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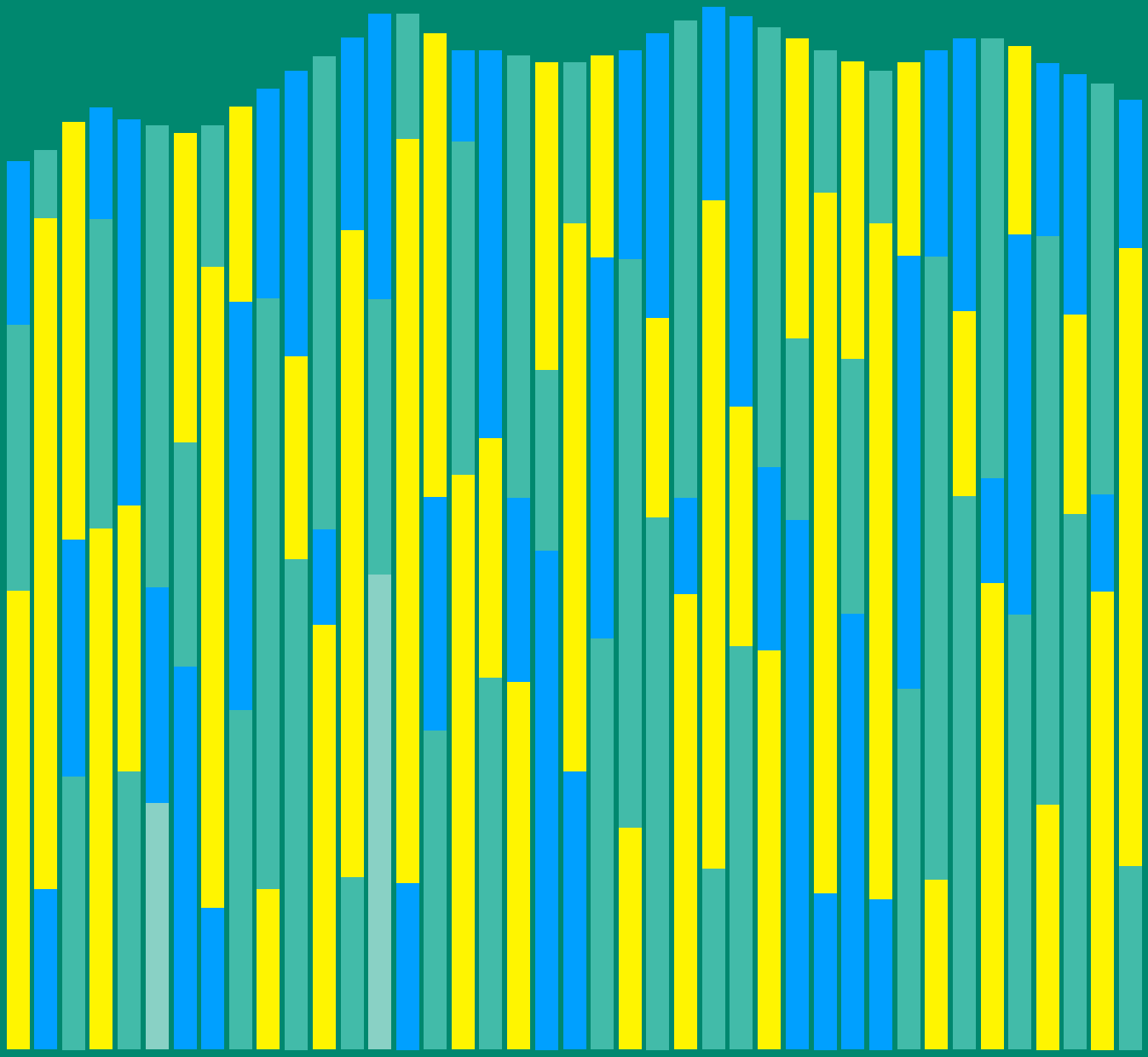


2023 Global Biopharma Resilience Index

How has the biopharma industry evolved over the past two years — and where should it look to improve?

Contents

SECTION 1

Intro

While the immediate shock of the COVID-19 crisis has faded, the spotlight on the global biopharma industry has not. There are many exciting areas where recent progress has the potential to transform lives — and the heightened threat of new pandemics and antimicrobial resistance means we may soon be looking to biopharma to save us again.

The rapid deployment of mRNA vaccines in response to COVID-19 catalyzed a new era in vaccinology and reignited interest in nucleic acid therapies. AI-enabled research is accelerating therapeutic development, with the opportunity to radically improve patient outcomes. Breakthroughs in cell and gene therapies (CGTs) have the potential to prevent, treat, and even cure genetic diseases.

Despite these breakthroughs and opportunities, however, sustained high growth is not a certainty for the industry. The emergency funding boost of 2020 and 2021 has fallen away, with financing for small and mid-size biotech firms in novel therapeutics pulling back in 2022[1]. The funding landscape remains challenging in 2023: cost of capital, economic insecurity, talent shortages, regulatory challenges, and disruption all continue to affect the sector. Furthermore, our latest research shows that the pandemic accelerated progress in aspects of the industry where biopharma firms have direct control (such as manufacturing), but ensuring collaboration between government, academia, and the industry remains challenging. The knock-on effect may jeopardize long-term improvement in patient outcomes.

1 Ramko R and Singhania A. Financing For Emerging Biotechs: Recent Trends & Predictions For 2023. Bioprocess Online. https://www.bioprocessonline.com/doc/financing-for-emerging-biotechs-recent-trends-predictions-for-0001 March 6, 2023

To assess the strength of the global industry in these turbulent times, Cytiva created the Global Biopharma Resilience Index. Introduced in 2021, the index scores and ranks countries on five factors:

- **Supply chain resilience**
- **Talent pool**
- **R&D ecosystem**
- **Manufacturing agility**
- **Government policy and regulation**

The 2023 index is based on data from a survey of 1250 pharma and biopharma executives across 22 countries. Countries are scored on a scale of 0 to 10, where 0 reflects the worst performance and 10 denotes best practice. (For more information on the methodology, please see page 38.) The overall index score for each country indicates the strength of its biopharma industry.

In addition to survey responses, this year Cytiva has incorporated additional data into the index — R&D activity and drug-approval timeframes, for example — to provide a more in-depth and accurate overview of the industry.

SECTION 2

Expert interviews

In addition to the survey, we also hosted in-depth interviews with 10 leading biopharma experts. We would like to thank the following individuals for participating:

Ian Alexander
Professor
Sydney Children's Hospitals Network and the University of Sydney

Aaron Cowley
Chief Scientific Officer
Arranta Bio

Killian O'Driscoll
Chief Commercial Officer
National Institute for Bioprocessing Research and Training (NIBRT)

Adrian Hill
Director
The Jenner Institute

Jerome Kim
Director General
International Vaccine Institute

Kyu-sung Lee
Global Head of Technical Operations and Manufacturing
BeiGene

Leszek Lisowski
Associate Professor
University of Sydney Children's Medical Research Institute

Aurélia Nguyen
Chief Program Strategy Officer
Gavi

Dave Tudor
Managing Director, Medicines Manufacturing Innovation Centre, Biologics and Quality
CPI

Wenjie Zhang
Chairman
Henlius

SECTION 3

Global outlook

Thirty years ago, this industry was brand new. A remarkable number of biologic products are on the market today.

And we're now at another inflection point, where cell therapies, gene therapies, RNA therapies, and other new technologies are treating diseases that were previously untreatable.

There are many new therapeutic modalities driven by excellent science, and from a clinical perspective, there's a huge amount of excitement about what's coming through the pipeline. But there are many challenges, too.

Killian O'Driscoll
Chief Commercial Officer
NIBRT

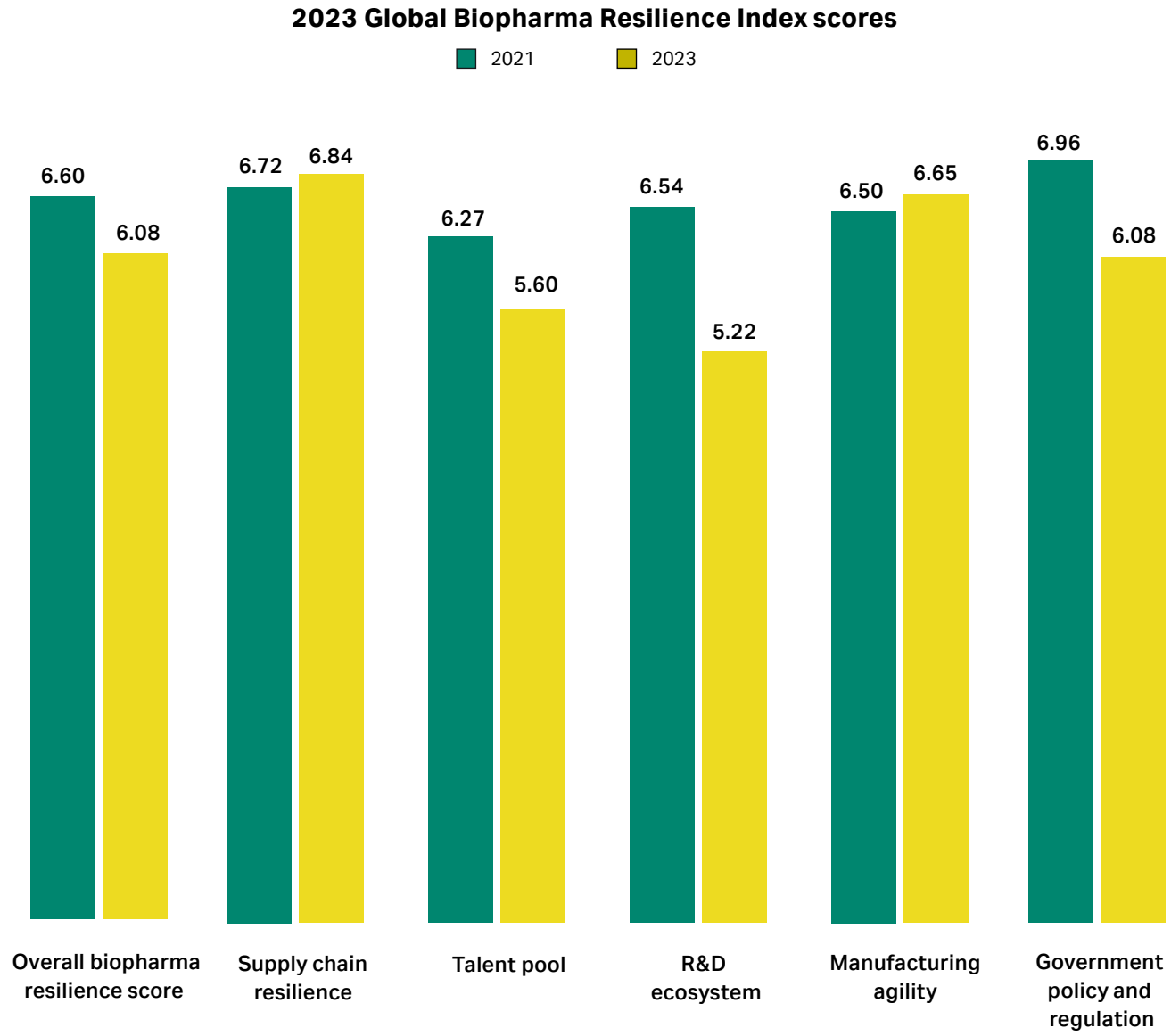


Fig 1. Overall, global biopharma resilience has weakened since 2021.

The overall 2023 Global Biopharma Resilience Index score is 6.08, which is lower than the 2021 score of 6.60. This decrease could be a result of the more granular methodology, which uses a broader data set, including publicly available data on biopharma trends, and offers a more extensive overview of the industry. Regardless, this finding points to specific areas of concern that the industry must address.

Performance across three of the five pillars — talent pool, R&D ecosystem, and government policy and regulation — has weakened. The pillar that has suffered most over the past two years is the R&D ecosystem, which fell from 6.54 in 2021 to 5.22 in 2023. The drop in the talent pool score may also reflect a swing back from the high talent mobility of the "Great Resignation" at the height of the COVID-19 pandemic, leading to a squeezed labor market and talent shortages in 2023.

The two pillars that have improved since 2021 are supply chain resilience and manufacturing agility. This shift may reflect the industry's need to strengthen these areas urgently during the pandemic, while deprioritizing other pillars. We may also be seeing the consequences of short-term fixes to temporarily boost progress in some areas without establishing longer-term resilience.

