

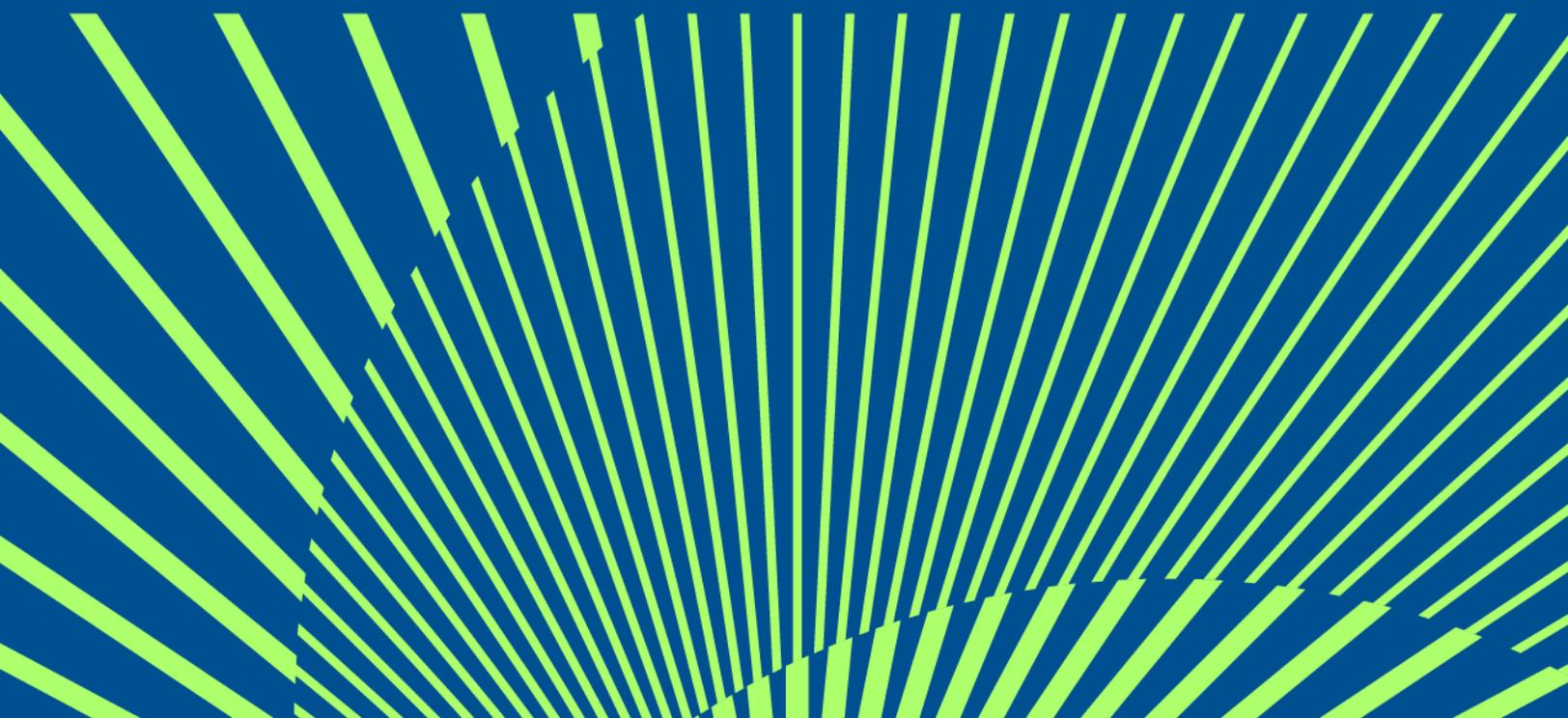


U.S. Chamber of Commerce
Global Innovation
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IP Rights and the Research-Based Biopharmaceutical Industry in the EU: An IP Index Out-of-Cycle Review

2023



Review Objective

Since 2012, the U.S. Chamber of Commerce's International IP Index has provided an important industry perspective on the IP standards that influence both long- and short-term business and investment decisions. The Index is a unique and continuously evolving instrument. It assesses the state of the international IP environment and provides a clear roadmap for any economy that wishes to be competitive in the 21st-century knowledge-based global economy. Today, the Index consists of 50 discrete indicators across nine separate categories that together measure the strength of a national IP environment. The latest edition of the Index, published in 2023, covers 55 economies that together represent both a geographical cross-section of the world and more than 90% of global economic output. Since 2015, the Index has also included a Statistical Annex that investigates the relationship between the strength of economies' national IP environments and different types of economic activity, including rates of research & development (R&D) spending, innovation, technology creation, and creativity. The most up-to-date data on the benefits of IP protection reveal that IP rights are, in fact, a critical instrument for economies that seek to enhance access to innovation, grow domestic innovative output, and enjoy the dynamic growth benefits of an innovative economy. Conversely, weak IP protection stymies long-term strategic aspirations around innovation and development. The Index's Statistical Annex has shown the strong, direct, and statistically significant relationship between IP protection and innovation—including attractiveness to venture capital and R&D investments, innovative activities, outputs, and early adoption of technologies.

This Index Out-of-Cycle Review comes in response to proposals from the European Commission that are under discussion with the European Parliament regarding revision of the EU's pharmaceutical legislation. The proposed Directive and Regulation touches on all facets of the EU's biopharmaceutical regulatory framework: R&D and manufacturing, sanitary registration and market authorization, patient and market access, and biopharmaceutical-specific IP rights.

Unfortunately, as currently constructed, this reform package is almost wholly negative. Instead of recognizing the strategic value of the research-based biopharmaceutical industry to the EU and its member states—as was so clearly demonstrated during the COVID-19 pandemic—and trying to strengthen and grow it, the reforms do the opposite.

The purpose of this review is to provide an estimate through a “what if?” scenario analysis of how the support and adoption of the current proposals to weaken biopharmaceutical-specific IP rights would affect individual EU member states' scores in upcoming editions of the IP Index.

Background

As has been noted in the Index over the past decade, at the EU level and among individual member states, growing uncertainty surrounds the biopharmaceutical IP environment. On the one hand, many European and national policymakers understand the industry's strategic value and importance as illustrated by the immense contributions and accomplishments in fighting the COVID-19 pandemic. For example, in the 2020 Pharmaceutical Strategy for Europe, the European Commission recognized the importance of the research-based industry, stating, "There is a strong and competitive pharmaceutical industry in the EU. Together with other public and private actors, it serves public health and acts as a driver of job creation, trade and science."¹ The European Commission is right. As an industry, the research-based biopharmaceutical sector is one of Europe's biggest success stories. European companies are some of the largest, most innovative, and most successful in the world. Not only does this industry have a long track record of producing lifesaving medical innovations that have been or are currently used by millions of patients, but the industry is also an engine of economic growth in the EU. Figures from the European Federation of Pharmaceutical Industries and Associations show that in 2021, the European research-based industry directly employed around 840,000 people (with more than 120,000 in high-skill R&D jobs), invested EUR41.5 billion in R&D activity, and generated EUR300 billion in production value².

On the other hand, the strategic value and economic contribution of this industry are not always recognized in the development of

IP policies. For example, in 2015, under the overarching initiative to reform and deepen the single market with the purpose of spurring economic growth, the European Commission announced its intentions to explore options, such as Supplementary Protection Certificates (SPCs), for recalibrating certain elements of patent term restoration for biopharmaceuticals. One option for change put forth by the Commission was to provide European manufacturers of generic drugs and biosimilars with an SPC manufacturing and export exemption (SPC exemption). The overriding purpose of the proposal was to provide European manufacturers of generic drugs and biosimilars a competitive advantage by weakening IP protection for innovators. As the Index pointed out at the time, many troubling assumptions underlay the Commission's proposal. Most basically, the proposal assumed that an actual market and demand exist for European generic manufacturers. Yet it was not at all clear what this market was or from where the demand for generic medicines produced in Europe would come. The markets that per definition would be targeted by European generic manufacturers under an SPC exemption are economies that do not provide IP protection and exclusivity for products under SPC protection in the EU for which the SPC exemption would apply. Generic follow-on products are likely already on the market in many of these economies and are produced by local manufacturers who are often preferred partners in local drug procurement. It was unclear why these targeted markets would favor European generic manufacturers as opposed to their own domestic ones. In many cases, these targeted economies already have

a health and pharmaceutical policy framework in place that actively discriminates against foreign manufacturers. Such localization policies often include price preferences in government tenders, import bans and increased taxation on foreign products, and local affiliation and/or production requirements. For those markets in which equivalent SPC protection mechanisms are in place, it is highly unlikely that an SPC exemption would grant the European generic and biosimilar manufacturers an exclusive status for early market entry of their products across the globe. Indeed, several key EU member states recognized this flawed logic. In 2019, Denmark, Sweden, and the United Kingdom all voted against the measure in the European Council (EC). The EC subsequently issued a statement whereby several member states raised concerns about the policy and its potential damage to Europe's research-based industries. Of note is the Danish government's perceptive criticism of the policy:

While reflecting a compromise, the final text of the regulation presents wide implications that may potentially benefit one side of the pharmaceutical industry in the future but may generate significant damage today for the other. By allowing storing of medicinal products and affecting acquired rights of the SPC holders, Denmark believes that the result is disproportionate and goes far beyond what is necessary in order to achieve with the objective of the proposal [emphasis added].

