Prepared for:

Vaccines Europe

Leopold Plaza Building, Rue du Trone 108

Brussels, B-1050

Improving the Attractiveness of the Vaccines Industry in the European Union

Final Report

Prepared by:

Tim Wilsdon, Ryan Lawlor, Milan Ferguson

Charles River Associates

8 Finsbury Circus

London EC2M 7EA

Date: June 2023

Executive summary

Vaccines Europe (VE) asked Charles River Associates (CRA) to research the current state of the vaccines industry in the European Union (EU). This study aimed to identify the factors affecting vaccine investment along the value chain and assess the attractiveness of the EU as a location relative to other global regions. Key policy recommendations for EU policymakers to enhance the EU's attractiveness for future vaccine innovation were then identified by examining the challenges affecting vaccines in the EU.

The report was developed through a comprehensive literature review, a quantitative analysis of key trends, and an interview programme with senior executives from 11 innovative companies which are active in the EU vaccine environment. Given that the current vaccine pipeline predominantly consists of prophylactic vaccines, this was the focus of our research.

Summary of key findings and challenges facing the EU vaccines industry

- **Limited funding, incentives, and support** for diverse vaccine types and platforms, as well as limited workforce capability, are barriers to early-stage vaccine research; this is evidenced by 56% fewer biotechs involved in vaccine research in the EU compared to the United States
- The **complexity of trial requirements and lengthy timelines** present challenges to conducting trials in the EU, with evidence of a 35% decline in global vaccine clinical trials conducted in the region since 2000
- Lack of financing and **complex manufacturing requirements and suboptimal infrastructure**, reduce the attractiveness of the EU for vaccine manufacturing
- Comparatively **limited regulatory flexibility and efficiency** pose barriers to timely regulatory approval of innovative vaccines

After considering the key findings from the research and the challenges facing the EU vaccines industry, we then developed policy priorities needed to improve the industry' attractiveness to support future innovation and ensure European populations realise the benefits of innovative vaccines.

Policy priorities: Improving the attractiveness of the EU vaccines industry

- Ensure there is **sufficient levels of funding and investment** to sustainably support vaccine research
- The EU needs the **appropriate infrastructure and skilled workforce** for vaccine R&D, manufacturing, and assessment
- Greater **coordination between the EU and Member States** to ensure processes are streamlined and harmonised to provide more timely population access to innovative vaccines
- The regulatory and access environment has the **necessary flexibility to support the assessment of innovative vaccines**
- Greater **accountability and EU-wide policy prioritisation** of prevention and immunisation to support more equitable population access to vaccines
- The **EU should demonstrate consistent support for the European vaccine industry** in global policy debates

1. Introduction

Charles River Associates ('CRA') was commissioned by Vaccines Europe ('VE') to undertake an analysis of the current state of the vaccines industry in the European Union (EU). The aim was to understand the factors affecting the investment in vaccines along the value chain to assess the attractiveness of the EU as a location for investment compared to other global regions. By examining the challenges affecting vaccines in the EU, key policy recommendations for European policymakers to enhance the EU's attractiveness for future vaccine innovation were then identified.

1.1. Background

The relative decline in Europe's attractiveness as a centre for innovation and manufacturing has been a concern for many years.[1] Much of the recent debate has been focused on pharmaceuticals. Pharmaceutical R&D expenditure in the United States in 2020 exceeded that in Europe by over €20 billion.[2] This gap is widening; twenty years ago, in 2002, the difference was only €2 billion. Less attention has been paid to vaccines.

Although the vaccines industry is a relatively small segment compared to the overall pharmaceutical industry (the most recent data showed it held 3.6 % of the total world market for pharmaceutical products)[3] it is particularly important for the EU. The European Commission (EC) industry scorecard shows that the health industry delivers the second highest level of investment value when compared to other innovative industries.[4] Data from 2019 demonstrates that the vaccine industry was an EU leader in R&D intensity.[5] The vaccines industry is also a significant contributor to the EU economy, creating 122,000 jobs (directly and indirectly) in 2016 alone (the most recent vaccine specific data available).[5] Traditionally the EU has been the location for investment in innovative vaccines, though in recent years manufacturers have been investing in sites in other regions, particularly Asia, to produce innovative vaccines at a larger scale to meet global demand.[6]

---

1 CRA first worked on this in 2004. "Innovation in the pharmaceutical sector" A report by Charles River Associates for DG Enterprise, 2004. https://media.crai.com/sites/default/files/publications/innovation-in-the-pharmaceutical-sector.pdf.