Table 1. Country rankings for the 2023 Global Biopharma Resilience Index

Country	Resilience score 2023	Resilience score 2021	Ranking change*
Switzerland	6.98	7.08	1
US	6.96	7.12	-1
UK	6.78	7.01	Same
Sweden	6.58	-	New country
Singapore	6.41	6.63	7
Germany	6.33	6.76	Unchanged
Canada	6.32	-	New country
Ireland	6.25	-	New country
France	6.18	6.71	2
Spain	6.18	6.77	-5
Japan	6.06	6.75	-3
South Korea	6.05	6.76	-5
Australia	6.02	6.73	-3
Italy	5.99	6.61	-1
Mexico	5.42	-	New country
South Africa	5.37	5.95	-1
Thailand	5.36	5.93	-1
Saudi Arabia	5.20	6.19	-6
UAE	5.17	-	New country

*If applicable

Of the 22 countries included in the index, Switzerland came out on top with a resilience score of 6.98. While lower than its 2021 score of 7.08, the country's overall position indicates strong industry performance.

This result is influenced by Switzerland's top-ranking education system, along with strong R&D tax incentives that reward companies investing in the pharma, biotechnology, and medtech industries[2].

The Swiss biopharma industry's strong performance allowed it to displace the US in the top spot, pushing the latter into second place, with a score of 6.96. The UK remains in third place, with a score of 6.78. All of the top three countries have seen a drop in resilience since 2021, a trend reflected across the index, which we'll explore in the following chapter.

2 Switzerland: R&D tax incentives for the pharmaceutical, biotechnology and medtech sectors. KPMG. https://kpmg.com/us/en/home/insights/2022/05/tnf-switzerland-tax-incentives-pharmaceuticual-biotech-medtech-sectors.html May 19, 2023

Ranking towards the bottom were Thailand (5.36), Saudi Arabia (5.20) and the UAE (5.17). While these countries have made strides in domestic biopharma manufacturing, they remain heavily import-dependent; both Saudi Arabia and the UAE import around 80% of their pharma products[3,4].

Overall, the data reveals a marked gap between the performance of the biopharma industry in countries with low gross national income (GNI) per capita and that in those with a higher GNI per capita. As Figure 3 shows, countries that the World Bank classifies as "high-income" are more likely to have a higher index score (China and India are outliers in this respect, scoring higher than expected given their GNI per capita).

3 Saudi Arabia Pharmaceutical Market Snapshot (2022 to 2032). Future Market Insights. https://www.futuremarketinsights.com/reports/saudi-arabia-pharmaceutical-market#:~:text=Saudi%20Arabia%20Pharmaceutical%20Market%20Snapshot%20(2022%20to%202032)&text=Saudi%20Arabia%20imports%2080%25%20of,dominated%20by%20many%20global%20corporations. October 2022.

4 Nagraj, A. UAE pharmaceutical market to be valued at $4.7bn by 2025 as it boosts local manufacturing. The National UK. February 23, 2022

2023 Biopharma Resilience Index: Regional scores overall

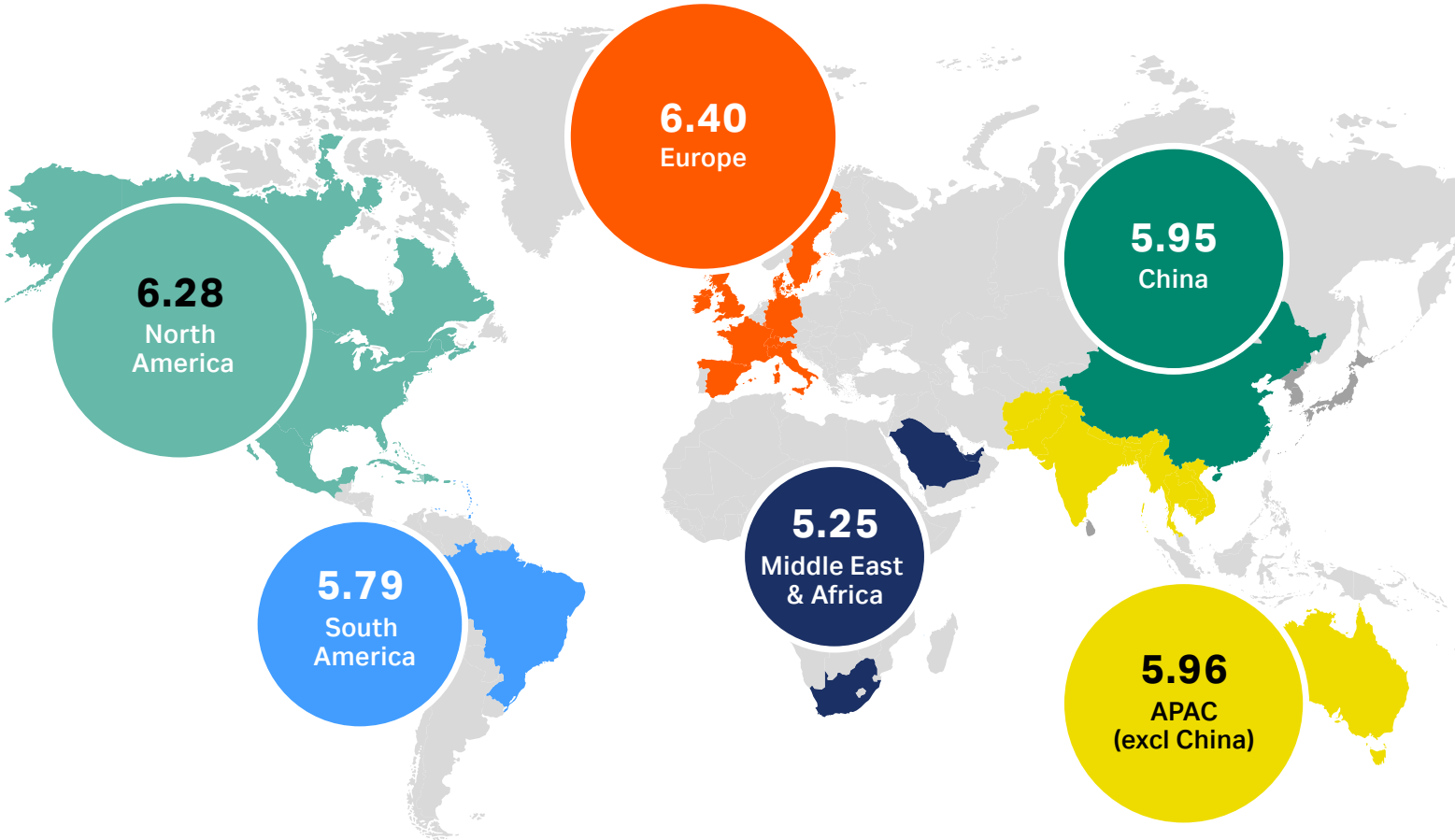


Fig 2. Across all regions, Europe has the highest biopharma resilience score.

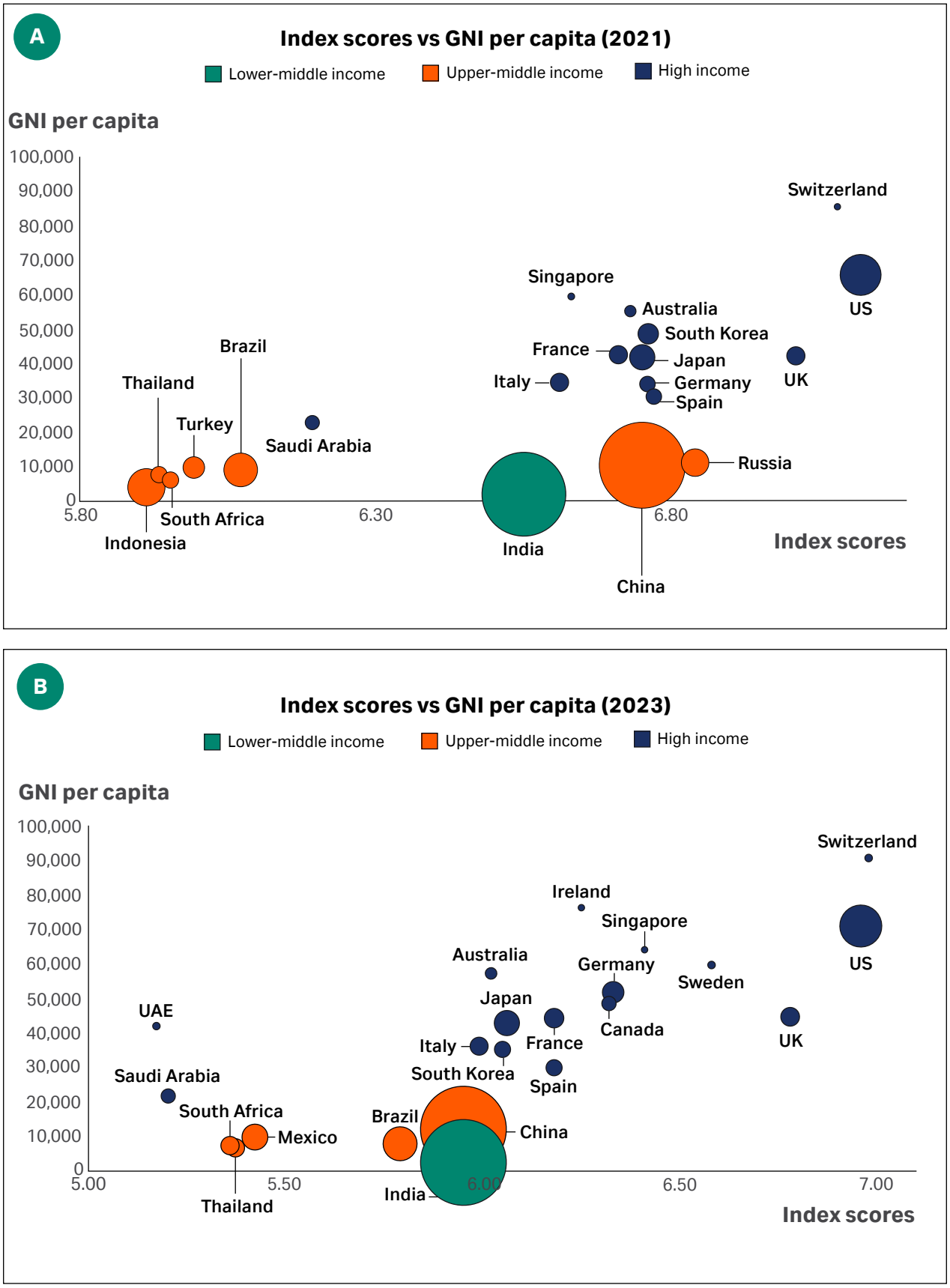
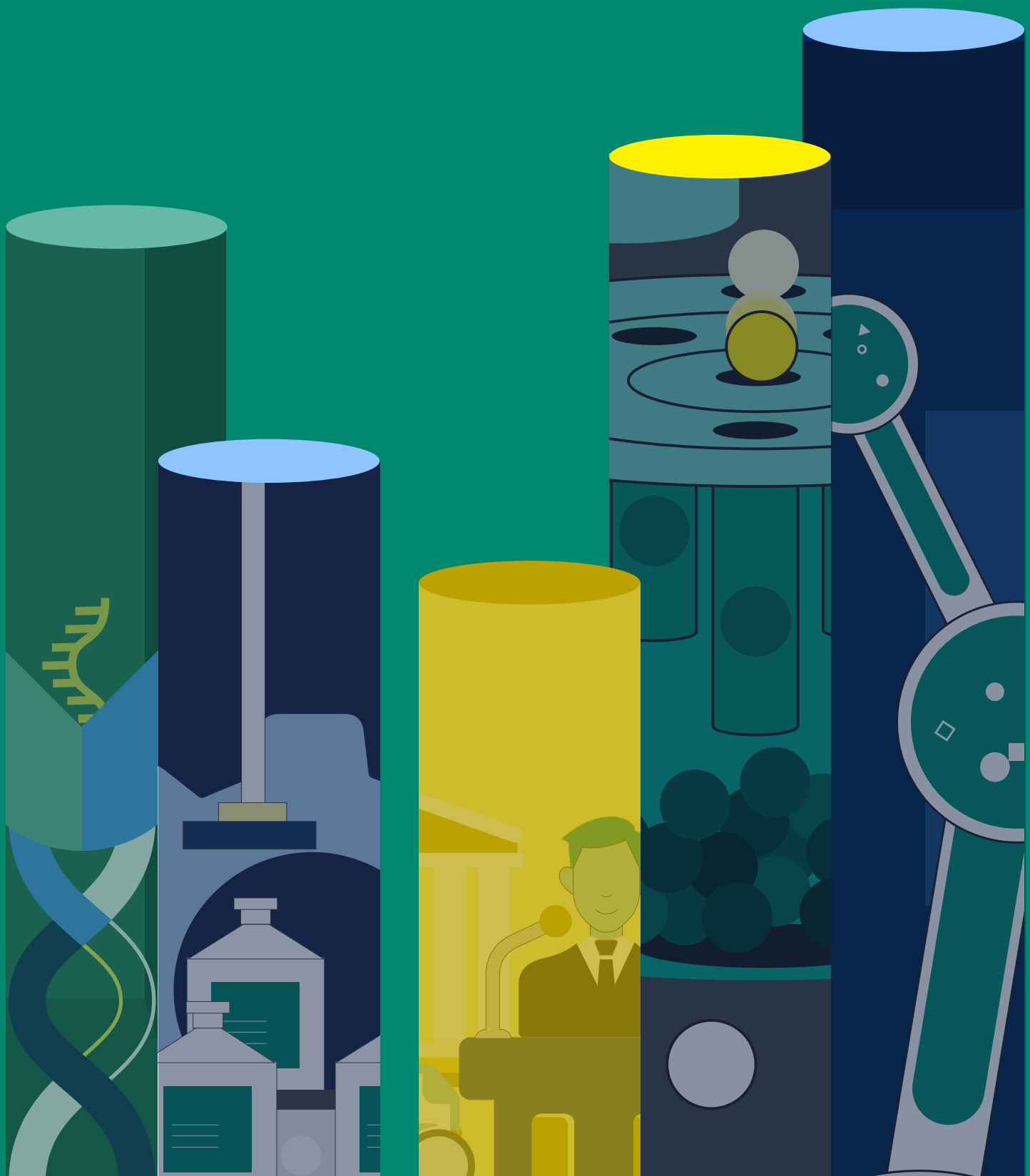


Fig 3. In both 2021 (A) and 2023 (B), the research reveals a strong correlation between biopharma performance and level of economic development.

