives du côté de l'ANSM. On pourrait imaginer que si c'est valorisé, les industriels seraient plus incités à développer des essais en France, ce qui éviterait les doutes sur la transposabilité de l'efficacité (par exemple si une population d'étude est exclusivement asiatique, le métabolisme peut différer).

Maëlys : La littérature montre que certains médicaments approuvés par l'EMA ne sont jamais disponibles dans certains pays. Est-ce un choix délibéré des industriels ou une défaillance du système ?

Représentant CEPS : Je ne dirais pas une défaillance du système. L'EMA donne une AMM sur un rapport bénéfice/risque positif. Mais il arrive que la HAS rende un avis (SMR) insuffisant, ou une ASMR 5 (le produit n'apporte rien de plus). Pour nous, si un produit n'apporte rien, il doit générer des économies pour le système de soins. Si l'industriel a des prétentions tarifaires incompatibles avec cette exigence d'économies, le produit peut ne pas être accessible. C'est donc parfois une simple raison économique.

Maëlys : Enfin, j'ai lu que certaines entreprises déposent de nombreux brevets pour un même médicament (*patent clusters*) afin de retarder les génériques. Observes-tu encore ces pratiques ?

Représentant CEPS : À titre personnel, je trouve qu'aujourd'hui c'est encore pire. Sur des produits "blockbusters", on peut trouver plus de 1200 brevets à l'international. On observe aussi des lancements de formes sous-cutanées juste avant la fin d'exclusivité de la forme intraveineuse (IV) pour capturer les volumes avant l'arrivée des biosimilaires. On essaie de sécuriser cela pour éviter les surcoûts liés à une forme galénique qui serait certes plus pratique, mais dont l'efficacité est identique à la forme tombée dans le domaine public. Sur ce point, la stratégie pharmaceutique européenne n'a pas encore apporté de réponse concrète ; on observe plutôt des changements négatifs.

Maëlys : Est-ce que tu penses que la stratégie pharmaceutique européenne est un vrai tournant réglementaire ou juste une couche supplémentaire sur un système qui a besoin d'une réforme plus profonde ?

Représentant CEPS : Je ne peux pas me prononcer sur l'ensemble du sujet que je ne maîtrise pas totalement. Ce qui nous impacte, c'est la modulation de l'exclusivité commerciale (pédiatrie, etc.) et le questionnement sur le statut orphelin (prévalence des maladies rares). Les critères d'octroi du statut orphelin

sont discutables quand ils concernent des produits très rentables. Il y a aussi des mesures sur les médicaments prioritaires (label PRIME) et les antibiotiques.

Maëlys : Pour le pilier innovation, j'ai analysé le label PRIME et, en effet, les délais d'approbation sont réduits de 4 mois et demi.

Représentant CEPS : Ce qui est plutôt positif. On espère que tout cela nous aidera, mais il reste beaucoup de défis techniques.

Maëlys : Merci beaucoup pour ton temps. Ça ne te dérange pas si j'intègre tes réponses dans mon mémoire ?

Représentant CEPS : Pas de souci, bon courage pour ton mémoire !

Maëlys : Merci beaucoup et bonne journée !

Représentant CEPS : De rien, bonne journée !

Participant C – Big Pharma Company

Maëlys: Hello!

Participant C: Hello! Good morning... just about, yes.

Maëlys: Yes, good morning. Thank you for taking the time to discuss this with me for my thesis.

Participant C: It is a pleasure.

Maëlys: I am not sure if Gab told you a bit about my master's thesis subject, or should I start from the top?

Participant C: He did tell me, and I thought it was very interesting. I am trying to remember exactly what he said, so apologies if I forget some details.

Maëlys: To make it short, I am trying to evaluate the impact of the Pharmaceutical Strategy for Europe that was implemented by the European Commission in 2020. To evaluate it, I analyze the impact of each main pillar: attractiveness of the market, competitiveness, market access, and innovation. For each pillar, I analyze one regulation implemented to support it. Based on public data, I have already gathered some results, but I thought it was also important to discuss this with people working in the market to get your insights on how it is experienced in decisions and day-to-day life. He told me you work at **Big Pharma Company** in the CMC department, is that right?

Participant C: That is right. I am also in the policy team, so I am very involved with all these things.

Maëlys: Okay. I have a few questions for you if that is okay.

Participant C: Yes, just before you get going: I have a CMC background and my role is in policy, so I am involved with quite a lot of these things. I would be very happy to follow up if we run out of time today or answer questions via email. I wanted to check, you are just using me for research? Am I anonymous?

Maëlys: I can make you anonymous, of course.

Participant C: Yes, that would mean I can be more candid if it is anonymous and not attributed to **Big Pharma Company**. Although there is nothing here that is confidential.

Maëlys: Of course. I have done this with other people as well by making them anonymous. Some also did not want me to mention their company, so I just mention that they are from a "Big Pharma" company without specifying which one.

Participant C: Great, okay, that is perfect. In which case, fire away. Oh, one more thing! I was involved in consultations on the Pharma Strategy in 2020 when it came out, and I have been involved in a lot of the work they have done to implement it. I assume you are aware that this is currently a very hot topic and things are shifting since the Draghi report. The current areas of focus include the Biotech Act, the Critical Medicines Act... there are all sorts of things being put together because of this strategy, but now some of the drivers are different from what they were in 2020.

Maëlys: Thank you, that is great context. From a CMC perspective first, I was wondering what it costs in time and resources to comply with EU manufacturing regulations compared to other jurisdictions. Is the EU regulatory burden on manufacturers a competitive disadvantage, or is it manageable?