Despite this criticism, Regulation 2019/933 has been in force since 2019, and the SPC export exemption is legal and operational in all EU member states. The decision to move ahead with the SPC exemption was a significant blow to biopharmaceutical rightsholders and has weakened the IP environment across the EU. Because of this action, the score on this indicator was reduced by 0.25 for all EU member states in the eighth edition of the Index.

Outside of the EU, the regulation continues to damage international rightsholders. Instead of allowing European generic manufacturers to gain a competitive advantage, other economies are simply emulating the EU. In a wide-ranging set of amendments to the Law on Protection of Rights to Inventions and Utility Models, in 2020, Ukraine introduced an export and stockpiling exemption explicitly modeled on EU Regulation 2019/933. Similarly, in 2021, the Israeli Ministry of Justice published draft amendments to the patent law "The Patents Law (Amendment No. 14) (Increasing the Competitiveness of the Israeli Economy), 5721-2021." The proposed amendments seek to introduce a manufacturing, export, and stockpiling exemption to the current term restoration regime. Like the Ukraine example, this law refers to and is explicitly modeled on Regulation 2019/933. As the Ukraine and Israel examples show, instead of benefiting the European generics industry, the introduction of the SPC exemption is hurting Europe's research-based industry and has led to a global race toward the bottom in weakening global IP standards. (Unlike Regulation 2019/933 and the SPC exemption, proposals for a new centralized process for granting and administering SPCs would be a positive addition to the IP environment in the EU. As part of the Unitary Patent system and Patent Court, in 2022, the European Commission issued a "Call for Evidence" consultation. This document outlines several options for reforming the SPC system, including the potential for introducing a new centralized system of SPC protection and application. At the time of research, the Commission had not adopted or proposed a final legislative proposal.)

In addition to the SPC system, since 2018, the European Commission has conducted a regulatory review of the Orphan Regulation and the Paediatric Regulation, which provide special incentives (including IP-based incentives and a defined period of market exclusivity) for products developed for rare diseases in children. In 2020,

the Commission published an “Inception Impact Assessment” with the view of proposing some legislative changes to both regulations. Orphan drugs are niche treatments for diseases with small patient populations and commercial markets. Since the 1980s, a series of financial and regulatory incentives in the United States (1983), Japan (1993), and the EU (2000) has managed to bring about a sea change in R&D, clinical research, and the development of new products globally for rare diseases. For, example, in the decade before the introduction of special incentives in the United States, only 10 products were approved for market, that is, only one drug per year on average.³ Since then, more than 575 drugs and biologic products have been developed and approved. A key driver of this success has been a clear and strong market exclusivity incentive. In the EU, the Orphan Regulation provides a 10-year term of marketing exclusivity (orphan status can be withdrawn after six years if designation criteria are no longer met, including if the drug is sufficiently profitable, and, in addition, exclusivity may be extended by two years if a pediatric investigation plan has been completed when requesting approval). On the back of these schemes, as well as key pharmacogenomic discoveries that fueled interest in the development of niche products⁴⁴, the number of orphan drugs developed and authorized for rare diseases has increased exponentially. Since its introduction in 2000, the EU Orphan Regulation had, as of 2017, resulted in the following:

- Nearly 2,000 orphan designations approved
- More than 150 orphan medicinal products approved by the European Medicines Agency (EMA) for over 90 rare diseases (up from only eight orphan products available in 2000)
- An increase of 85% in the number of rare diseases for which an orphan designation exists in the EU

- An increase of 88% in clinical research activity on rare diseases between 2006 and 2016, with the EU-5 countries experiencing an even bigger increase of 104% during that period⁵

The data are clear: the Orphan Regulation and its IP rights-based 10-year market exclusivity incentive have been a success and have done exactly what they were intended to do—place more orphan medicines on the EU market.

The real challenge facing European policymakers, both regionally and nationally, is to ensure that patients gain effective access to these new medicines. Timely and equitable access to orphan medicines is not guaranteed in the EU, and substantial differences exist among member states with respect to both the number of products publicly reimbursed and the average time it takes for patients to gain access to them. This should not be news to the European Commission. In a 2006 assessment report, the Commission cited a survey conducted by the pan-European patient group EURORDIS, which found that for a sample of 12 orphan products approved by the end of 2003, only one member state demonstrated the availability of the entire sample, whereas only half of the sample or less were available in the rest of the then 25 EU member states.⁶ The report concluded the following:

The full benefits of the EU orphan regulations require optimal synergies between action on Community and on Member State level. Incentives at the European Union level need to be translated into rapid access of patients to the new products throughout the entire Community and they need to be supplemented by incentives at Member States level. In this regard, the past experience was not entirely satisfactory.⁷ [emphasis added]

More recent evidence suggests that not much has changed since 2006. A 2017 study by the Office of Health Economics (a British research institute) compared access to 143 orphan products that were approved for marketing in the EU between 2000 and 2016 across the then EU-5 (including a division between England, Scotland, and Wales that constitutes the United Kingdom).⁸ The study found the following:

- Access to authorized orphan products through public reimbursement varied substantially among the sampled member states, ranging from 93% in Germany to 33% in Wales.
- The average duration between the granting of marketing authorization by the EMA and reimbursement decision by the national authority was 23.4 months—nearly two years.⁹
- That duration is also considerably longer for orphan medicines when compared with nonorphan medicines. For example, in the United Kingdom, the median number of months between the marketing authorization and the first National Institute for Health and Care Excellence appraisal was 20.2 months for orphan medicines compared with 12.7 months for nonorphan medicines.

The EU Orphan Regulation has succeeded in promoting research of rare diseases and incentivizing the development of orphan medicinal products, just as similar IP incentives in other economies—such as the United States—have produced similar positive outcomes. However, the last step—providing patients with rare diseases access to these medicines—is member states’ responsibility. As the cited evidence suggests, access to orphan medicinal products is hampered by insufficient reimbursement and long delays, which result in unequal access to care for patients with rare diseases across the EU. Instead of

questioning or reviewing the efficacy of the IP incentives enshrined in the Orphan Regulation—which is what has produced this innovation in the first place—the Commission and EU policymakers should put more effort and thought into how to address this access barrier more effectively.

This line of thought can also be applied more broadly to access to all new and innovative biopharmaceutical products and technologies. The European Commission rightly pointed out in the Pharmaceutical Strategy for Europe that “innovative and promising therapies do not always reach the patient, so patients in the EU still have different levels of access to medicines.”¹⁰ However, just as with access to orphan drugs, substantial differences exist among member states with respect to both the number of products publicly reimbursed and the average time it takes for patients to gain effective access to them within a health system. Again, within this context, IP rights play no part. The design of a health system’s biopharmaceutical market access policies takes place at the member state level. Each member state, through its broader health and biopharmaceutical policies, decides on market access policies and how to control the cost of medicines. Some EU member states and health systems seek to eliminate barriers to the introduction and use of new products and technologies. Others focus solely on cost containment and do not prioritize patient access to new products and innovation. Proposals for solving the access issue should recognize this fundamental fact. Existing IP incentives are not part of the problem.

Finally, at both the member state and EU levels, there has been a growing focus on compulsory licensing for biopharmaceuticals. In 2017, health authorities in the Netherlands promised to explore the use of compulsory licensing for medicines whose price was deemed excessive, acting on the advice included in a report by the Council for

Public Health and Society, Development of New Medicines— Better, Faster and Cheaper—which encouraged the use of compulsory licensing to strengthen the government’s position in price negotiations. In 2020 in Hungary, the government introduced an expedited compulsory licensing mechanism for biopharmaceuticals. In a separate development later that year, a Hungarian manufacturer began producing a local version of the drug remdesivir for use in a local clinical trial. Registration data in the European Union Clinical Trials Register show the trial was supported by the Hungarian government (the Ministry of Innovation and Technology through a consortium). Industry sources suggest that a compulsory license was granted by the Hungarian authorities in late 2020.