SECTION 4

The five pillars of resilience



PILLAR 1

Supply chain resilience

If you want to support one cGMP facility for the whole year, you need a massive GMP-compliant warehouse with storage at different conditions, temperatures, and humidities.

It is a logistical nightmare. Running out of even a single component of manufacturing can break the whole chain. Sometimes, it's as simple as a delivery that depends on shipping from the US or Europe.

And, if it's a biologic, then it triggers all the different import requirements, and sometimes the things you don't even think about are the ones that break the whole process.

Leszek Lisowski
Associate Professor
University of Sydney Children's Medical Research Institute

The supply chain pillar measures the extent to which each country has reliable access to the medical products required by its domestic population, including vaccines, therapeutics for chronic conditions, and personalized medicines such as CGTs. The score indicates whether a country is considered at risk of shortages due to over-reliance on imported active pharma ingredients, drug-production equipment, or finished pharma products.

Our research indicates that overall supply chain resilience grew slightly from 6.72 in 2021 to 6.84 in 2023. This increase reflects the benefits of efforts to strengthen the security of global supply.

Despite the overall improvement, just 44% of pharma leaders feel that their supply chains are more robust than they were one year ago.

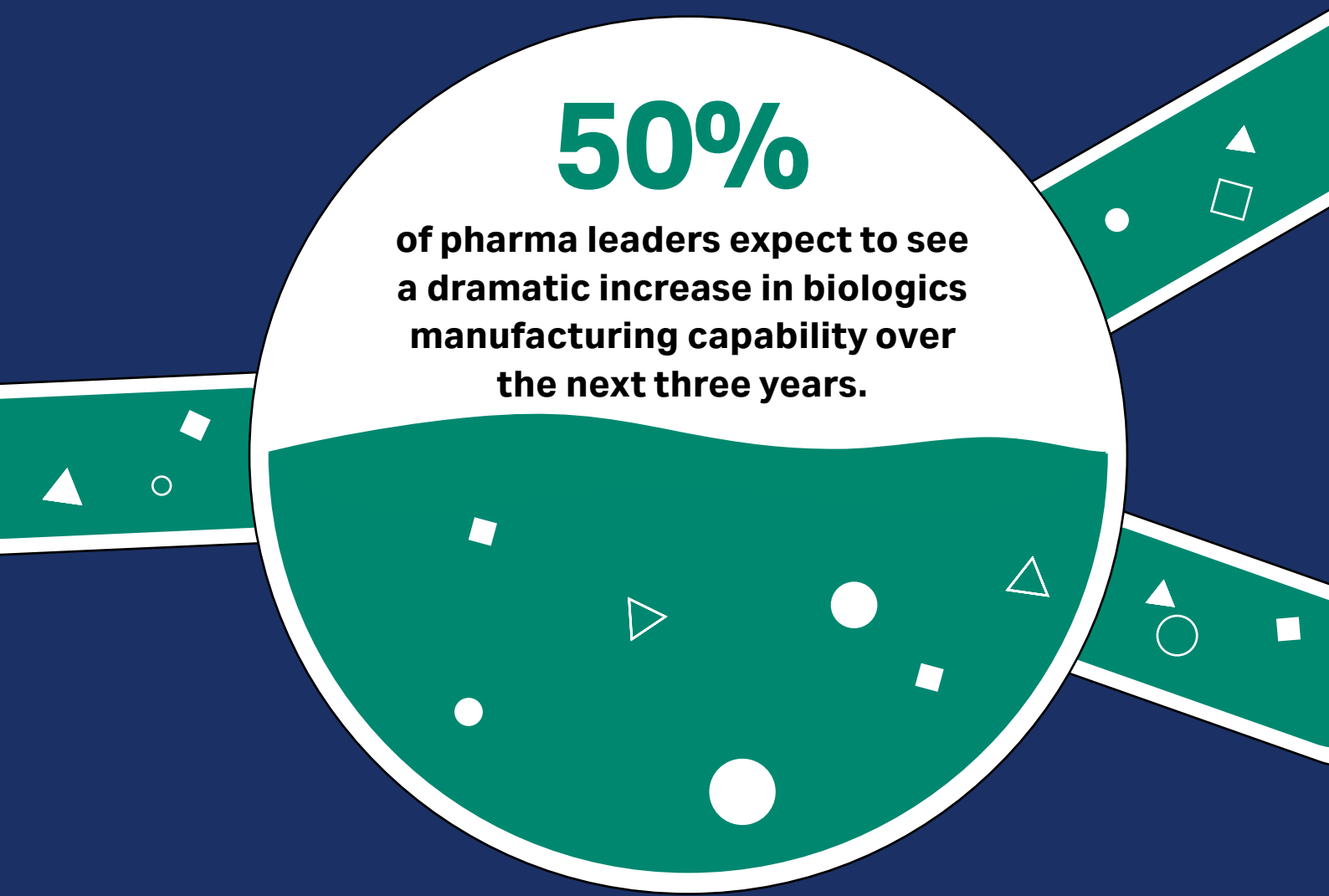
Around half of respondents say their country is moderately to highly dependent on the import of many components of drug production, as well as the import of finished pharma products.

Nearly two in 10 (19%) pharma executives say that increasing supply chain resilience is a domestic priority for the next two years. Companies are setting their attention on nearshore and onshore manufacturing, with many countries trying to establish or strengthen domestic manufacturing operations in order to stabilize supply.

But this narrow measure will not guarantee security of supply. Countries need to take a more comprehensive approach, explains Aurélia Nguyen, Chief Program Strategy Officer for Gavi, the Vaccine Alliance.

"There's a huge number of enabling factors, not least a supportive regulatory and trade environment that helps you pivot quickly between different products, if needed. For example, we saw with COVID-19 that one of the big hurdles we faced was the export ban on vaccines from India," she says.

"We need to ensure we have in place a level of protection for the smooth flow of health products — or, if not, then a reasonably diversified supply chain that can absorb shocks as and when they happen."



Percentage of executives who report a stockout or period of insufficient supply at least once a year, in the following categories

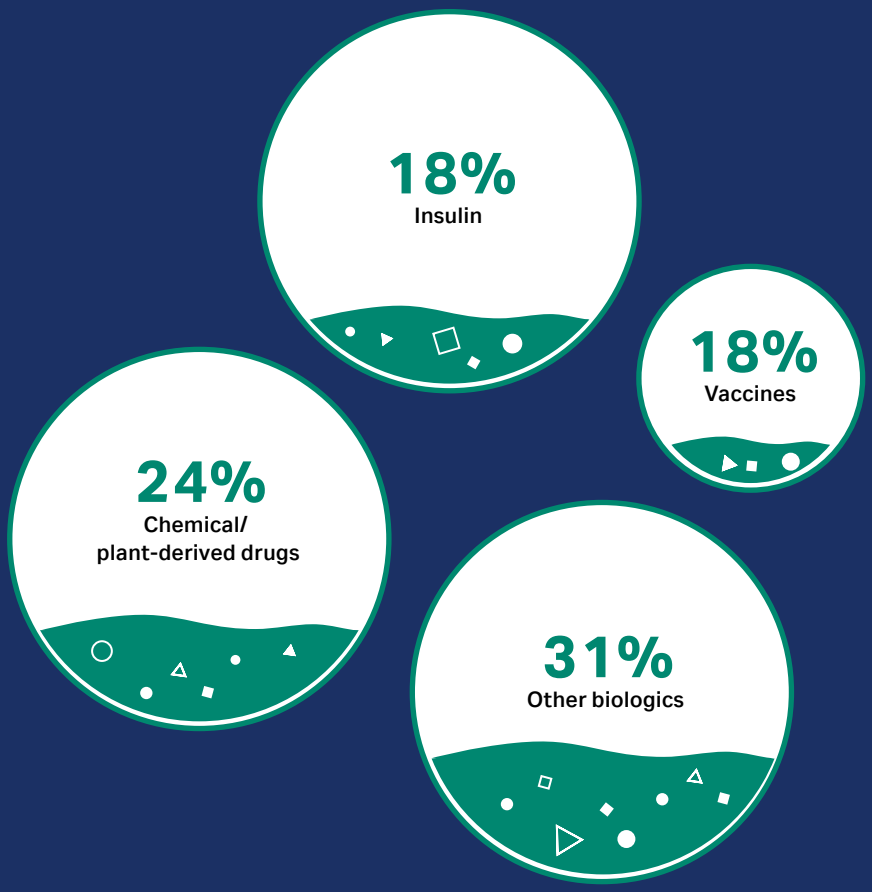
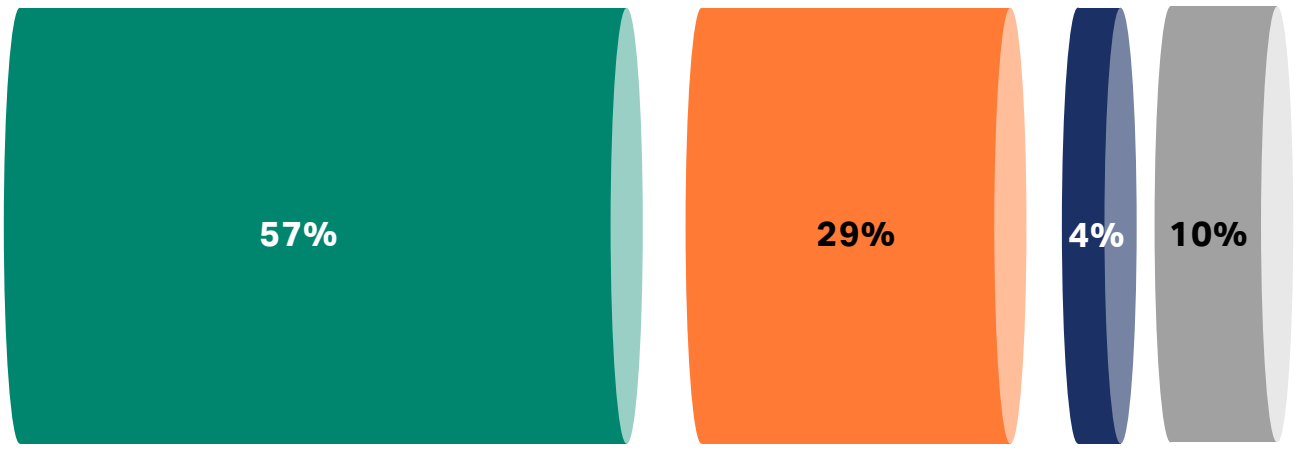


Fig 4. Around three in 10 executives report that their country experiences shortages of biologic drugs at least once a year.

How capable is the supply chain in your country at providing the necessary support for the rollout of personalized medicines and cell and gene therapies?



- Somewhat adapted, we need to look to foreign countries for some of the essentials of delivering these medicines
- Not well adapted, the weakness of supply chains in this area impedes the domestic rollout of these kinds of treatments
- Not at all adapted, we lack the capacity to support the use of these complex treatments
- Extremely adapted, we have access to everything we need domestically

Fig 5. Only one in 10 executives says their country is "extremely adapted" to support the rollout of cell and gene therapies.