Participant C: Good question. Global standards, GMPs (Good Manufacturing Practices) in particular, and technical requirements are standardized via ICH and a process called PIC/S. In essence, the differences between requirements in Europe, the US, or even China or South America are marginal. Everything is globally harmonized, so there is no additional burden from European regulatory requirements. You need to think about it this way: European regulatory requirements for pharmaceutical manufacturing apply to products supplied to Europe, not to products made in Europe. If you are manufacturing in the US, China, or Australia for the European market, it is the same requirement as if you were making it in Brussels or Rome. The requirements are agnostic of geography.

Maëlys: So there is no additional burden at all?

Participant C: No.

Maëlys: Okay, thank you. For the competitiveness pillar, I analyzed the regulation regarding the SPC (Supplementary Protection Certificate) manufacturing waiver. I was wondering if, in practice, it has changed manufacturing decisions at GSK or among other companies.

Participant C: Not yet, because it is too soon. Manufacturing investments are very large and expensive, and they are typically made a long time in advance. It is the proverbial oil tanker; it takes time to turn it around. Are companies paying close attention to it? Yes. If it is implemented, there are several things to consider. You have to understand the scope (which products it might apply to), the duration (the current proposal is 12 months; if that shrank to 6 or expanded to 24, the incentives would be very different), and then the criteria (what do you need to comply with to qualify).

Currently, the Biotech Act defines biotechnology as any area where recombinant or genetic modification technologies are used. That is the definition the industry recognizes. However, the definition for the SPC to qualify is not that broad; it is currently a subsection of that definition and basically only applies to products made in a biological system (vaccines, monoclonal antibodies, etc.). If you look at that narrow definition, it is not as impactful as it would be with the broader definition.

Then there is the criterion that you must have one part of the manufacturing process inside the EU. Even that is controversial because some countries say it must be strictly the EU, while others argue we should

adhere to principles of free trade and include countries outside the EU where we have free trade agreements. All of this is a white-hot piece of controversy.

The answer to your question is: it depends on what the final wording will be. But I will say that the idea of getting extended exclusivity for a product at the end of its life cycle is definitely very important to companies in terms of planning their manufacturing. Also, every other region is pushing for this. Most of the big investments in manufacturing have gone to the US in the last two years because they are trying to pull it in. Europe is competing.

There are two other mechanisms that pull manufacturing into a region, which are different from extended exclusivity. One is what they use in Singapore: tax. Low tax, basically zero tax on everything you manufacture. That is hugely effective, but taxes are set at a national level in Europe and no one is interested in reducing them. The last one is reimbursement, which is the US model. Americans pay more for their medicines, which means when they say "we will introduce tariffs on your imports unless you make them here," people listen because of the impact on sales.

If you are a country with a pharmaceutical manufacturing footprint like Belgium, Italy, France, Germany, or Ireland, then the Biotech Act makes complete sense. You will be paying more for your medicines for longer, but the investment you get will pay for it. If you are Romania, Bulgaria, or Hungary, where you do not have a manufacturing footprint, there is no upside. It is all higher costs.

Maëlys: So it does not make sense for them.

Participant C: Exactly. So how the European Commission and Parliament are going to square that, I have no idea. I can see why Greece would not be in favor of it. You asked a simple question and I gave a complicated answer (Laughs) The short answer is: Yes, companies are paying attention. Is it the best model to incentivize localization of manufacturing? No. Low tax and higher prices are better models.

Maëlys: That is very interesting. Is it too early to evaluate the general impact of this SPC manufacturing waiver?

Participant C: I think it is way too early. It needs to be finalized. The scope, criteria, and duration need to be clear. Once those are clear, you should see the impact relatively quickly as companies start making announcements about manufacturing locations.

However, we should look at what has happened in the last 12 months in terms of investments based on the new US position. There is a lot of data around manufacturing and exports in Europe that looks positive up until 2024. But if you look at everything since 2024, it has all gone in the other direction.

Maëlys: Yes, I analyzed the exports going out of Europe, but the public database puts all pharmaceutical exports in one category. I could not separate vaccines, for example, so the analysis was not significant. I thought maybe it was also because of COVID masking the effects.

Participant C: That is true as well. It is definitely too soon to evaluate the SPC because it is not finalized.

Maëlys: Jean-Gonzague mentioned that you participate in forums where upcoming regulatory frameworks are discussed. What are the CMC-specific regulatory changes in the EU pipeline that the industry is most focused on right now? Are they likely to improve or worsen Europe's manufacturing competitiveness?

Participant C: Good question. Let me come back to my original point: regulations apply to manufacture *for* Europe, not *in* Europe. Having said that, there are things that are a direct measure of European competitiveness in the CMC space. You can look at them in the context of the regulatory processes themselves. Where Europe is less competitive than the US is the time taken to review and approve regulatory submissions. It is slower in Europe, not massively, but slower nonetheless. The industry would like to see faster reviews and approvals.

But that is not the area where we are most focused. We want to be able to introduce more innovation into manufacturing. In that context, Europe is good; they support innovation. Europe is a global superpower when it comes to regulation because so many countries look to European approval as the basis for their own. Europe is focused on enabling new technologies: digital technologies, modeling-based controls, AI, etc.

The European regulatory system is competitive, but it could be better. It could be faster and make changes easier. Proximity to regulators and having good relationships, being "down the road" and able to engage face-to-face, is really important. It does have an influence.

The flip side is that European regulators are probably under-resourced compared to the US. The industry is pushing the Commission and the European framework to put more resources into this, to increase capacity, capability, and expertise, particularly in new digital areas. But that seems like an uphill struggle because nobody wants to spend more money on people.

Maëlys: I also analyzed the Priority Medicines (PRIME) program from the EMA. According to my analysis, a medicine with PRIME status has its approval time reduced by about 4.7 months. However, when there is an ATMP (Advanced Therapy Medicinal Product) status, it adds 3.7 months to the review. From a CMC standpoint, ATMPs are complex to manufacture and regulate. Do you think the EMA's CMC review process for ATMPs is fit for purpose?