In 2022, the European Commission issued a Call for Evidence on the current compulsory licensing regime across the EU. It is difficult to understand the rationale for this Call for Evidence. Each individual EU member state has national laws in place that address compulsory licensing in line with their World Trade Organization (WTO) commitments. The Commission posits in the Call for Evidence that a pressing need for “coordination and harmonization” exists at the EU level on compulsory licenses but provides no actual evidence that this is the case. The document asserts that the COVID-19 pandemic shows the need for clearer and more “effective” compulsory licensing mechanisms:

The COVID-19 pandemic has underscored the importance of having a strong and balanced IP system (to provide the necessary incentives to develop new treatments and vaccines) and a suitable framework (for sharing technologies, know-how and data). It has also triggered many debates, at national, EU and multilateral levels, on the need for effective IP tools to ensure proper and global access to essential technologies in a crisis. Close public-private cooperation based on voluntary

solutions for sharing the relevant IP and know-how, e.g. licensing or manufacturing agreements, is the fastest and most effective way to develop and scale up the production of critical medicine and medical supplies. However, if voluntary arrangements between rightsholders, third parties (such as manufacturers), and public authorities fail or are unavailable, the use of last-resort tools, namely compulsory licensing, might be needed. A compulsory license issued by a government authorises a party other than the patent holder to use a patented invention without the consent of the patent holder. In particular during a crisis, these tools must be effective to make an orderly EU response possible. [Emphasis added]¹¹

This was followed up with a proposal for new EU legislation in April 2023. Unfortunately, the proposed regulation is based on the same flawed logic as the Call for Evidence. For example, the preamble of the draft regulation explains the rationale and need for an EU-wide compulsory licensing regime as follows:

In the context of the Union crisis or emergency mechanisms, the Union should therefore have the possibility to rely on compulsory licensing. The activation of a crisis or an emergency mode or the declaration of a crisis or a state of emergency addresses obstacles to free movement of goods, services, and persons in crises and shortages of crisis-relevant goods and services. In cases where access to crisis-relevant products and processes protected by a patent cannot be achieved through voluntary cooperation, compulsory licensing can help in lifting any patent-related barriers and thus ensure the supply of products or services needed to confront an ongoing crisis or emergency. It is therefore important that,

in the context of said crisis mechanisms, the Union can rely on an efficient and effective compulsory licensing scheme at Union level, which is uniformly applicable within the Union. This would guarantee a functioning internal market, ensuring the supply and the free movement of crisis-critical products subject to compulsory licensing in the internal market.

If anything, the evidence and experience from the COVID-19 pandemic show the complete opposite. For example, the much-discussed Trade-Related Aspects of Intellectual Property Rights Agreement (TRIPS) waiver and subsequent 2022 WTO Ministerial Decision have proven to be unnecessary. They address a problem of vaccine shortages that does not exist, and no WTO member has yet made use of it. As the Index stated clearly and unequivocally when the idea for a waiver was first broached in 2020, waiving and overriding of IP rights are completely irrelevant within the context of fighting the COVID-19 pandemic. At more than 15 billion doses produced, the global manufacturing and supply of COVID-19 vaccines today outstrip global demand. In fact, the International Monetary Fund, World Health Organization, and WTO have all suspended their respective monitoring of the global vaccine supply chain because it no longer needs to be monitored^{12d}. Similarly, only one compulsory license was issued during the pandemic by the Israeli government to specifically address a perceived shortage of medicines, but the generic product was never distributed to Israeli COVID-19 patients. Other licenses were issued based on the cost of a given treatment as opposed to its availability. See, for example, the involuntary licenses issued in Hungary and Indonesia.

Much like the WTO's TRIPS waiver, the European Commission's fascination with expanding involuntary mechanisms for sharing IP through a more "effective" compulsory licensing mechanism

does not seem to be based on real-world data and need. More broadly, threats and the use of compulsory licensing of medicines as a basis for price negotiations are usually associated with low-income developing economies with underdeveloped health systems and limited financial resources, not the European Commission or high-income EU member states with advanced sophisticated health systems. The issuing of a compulsory license undermines the basic idea of the protection and sanctity of property rights, including IP rights in place to protect and incentivize biopharmaceutical innovation. Cost is not a relevant justification or basis for compulsory licensing or the overriding of any granted form of biopharmaceutical exclusivity. Moreover, the use of these types of licenses threaten the very foundation of the EU's position as a global leader in innovation and high-tech industries, including biopharmaceuticals. As the cited data from European Federation of Pharmaceutical Industries and Associations (EFPIA) show, as an industry, the research-based biopharmaceutical sector is one of Europe's biggest success stories and includes some of the largest, most innovative, and successful research-based biopharmaceutical companies in the world. The overriding of biopharmaceutical IP rights based on cost and price negotiations sets a wholly negative precedent that may be applied to other industries and sectors. If the EU or individual member states wish to pay less, or nothing, for medicines using compulsory licenses, these measures could subsequently be applied to the procurement of medical devices, software, trains, automobiles, or any other high-tech product that the public sector purchases.

Fast-Forward to 2023: European Commission Proposes a New EU Pharmaceutical Legal Framework

In April 2023, the European Commission published a package of proposed legislative changes to almost all facets of the biopharmaceutical market authorization process and related incentives, including for orphan and pediatric drugs. The proposed changes would fundamentally weaken the EU’s legal framework as it relates to biopharmaceutical IP rights. Specifically, rights related to regulatory data protection (RDP), orphan drugs, and patent protection—through an expansion of existing so-called Bolar exemptions—would be materially weakened.

With respect to RDP, the proposed revised directive would replace the current RDP regime and 8+2+1 formula with a baseline formula of 6+2, which represents a defined data exclusivity term of protection of six years and a two-year market exclusivity window. Article 81(2) of the draft directive includes the possibility of extending this exclusivity to the existing 10-year period or even, under unique circumstances, to 12 years. The conditions that must be fulfilled to gain these additional periods of exclusivity are so convoluted and complex that it is unlikely that any research-based entities will be able to access them. This includes the extension of the term of exclusivity on external factors, such as market access. For example, under Article 82, the possibility of a 24-month extension of the term of data exclusivity is contingent on the relevant product being “continuously supplied into the supply chain in a sufficient quantity and in the presentations necessary to cover the needs of the patients in the member states in which the marketing

authorization is valid.” Such “conditionality” of IP or regulatory protection establishes a counterproductive precedent because it makes the availability of such protection contingent on factors outside of rightsholders’ control. The Commission has not considered that biopharmaceutical innovators are not responsible for the procurement, prescribing, and dispensation of medicines and health technologies. Individual EU member states and their respective health systems oversee all processes related to “the needs of the patients in the member states,” that is, actual patient access, including pricing and reimbursement, procurement, and prescription and dispensation practices.

The legislation also reduces the market exclusivity period for orphan drugs. As mentioned, the current Orphan Regulation has provided a 10-year term of marketing exclusivity. However, orphan status can be withdrawn after six years if designation criteria are no longer met, including if the drug is sufficiently profitable, and, in addition, exclusivity may be extended by two years if a pediatric investigation plan has been completed when requesting approval. Like the proposed RDP changes, Article 71 of the draft regulation provides a variable set of terms of protection for orphan medicinal products; in this case, the exclusivity periods are 10, 9, and 5 years. Eligibility for the maximum period of 10 years of protection is to be restricted and will be made available only for products that address what is described as a “high unmet medical need.” Under Article 70, products will need to provide an “exceptional therapeutic advancement,” and the use of the

product should result “in a meaningful reduction in disease morbidity or mortality for the relevant patient population.” This reduction in eligibility for the maximum period of protection will, per definition, reduce the incentives to invest and develop new products and treatments for patients with rare diseases. Ultimately, it will result in fewer products developed, commercialized, and made available to these patient populations. It remains unclear why the Commission wishes to actively reduce the future development and supply of medicines for these patient groups.

Finally, the proposal expands existing Bolar exemptions to include health technology assessment and pricing and reimbursement processes. A Bolar exemption (or exception) allows follow-on applicants to begin the testing and regulatory approval processes for their follow-on products without acquiring consent from the rightsholder, in this case, the market authorization holder of the reference product. This type of exception originates in the United States and, specifically, in the 1984 Drug Price Competition

and Patent Term Restoration Act (Hatch-Waxman Act). The rationale behind these types of exceptions or exclusivity exemptions is to ensure that there is no undue delay in the market supply of follow-on products once the relevant exclusivity of the reference product expires. Bolar exceptions are not intended to be used to undermine rightsholders’ legitimately granted exclusivity periods. The expansion of the Bolar exemption to include health technology assessment and pricing and reimbursement processes would potentially weaken existing exclusivity periods—including duly granted patent protection—through the premature launch of patent-infringing generics or biosimilars. This would put rightsholders in a position whereby their IP rights are potentially infringed during the period of duly granted exclusivity whether through patent protection or a different IP right.

Proposed Pharmaceutical Legislation and the Index: Quantifying the Negative Impact on Economies' National IP Environment

The support and adoption of the current proposals to weaken existing biopharmaceutical IP incentives in the EU will have a direct and tangible negative impact on EU member states' national IP environments and corresponding Index score. This section of the review provides an estimate of this impact and quantifies the negative impact on individual EU member states' Index scores.

As currently constructed, the Commission's proposals would primarily affect two Index indicators: Indicator 5, Pharmaceutical-related patent enforcement and resolution mechanism, and Indicator 25, RDP term.