Small–molecule medicines, including aspirin and other long–standing, familiar drugs you might find in your home, are easier to commoditize and offshore. Cell and gene therapy products are significantly more complex to manufacture and need to be produced close to the patient. Our research shows that, currently, most countries cannot meet this requirement.

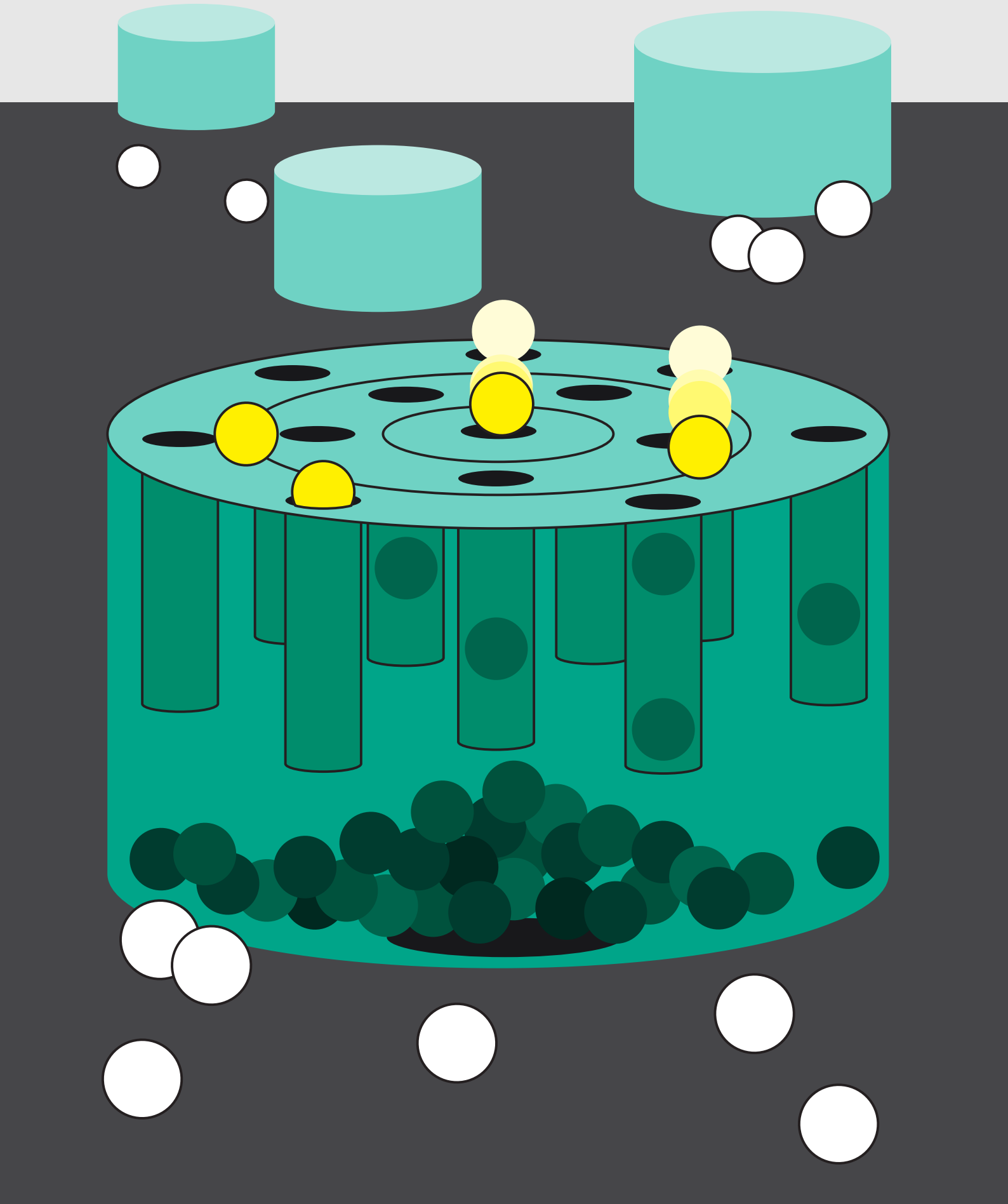
With the global biologics market expected to reach $787 billion by 2028[5], many pharma companies will be forced to reconfigure their supply chains to keep pace. According to Aaron Cowley, Chief Scientific Officer at Arranta Bio, a US-based contract development and manufacturing organization, companies must remember that diversity of suppliers is key to resilience.

"It's important to decentralize supply chains so that you have multiple suppliers spread across the globe," he says. "One of the biggest challenges we've had is that large companies are constantly acquiring smaller companies in the supply chain, which means there are now fewer suppliers and more bigger players that are increasingly controlling the supply chain instead of decentralizing it."

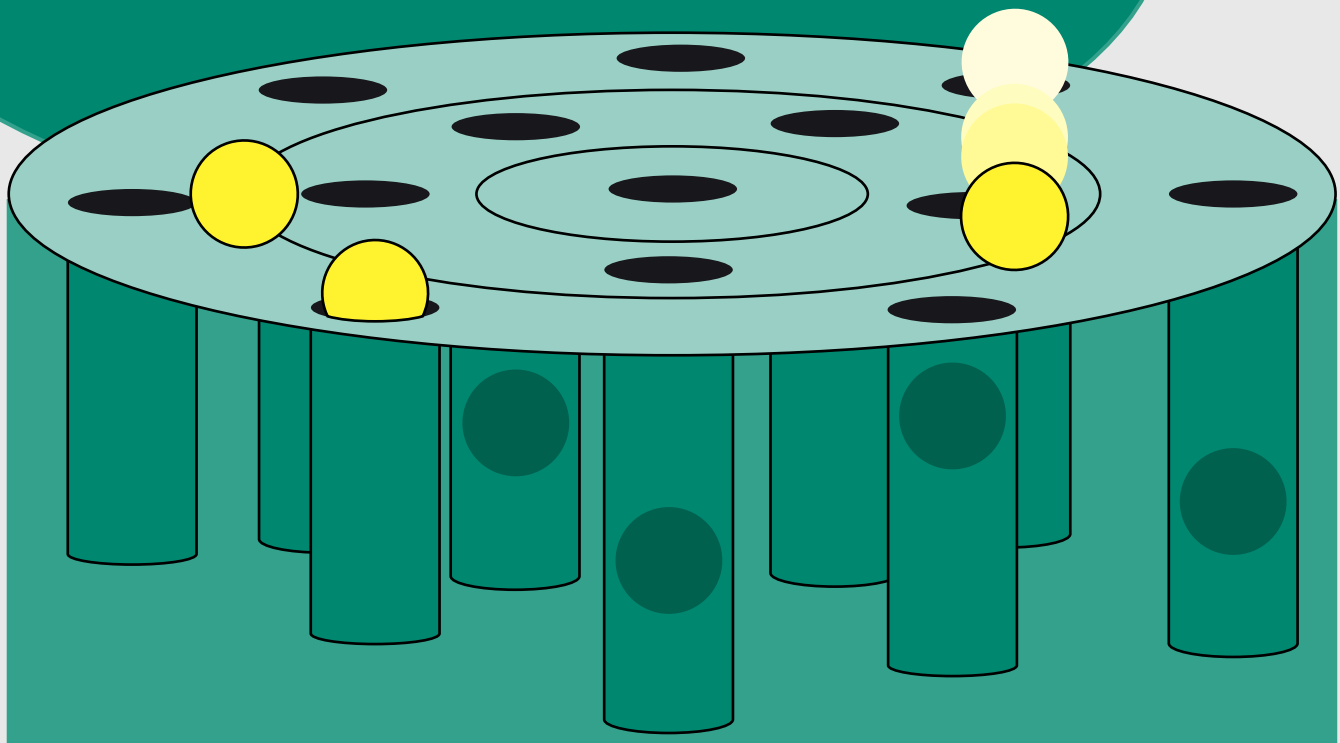
5 Biologics Sales & Consensus Forecast. London, UK: GlobalData; 2023. https://www.globaldata.com/data/. Accessed May 02, 2023.

PILLAR 2

Talent pool



Academia keeps training new people and losing them to commercial, where there's more money, which actually undermines the whole pyramid because most of the developments still come from academia.



We can never compete with the commercial sector when it comes to salaries and career opportunities — and as we keep losing people, that backfires and slows down the overall progress.

Leszek Lisowski
Associate Professor
University of Sydney Children's Medical Research Institute

Our research sought to assess how easily each country can access the talent it needs to grow. This pillar considers how effective academic institutions are at delivering a strong pipeline of biopharma talent, and how effectively labor regulations enable biopharma firms to access talent from overseas.

The 2023 data shows that overall talent pool resilience fell to 5.60 from 6.27 in 2021 — the steepest decline seen across all the pillars (it was also the weakest pillar in 2021). Advances in biotech have created a surge in demand for highly qualified individuals. Many countries' academic institutions have been unable to meet this demand, creating fierce competition for a limited pool of R&D talent in biologics manufacturing.

Almost a quarter of pharma executives report that it is a substantial challenge to find and retain pharma manufacturing talent. This problem is made even worse by the increasing call for AI-modeling skills across biopharma processes, meaning that the required skill sets are much more specific than in the past. The "Great Resignation" ushered in an era of remote work and talent mobility[6], yet the recent transition to hybrid work patterns may see mobility decline, leading to challenges in hiring biopharma expertise in 2023. This shift will force employers to explore new solutions that may oblige them to be more flexible in accepting different working formats and skill sets.

"The growth of the biopharma industry has been exponential, and it's been hard for traditional education providers to keep pace with that," explains Killian O'Driscoll, Chief Commercial Officer at NIBRT, based in Ireland. "The universities and community colleges do a fine job of training people in the core principles of genetic engineering, bioprocessing, chemical engineering, and related areas. But it's a challenge for them to provide the very specific skill sets that you need for biopharma manufacturing."

The talent shortage has highlighted the importance of staff retention, prompting some companies to offer more competitive salaries or opportunities to upskill[7]. However, smaller firms, particularly non-profits, struggle to compete with the money and resources of bigger companies.

6 Klipfel, M. Four Ways To Turn The Great Resignation Into The Great Return. Forbes. https://www.forbes.com/sites/forbeshumanresourcescouncil/2022/08/15/four-ways-to-turn-the-great-resignation-into-the-great-return/ August 15, 2022

7 Talent Trends Shaping the Future of the Pharmaceutical Industry. SRG. https://www.srgtalent.com/blog/future-of-pharma-talent-trends March 20, 2023

Top 3 most difficult skills to attract and retain:

1. Manufacturing talent for GMP-certified or equivalent facilities
2. R&D talent
3. Digital technology talent

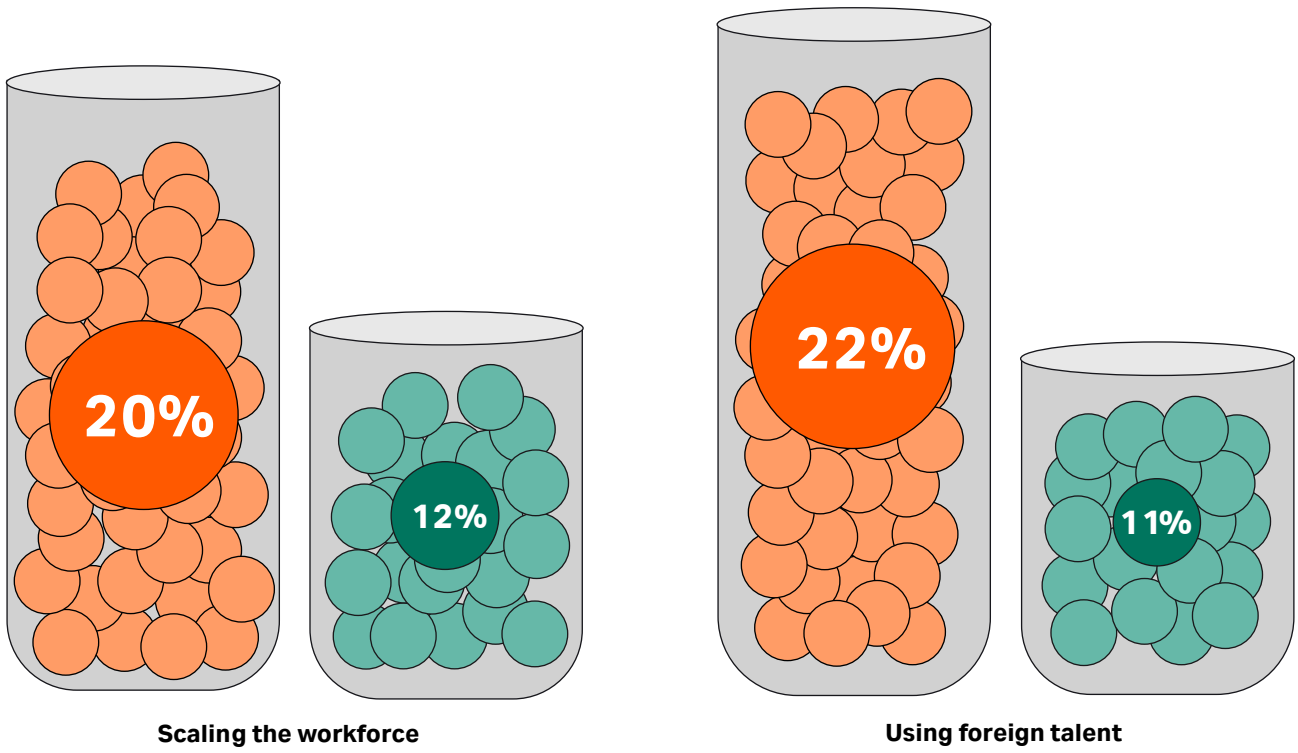


Fig 6. Executives in emerging economies are more likely to describe their country's labor regulations as "rigid" or "very rigid."