Participant C: I think ATMPs are a complicated area. The EMA is focusing on them, but I think that is actually disproportionate. I do not think there are that many ATMPs in the pipeline. You would do better looking at transformational modalities that are not ATMPs, like antibody-drug conjugates, complicated oligonucleotides, and complex vaccine platforms. That is where the big impact will be.

In the context of CMC, it is not the review time that is the critical path. Whether it is 30 days or 80 days does not matter as much as where they set the bar in terms of the development and data requirements. Your critical path is generating evidence to support the approval.

The EMA introduced something in 2021 just in time for COVID, without which we wouldn't have been able to get the vaccines on the market as quickly as we did. It was based on the PRIME process and the unmet medical need process. It involves concepts of benefit-risk leading to alternative CMC evidence. Accepting different data, that is what will make the difference. Europe is at the cutting edge in that space. I would say they have gone backwards a bit since COVID and are slightly more conservative now, but they are still among the best. It is called a "toolbox" because it includes different technical ways of doing things, different regulatory engagement processes, and consultation tools. It makes a massive difference.

Maëlys: Do you think the complexity of these products is creating regulatory bottlenecks that PRIME cannot compensate for?

Participant C: The more complicated the product, the more likely you are to have a bottleneck. I agree on that. But I still think there is enough knowledge for most ATMPs not to be the bottleneck. They have been working on this since before PRIME. They figured out over 10 years ago that CMC was going to be on the critical path. The more you shrink the clinical timelines, the more the CMC package becomes the critical path if it does not change. So they have been really focused on that. But you are right: the more complex the biological, the more likely it is on the critical path.

Maëlys: One last policy question: across the forums you participate in, where do you think the EU pharmaceutical regulatory framework is world-class and where is it behind?

Participant C: The best thing about Europe is the focus on innovative products and manufacturing. It is world-leading.

Where it is behind is "post-approval changes." It is harder to make changes to products once they are on the market in Europe than it should be. The US (FDA) is ahead of the EU (EMA) in terms of enabling post-approval change. I worry that the EMA will fall further behind. The process of changing products and getting regulatory approval for new manufacturing processes is called the "variations" process. They have just updated the variations regulation, and while the EMA and Commission are patting themselves on the back, the industry feels they have done almost nothing and could have gone much further.

The other problem in Europe is not related to medicines manufacturing directly, but there is pressure from other legislation. Europe is uniquely complicated in how these things link together. Chemicals legislation (REACH) is a big one. Essential chemicals needed to manufacture medicines are being banned in Europe, and nowhere else in the world, for environmental reasons. While the environmental goal is good, it is bad for medicines because they are not exempting them. Other countries will exempt medicines from those controls so they can keep manufacturing them. This will push manufacturing out of Europe. We can manufacture in Switzerland, the UK, the US, or Singapore using chemicals we can no longer use in the EU.

Maëlys: They should take that more into consideration.

Participant C: They should focus on the specifics of medicines manufacturing and not treat it the same as bulk chemical manufacturing.

Maëlys: Other people I have interviewed mentioned a lack of harmonization in Europe, for example, differences in the competence of the European Commission versus member states for clinical trials.

Participant C: There is some truth to that. In the CMC space, it is probably not as significant as in clinical or non-clinical areas, but there are definitely countries in Europe that have different CMC expectations. It is supposed to be harmonized, but there are differences. Spain is the one everyone complains about in CMC, and to a lesser extent, Germany.

Maëlys: So you agree harmonization is still a problem where Europe is behind.

Participant C: Yes, I agree.

Maëlys: Thank you very much for your answers to my questions.

Participant C: It was a pleasure, Maëlys. Good luck, and let me know if you need help for anything else. Goodbye!

Maëlys: Goodbye!

Participant D – European Commission, DG COMP

Maëlys: Hello! Thank you for taking the time and for accepting this interview. As I told you, this is for my master's thesis. I'm trying to evaluate the impact of the EU pharmaceutical strategy that was implemented in 2020. To do this, I'm analyzing each pillar of this strategy: attractiveness, competitiveness, innovation, and access to medical care. I've already completed a quantitative part where I gathered results based on public data, and now I'm conducting interviews with people working in the sector, whether in pharma companies or, like you, in the European Commission, to gather insights. So, you work in the DG of Competition, right?

Participant D: Yes. Specifically, I work with antitrust enforcement, which means restrictive agreements by pharma companies. In the past, there were many pay-for-delay agreements between originator and generic companies, as well as abuses of dominant position. You might have heard of the *Teva Copaxone* decision from 2024, where the dominant originator engaged in conduct to delay or disable competing entry with off-patent products like generics. We also had an excessive pricing case involving *Aspen* a few years ago. Essentially, we enforce competition law to support two objectives of the pharma strategy: access to affordable and innovative medicines.

In terms of affordability, we correct market failures where companies try to prolong their exclusivity at the expense of timely access for health systems and patients to drugs that should have been cheaper. Health systems continue paying very high sums for legacy drugs because companies found ways to prolong exclusivity by six months, a year, or even two. For a blockbuster drug, that translates into hundreds of millions of euros. If we manage to avoid that conduct, those funds can be spent on new treatments or surgeries instead. If companies are allowed to unduly extend their quasi-monopolies, money is misspent on legacy technology instead of cutting-edge innovation. By rigorously enforcing competition law, we're trying to make the entire innovation cycle turn so that money is spent on the right side of the cycle, the innovative side.

Maëlys: That's very interesting. In the literature I analyzed for my thesis, there is a sector inquiry from 2009 that mentions patent clusters, when a company files hundreds of patents for one drug to delay generic entry. Do you still see many patent clusters 15 years later, or has it improved?