Indicator 5 measures the existence of primary and/or secondary legislation (such as a regulatory and/or administrative mechanism) that provides a transparent pathway for adjudication of patent validity and infringing issues before the marketing of a generic or biosimilar product. This score is evenly divided between the existence of a relevant mechanism and its application or enforcement. If no mechanisms are in place, the maximum score that can be achieved is 0.5. Such a score is based on the extent to which de facto practices (such as expeditious preliminary injunctive relief) are in place that achieve a similar result. The European drug regulatory authority, the European Medicines Agency, does not evaluate or adjudicate patent validity or other IP rights infringing issues before the marketing of a generic or biosimilar product. Instead, rightsholders in all EU member states must seek injunctive relief through a national court of law once a potentially infringing product reaches the market. This is readily available in most EU member

states. However, from the Index's perspective, this is a limitation because it does not effectively address the issue of a potentially infringing product being approved for market before sanitary registration and approval. Consequently, the maximum score that all EU member states have achieved until now on this indicator has been 0.5.

Indicator 25 measures the term of RDP exclusivity granted to new biopharmaceutical products containing new active ingredients regardless of molecular size and/or complexity. The baseline numerical term used is the existing EU term of 10 years (8+2) of marketing exclusivity. Half (0.5) of the available score is based on the term available for biologics or large molecule compounds. If an economy's relevant RDP legislation or regulation, either de jure or de facto, does not cover such compounds, then the maximum score that can be achieved in this indicator is 0.5. As mentioned, until now, RDP legislation in the EU is provided by Article 10 of Directive 2004/27/EC (amending 2001/83/EC). Before 2004, the EU's RDP regime was not harmonized among EU members, and the term of protection varied between 6 and 10 years. The 2004 amendments harmonized the term of protection according to the 8+2+1 formula. According to this formula, new pharmaceutical products are entitled to eight years of data exclusivity, two years of marketing exclusivity (in which generic and follow-on applicants are allowed to submit bioequivalence studies), and an additional year of protection for new indications of existing products. This period of protection is not limited to chemical entities and extends to biologics. Under this formula of data and market exclusivity, the EU's practice has

matched that of the Index benchmark, and all EU member states have achieved the maximum available score of 1.00 on this indicator.

As Table 1 shows, the latest edition of the Index includes 10 EU member states.

Table 1. EU Member States Included in the 11th Edition of the Index

• France	• Italy
• Germany	• Netherlands
• Greece	• Poland
• Hungary	• Spain
• Ireland	• Sweden

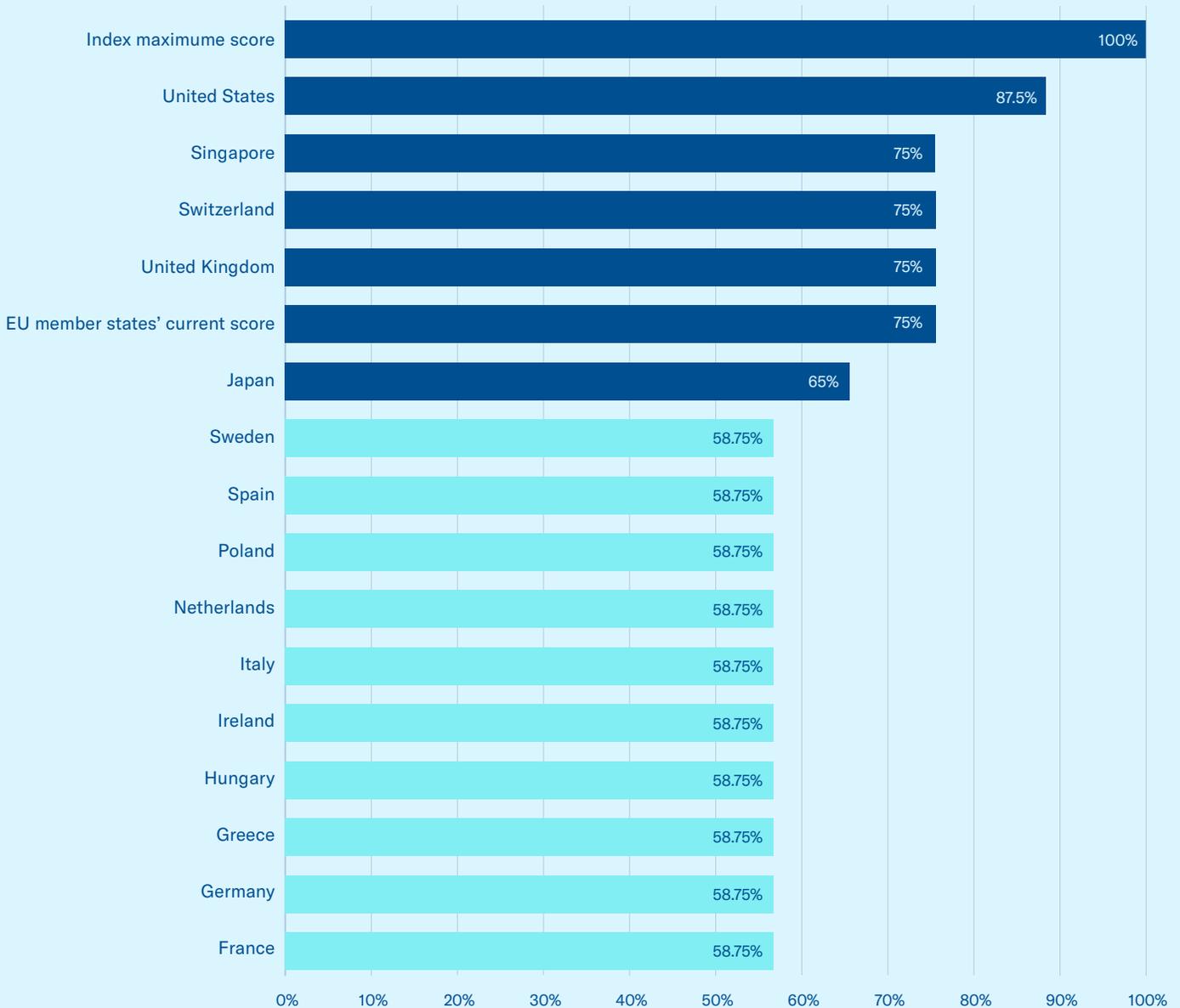
What would the impact of the Commission’s proposal be on these Index economies’ Index scores and specifically on the scores for indicators 5 and 25?

As discussed, under the current Commission proposals, the effective term of RDP would be reduced from 10 years to 8 years. This would result in a reduction of 0.20 on indicator 25. Similarly, the reduction in effective patent protection for pharmaceuticals due to the expansion of the Bolar exemption will result in a reduction of between 0.25 and 0.50 on indicator 5 depending on the implementation in each jurisdiction. As with all EU legislation, substantial differences can exist among EU member states in how the relevant statute is transposed and/or interpreted in national courts. How such implementation and

interpretation take place will determine the total impact of these legislative changes on the national IP environment and accompanying score for this indicator. The following estimated score reduction is based on an average score of the midpoint score between a 0.5 reduction and a 0.25 reduction.

Figure 1 shows the results of this reduction for all 10 EU member states included in the Index.