Labor regulations can also pose a challenge. Only around two in 10 respondents say that their country's labor regulations around foreign talent and scaling the workforce are "very flexible"; the data shows this problem is more pronounced in emerging economies.

Generating talent requires specialist institutions to train and employ graduates. Around four in 10 executives are either ambivalent or negative about the ability of their country's educational system to deliver on this need.

The UK sets a strong example to follow. Ranking third in the Global Biopharma Resilience Index with a talent score of 6.44, the UK pharma industry benefits from strong collaboration between academia and industry.

Initiatives such as Knowledge Transfer Partnerships[8] encourage the sharing of talent, resources, and research facilities between organizations, creating a wealth of opportunities that attract skilled candidates. "The quality of core scientific and engineering skills in the UK is exceptionally good," agrees Dave Tudor, Managing Director of the Medicines Manufacturing Innovation Centre at CPI, the process-manufacturing partner in the UK government's High Value Manufacturing Catapult (HVMC).

He still advises British pharma leaders to avoid complacency. "We need to have one eye on the future. Do we have enough data scientists for AI and advanced digital solutions, for example?" he asks. "We also need to make sure our scientific curriculum is modified to bring in oligonucleotides and ribonucleic acid, the advanced drug modalities that are coming through. We need to keep up with all the latest developments."

8 Knowledge Transfer Partnership guidance. UK Research and Innovation. https://www.ukri.org/councils/innovate-uk/guidance-for-applicants/guidance-for-specific-funds/knowledge-transfer-partnership-guidance/ March 3, 2023

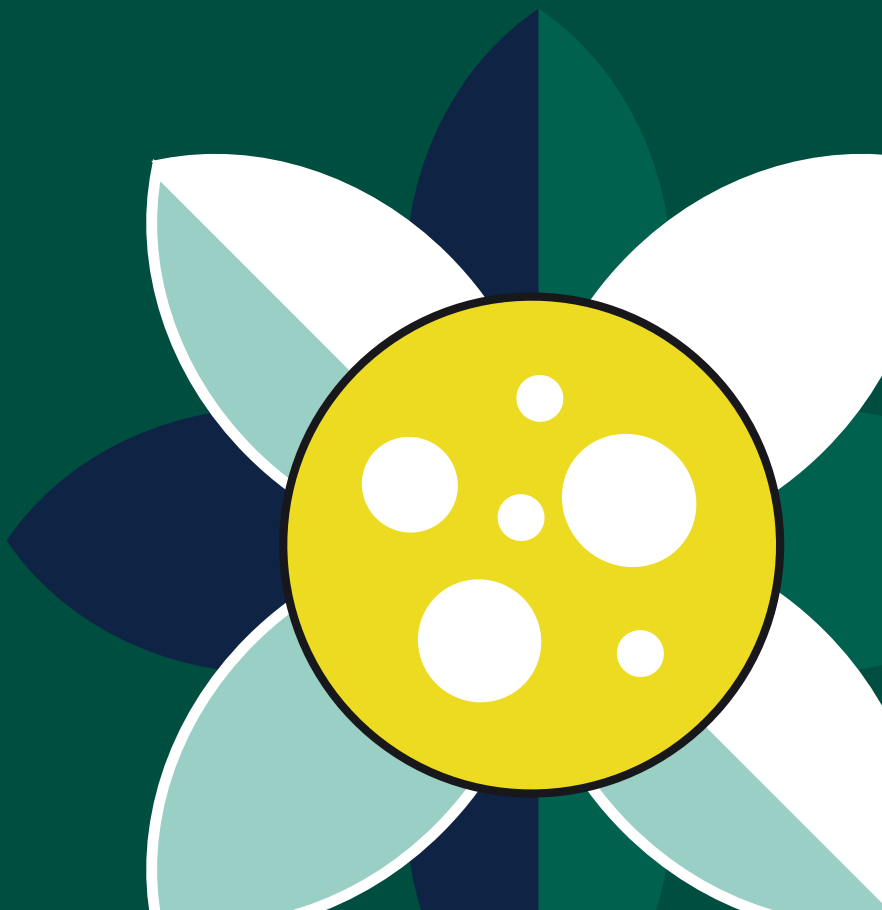
PILLAR 3

R&D ecosystem

The Japanese have a model for supporting R&D; $2billion is going to R&D to develop the industry. Something similar is happening in Korea.

Sweden, which has always been very forward-thinking around innovation, has put forward a similar idea, whereas other countries, like the US, have gone back to pre-COVID.

Jerome Kim
Director General
International
Vaccine Institute



The R&D ecosystem pillar explores how easy it is for a biopharma firm in a given country to find a range of high-quality development and R&D partners to choose from. It assesses the extent to which the industry fosters a strong culture of collaboration, as well as the technological capability to develop, test, and scale new research rapidly.

The global R&D ecosystem index fell from a 2021 score of 6.54 to 5.22 in 2023, the lowest score of all five pillars.

It is striking that this comes after a period of intensive industry collaboration during the COVID-19 pandemic. Recognizing the benefits of a collaborative approach, the majority of pharma firms we surveyed put enhancing their national R&D ecosystem as their top domestic priority over the next two years.

"I think having a dialog within the R&D community can make a clearer results chain between the work that we do, the products we develop, and the applications for patients," says Aurélia Nguyen. "It has been hugely beneficial for Gavi in terms of making sure that we have access to new vaccines and technologies that increase the reach of our programs. It's highly motivating to the R&D community to really understand the value of the work that they do."

With so many firms now facing talent shortages, a healthy R&D ecosystem is essential to bridge the gap. However, fewer than half of respondents believe their country has a collaborative R&D ecosystem.

While the majority of those surveyed are positive about the quality of potential R&D partners in their country, only around a quarter would rate them as "excellent," indicating significant room for improvement.

Leszek Lisowski, an Associate Professor of Molecular Biology at the University of Sydney specializing in developing and optimizing viral vector technologies, explains this reluctance to collaborate. "We have a lot of handpicked collaborations with companies, and we've been quite lucky. But collaboration involves a whole spectrum of interactions," he says. "A lot of companies, by their nature, have to be competitive. They have to hide their research; they cannot just share all their data."

As with the talent pool pillar, the R&D data shows a clear distinction between developed and emerging economies. Respondents in developed economies often rank prospective partners as "excellent"; in contrast, those in emerging economies frequently report a paucity of adequate prospective partners.

Percentage of executives who report that there is a culture of widespread cooperation and open innovation in the following areas of the biopharma industry, within the country in which they are based

Fig 7. Fewer than half of executives perceive a strong culture of collaboration across their country's biopharma ecosystem.

Country most likely to rate the quality of the following biopharma partners “excellent” or “among the best in the world”:

US

40%

of executives rated the country’s academic institutions as “excellent”

Singapore

40%

of executives rated national government laboratories/think tanks as “excellent”

Spain

38%

of executives rated contract manufacturing organizations as “excellent”

Sweden

37%

of executives rated biopharma companies as “excellent”

Australia

36%

of executives rated traditional pharma companies as “excellent”

US

34%

of executives rated contract research organizations as “excellent”

"The intensified geopolitical situation makes global collaboration a challenge. But collaboration between academia and biotech should cross borders because medicine is medicine, not politics," suggests the president of a global biopharma company headquartered in China. "I hope there can be wider collaboration between Chinese biotech companies and their counterparts in Europe and the US, not only from a commercial perspective but also with academia across the world."

A collaborative R&D culture that allows researchers mutual access to one another's findings is essential to accelerating development, reducing risk, and improving health outcomes for patients. If denied access to an innovation network, individual talent remains isolated, limited by a lack of stimulation and, often, without access to essential resources. Pharma leaders must consider the benefits of instilling a collaborative culture into their firms.

"It's important that the innovation ecosystem is sustained by the triple helix of government, industry, and academia funding.

Don't just invest for two or three years; it's got to be a 10-year strategy. We need a continued way of innovation funding that really drives what needs to happen to keep the ecosystem hungry and alert to what's coming through.

Dave Tudor
Managing Director
Medicines Manufacturing Innovation Centre, Biologics and Quality, CPI

PILLAR 4

Manufacturing agility

It’s not just about developing therapies that might be used one day.

There are therapies that are ready to go now — so how do we get them to the clinic, and what are the challenges involved? Most people think about how you scale manufacturing up from a technological perspective.

But depending on the target disease, there are issues about how you scale it down, particularly for rare and ultra-rare diseases, and how you make this economically viable.

Ian Alexander
Professor
Sydney Children’s Hospitals Network
and the University of Sydney

The manufacturing agility pillar explores each country's level of access to the technology, talent, and external partners required to rapidly scale manufacturing of essential medicines. It also considers any barriers the industry faces to strengthening its manufacturing capability.

The data shows that overall manufacturing agility grew slightly from the 2021 score of 6.50 to 6.65 in 2023. This pillar is closely linked to supply chain resilience, which was the only other pillar to see a similar level of growth over this period.

Being equipped to scale manufacturing up or down at short notice is key to overall resilience; however, many countries have a limited ability to do this. Most executives believe that their country would be slow or very slow in scaling up the production of critical therapeutics, should shortfalls occur.

One therapeutic area of particular concern is biologics other than vaccines and insulin, such as monoclonal antibodies. Only 8% of executives say their country could immediately ramp up production of these medicines in response to a shortfall.

Why are novel therapeutics so challenging to scale?

"The products coming through the clinical pipeline are getting more diverse and complex," NIBRT's Killian O'Driscoll explains. "They're driven by fantastic science, they've got great clinical efficacy, but they are more challenging to manufacture, and that's putting strain on supply chains. We're also seeing that the actual manufacturing processes are getting more complex in response to that more diverse pipeline, along with the increasing need for efficiencies for sustainability."

How quickly could companies in the country where you are based ramp up production of the following products should a shortfall occur in the global market?

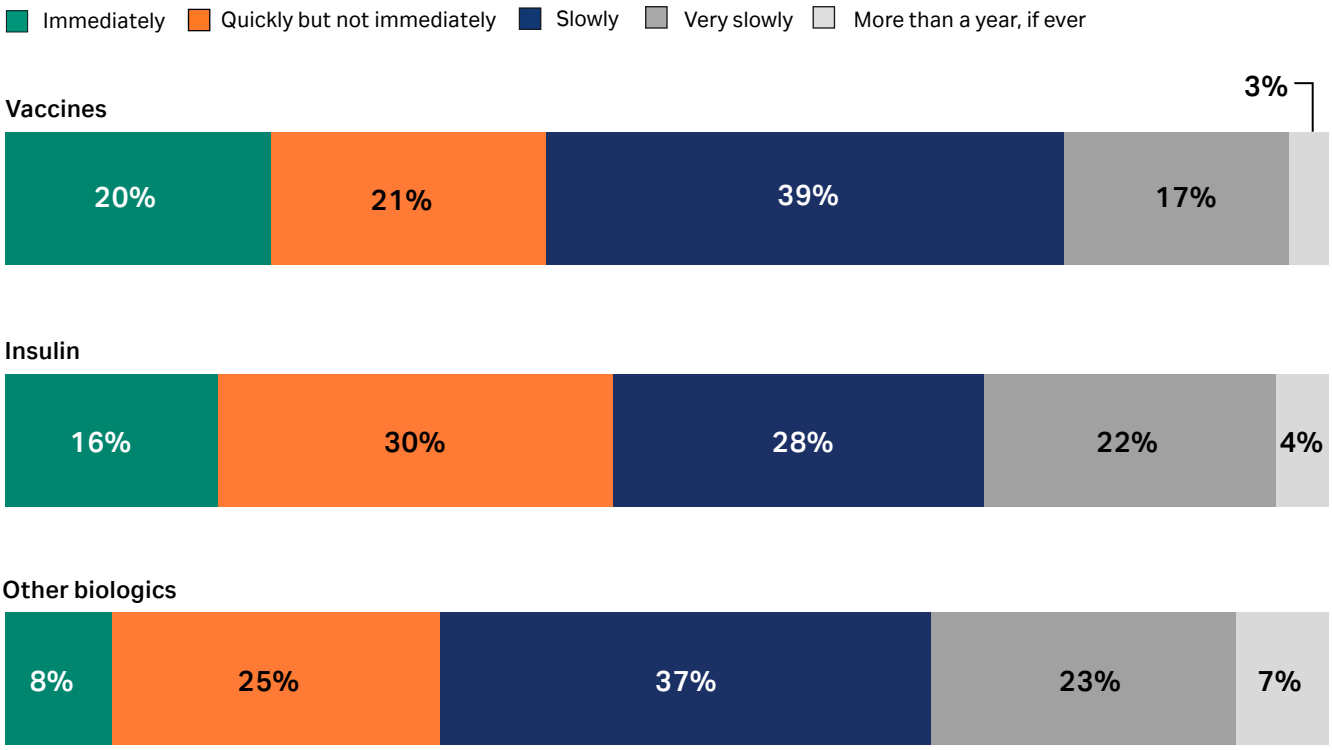


Fig 8. Fewer than one in 10 executives say their country could immediately ramp up production of biologic drugs if faced with a shortfall.