Participant D: It remains a very relevant topic and, sometimes, a problem. We receive many complaints from the market that we cannot act on because the problem doesn't only come from company conduct, but from how the patent system itself is crafted. One aspect is "divisionals," where divisional patents are granted quite uncritically. You have a parent patent and then can split it while the application is pending, creating many similar-looking patents. We've been looking into how that's misused to gain an undue advantage. This continues to be an issue in medical devices and pharma. Often, these patents were filed a decade ago and have been pending for 15 years. They are tweaked to effectively mimic what another innovator has been doing, creating a great degree of uncertainty for competitors. If a company can update its patent claims with actual developments they see in the market, it creates a situation where you cannot get patent certainty even for innovative products until very late. So yes, it's still an issue, probably not on a smaller scale than in 2009. There was an attempt by the EPO to shorten the duration for divisional patent applications, but it just led to huge tactical filing and was not practically possible for the EPO to treat, so they abandoned the rule.

Maëlys: Regarding the competitiveness pillar, I analyzed the SPC (Supplementary Protection Certificate) manufacturing waiver, which allows generic manufacturers to produce during the SPC period for export. From a competition law perspective, is this the right instrument to rebalance the market, or does it create other risks of competition distortions?

Participant D: That's a good question for competitiveness, but I'm not sure it's a question for competition law. We are responsible for enforcing competition law in the EU or EEA, and by definition, the SPC waiver is meant to cater to products sold outside the EU. However, SPC was mentioned in the strategy as an area where the system could be optimized. We've had a number of complaints about SPC abuses since 2005 because the regulation wasn't specific enough. More recent complaints allege conduct where companies try to go against the spirit of the SPC regulation. Our colleagues in DG GROW, who are responsible for SPC proposals, are trying to fill the gaps and correct possible leeway, but we're always one step behind because the industry is very creative. Incentives are huge to gain an extra year or two of exclusivity, up to five years. This sometimes comes to us as a competition law issue when a company is allegedly misusing the system to get an SPC it's not entitled to.

Maëlys: The pharma strategy seems to have a tension at its core: it wants to strengthen IP protection and extend exclusivity to incentivize innovation, while also ensuring faster generic entry and lower prices. How do you navigate this tension, and do you think the strategy resolves it?

Participant D: You're right that there is tension, but that's for the legislator to resolve. As you've seen with the pharma package, there were movements in regulatory exclusivities and a "clash of the giants" involving the EFPIA (originator association) pushing for more, and generic associations pushing the other way. Member States also had an interest in instilling conditionality to achieve a more level playing field for access to drugs in low-price countries. This tension was ultimately resolved by the co-legislators adopting the pharma package, which maintains the overall period of exclusivity but makes some parts more conditional.

Our role is complementary to the regulatory regime. If regulation doesn't work, we can fix some anomalies, but we do it on a case-by-case basis, which takes four to five years for a final decision. We cannot *ex post* fix a regulatory problem. What we try to do is ensure the "creative destruction" cycle continues to turn. Imagine if companies found ways to prolong exclusivity indefinitely; what would be their incentive to invest in new drugs? We've seen mid-tier companies focus on finding ways to prolong exclusivity, for example, by issuing a new version of an old active substance in a new formulation or with a slightly different release, rather than going for cutting-edge new products. These are incremental "line extensions" rather than real new generation products. When competition isn't working, companies don't have the incentive to move forward because no one comes at the end of the patent term and offers the same product ten times cheaper. We try to ensure there is creative destruction so that there is also creation in terms of innovation.

Maëlys: For the pillar of access, I found a convergence in patient access across EU Member States since 2020, but structural inequalities remain huge, comparing Germany to Romania, for example. Is this a competition problem or a matter of national health policy?

Participant D: I touched upon this with conditionality. These disparities lead to competition law issues, such as parallel trade. Parallel trade is a phenomenon where drugs are bought in low-price countries (typically in the South and East) and resold in the West. If the quantities aren't out of the ordinary, the supplier cannot refuse supply or contractually limit exportation. This has led to shortages in procurement

countries because exporting was more lucrative for wholesalers than selling locally. This prompted public health reactions where countries started limiting exportation.

An unwanted consequence is that originators launching new, expensive products may hesitate to make them available in low-price Member States because they fear the product will be exported and ruin their higher-price markets in the West. Another connection is International Price Referencing, where countries determine pricing based on a basket of other countries. As a smart operator, you don't want those cheap prices in the basket, so you don't launch there. We've even seen companies in Western countries consider withdrawing their product if upcoming generic competition might drop the price so much that it ruins their pricing status in neighboring countries.

Maëlys: Does this happen a lot?

Participant D: What I've seen is anecdotal, but I've seen it as an actual consideration.

Maëlys: One last question: In your perspective, has the EU pharma strategy enhanced the competitiveness of the EU market yet?

Participant D: My private reply would probably be "no." Where it has helped is by accelerating developments on the biosimilar side. Europe has a strong biosimilar industry, and the strategy led to positive developments, such as the European Medicines Agency issuing a statement on the interchangeability of biosimilars with originator biologicals. Rules of engagement have been simplified, and there's been regulation to cut red tape in the EMA.

But at the end of the day, it's the macro picture, like Trump's tariffs and the overall attractiveness of the business environment, that determines how competitive we are and where the money goes. These steps go in the right direction, but the question is how strong they are compared to incentives to move to the US.

Maëlys: Thank you for your answers and for your help.

Participant D: No problem. Good luck!

Participant E – Big Pharma Company

Maëlys: So I am trying to evaluate the impact of the pharmaceutical strategy for Europe that was implemented by the European Commission. To do this, I try to evaluate the impact of the four main pillars, which are attractiveness, competitiveness, access, and innovation. For each of them, I analyzed one specific regulation, looking at public data to see if there is a real change between 2020 and now. I thought it was also important to gather insights from people working in the market, in the sector, to complement and explain the results on how the strategy is perceived inside. And so you work at Roche, and you used to work in a biotech in the United States that was then acquired?