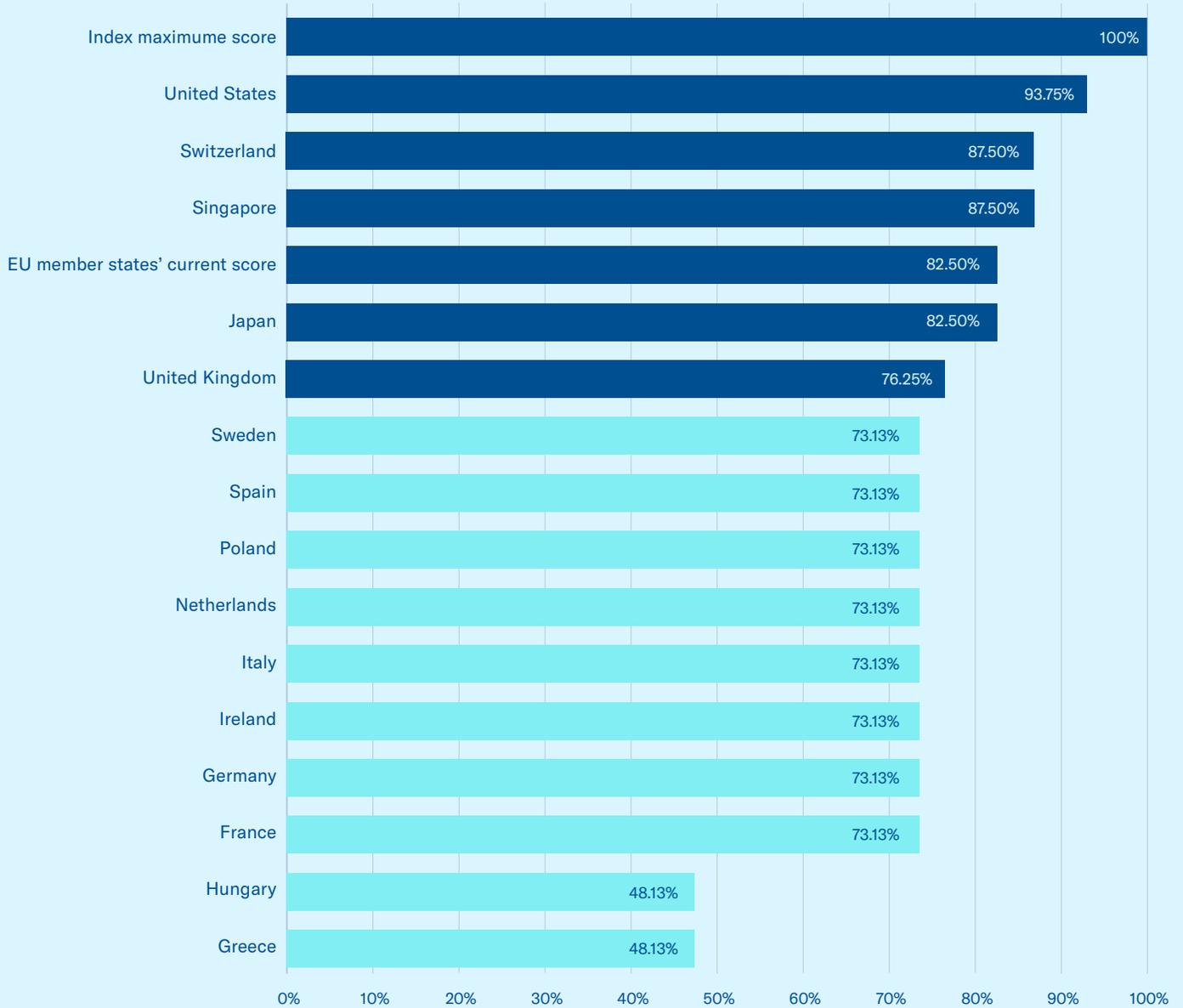
Figure 1. Current Scores, Indicators 5 and 25, Select Index Economies and EU Member States versus Estimated Score Reduction, EU Member States (Current Scores Are in Red; Estimated Reduced Scores Are in Blue)



It is also possible to broaden this comparative analysis and to estimate the negative impact of the Commission's proposal on the total national IP environment as it relates to biopharmaceutical IP rights measured in the Index. This broadens the analysis to include

two additional indicators: 6, Legislative criteria and use of compulsory licensing of patented products and technologies, and 7, Patent term restoration for pharmaceutical products. Figure 2 shows the results of this reduction for all 10 EU member states included in the Index.

Figure 2. Current Scores, Indicators 5, 6, 7, and 25, Select Index Economies and EU Member States versus Estimated Score Reduction, EU Member States (Current Scores Are in Blue; Estimated Reduced Scores Are in Red)



As Figure 1 shows, the adoption of the Commission’s proposals as currently drafted would result in a reduction of 16.25% for all EU member states for these two indicators from 75% of the maximum available Index score to 58.75%. Compared with other Index economies, it would result in the national IP environment in all 10 EU

member states for these two indicators becoming weaker than that in the United States, Singapore, Switzerland, the United Kingdom, and Japan. Currently, all EU member states’ scores are tied with or are higher than all these comparator economies with the sole exception of the United States.

Similarly, Figure 2 shows that broadening this analysis would result in a negative impact and reduction on all EU member states' scores. Currently, the average score for all 10 EU member states for these indicators is 82.50%; this score

ranks higher than that for both Japan and the United Kingdom. Under the Commission's proposals, this would drop to 73.13%, and all EU member states would rank in the bottom below other comparator economies.

Relationship Between IP Rights and Biopharmaceutical Innovation and R&D

Developing new medicines is a long-term, high-risk, resource-intensive process. The fixed costs in terms of laboratory, research facilities, and researchers are high. Compared to many other high-tech industries—for example, computer software—developing the next ground-breaking treatment for cancer or Alzheimer's disease requires more than just a laptop and a great idea. As medicines become more targeted and technically sophisticated, the cost of development rises dramatically. In 1979, the total cost of developing and approving a new drug stood at \$138 million. Almost 25 years later, in 2003, this figure was estimated at \$802 million.¹³ A 2012 estimate points to the total cost of drug development being approximately \$1.5 billion.¹⁴ Tufts University research from 2016 suggests that it costs \$2.6 billion, on average, to develop a new drug.¹⁵ International experience and the basic economics of the biopharmaceutical industry show how critical IP rights are to incentivize and support this R&D of new medical technologies and products.¹⁶ In particular, patents and other forms of exclusivity for biopharmaceuticals, such as RDP and special exclusivity incentives for the protection and production of orphan drugs, enable research-based companies to invest vast sums in R&D and in the discovery of new drugs, products, and therapies. On average, only one to two of every 10,000 synthesized, examined, and screened

compounds in basic research will pass through all stages of R&D and go on to become a marketable drug. IP rights provide a limited-term market exclusivity that gives firms sufficient time to recoup R&D investments made ahead of competition from additional market entrants who bore none of the costs of early-stage investment, R&D, and product commercialization. Many drugs and therapies may not have been discovered without the legal rights provided to innovators through IP laws.

Indeed, the available evidence on clinical research and rates of innovative clinical trials bear this out. Clinical trials represent one of the most important activities conducted by biopharmaceutical companies in different countries. Clinical research is a cornerstone of the drug development process. Conducting clinical trials is part of an extensive process for determining which compounds out of hundreds under investigation may be further developed and eventually brought to market and in what manner. The main purpose of clinical trials is to test and provide proof of the safety, quality, and efficacy of new drugs or new uses, forms, or dosages of existing drugs. Clinical trials are conducted within a highly controlled and studied environment where all aspects of a drug candidate are monitored, recorded, and subjected to high levels of scrutiny and evaluation. The clinical

research process includes complying with a wide range of regulations that govern international best practices related to the quality, safety, and efficacy of drugs, for instance, Good Laboratory Practice guidelines on conducting toxicity studies, Good Manufacturing Practice, and protecting the rights of patients through Good Clinical Practice.¹⁷ Without clinical trials, it would be exceedingly difficult to test the safety, quality, and efficacy of a proposed new medical technology. Although the nature of clinical research has changed over the past few decades with new development technologies emerging, clinical research is still a cornerstone of modern medical development. Clinical trials also provide patients with early access to innovative drugs, which may revolutionize existing treatments available domestically for prevalent diseases.¹⁸ In fact, clinical trials enable advance access to treatments that may continue beyond the duration of the clinical trial.¹⁹ In this sense, the availability of a trial in a host country can be the difference between a patient gaining access to a given novel treatment in research and waiting years until the product has been fully developed and globally launched. For patients with rare and/or terminal diseases, the availability of local trials can be a matter of life or death. Clinical trials also help local physicians participate in cutting-edge research and become members of a multicenter research network. Such experience helps build R&D expertise, experience, and prestige and expands the ability of local researchers to publish their research and become key opinion leaders in their field. They often involve improvements to infrastructure—hospitals, clinics, and health technologies—in local communities.²⁰ Participation in multinational, cutting-edge research helps ensure that clinical trials and sites meet international standards of Good Clinical Practice and exposes clinicians to new techniques and treatment strategies. Thus, the growth and conduct of clinical trials improve the overall medical research infrastructure and experience

in a country or region. Finally, clinical research can have significant positive direct and indirect macroeconomic benefits because they represent the largest portion of biopharmaceutical R&D spending. In 2019, Deloitte estimated global life sciences R&D spending to be around \$177 billion. A substantial proportion of this expenditure comes from members of the Pharmaceutical Research and Manufacturers of America trade association. The association's annual 2020 membership survey estimated that R&D expenditure by member companies totaled more than \$83 billion.