2 Charles River Associates (2022). Factors affecting the location of biopharmaceutical investments and implications for European policy priorities. Available at: https://www.efpia.eu/media/676753/cra-efpia-investment-location-final-report.pdf

3 Lobo, F. (2021). Restructuring the global vaccine industry (No. 134). Research Paper.

4 European Commission (2018). The 2018 EU Industrial R&D Investment Scoreboard. Available at: https://iri.jrc.ec.europa.eu/scoreboard/2018-eu-industrial-rd-investment-scoreboard

5 Vaccines Europe (2020). The EU Vaccines Industry in Figures. Available at: https://www.vaccineseurope.eu/about-us/the-eu-vaccine-industry-in-figures/

6 For example, Sanofi to invest in a leading-edge production site in Singapore; continues to strengthen its vaccines manufacturing capacities. Available at: https://www.sanofi.com/en/media-room/press-releases/2021/2021-04-12-05-00-00-2207870

The factors affecting vaccine decision-making have been affected by the pandemic. Prior to the COVID-19 pandemic there was concern from key stakeholders (e.g., industry, policymakers) that the EU vaccines industry was facing several challenges, with disinvestment superseding investment and reductions in policy prioritisation.[7] The pandemic highlighted the value of the innovative vaccine industry, with EU policymakers highlighting the need to build more strategic autonomy and resilience and the importance of accelerated marketing authorisation procedures which were seen as vital for the development of COVID-19 vaccines. Even so, the debate regarding attractiveness and competitiveness has focused on pharmaceuticals with the result that the proposals for revising the General Pharmaceutical Legislation outline a series of legislation aimed at supporting the competitiveness of the broader pharmaceutical industry in the EU affecting vaccines but with little specific consideration.[8]

Given the vaccines industry's specificities and complexities, there is a need for an analysis of what would make the EU region more attractive.[9] Only by understanding the challenges facing the vaccines industry in the EU is it possible to develop the policy priorities needed to secure the region as a worldwide leader in vaccine innovation and ensure a sustainable ecosystem.

1.2. Approach

The research-based vaccine industry is highly successful at developing life-saving vaccines. There is a rich pipeline of vaccines in development. A review of Vaccine Europe members found that of the 100 vaccine candidates in the pipeline in July 2022, 92 were for prophylactic vaccines and 8 were for therapeutic vaccines.[10] Given the differences in the policy environment for therapeutic vaccines to prophylactic vaccines, this report focuses on improving the attractiveness for innovative prophylactic vaccines across classical and next-generation technology platforms (see Figure 1).