Participant E: Yes, I used to work at Genentech, and then Roche bought Genentech back in 2009.

Maëlys: Okay, so you followed the acquisition. Thank you. And so with this, you've been exposed to both the EFPIA and the United States version with PhRMA?

Participant E: Yeah, I mean, I think my exposure is more recent because I work in regulatory policy. So we gather as an industry with the PhRMA trade organization or the EFPIA trade organization and then we

bring our positions to EMA, the member state authorities, or FDA. So I work on both sides, actually; my role is global.

Maëlys: Okay, nice. And so with your perception from both, I was wondering when a regulatory technology policy debate comes up, is there a meaningful difference in how the US and the European industries approach it, or is it essentially the same industry speaking but with two different voices?

Participant E: There are some differences. I think because in EFPIA, the trade association, we look at primarily focus on how we can change or modernize the regulatory system in Europe. So that requires us to put emphasis on certain things. And then in FDA (PhRMA), it's a little bit different because it's more about just how can we accelerate the FDA in their assessment.

Maëlys: So the focus is on different things.

Participant E: Yeah, I mean, even a company like Roche, we have representation on both sides. Sometimes the positions of PhRMA are a little bit different from the ones in EFPIA, but they are in general not conflicting. It's just like competing priorities that we have to balance a little bit. For example, if in Europe we want to focus on aligning regulatory requirements with the rest of the world, that's a big focus for us. The EU is actually a reference agency for a lot of places internationally. So in EFPIA, sometimes we put more emphasis on things like how can the EMA support reliance, how can they align their requirements to WHO, or how transparent they are in these terms. And then for PhRMA, it could be more about how can we make sure that our PDUFA commitments are being met, that the FDA doesn't go into some crazy direction that has nothing to do with the rest. We also work in ICH, the International Council for Harmonization. I've been in ICH representing PhRMA, other colleagues are representing EFPIA from other companies, and sometimes we do have to negotiate a little bit the positions between PhRMA and EFPIA even if we are the same company.

Maëlys: Okay, thank you. And so the integration of Genentech into Roche, I think, must have created a very specific view on how the US and European regulatory environments compare from the inside of one company. I was wondering what does that internal dual experience tell you about why Europe keeps losing ground in clinical research attractiveness? Because in my analysis, I could see that the European market share of clinical trials keeps declining year after year.

Participant E: Yeah, I think a good way to look at it is that we need to look at the EU as 27 countries and the US as a single country. I think just the fact that in Europe you have this very complex political environment in terms of what is actually competence of the European Union and what is competence of the member states. They have to balance this across this complex governance of the European Union with the Parliament, the Council, the Commission. And then the interests of the countries are not always aligned and there's always silos by industry or ministry. So I think it's the combination of all these factors that makes it super complicated. Specifically on the clinical trials stuff, what happens is we have some ability to centralize with the new clinical trial regulation in terms of looking at the documentation and looking at safety, efficacy, etc. But then we have these ethics committees. And the ethics committees are not centralized, not coordinated well, and that is making it super difficult. And then member states, they issue additional guidelines or regulation that makes it just super complex. The other issue is also with China. It's now a competition with not just the US but also with China in terms of attracting the clinical trials.

Maëlys: I analyzed in my thesis the fact that the competence is really divided between Europe and the member states, and the fragmentation is a problem. So I analyzed the clinical trial regulation with the new CTIS portal. As I said, my data shows that the CTIS portal transition did not reverse Europe's declining market share. Do you think that the CTIS portal was the right solution to the right problem, or is it too much a technological fix for a problem that is more economic?

Participant E: I think that they're all parts of the problem. I think the CTR regulation didn't go far enough because it did not address these competencies and it did not address the alignment of the ethics committees and all this stuff. But then on top of that, the design of CTIS is introducing more restrictions than even CTR put in place. So I'll give you one example: there's this concept of a "substantial amendment". A substantial amendment in CTR doesn't say how the operation of the substantial amendment works, but in CTIS they restricted it so that you can only have one amendment at a time. Clinical trials no longer work like they did 20 years ago; they have to be a lot more agile. You need to be adjusting things over time—the protocol—as things develop, and that's basically not possible with CTIS and CTR. CTIS is making it worse to some extent. Even though you have this central system to put the documentation and run the procedures, it's also placing a lot of burden and restriction on sites—administrative and just operational. In comparison to the US, in the US they use the IND model, which is based on the product. You have product application and then you have protocols around it and investigator brochures. It's way easier to use.

Maëlys: So they are thinking about doing a more "core dossier" concept in Europe where it could be centered around the product as well?

Participant E: EFPIA has already put a lot of efforts in advocacy around this and the Commission is now open to considering that. The issue is when we talk about technology, every member state has to own their own systems and tools and IT, and they also have to get the budget for them. To really take advantage of the technology that we have available today, you need to have a more coordinated funding, procurement, budgeting, operation, installation of all of it. If you say now "let's replace CTIS with something more modern, more flexible," I don't know that EMA would be on board with that. If you say now "let's replace all of the national regulatory assessment systems so that the regulatory process can flow more readily," then you would have resistance from the member states because obviously it's people, it's resources, it's funding, it's departments.

Maëlys: From your position, when you look at the pharmaceutical strategy for Europe as a whole, is it perceived in the US industry as a serious strategic reorientation that changes the whole competitive landscape, or is it more something that affects the European operations but it doesn't really register as a geopolitical signal?