The level and complexity of clinical research and the number of active clinical trials are a good proxy for levels of biopharmaceutical innovation and R&D capacity. This is true for the most complex and cutting-edge biopharmaceutical innovations represented by early-phase trials (phases I and II), trials involving large-molecule biologics, and novel biotechnologies. The presence of high levels of per capita early-phase trials suggests cutting-edge, innovative research is taking place because these trials represent initial human testing of drug candidates' safety and efficacy and therefore require controlled environments and high-quality human resources and infrastructure. Similarly, biologic and biotechnology-based medicines and technologies are increasingly used in the treatment of some of the most complex medical conditions today and in cutting-edge medical research. For example, most COVID-19 vaccines and therapeutics are based on new, complex biotech research. Both the Moderna and Pfizer-BioNTech vaccines are based on novel mRNA biotechnology. Unlike traditional vaccines that inject a weakened or inactive pathogen, mRNA technology contains instructions on how our bodies should make a specific protein that elicits the desired immune system response.²¹ Although scientists and biopharmaceutical researchers have studied mRNA technologies for decades, the COVID-19 vaccines are the first vaccines that have been

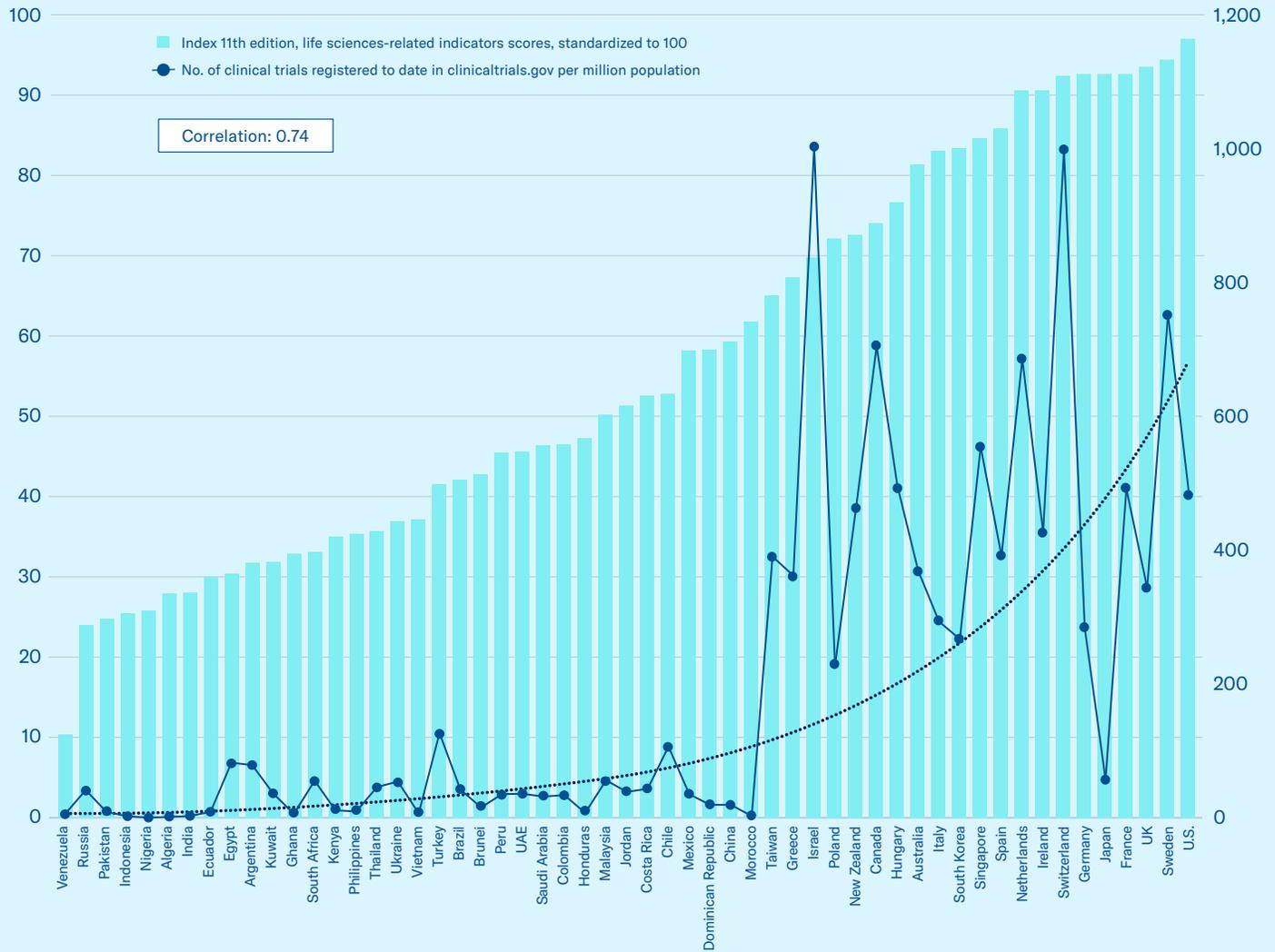
approved and used with this technology. Given a biologic's size, complexity, and inherent instability, the R&D process requires a level of stability and technical capacity. Testing of a biologic drug candidate's safety and efficacy within a clinical trial requires a highly controlled environment in which transportation and storage of the drug are controlled, the trial protocols are strictly adhered to, and patients are monitored carefully.

Regarding biopharmaceutical R&D and IP incentives, a strong and direct relationship exists between levels of clinical research and IP protection. Economies with higher levels of biopharmaceutical IP protection that do not exist in the patenting of biopharmaceutical innovation and that provide RDP and full patent term restoration tend to have higher levels of biopharmaceutical innovation as represented by clinical research. This year's Statistical Annex includes four relevant correlations related to biopharmaceutical innovation:

1. Clinical trials
2. Early-phase clinical research
3. Development of biologic therapies
4. Biotechnological innovation

These correlations measure the relationship between IP rights specific to the biopharmaceutical sector and rates of the described indicators for biopharmaceutical innovation and R&D for the 55 economies included in the Index. Overall, the results are clear—a strong correlation exists between the availability of biopharmaceutical IP rights and levels of biopharmaceutical innovation as measured through levels of clinical research and by Scientific American's WorldView Scorecard. All correlations achieved a score between 0.74 and 0.81, which suggests a strong relationship between the availability of relevant biopharmaceutical IP rights and the biopharmaceutical innovation variables measured.

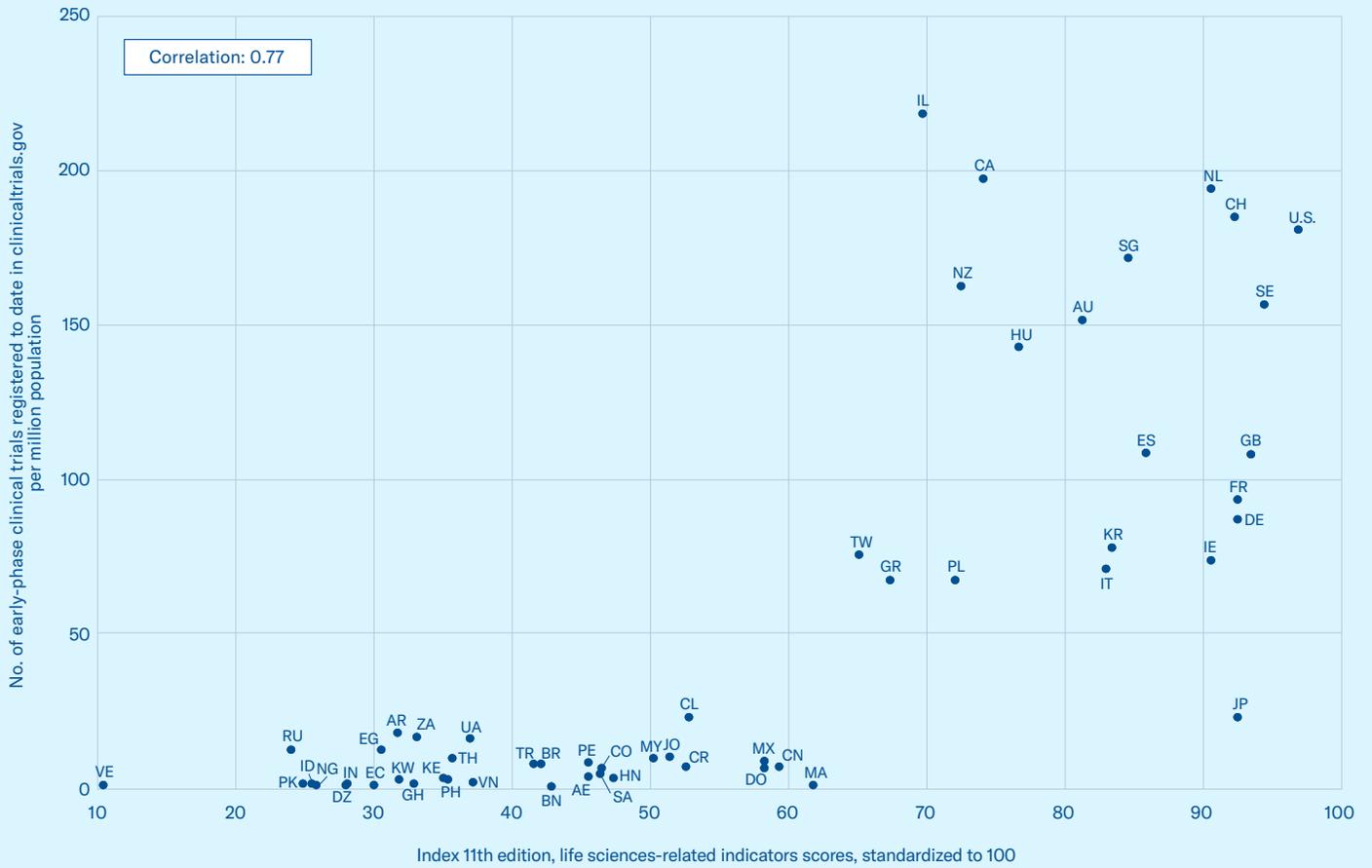
Figure 3. Association Between the Index Life Sciences–Related Indicator Scores and Clinical Trial Activity



The availability (or lack) of IP rights acts as a powerful incentive for attracting clinical research, which accounts for approximately 60% of biomedical foreign direct investment

in R&D. Economies that score 50% or more on the Index’s life sciences–related indicator host more than 10 times the number of clinical trials than do low-scoring economies.