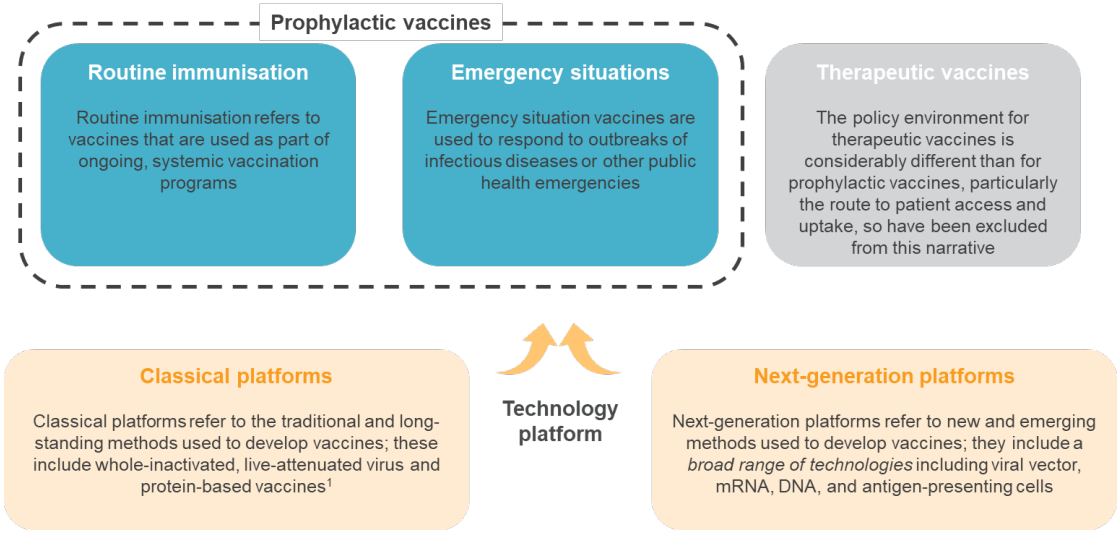
7 EU Vaccine Industry Roundtable 2019. Available at: https://irp-cdn.multiscreensite.com/4b9fd501/files/uploaded/kENUP%20Vaccine%20Roundtable%20Findings%207-Sep-2019%20WEB.pdf

8 European Commission. (2020). Pharmaceutical Strategy for Europe. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52020DC0761

9 EU Vaccine Industry Roundtable 2019. Available at: https://irp-cdn.multiscreensite.com/4b9fd501/files/uploaded/kENUP%20Vaccine%20Roundtable%20Findings%207-Sep-2019%20WEB.pdf

10 Vaccines Europe Pipeline Review 2022

Figure 1: Innovative prophylactic vaccines and associated technology platforms



Source: CRA analysis

To understand the current state of attractiveness of the vaccines industry in the EU and potential policy reforms to improve this, the research approach involved three key steps:

1. First, a literature review was undertaken to identify the key drivers affecting investment and identify recent trends and policy challenges affecting the EU vaccines industry[11]
2. Second, quantitative evidence was collected on factors affecting investment decisions to see how the environment is changing. The EU policy environment was compared to other regions, including the US, to identify implications on investment and performance
3. Finally, an interview programme was undertaken with 11 VE members to validate the investment drivers and challenges for vaccines, understand the impact of the policy environment on investment decisions and identify policy asks to improve attractiveness.

2. Investment drivers for Vaccines

Fostering future vaccine innovation requires a healthy ecosystem that recognises the benefits of the vaccines industry and incentivises industry investment. The activities involved in research and development of new vaccines are incentivised by (1) supply-side policies - industrial policy supporting basic research, enabling clinical development, and regulatory

11 The literature review was conducted over a 4-week period during January and February 2023 and included a search of academic databases, a grey literature search to identify reports which were not published in academic journals and a supplementary search which included a targeted Google search and checking the references of relevant publications. We used the following key search terms: vaccines; vaccine market; investment; attractive; attractiveness; European Union; EU; pharmaceutical industry; development; manufacturing; research; innovation; regulatory; access; funding; immunisation. Our searches identified over 300 publications, of which 57 were selected for further review due to their relevance.

approval, and (2) demand-side policies, ensuring national recommendations are issued for interventions in due time, with appropriate demand planning to support supply. Adopting innovation in a timely manner requires appropriate reimbursement policies and implementation of immunisation programmes to ensure interventions reach target populations. This has commonly been presented as an interconnected value chain.[12]

Looking along the vaccines value chain we can connect the factors that drive investment to the policies that increase attractiveness. Table 1 sets out the key investment drivers for vaccines across each phase of the value chain.