Main factors impeding manufacturing operations:

The good news? 52% of respondents say that, over the past two years, it has become more affordable to manufacture biopharmaceuticals. However, manufacturing for cell and gene therapies continues to suffer from a lack of streamlining and limited standardization. Many new therapies come from start-ups or academic labs that are innovative but lack the ability to scale up.

Aaron Cowley of Arranta Bio highlights the need to increase manufacturing standardization and efficiencies by developing process flows and applying new technologies. Lower costs will, of course, increase accessibility and adoption of therapies.

"We have a huge disconnect right now between the cost of biologics and their impact on the healthcare system. A lot of biologics are for super-rare conditions and can cost $500,000 to $4million for a single treatment. For example, the manufacturing costs are so steep that firms risk losing money by putting their molecules in markets outside the US," he says.

"If we want to take these biologics and expand them to a larger market, we've got to focus on the manufacturing strategy and capabilities to make it a reality from an economic standpoint, because right now it's just not working. What we're missing is a piece in the middle between the CDMO and the product innovators. We're lacking the innovation to make these biologics a scalable platform process."

Advanced digital technologies such as AI, data analytics, robotics, and automation could allow manufacturers to scale production up or down on demand. But our research suggests pharma companies are not making the most of these tools.

Fewer than one in 10 executives believe their company is "very effective" at using digital tech to drive a competitive advantage in drug manufacturing, and 47% believe that overly restrictive regulations are holding back digitalization.

Better collaboration with regulators could help ensure digitalization is not impeded by lengthy approval processes. CPI's Dave Tudor suggests that companies use technology selectively to get the best results — from both a regulatory and an environmental perspective.

"How do companies choose the right advanced manufacturing and digital technology solution to drive efficiency?" Tudor asks. "If they get that right, they can deliver productivity, they can drive a better regulatory compliance performance, and, nine times out of 10, if you get productivity, you get a reduction in your carbon footprint."

PILLAR 5

Government policy and regulation

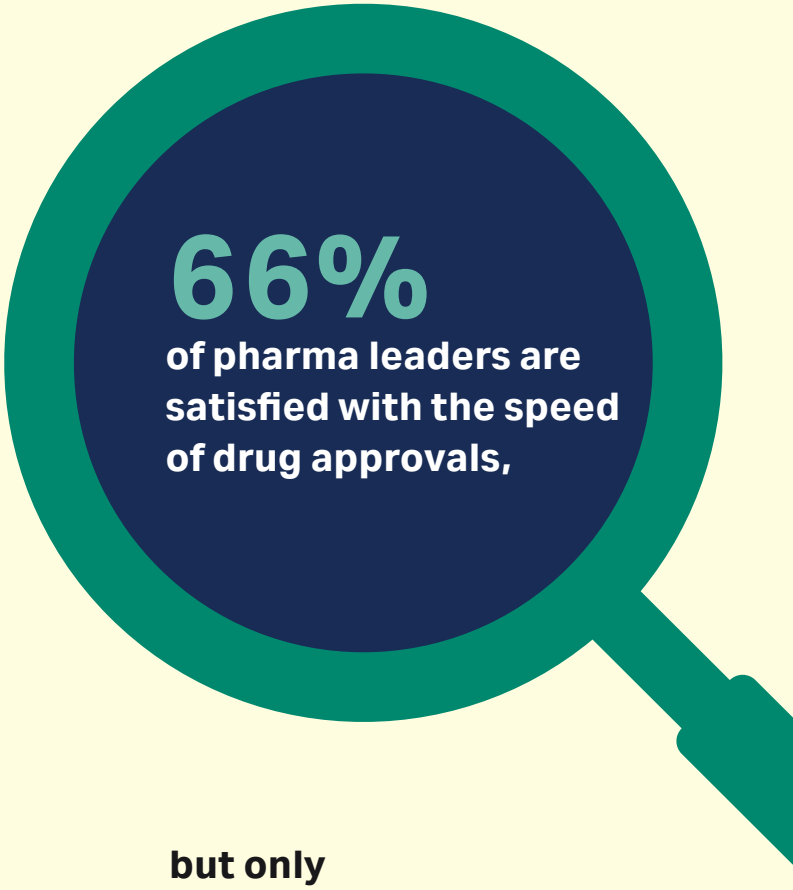
The resilience index's final pillar considers the effectiveness of each country's policies and regulations on the development landscape and healthcare system. This part of our research looks into policies around tax, trade, and IP, as well as interactions with regulatory agencies that govern drug development and approval. Collectively, these policies and regulations impact the ability of novel therapeutic developers and commercial pharma manufacturers to produce and commercialize medicines.

Overall, perceptions of government policy and regulation fell to 6.08 in 2023, from a previous high of 6.96 in 2021. The high in 2021 likely reflects that year's accelerated regulatory-approval environment for certain products (notably vaccines authorized during the COVID-19 pandemic).

In 2023, updated policies and regulations pose near-term challenges for firms. Nevertheless, some of these changes — such as regulatory alignment and harmonization — may benefit industry in the long term. Indeed, many key regions are now implementing major policy changes, often ones that were delayed or held up by political complications at the height of the pandemic. These include the EU Clinical Trials Regulation (CTR)[9], updates to GMP guidelines, and significant changes in the US Prescription Drug User Fee Act (PDUFA VII)[10].

The resilience index data is consistent with the short-term disruption of the current dynamic policy and regulatory landscape. While introducing near-term challenges, this shift also creates opportunities for manufacturers to engage early with regulatory agencies to de-risk and reduce development costs. These policies, which focus on innovation and new and more efficient manufacturing and clinical technologies, will also provide structural long-term benefits for manufacturers. Our survey shows that many executives are generally satisfied with the drug approval process, which is the final step in a year- or even decades-long development program for new therapeutics; however, they also feel that regulatory consultation during development could be more efficient and transparent.

In 2023, meeting new compliance requirements and navigating short-term uncertainty while taking advantage of new programs will remain a focus area for the industry.



but only

59%

are satisfied with the structure for consultation between regulators and other stakeholders, including patients and industry.

9 Clinical Trials Regulation. European Medicines Agency. https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-regulation 15 February, 2023

10 PDUFA VII: Fiscal Years 2023 – 2027. FDA. https://www.fda.gov/industry/prescription-drug-user-fee-amendments/pdufa-vii-fiscal-years-2023-2027#:~:text=The%20new%20law%20ensures%20that,critical%20new%20medicines%20for%20patients April 4, 2023

Innovative therapeutics in the cell and gene therapy space continue to be subject to a lengthier approval process, requiring additional testing and long-term patient follow-up[11,12] — all of which increase development costs and time. The vast majority (90%) of executives reported that their country needs to do more to support the delivery of cell and gene therapies.

Recently, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) announced the first internationally "harmonized" guidelines for gene therapy biodistribution[13], a major step forward for gene therapy developers. Further, many countries have been working toward establishing harmonized guidance for cell and gene therapy developers, including finalization of the guidance framework in the US [14].

While the international standardization of recommendations for cell and gene therapy development may have initially increased uncertainty, it constitutes a positive sign for the alignment and transparency of policy and the regulatory landscape in 2023 and beyond.

11 ICH guideline S12 on nonclinical biodistribution considerations for gene therapy products. European Medicines Agency. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ich-guideline-s12-nonclinical-biodistribution-considerations-gene-therapy-products-step-2b_en.pdf June 24, 2021

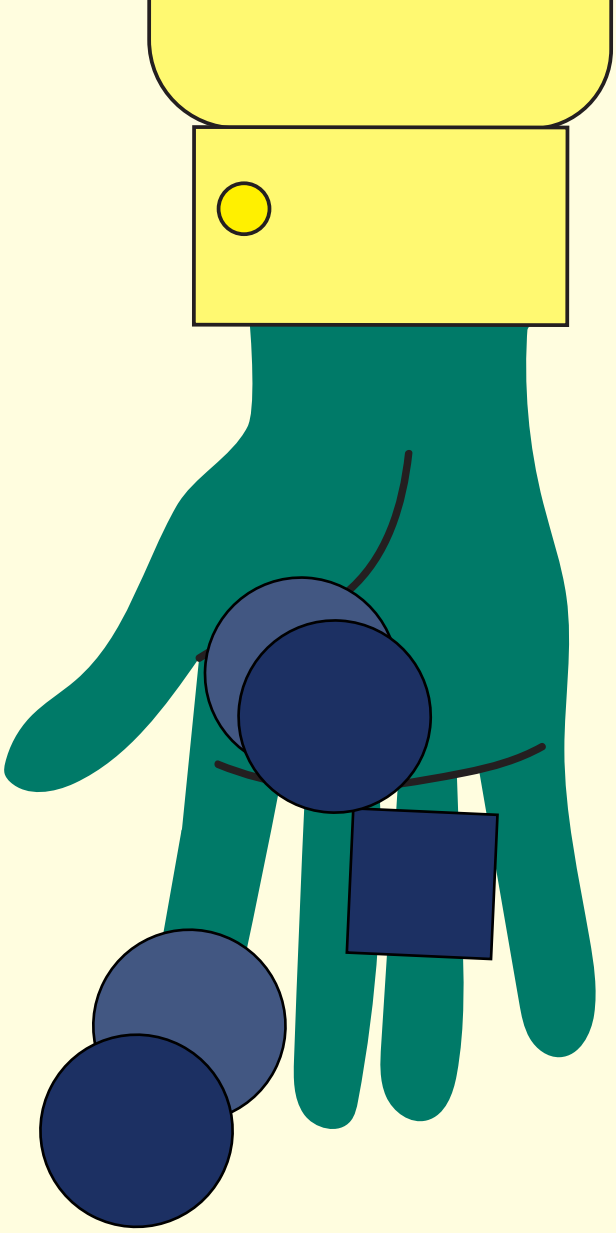
12 Long Term Follow-Up After Administration of Human Gene Therapy Products. FDA. https://www.fda.gov/media/113768/download January 2020

13 ICH adopts S12 guideline for gene therapies. Regulatory Focus. https://www.raps.org/news-and-articles/news-articles/2023/3/ich-adopts-s12-guideline-for-gene-therapies March 20, 2023

14 Cellular & Gene Therapy Products. FDA. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products March 20, 2023

45%
of executives say government policy is pursuing inconsistent goals.

46%
believe government tax or trade policies actively encourage domestic pharma/ biopharma manufacturing.



In recent years, policymakers and regulatory agencies worldwide have focused on enabling biopharma innovation important to public health. The 21st Century Cures Act 2.0 in the US[15] and the DARWIN EU® Coordination Centre launch in 2022 are key examples of policy intended to stimulate innovation[16]. These initiatives, among others, focus on enabling biopharma development by using real-world evidence (RWE), streamlining payment and coverage processes, enabling digital health, and optimizing the drug-approval process.

While these and related legislation take some steps to promote innovation and ensure security of domestic supply, our data shows that many countries could further refine tax and trade policies.

In both new policy development and direct interactions with regulatory agencies during drug development, communication is key. At policy level, governments can foster industry relationships through open forums and channels such as public hearings, consultations, advisory committees, trade associations, and partnerships. Developers and manufacturers can engage in meetings and designation programs during product development.