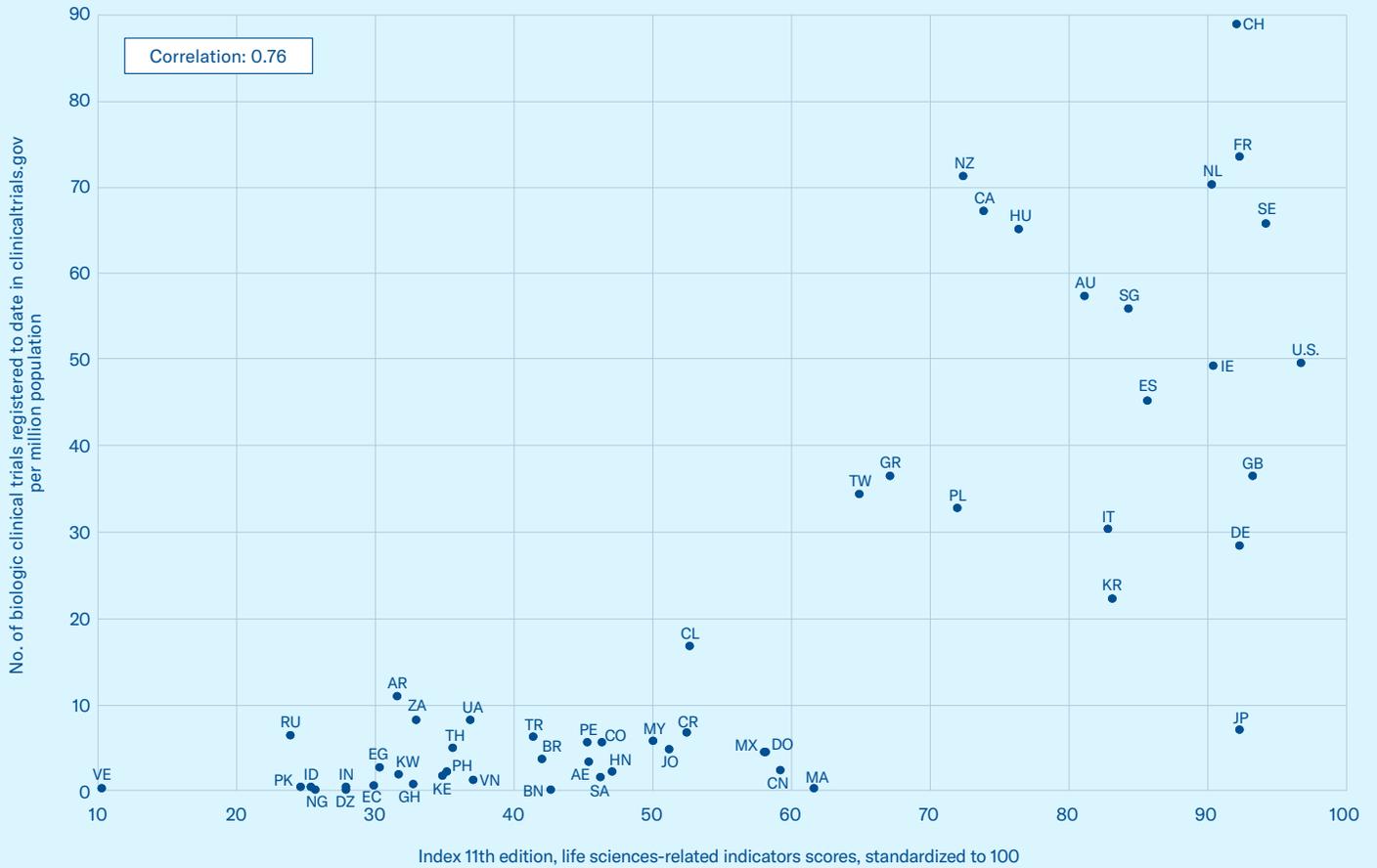
Figure 4. Association Between the Index Life Sciences–Related Indicator Scores and Early-Phase Clinical Trial Activity



Economies that maintain robust IP environments tend to see more than 17 times the number of early-phase clinical trials on average

compared with economies whose life sciences–related IP environments trail behind.

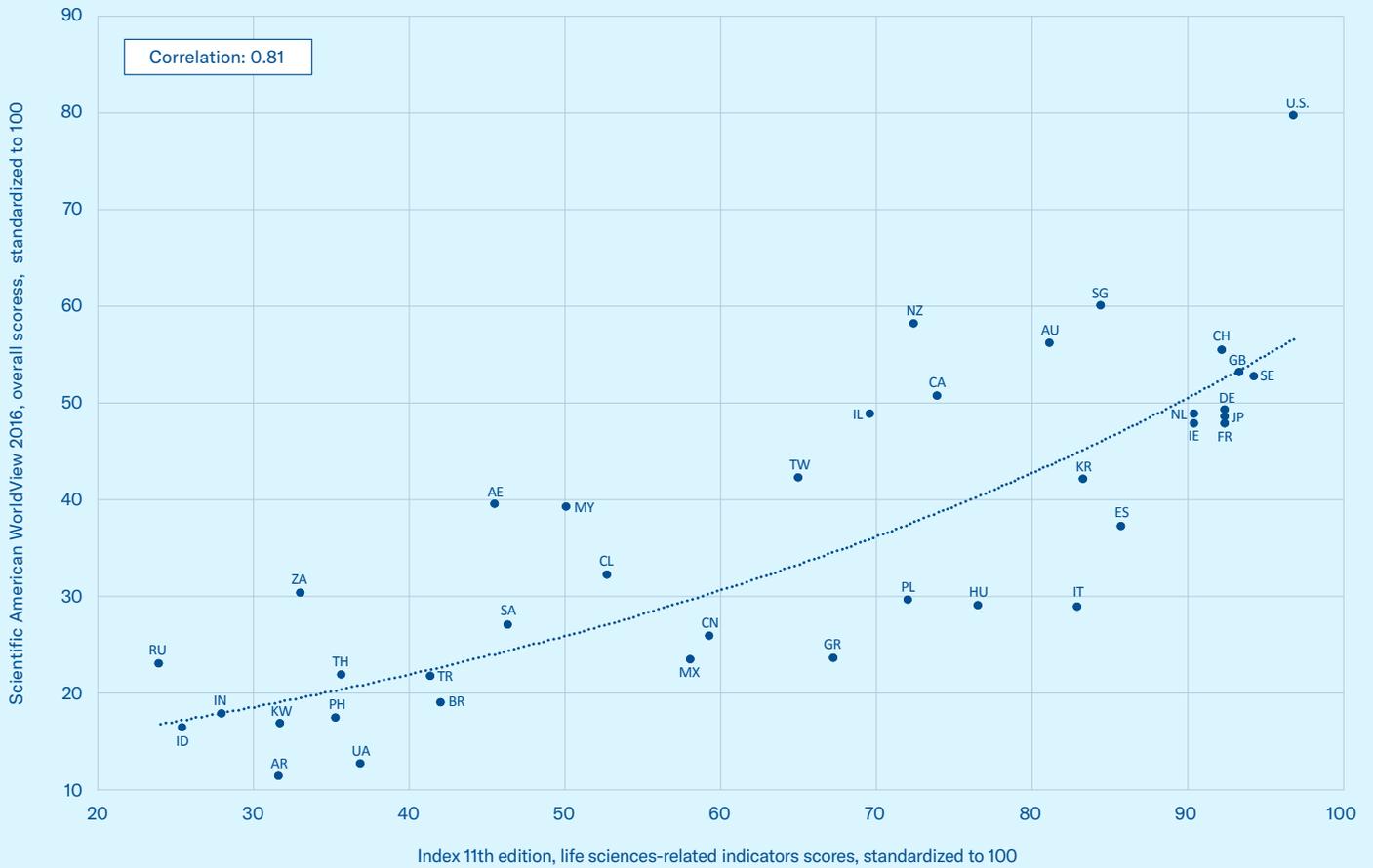
Figure 5. Association Between the Index Life Sciences–Related Indicator Scores and Biological Clinical Research Intensity



Clinical trials in biologics have a similar story. Economies with strong to robust IP frameworks for life sciences host more than 11 times the number of

clinical trials in innovative biologic drugs compared with economies that have a weaker environment.