Table 1: Key investment drivers for vaccines across the value chain

Value chain	Key investment drivers
Research	• Vaccine research contributions from public/private partners, e.g., governments, venture capitals • Push incentives to stimulate research, e.g., grants, tax breaks • Innovation clusters, i.e., location and performance of existing research footprints
Development	• Skill of vaccine development workforce • Efficiencies in setting up clinical trials, e.g., approval timelines • Enabling digital infrastructure, such as e-health registries and high-quality RWE generation
Manufacturing	• Skill of vaccine manufacturing workforce • Infrastructure capabilities which support continuous improvement in production • Incentives to establish and/or transform vaccine manufacturing capacity (e.g., green/digital transition) • Effective demand forecasting • Availability of local public-private partnerships to support vaccine manufacturing
Regulatory	• Regulatory expertise and capabilities in assessing novel vaccines • Harmonised regulatory requirements for vaccine quality, efficacy and safety • Availability of alternative pathways for regulatory assessment • Sufficient and predictable Intellectual Property protection
Access	• Pull incentives which improve market certainty • Expertise and use of appropriate models in vaccine assessment • Access environment that encourages vaccine innovation • Sufficient budgets to purchase and implement immunisation programs across the life-course

12 Ilin, I et al (2022). Innovation Ecosystem Model of Vaccines Lifecycle Management. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9906693/

- Immunisation programs with sufficient flexibility and funding to adopt innovative vaccines in a timely manner
- Prevention policies to increase vaccination rates and reduce hesitancy

Source: CRA analysis based on the literature review and interviews with VE members

By recognising these investment drivers and providing support to the EU vaccines industry in global policy debates, the EU can support vaccine innovation. This will help ensure that the European population benefits from innovative vaccines, whilst also achieving most of the Sustainable Development Goals and covering the key principles of ESG (environmental, social and governance).[13]

3. Vaccine market attractiveness in the EU

In determining market attractiveness in the EU, we need to take into account that EU Member States are responsible for organising and delivering health services and care. The EU's role in health policy is therefore complementary to national policies and aims to:[14]

- Protect and improve the health of EU citizens
- Support the modernisation of health infrastructure
- Improve the efficiency of the EU's health systems
- Strengthen preparedness and response measures to cross-border health threats

Here, we review each phase of the value chain to identify the policy challenges affecting the industry and set out the implications on attractiveness.

3.1. Research

The EU is a global leader in vaccine research, with many of the world's largest vaccine companies having established research facilities within the region. This is due to the presence of several key investment drivers across certain countries, including innovation clusters in Belgium and France, and a strong research ecosystem that has been supported by national government funding.[15] The research strength of the EU vaccines industry was highlighted during the COVID-19 pandemic, which saw nearly half (47%) of patent applications for COVID-19 vaccines coming from European companies.[16]

13 Gavi, the Vaccine Alliance. Sustainable Development Goals. Available at: https://www.gavi.org/our-alliance/global-health-development/sustainable-development-goals

14 European Council. EU Health policy. Available at: https://www.consilium.europa.eu/en/policies/eu-health-policy/

15 CRA interviews with VE members

16 European Federation of Pharmaceutical Industries and Associations (2022). Getting the world vaccinated against COVID-19. Available at: https://www.efpia.eu/media/637039/efpia-vaccines-infographic-may-2022-1.pdf

However, there are a number of challenges facing early-stage research in the EU, which have led to some companies to focus their research investments in other regions.[17] This is particularly concerning when we consider the development of small and medium-sized enterprises (SMEs) investing in vaccine research. A notable challenge facing the EU vaccines industry is the ***difficulty early-stage actors face in raising capital due to limited exit opportunities*** (that exist in other parts of the industry, allowing investors to crystallise gains earlier in the development process). Vaccine development is highly complex and requires significant investments of both time and capital. These factors can create concerns about the return on investment, which in turn, can make it difficult to raise funding for vaccine research, particularly for SMEs that are heavily reliant on external funding. The lack of exit opportunities in the EU reduces the availability of funding, creating a barrier to innovation and hindering the development of new vaccines.

Research into new targets is enabled by next-generation technology platforms, which have the potential to develop vaccines for new diseases or accelerate the time of development.[18] Another challenge is the ***lack of sufficient incentives to diversify vaccine technology platforms***. In the EU, there is currently limited support at both the EU and national level, compared to other regions, for vaccine research into technology platforms, discouraging researchers from investing in new technologies and risks preventing future innovation. In addition, there are often ***significant barriers to receiving EU-level funding***. For example, the EC's Health Emergency Preparedness and Response Authority (HERA) is a new agency to support the development of medical countermeasures, including vaccines, for future health threats. However, there are already concerns that securing funding from HERA can be challenging due to extensive conditions and a complex, non-transparent decision-making process which focuses more on public accountability than the value of innovation.[19,20] Barriers to EU-level funding make it challenging for companies to secure investment for their research activities, negatively impacting vaccine innovation.