Participant E: I think it doesn't go far enough. Even the new pharmaceutical legislation did not really address the core problems. Looking at the geopolitical landscape, Europe should really be pushing the boundaries more and getting closer, making it more accessible for industry in terms of the process, the investment. We're now kind of putting our hopes on the EU Biotech Act because that seems to be something that could come on top of the NPL. We did a lot of advocacy before the NPL to explain what we needed, and it kind of fell on deaf ears. And what we end up with is something that is more punitive in a way that doesn't bring Europe together and that is not going to really help in the competitiveness thing. And then you have on top all the crazy stuff that Trump is doing, like "most favored nation pricing," which is affecting things as well. And just last week, FDA announced that they're going to do real-time review of clinical trials

so they're going to start to accept ongoing data right away so that they can approve quickly. Europe has no response to that.

Maëlys: As a last question, where do you think the pharmaceutical strategy for Europe is a success in reaching their objectives and where are there a lot of shortcomings in your opinion?

Participant E: I think the aspirations are good; the goals and objectives make sense. But where it always falls is in the actual implementation and execution because of the complex governance and all the different interests. When it says the strategy to 2028, you could say it's the strategy to 2035 because in reality how long it takes just to get there. It feels to me very aspirational and not really followed up with money, focus, energy, and alignment. You really can feel that in the industry. Maybe there's a lack of recognition that the pharmaceutical and biotech industries are strategic priorities for the European Union, so they don't get as much attention as energy or other things.

Maëlys: Okay, thank you. These were my questions. Is that okay for you if I integrate this in my thesis?

Participant E: Yes, I just don't know if you could avoid my name?

Maëlys: I can make it anonymous if you want and your company as well

Participant E: That would be very good.

Maëlys: Perfect. Thank you so much for your time.

Participant F – ICH & European Commission (DG SANTE)

Maëlys : Bonjour madame ! Vous m'entendez ?

Participant F : Oui, maintenant je vous entends. Je suis vraiment désolée pour hier, j'ai commencé une réunion et je voyais le temps passer et mon aide n'arrivait pas à se délier sur les différents points financiers, et je déteste les chiffres.

Maëlys : Pas de souci, je comprends tout à fait, c'est trop bien que vous ayez un créneau aujourd'hui, donc merci beaucoup. Je ne sais pas si vous avait déjà expliqué sur quoi porte ma thèse ?

Participant F : Un peu de quoi il s'agissait dans les grandes lignes.

Maëlys : D'accord. Pour ma thèse de Master, j'évalue l'impact de la stratégie pharmaceutique pour l'Europe que la Commission a implémentée il y a six ans maintenant. Pour évaluer son impact, j'ai d'abord fait une analyse quantitative où j'ai voulu évaluer chaque pilier séparément : l'attractivité, la compétitivité, l'accès et l'innovation du marché. Pour chaque pilier, j'ai tenté d'évaluer une régulation spécifique. J'ai obtenu des résultats avec les données publiques, mais je pensais qu'il était aussi important de m'entretenir avec des gens qui travaillent sur le terrain pour comprendre comment la stratégie est vécue de l'intérieur. Vous travaillez à l'ICH si j'ai bien compris, et avant vous étiez à la Commission européenne ?

Participant F : Alors oui j'ai fait un petit moment à la Commission européenne, et ensuite j'ai travaillé pour GS1, un organisme de standardisation internationale, où j'ai dirigé le département santé pendant quatre ans. Maintenant, je suis à l'ICH, que je dirige depuis un peu plus d'un an.

Maëlys : Est-ce que vous pensez que la stratégie pharmaceutique pour l'Europe représente vraiment un changement de paradigme dans la façon dont la Commission conçoit la politique pharmaceutique, ou est-ce plutôt une continuité dans un nouvel emballage ?

Participant F : Elle souffre un peu du contexte. C'est bien d'avoir une stratégie, mais quand elle est publiée, c'est toujours très pertinent et enthousiaste. Quand on arrive vers la fin ou quand il se passe des choses au milieu, il faut pouvoir l'ajuster. Notamment, il y a eu le COVID qui a changé pas mal de choses sur les évaluations, les essais cliniques, la gestion des stocks de médicaments par l'Europe, l'accès aux médicaments, la gestion des données patients. On n'avait jamais eu de crise telle que celle du COVID avant, on n'avait jamais eu un bond en termes de digitalisation dans la santé, ni de problèmes géopolitiques qui perturbent l'accès aux ingrédients actifs. Il y a aussi toutes les nouvelles thérapies cellulaires et géniques qui sont passées d'une phase d'essai à une utilisation plus concrète aujourd'hui. Elle était pertinente, elle l'est toujours sur certains points, mais il faudrait un petit coup de lifting.

Maëlys : Donc les objectifs de base étaient intéressants mais il n'y a peut-être pas assez d'énergie et de ressources pour vraiment tout atteindre ?

Participant F : Voilà, les priorités sont toujours les bonnes, mais c'est la mise en œuvre qui est toujours difficile, surtout quand on rentre dans les tactiques pour chaque priorité.

Maëlys : Par rapport au modèle ICH, fondé sur le consensus volontaire entre les régulateurs et l'industrie, est-ce un bon modèle pour répondre à la vitesse des avancées technologiques comme l'IA ou la médecine personnalisée ?

Participant F : Ça dépend, il n'y a pas de réponse standard. Le consensus est sur le développement de la guideline, mais à la fin ce sont les régulateurs qui l'adoptent. Sur l'intelligence artificielle, on n'a encore rien produit car on se demande si l'outil "guideline" est le bon outil pour être aussi agile que les progrès sur l'IA. Par contre, sur les thérapies cellulaires et géniques, on a un "discussion group" qui fait un état des lieux des risques et bénéfices avec l'industrie et les régulateurs pour garantir la sécurité des patients. Une fois le socle commun défini, on produit la guideline.