There is also a need for clear conversations around strategy, suggests the University of Sydney's Ian Alexander. "Too often, the people [having the conversation] are three steps down the food chain in terms of where the critical decisions will be made," he says. "This creates a lot of uncertainty and frustration, and often a lot of hard work comes to nothing. So, you've got to make sure that the right interactions happen between the right people."

While early interactions with regulators have existed for some time — such as Innovation meetings, Scientific Advice, and Pre-IND (Investigational New Drug) meetings — many countries are streamlining the process for early development. These early meetings include the FDA's newly launched Type D meeting[17] and centralized EU EMA meetings under the Clinical Trials Regulation (CTR)[18]. The EU Commission has also announced plans to reduce the burden on pharma firms through a regulatory "sandbox" approach, which enables new technologies to be tested in a "real-world" environment sooner, with appropriate oversight and safeguards[19]. These, and other policies originating in the pandemic with the goal of streamlining innovation, are now coming into effect, creating both uncertainty as well as new opportunities for industry-regulator interaction.

Many of the countries with the highest biopharma resilience scores benefit from strong government investment and engagement with the pharma sector.

For example, in March 2023, the US government launched an executive order on advancing biotechnology and biomanufacturing innovation, which will serve as a guide for the public and private sectors to harness the full potential and power of this technology[20].

In Sweden, public–private partnerships such as Vinnova and Business Sweden offer funding and support to

15 21st Century Cures Act 2.0. Duke-Margolis Center for Health Policy. https://healthpolicy.duke.edu/cures2.0#:~:text=The%20Cures%202.0%20Act%20draft,and%20gene%20therapies%2C%20accelerated%20approval%2C

16 Initiation of DARWIN EU® Coordination Centre advances integration of real-world evidence into assessment of medicines in the EU. European Medicines Agency. https://www.ema.europa.eu/en/news/initiation-darwin-eur-coordination-centre-advances-integration-real-world-evidence-assessment February 9, 2023

17 Guidance for Industry: Formal Meetings Between the FDA and Sponsors or Applicants. FDA. https://www.fda.gov/media/72253/download May 2009

18 EudraCT & EU CTR Frequently asked questions. European Medicines Agency. https://eudract.ema.europa.eu/docs/guidance/EudraCT%20FAQ_for%20publication.pdf January 31, 2023

19 Peseckyte G. EU Commission aims to reduce regulatory burden for pharmaceuticals. Euractive. https://www.euractiv.com/section/health-consumers/news/eu-commission-aims-to-reduce-regulatory-burden-for-pharmaceuticals/ April 28, 2023

20 Executive Order on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy. The White House. https://www.whitehouse.gov/briefing-room/presidential-actions/2022/09/12/executive-order-on-advancing-biotechnology-and-biomanufacturing-innovation-for-a-sustainable-safe-and-secure-american-bioeconomy/ September 12, 2022.

How have biopharma regulatory processes/frameworks changed in your country over the past two years?

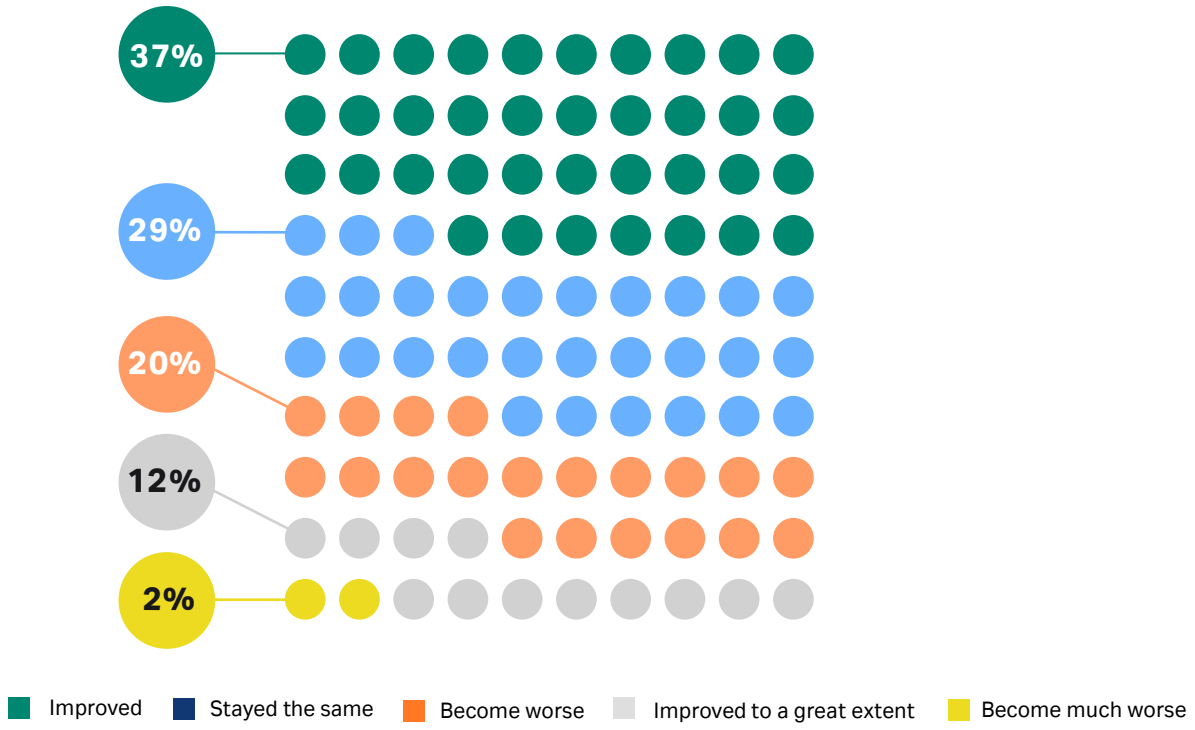


Fig 9. Less than half of executives believe that regulatory processes/frameworks in their country have improved over the past two years.

companies looking to collaborate with Swedish research institutions. A robust system for intellectual property (IP) rights helps protect companies' investments[21].

And in Singapore, the Pharma Innovation Programme Singapore (PIPS) brings together a consortium of experts from industry, academia, the public sector, and government agencies to harness new manufacturing technologies and data analytics[22]. This effort has played a significant role in the country moving seven positions up the Global Biopharma Resilience Index from 2021 to 2023.

Government policies and regulations play a key role in the success of these leading countries — but these factors alone are not enough to maintain their resilience; ongoing financial support is essential.

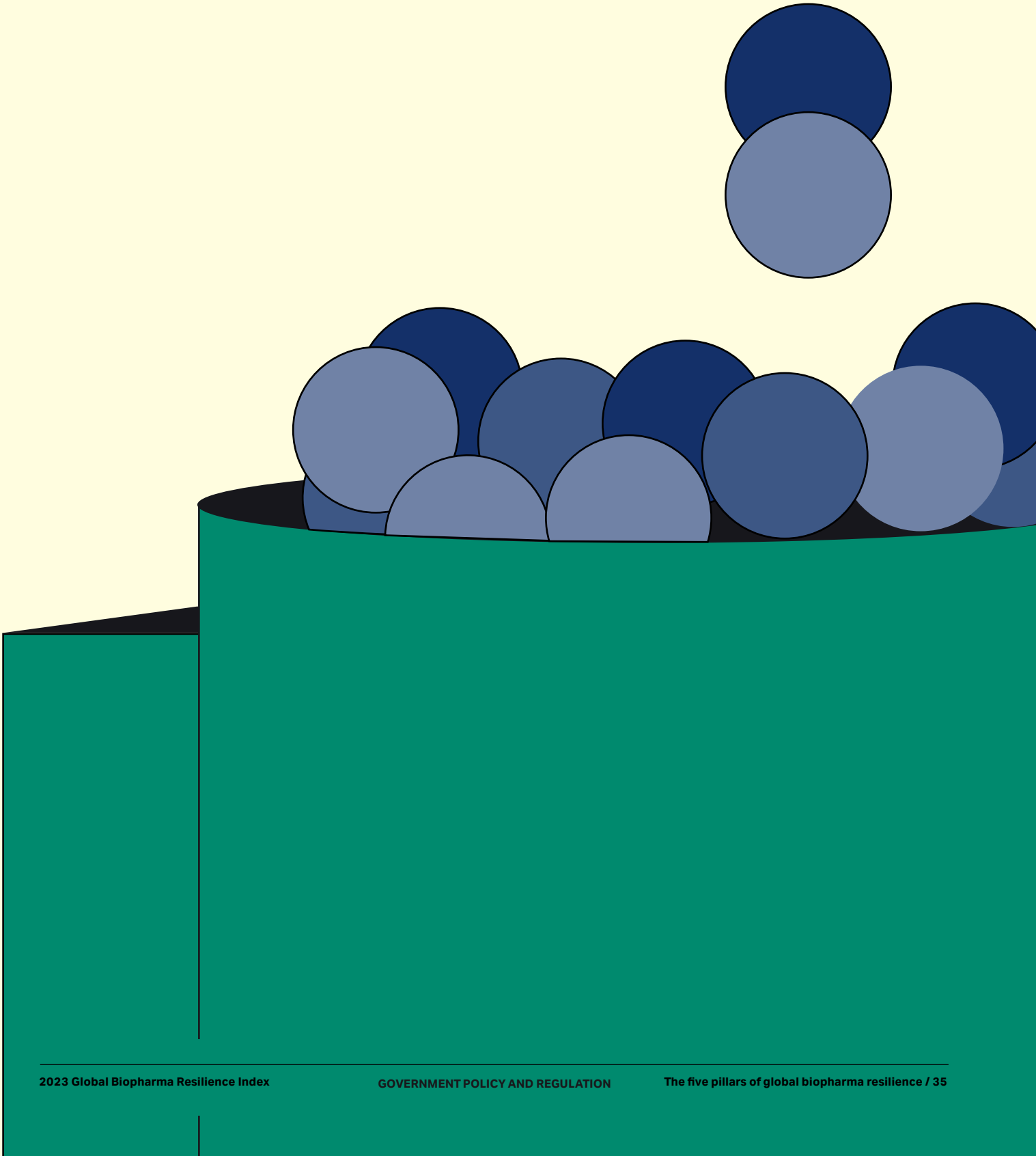
"Fiscal competitiveness is essential for the sustained growth of life science innovation and manufacturing, whether that's capital grant allocation, corporation tax, R&D incentives, or a combination of all of these," says CPI's Dave Tudor. "We've got to protect our existing supply chain and infrastructure by incentivizing companies to continue to invest in the UK, and advanced technologies and competitive fiscal products are two key ways of achieving this. By getting this right, we will attract new companies as well. They need to see that our country is a great place to do business because we've got some of the best scientists to support their new, innovative science."

21 Albert H. How Sweden's Intellectual Property Law Boosts Biotech Innovation. Labiotech. https://www.labiotech.eu/expert-advice/interview-uhlen-kth-2/ November 5, 2019 (updated June 24, 2022).

22 Pharma Innovation Programme Singapore (PIPS). Agency For Science, Technology and Research (A*STAR). HYPERLINK "https://www.a-star.edu.sg/pips%202023"https://www.a-star.edu.sg/pips 2023.

Our data shows the perceived importance of both public funds and supportive but firmly enforced policy, as well as regulatory process efficiencies. Only with these elements in place will translational and early-stage firms appeal to venture partners with access to the private capital needed at clinical-stage development. In particular, in a macroeconomic climate where venture capital may be more limited and many larger pharma firms are slimming their pipelines, both policy and regulation must come together to enable translational and clinical development of the next generation of medical technologies.

Regions that achieve cohesive domestic policies and regulatory processes with an eye to international collaboration will continue to attract investment in biopharma development.



SECTION 5

Conclusion

Here are five ways for countries to boost the resilience of their biopharma industries in the years ahead:

1. Develop a long-term roadmap that aligns government policy and biopharma regulations

- Policy initiatives on fostering innovation should be designed to translate into clear regulatory guidelines. The pandemic demonstrated that government policy and regulation can coordinate effectively to promote rapid innovation (that is, urgent development and distribution of COVID-19 vaccines). Other areas, such as digital health and gene therapy, continue to face challenges. In Brazil, changes to clinical trial and approval regulations in rare disease are providing benefits for cell and gene therapies, in particular[23]. Meanwhile, the UK government recently announced that the Medicines and Healthcare products Regulatory Agency will implement rapid sign-off for medicines and technologies approved by other trusted regulators, such as the United States, Europe, and Japan[24].
- Going forward, industry must work in closer collaboration with both government policymakers and regulatory-agency leadership to ensure regulatory processes are adapted to suit emerging technologies and therapies. Although there has been progress on facilitating faster drug approvals (while continuing to ensure safety and efficacy), that is just the last of a number of regulatory barriers that new products must overcome to reach the market.
- International and domestic regulations must be much more closely aligned. Switzerland, the highest-performing country in the Global Biopharma Resilience Index, is particularly strong in this regard. Swissmedic, the Swiss Agency for Therapeutic Products, is known for being rigorous yet flexible in allowing expedited drug approvals and streamlining international data use in the local drug-approval process. The organization works closely with international partners to accelerate market access for innovative therapies, and is supporting "regulatory harmonization" as a priority for the next three years[25]. Further, programs like the US FDA's Project Orbis aim to make concurrent international drug approvals a reality[26], although scope presently remains limited to high-priority oncology projects.