Lastly, there is a ***current shortage of skilled workers for vaccine research across the EU***. Given that vaccine research is a highly complex and technical process, it is essential that workers have the necessary specialised skills and knowledge. A recent gap analysis of vaccine R&D in Europe involving over 50 organisations highlighted the need for greater access to workers with technical expertise to support vaccine research in Europe.[21] The absence of skilled workers reduces the attractiveness of the EU as a region for vaccine research and forces companies to consider other regions for investment.

17 CRA interviews with VE members

18 Van Riel, D., & de Wit, E. (2020). Next-generation vaccine platforms for COVID-19. Nature materials, 19(8), 810-812.

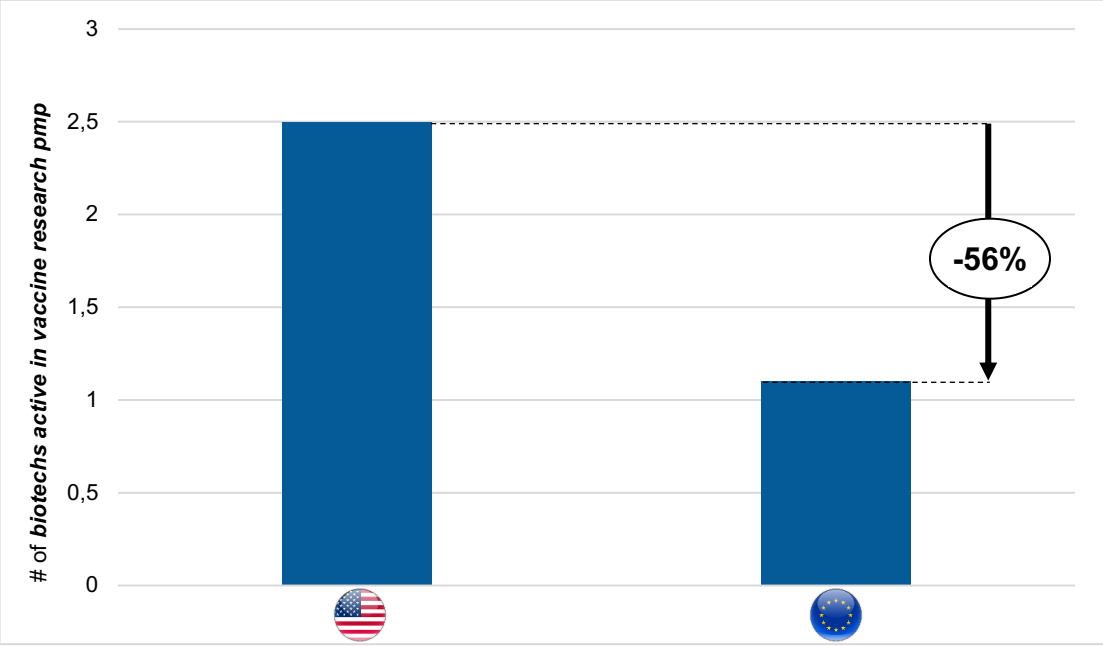
19 Covid-19 Response. Health Emergency Response Authority (HERA). Available at https://covid19response.org/hera/

20 Valneva position paper on vaccine policymaking in Europe [to be published]

21 Jungbluth S et al (2022). A gaps-and-needs analysis of vaccine R&D in Europe: Recommendations to improve the research infrastructure.

The research challenges facing the EU vaccines industry are evident in the ***relatively low number of biotechnology companies*** (biotechs) in the EU that are actively engaged in vaccine research compared to other regions. Taking into account the EU's historical strength in vaccine development it is concerning that, as shown in Figure 2, there are 56% fewer biotechs involved in vaccine research in the EU compared to the United States (US). This indicates that the current EU research ecosystem is less attractive as a region for vaccine research, highlighting the need for action to address the aforementioned challenges of the EU vaccines industry.