Maëlys : Depuis votre position à l'ICH, est-ce que vous voyez l'Europe comme un leader, un suiveur ou un acteur parmi les autres en termes de standards pharmaceutiques ?

Participant F : Je dirais comme un leader, notamment grâce à l'Agence européenne des médicaments (EMA) et toutes les institutions européennes qui apportent une compétence en termes d'essais cliniques, de priorisation d'accès et de réglementation des stocks essentiels. On n'a pas ça dans les autres pays. Le FDA est différent car au niveau du FDA on n'a personne qui est l'équivalent de la Commission européenne qui apporte une partie politique, une coordination et une cohésion, puis qui vérifie la mise en œuvre avec un "bâton" pour forcer les pays à suivre. Si on regarde en termes d'intérêt des patients, l'Europe est assez précurseur. Par contre, on voit pas mal d'hésitations à prendre le lead, liées au contexte actuel où l'Europe a été très attaquée sur la défense récemment, ce qui crée une certaine timidité dans le domaine de la santé.

Maëlys : Sur les délais d'accès aux médicaments, mon analyse montre une réduction des inégalités entre les pays de 3,75 jours par an, mais les inégalités structurelles restent énormes entre l'Allemagne et la Roumanie. Est-ce que cette convergence est réelle et durable ou est-ce le résultat d'une période post-COVID qui va se stabiliser ?

Participant F : Il est intéressant de regarder le type de médicament, par exemple les médicaments génériques où les frontières sont plus poreuses que pour les médicaments traditionnels. J'ai habité en Belgique et ma fille avait un traitement immunosuppresseur qui était régulièrement en rupture de stock, alors qu'en France il était disponible tout le temps sur simple prescription. Les médicaments d'oncologie n'ont pas une chaîne d'approvisionnement équivalente à un autre médicament. Il faut regarder quels sont les points d'administration dans le pays. L'ICH a des guidelines sur les essais cliniques, et il y a des pays très matures comme l'Australie qui ne répondent pas aux critères d'ICH pour l'instant car ils ont un système d'évaluation propre.

Maëlys : Quelle est selon vous la limite la plus importante de la stratégie pharmaceutique pour l'Europe ?

Participant F : Je pense que c'est le pilier 1, l'attractivité. On l'a vu pour les vaccins COVID : on a parlé du vaccin Sanofi pendant longtemps et il n'est pas sorti. Quand Trump met une politique de tarifs très agressive, les entreprises ont tendance à délocaliser pour prendre moins de risques. Essayer de garder la connaissance en France et une possibilité de recherche et d'innovation est assez difficile. En Suisse, il y a de gros labos, on en a plus sur ce petit pays que sur toute l'Europe. L'attractivité devrait être l'inquiétude principale.

Maëlys : Sur l'attractivité, j'ai analysé la régulation des essais cliniques avec le portail CTIS, et mon analyse montre que ça n'a pas inversé le déclin de la part de marché de l'Europe. Certains disent que c'est dû au fait que l'Europe est trop fragmentée avec un manque d'harmonisation entre l'Europe et chaque État membre.

Participant F : Oui, et ça ne va pas changer car il n'y a pas de proposition pour le changer. Ça ajoute une couche de complexité énorme à gérer pour les entreprises et les régulateurs. Il y avait une directive européenne pour lutter contre la contrefaçon (EU FMD) où l'idée était d'avoir une organisation européenne qui coordonne les activités de tous les pays. Comme personne n'avait l'obligation de scanner en pharmacie et que personne n'avait mis en place les technologies, ça a créé beaucoup de bureaucratie mais c'est très difficile pour les pays de se coordonner et pour l'industrie de s'y retrouver. C'est beaucoup moins agile aussi. Certains pays bénéficient de crises, nous on n'en tire pas bénéfice du tout.

Maëlys : C'était mes questions. Est-ce que vous êtes d'accord que j'intègre tout ça dans mon mémoire ? Je peux vous anonymiser.

Participant F : Oui bien sûr !

Maëlys : Merci beaucoup pour votre aide. Au revoir madame.

Participant F : Avec plaisir. Bonne après-midi. Au revoir.

R script

Pillar 1

1. Préparation des données

```
library(readxl)
```

```
data_p1 <- read_excel(file.choose())
```

```
# On crée les variables pour la régression "Interrompue"
```

```

data_p1$Time <- 1:nrow(data_p1) # Tendance générale (1 à 10)
data_p1$CTR_Effect <- ifelse(data_p1$Year >= 2022, 1, 0) # Choc immédiat après 2022
data_p1$Time_Since_CTR <- ifelse(data_p1$Year >= 2022, data_p1$Year - 2021, 0) # Changement de
pente
# 2. La Régression (Modèle Scientifique)
# On explique la part de l'UE par le temps et l'effet de la réforme,
# en contrôlant par la part des Amériques (pour voir si c'est un effet mondial)
model_attractiveness <- lm(`EU share` ~ Time + CTR_Effect + Time_Since_CTR + `Americas share`,
data = data_p1)
# 3. Résultat
summary(model_attractiveness)

```

Pillar 2

```

# PILIER 2 - COMPÉTITIVITÉ
# Impact du SPC Manufacturing Waiver sur les exportations EU
# Source données : Eurostat (catégorie SITC 54)
# --- 0. Packages ---
library(ggplot2)
library(readxl)
# --- 1. Import des données ---
# Fichier Excel attendu : "pilier 2.xlsx"
# Colonnes attendues :
# - Year      : année (ex. 2011, 2012, ..., 2025)
# - exports   : valeur des exportations extra-EU en milliards d'euros
data_pillar2 <- read_excel("pilier 2.xlsx")
# --- 2. Construction des variables de régression ---
# Variable de tendance temporelle (1, 2, 3, ...)
data_pillar2$time_trend <- seq_len(nrow(data_pillar2))
# Variable dummy SPC Waiver :
# 0 = avant la réglementation (2011–2018)
# 1 = après l'entrée en vigueur (2019–2025)
data_pillar2$waiver_active <- ifelse(data_pillar2$Year >= 2019, 1, 0)
# --- 3. Régression OLS (Ordinary Least Squares) ---