2. Bridge the gap between emerging and developed economies

- Strong areas among the cohort of less-developed countries — such as India's efficient supply chain and China's manufacturing agility — should be studied by other developing countries for ways in which they could emulate these successes and thereby accelerate their own progress.
- China is attempting to reverse the "brain drain" of biopharma professionals seeking opportunities abroad using a series of talent-recruitment policies encouraging Chinese nationals to return to the country[27].
- The biopharma industries of developed economies can also help strengthen the global R&D ecosystem. For example, the Global Gene Therapy Initiative, an international alliance of clinicians, scientists, engineers, advocates, and community members, is working to establish pathways to cell and gene therapies in Uganda and India, focusing on HIV and sickle cell anemia[28].

23 How Effective is ANVISA's Rare Diseases Expedited Approval Pathway [RDC 205]? Trinity. https://trinitylifesciences.com/blog/how-effective-is-anvisas-rare-diseases-expedited-approval-pathway-rdc-205/ March 18, 2022.

24 Cowlishaw S, Castle G, Handy E, Dirkzwager R. UK MHRA to recognize foreign regulatory approvals for medicines and medical technologies and promote digital innovation. Covington. https://www.insideeulifesciences.com/2023/03/20/uk-mhra-to-recognize-foreign-regulatory-approvals-for-medicines-and-medical-technologies-and-promote-digital-innovation/ March 20, 2023.

25 Strategic objectives 2023–2026. Swissmedic. https://www.swissmedic.ch/dam/swissmedic/en/dokumente/direktion/strategische_ziele_2023-2026.pdf.download.pdf/strategische_ziele_2023-2026.pdf September 16, 2022.

26 Project Orbis. U.S. Food & Drug Administration. https://www.fda.gov/about-fda/oncology-center-excellence/project-orbis March 17, 2023.

27 Yang L, Marini G. Research Productivity of Chinese Young Thousand Talents. International Higher Education. 2019(97):17-18. DOI: https://doi.org/10.6017/ihe.2019.97.10944.

28 Global Gene Therapy Initiative. Caring Cross. https://caringcross.org/global-gene-therapy-initiative/ 2023

3. Address the talent shortage through training, upskilling, and retention

- Biopharma talent is in short supply worldwide, partly owing to rapid advances in biologics, which require a highly specialized skill set, and the increasing need for digital expertise. Organizations struggling to fill this gap can focus on upskilling their existing workforce in digital and investing in staff training and development.
- Improving retention through flexible working conditions and other approaches (see Section 2) can alleviate some of the anxiety around the short supply of talent.
- Attracting talent from the technology sector — particularly as it experiences a lag in hiring — may help supply some digital talent in the short term, but a longer-term talent pipeline is needed. Specialist training facilities, such as NIBRT in Ireland, are critical to providing the hands-on experience that many universities cannot, working directly with industry to design, develop, and deliver bespoke training programs for new and existing staff.

4. Strengthen digitalization through targeted investment

- The difficulty in sourcing talent with expertise in digital solutions may be contributing to biopharma's lack of momentum in adopting new technology. A focus on industry-specific applications — such as continuous manufacturing and Real Time Release Testing (RTRT), which uses data collected during the manufacturing process — could boost adoption rates.
- A move towards roboticization of all or part of the manufacturing process would significantly reduce costs and support scalability to meet demand.
- There is a clear need for greater investment in the platforms that enable continuous manufacturing for biologics. In the US, significant funding is coming from the government and contract manufacturing organizations[29], but companies based in countries without this support may need to seek private investment.

5. Learn from leading countries' investment models

- There are some small, high-performing ecosystems that are high on the list for their unique investments in the market. For example, Ireland, Switzerland, and Sweden are pairing government investment with R&D hubs for training and development, fostering a "small but mighty" approach to biopharma.
- There are also positive trends around mid-ranking countries in the index, in particular South Korea, where the government has promised an annual investment of $303 million to nurture the national biotech industry[30]. This investment is combined with a raft of regulatory reforms intended to streamline innovation, decentralize clinical trials, and de-risk investment in new therapies[31]. And in Japan, the government has secured $420 million to strengthen the domestic ecosystem for drug and vaccine development[32].
- India and China provide a strong example of how robust government policy paired with a strong scientific culture can power growth in biopharma.
- Governments can make their investments go further by developing tax policies with an eye to the global market, ensuring competitiveness, attracting business from overseas, and encouraging established companies to remain in the country.

Since 2021, our research shows the industry has made critical strides towards improved resilience, but it also reveals that it is not enough to secure the full benefits to global health of opportunities in innovative disease management and new life-saving treatments. Following these recommendations, building towards a streamlined system that prioritizes alignment of internationally agreed standards and domestically applied regulations, will boost resilience for individual countries and for the global biopharma ecosystem as it works towards increased access and equity in healthcare.

29 Non-stop investment from CMOs and US Government into continuous manufacturing. Pharmaceutical Technology. https://www.pharmaceutical-technology.com/comment/investment-continuous-manufacturing/ June 23, 2022.

30 Woo-hyun S. S Korea rolls out biotech plan. The Korea Herald. https://www.koreaherald.com/view.php?ud=20221207000703 December 7, 2022.

31 Shin JW. Korea's Biopharma Regulatory Reform Push To Focus On Innovation, Streamlining. Citeline Regulatory Pink Sheet. https://pink.pharmaintelligence.informa.com/PS147841/Koreas-Biopharma-Regulatory-Reform-Push-To-Focus-On-Innovation-Streamlining March 8, 2023.

32 Takagi L. Japan Kicks Off $366m Bioventure Support Program. Citeline Commercial Scrip. https://scrip.pharmaintelligence.informa.com/SC146914/Japan-Kicks-Off-$366m-Bioventure-Support-Program August 19, 2022.

SECTION 6

Research methodology

Quantitative research

The Cytiva Global Biopharma Resilience Index is built using data from a survey of 1250 senior pharma and biopharma executives across 22 countries. The research was carried out by Cytiva in partnership with Longitude, a Financial Times company, in January and February 2023. Of the survey respondents, 25% held C-suite/board-level roles, and just under one-third (30%) were from organizations with annual revenues of more than $1billion.

The index results are based on 22 different performance indicators across five different pillars. While 18 of the indicators are scored on the survey data, four are based on publicly available third-party data.

The indicators (or questions) by pillar are:

Supply chain resilience

- How prone is a country to drug shortages?
- How easy is it for a country to secure high- quality drugs?
- How much dependence is there on imports?
- How prepared is a country to roll out personalized medicines, and cell and gene therapies?
- To what extent can a country meet the population's need for medications? Based on the UN Comtrade database for total pharma imports and exports[33], as well as IQVIA and OECD data on market size[34].

Talent pool

- Can talent be sourced easily?
- Is there sufficient education and training to nurture talent?
- How supportive are labor regulations of accessing talent overseas and scaling the workforce?
- What is the availability of highly qualified R&D talent? Based on the Nature Index data on number of high-quality publications in internationally recognized journals[35], adjusted using UN data on population size[36].

R&D ecosystem

- Are partners readily available in the ecosystem?
- How sufficient are existing R&D capabilities?
- Is there healthy cooperation among industry actors to drive innovation?
- How effective are the country's pharma and biopharma industries at incorporating digital technologies into their R&D efforts?
- How effective are the country's pharma and biopharma industries at developing new medications? Based on OECD data on IPS patent outputs[37], adjusted using UN data on population size (as above).

33 UN Comtrade Database. https://comtradeplus.un.org/ 2022.

34 Patents by technology. OECD. HYPERLINK "https://stats.oecd.org/Index.aspx?DataSetCode=PATS_IPC"https://stats.oecd.org/Index.aspx?DataSetCode=PATS_IPC# May 23, 2023.

35 2022 tables: Countries/territories — life sciences. Nature. HYPERLINK "https://www.nature.com/nature-index/annual-tables/2022/country/life-sciences/all%202023"https://www.nature.com/nature-index/annual-tables/2022/country/life-sciences/all 2023.

36 World Population Prospects 2022. United Nations Department of Economics and Social Affairs, Population Division. https://population.un.org/wpp/Download/Files/1_Indicators%20(Standard)/EXCEL_FILES/2_Population/WPP2022_POP_F03_1_POPULATION_SELECT_AGE_GROUPS_BOTH_SEXES.xlsx 2022.

37 Patents by technology. OECD. HYPERLINK "https://stats.oecd.org/Index.aspx?DataSetCode=PATS_IPC"https://stats.oecd.org/Index.aspx?DataSetCode=PATS_IPC# May 23, 2023.

Manufacturing agility

- How quickly can the industry accelerate production when faced with a shortfall?
- How many barriers does the industry face when it comes to domestic manufacturing (such as access to the right skills and/or equipment)?
- How effective are contract manufacturing organizations in terms of quality, adaptability, and speed?
- How effective is the industry at using digital technologies to improve manufacturing?

Government policy and regulation

- How effective is the national drug-approval agency?
- What policies are in place to promote industry integrity?
- How much funding is available?
- How efficient is the regulatory decision-making around approving new drugs? Based on CIRS data on regulatory approval times[38].

Survey responses were scored out of 10, with a score of 10 indicating excellent performance and a score of 0 indicating complete failure.

The scores were then aggregated and averaged to provide an overall index score for each country, as well as individual scores for each of the five pillars. The scores act as a proxy for the resilience of the biopharma industry overall, and in each of the five areas.

38 CIRS: Centre for Innovation in Regulatory Science. https://cirsci.org/ 2023.

SECTION 7

Scoring methodology

Supply chain resilience

- The biopharma supply chain is resilient enough to meet the global demand for medications, without shortages
- The biopharma supply chain can provide reliable global access to high-quality drugs and is increasing its capability to produce biologic drugs
- The world/country is not overly dependent on a small number of countries to produce essential medicines
- The world/country is well prepared to roll out personalized medicines, and cell and gene therapies

Talent pool

- The biopharma industry is able to source all of the talent it needs easily — in particular, digital and technical talent
- The biopharma industry has access to high-quality R&D talent
- Education and training are sufficient to nurture talent
- Flexible labor regulations make it easy to source talent from other regions, and to scale the workforce when required

R&D ecosystem

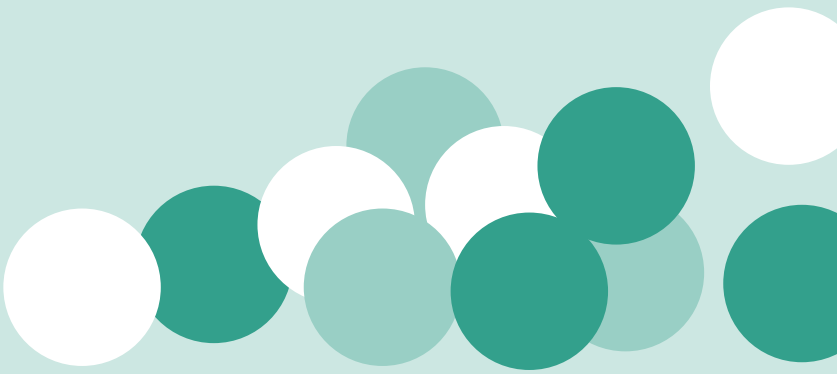
- The biopharma industry has a strong culture of collaboration, and companies can easily find partners to work with them on R&D
- All aspects of the biopharma ecosystem have sufficiently strong R&D capability
- The industry is producing a reliable pipeline of new medications
- The industry is effectively harnessing digital technologies to strengthen R&D activities

Manufacturing agility

- Biopharma is able to quickly ramp up production of medications in response to shortfalls
- The global industry doesn't face any barriers to increasing manufacturing capability (such as difficulty accessing the right skills or equipment)
- The industry has access to contract manufacturing organizations that excel in quality, speed, and adaptability
- Emerging technologies — such as artificial intelligence (AI) and automation — are effectively adopted to continuously improve biopharma manufacturing

Government policy and regulation

- Agencies responsible for drug approval excel across the following areas: speed, technical capacity, openness to innovation, and cost-effectiveness
- Governments are implementing policies that support the biopharma industry (such as tax and trade policies, and intellectual property laws)
- Funding for start-ups is sufficient to drive growth and innovation in the biopharma industry



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