Figure 2: Comparison of biotechs active in vaccine research, EU vs US, pmp[22]



Source: ClinicalTrials.gov

Notes: CRA conducted a review of ClinicalTrials.gov and a targeted literature search to identify biotech companies active in vaccine research. We then used company data to determine the location of their headquarters, which was used as the basis of the analysis.

The implications of Research challenges affecting the attractiveness of the EU vaccines industry

- Limited funding and incentives for vaccine manufacturers is a barrier to early-stage vaccine research needed to ensure continued innovation
- There is limited support for diverse vaccine types and platforms for a continued pipeline of innovation to maximize public health impact
- It is more challenging for the industry to innovate and upscale due to limited workforce capability

22 Pmp = Per million population

3.2. Development

The EU has traditionally been an important region for vaccine development, with approximately 22% of global vaccine clinical trials taking place in the EU over the last two decades.[23] This can be attributed to the relatively advanced clinical trial infrastructure present in many EU countries, which has provided a solid foundation for vaccine development. However, there are several key issues related to clinical development currently affecting the EU vaccines industry.

One of the main challenges reported for vaccine development in the EU is that ***clinical trial requirements can be extensive***. While clinical trial requirements are necessary to appropriately demonstrate the safety and efficacy of vaccines, when these requirements become increasingly burdensome they can prolong the development process and delay access to innovative vaccines.[24] This has been the case across some EU countries, where vaccine developers have been required to meet additional requirements (compared to other EU countries) to ensure that they can conduct clinical trials.[25] While the Clinical Trials Regulation[26] has recently been updated to reduce disparities between countries in their trial requirements, there is still a notable risk that the requirements for developers will still be extensive.

Considering the lengthy timelines for vaccines development, it is vital that processes are streamlined and efficient to deliver innovation quickly. In the EU, the ***speed of overall clinical trial timelines can be relatively slow***.[27] Supporting evidence for this in the literature was limited, however, it was frequently reported during the interview program. This challenge relates in part to the requirements which can delay the initiation of clinical trials, but it is also due to other factors such as difficulties in patient enrolment.[28]

Another related issue is the ***significant disparity in clinical trial approval timelines*** across Member States. While regulatory approval for trials can be relatively quick in some countries, in others this can be notably slow. A recent analysis found that the time to approve and set up a study was 100 days faster in the US than in some EU countries such as France and Italy.[29] This has a negative impact on clinical trials in the respective country and in the EU, as

23 CRA analysis of global clinical trials, further information can be found in Figure 3

24 Sertkaya, A et al (2014). Examination of Clinical Trial Costs and Barriers for Drug Development.

25 CRA interview with VE members

26 The Regulation aims to harmonise processes and requirements for the approval, assessment and supervision of clinical trials throughout the EU. Prior to its introduction clinical trial sponsors had to submit clinical trial applications separately to each national competent authority, whereas now one application is submitted. Further information can be found at: https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-regulation