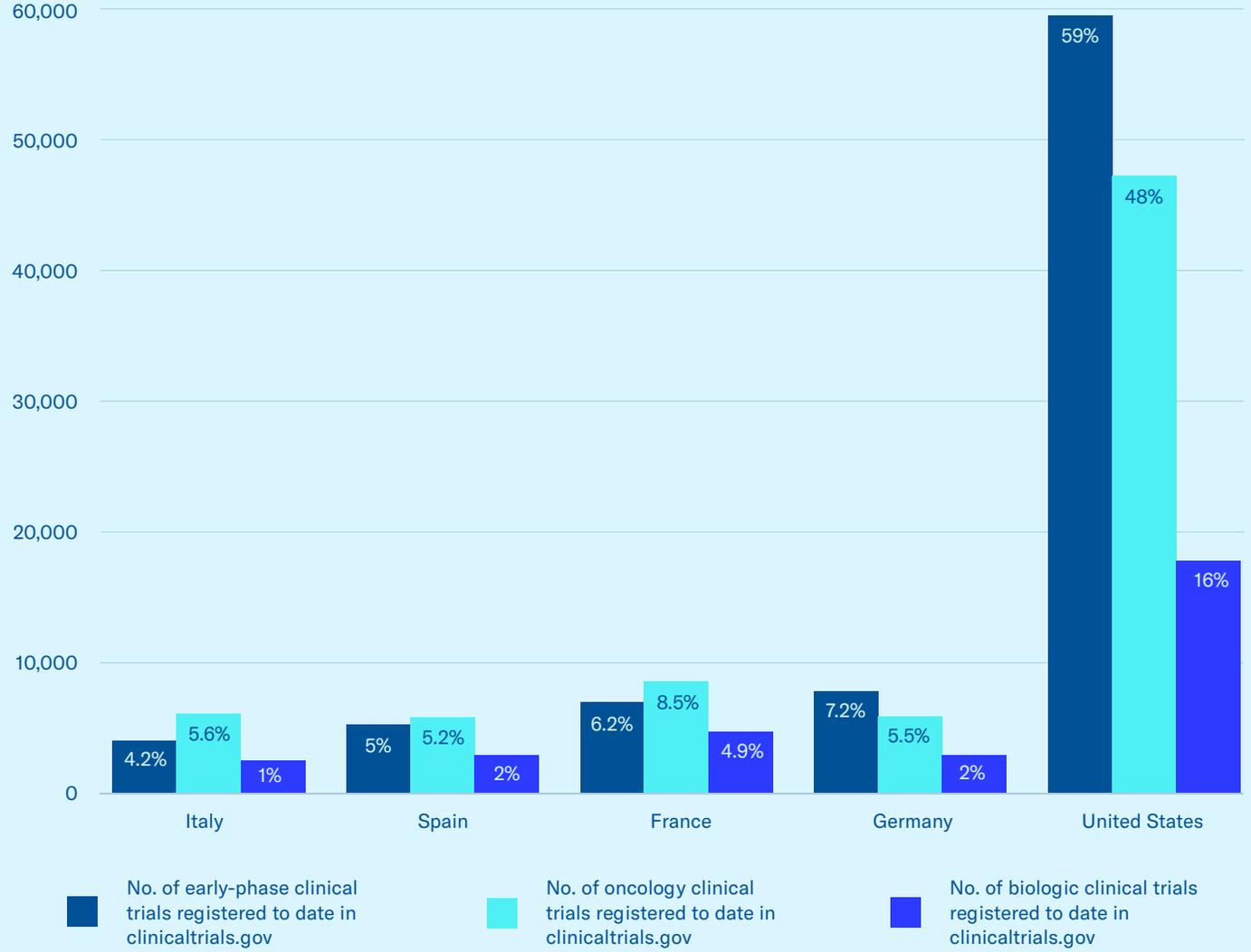
Figure 6. Association Between the Index Life Sciences–Related Indicator Scores and the Scientific American WorldView Scores



Protecting IP rights related to the life sciences (such as patents, regulatory data protection, and patent term restoration) has a clear and direct correlation with an environment in which biotechnology innovation can thrive. Economies that score 50% or more on the Index are more than twice as likely to provide environments that are conducive to biotech innovation, as measured by Scientific American, than economies with weaker national IP environments.

Many EU member states have significantly lower levels of clinical research and biopharmaceutical R&D compared with major R&D centers such as the United States. For example, as Figure 7 shows, compared to the United States, rates of clinical research in early-phase research, cancer, and biologics for the largest EU member states are far behind. This is before the EU weakens its IP rights and incentives through the Commission’s proposals.

Figure 7. Number of Early-Phase, Cancer-Related, and Biologics-Related Clinical Trials Registered to Date in clinicaltrials.gov, United States and Select EU Member States



Conclusion

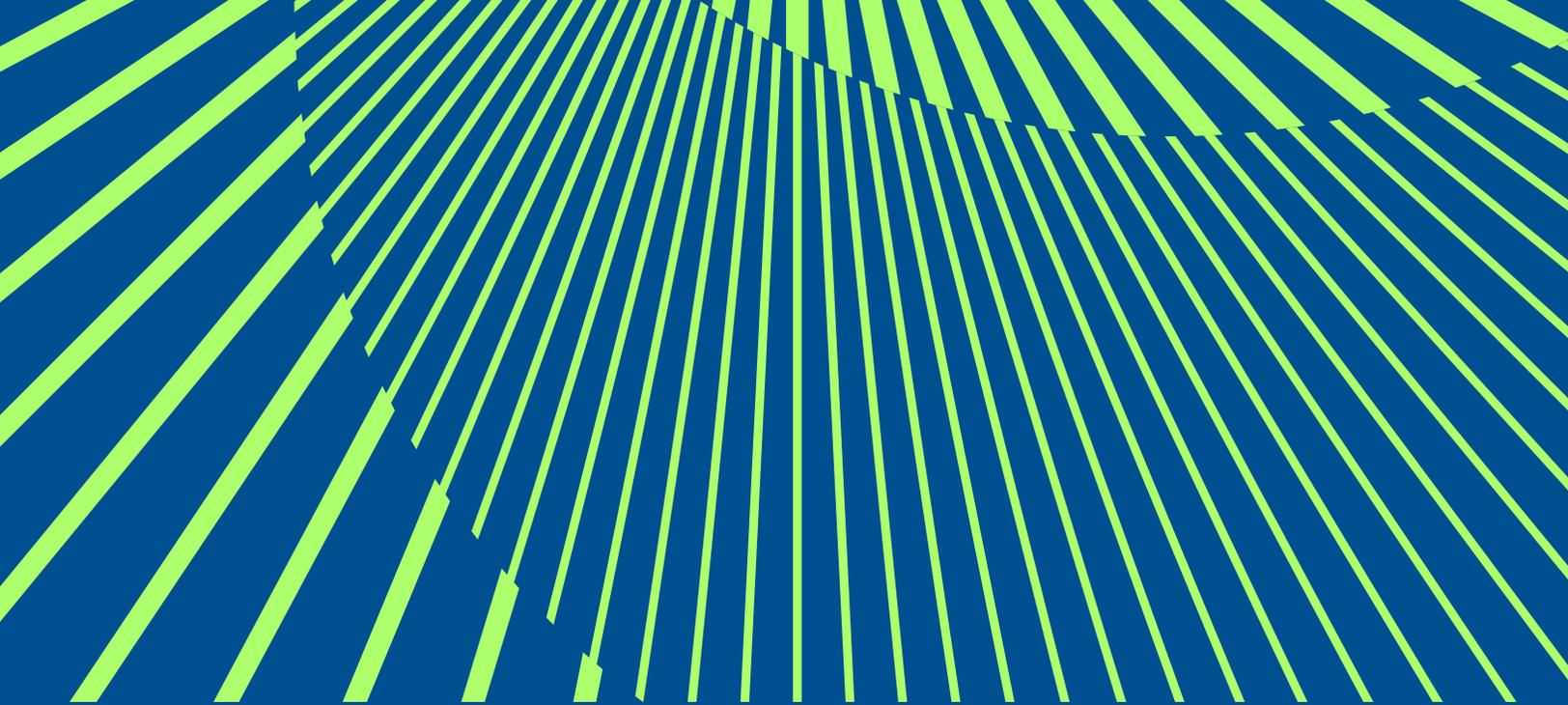
Although the General Pharmaceutical Legislation aims to create a 21st-century life sciences landscape that fosters innovation and enhances patient access, the proposed legislation will fundamentally weaken the ecosystem for biopharmaceutical innovation. Over time, such action will simply hollow out the national IP environment and framework for future biopharmaceutical innovation. With fewer resources, it stands to reason that

biopharmaceutical manufacturers will have less to invest in R&D and will be less likely to develop new biopharmaceutical products and services at the same rate as in the past. The negative effect will be felt most in the EU, which will continue to see rates of biopharmaceutical R&D and clinical research drop. Before the Commission moves forward with its reform efforts, it should pause and consider the full ramifications of its proposed policies.

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