```

```

# Modèle : exports ~ time_trend + waiver_active
# Le time_trend capte la croissance naturelle du marché mondial.
# waiver_active mesure l'effet spécifique du SPC Waiver.
model_pillar2 <- lm(exports ~ time_trend + waiver_active, data = data_pillar2)
summary(model_pillar2)
# --- 4. Interrupted Time Series (ITS) — visualisation ---
# Valeurs ajustées par le modèle
data_pillar2$fitted <- fitted(model_pillar2)
ggplot(data_pillar2, aes(x = Year)) +
  geom_point(aes(y = exports), size = 2.5, color = "#1D9E75") +
  geom_line(aes(y = fitted, linetype = "Modeled Trend (Controlling for Time)",
    color = "#1D9E75", linewidth = 0.8) +
  geom_vline(xintercept = 2019, linetype = "dashed", color = "red", linewidth = 0.8) +
  annotate("text", x = 2019.2, y = min(data_pillar2$exports) + 10,
    label = "SPC Waiver\nImplementation",
    hjust = 0, size = 3, color = "red") +
  scale_linetype_manual(values = c("Modeled Trend (Controlling for Time)" = "solid")) +
  labs(
    title = "Interrupted Time Series: SPC Waiver Impact on Exports",
    x = "Year",
    y = "Extra-EU Exports (Billion €)",
    linetype = NULL
  ) +
  theme_minimal(base_size = 11) +
  theme(legend.position = "bottom")

```

Pillar 3

```

# PILIER 3 — ACCÈS
# Impact de la réglementation HTA sur l'équité d'accès (W.A.I.T.)
# Source données : rapports annuels EFPIA
# --- 0. Packages ---
library(ggplot2)

```

```

library(readxl)
library(tidyr)
library(dplyr)

# --- 1. Import des données ---
data_pillar3 <- read_excel("pilier 3.xlsx")

# --- 2. Test F de Fischer — comparaison des variances 2020 vs 2024 ---
# H0 : la variance en 2024 est égale à celle de 2020.
# On teste si l'inégalité entre pays a significativement diminué.
var_2020 <- var(data_pillar3$Delay2020, na.rm = TRUE)
var_2024 <- var(data_pillar3$Delay2024, na.rm = TRUE)
cat("Variance 2020 :", round(var_2020, 2),
    " Variance 2024 :", round(var_2024, 2), "\n")
f_test <- var.test(data_pillar3$Delay2024,
                   data_pillar3$Delay2020,
                   alternative = "less")

print(f_test)

# --- 3. Graphique — Évolution de la variance 2018–2024 ---
years <- 2018:2024
delay_cols <- paste0("Delay", years)
variances <- sapply(delay_cols, function(col) var(data_pillar3[[col]], na.rm = TRUE))
df_var <- data.frame(Year = years, Variance = variances)
ggplot(df_var, aes(x = Year, y = Variance)) +
  geom_line(color = "#178FD4", linewidth = 0.8) +
  geom_point(color = "#178FD4", size = 3) +
  labs(
    title = "Evolution of Access Delay Variance in Europe (2018-2024)",
    subtitle = "Measuring inequality in patient access to innovative medicines",
    x = "W.A.I.T. Cohort Year",
    y = "Variance (Inequality Indicator)",
    caption = "Source: Based on EFPIA W.A.I.T. Indicators"
  )

```

```
) +
theme_minimal(base_size = 11)

# 4. Sigma-convergence régression sur l'écart-type 2020-2024
# On mesure si l'écart-type (sigma) des délais diminue significativement au fil du temps.
# Modèle : Sigma ~ Year
sigma_vals <- sapply(paste0("Delay", 2020:2024),
                     function(col) sd(data_pillar3[[col]], na.rm = TRUE))
df_convergence <- data.frame(
  Year = 2020:2024,
  Sigma = sigma_vals
)
model_sigma <- lm(Sigma ~ Year, data = df_convergence)
summary(model_sigma)
```

Pillar 4

```
library(readxl)
library(dplyr)

# 1. Chargement
df <- read_excel(file.choose(), skip = 1)

# 2. Nettoyage et Fusion
prime <- df[, c(1, 9, 10, 11, 12)]
colnames(prime) <- c("Name", "Submission", "Auth", "Orphan", "ATMP")
prime$Is_PRIME <- 1

std <- df[, c(14, 16, 17, 18, 19)]
colnames(std) <- c("Name", "Submission", "Auth", "Orphan", "ATMP")
std$Is_PRIME <- 0
final_data <- rbind(prime, std) %>% filter(!is.na(Name))

# 3. Conversion forcée des dates (Gestion des erreurs de saisie)
# On s'assure que R comprend bien le format Date
final_data$Submission <- as.Date(final_data$Submission)
```

```

final_data$Auth <- as.Date(final_data$Auth)

# 4. Calcul du délai EXPLICITEMENT en MOIS

# On calcule en jours, puis on divise par 30.44

final_data$Delay_Months <- as.numeric(difftime(final_data$Auth, final_data$Submission, units =
"days")) / 30.44

# 5. Vérification visuelle

print("Aperçu des délais calculés (en mois) :")

print(head(final_data[, c("Name", "Delay_Months")]))

# 6. RÉGRESSION FINALE

model <- lm(Delay_Months ~ Is_PRIME + ATMP + Orphan, data = final_data)

summary(model)

```