27 CRA interview with VE members

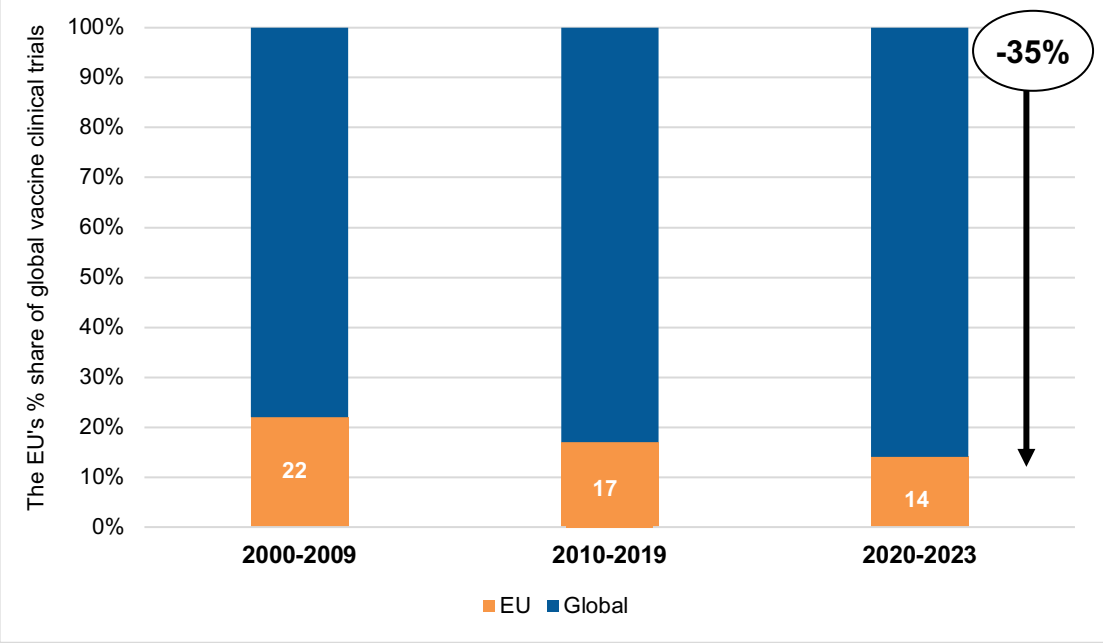
28 Goossens, H et al (2022). The European clinical research response to optimise treatment of patients with COVID-19: lessons learned, future perspective, and recommendations. The Lancet. Infectious diseases vol. 22,5

29 UK Government report on life science competitiveness indicators (2022). Available at: https://www.gov.uk/government/publications/life-science-sector-data-2022/life-science-competitiveness-indicators-2022

developers may prioritise conducting clinical development in other EU countries or outside the EU. As noted above, the Clinical Trial Regulation has been updated in an effort to harmonise approval timelines across Member States, however, it remains to be seen what impact this will have.

These challenges are reflected in the ***declining share of global vaccine clinical trials conducted in the EU over the last decade.*** Figure 3 shows that between 2000 and 2009, the EU accounted for 22% of global trials, whereas in 2010-2019, there was a notable decrease to 17%. This trend has continued during and after the COVID-19 pandemic, with the period of 2020-2023 registering a further drop to 14%. Overall since 2000, there has been a 35% decline in vaccine clinical trials conducted in the EU.

Figure 3: The EU's declining share of global vaccine clinical trials



Source: ClinicalTrials.gov

Notes: CRA conducted a review of vaccine clinical trials registered on ClinicalTrials.Gov between three time periods, 2000-2009, 2010-2019 and 2020-2023. Analysis of these trials led to the above findings.

Finally, there is ***limited real-world evidence (RWE) infrastructure to support development*** in the EU. RWE can play a key role in providing data on the safety and efficacy of existing vaccines. In turn, this can be used to optimise the development of innovative vaccines by improving their effectiveness and/or safety. Furthermore, RWE can provide context on vaccine uptake and use, which can support developers to make more informed decisions related to vaccine development. A recent academic review of real-world evidence in Europe found, there are significant disparities in RWE infrastructure, with several Member States (especially in

Central and Eastern Europe) lacking the capability to collect RWE.[30] It is worth noting that there are several ongoing EU initiatives aimed at improving the RWE environment in the EU e.g. DARWIN Initiative.[31]

The implications of Development challenges affecting the attractiveness of the EU vaccines industry

- Increasing complexity in clinical trial requirements reduces the attractiveness of conducting vaccine trials in the EU and may lead to trials being conducted elsewhere
- Lengthy clinical trial timelines in the EU may drive companies to conduct trials in regions with faster or simpler processes
- Disparities lead to certain countries being prioritised for vaccine clinical trials – there is scope for this to be improved through CT Regulation
- Limitations and heterogeneity in RWE infrastructure across MS can result in sub-optimal clinical development in the EU – this may be improved through ongoing EU initiatives

3.3. Manufacturing

The EU is home to many of the world's leading vaccine manufacturers and played an important role in supplying vaccines globally. This was seen very clearly during the COVID-19 pandemic – by January 2022 the EU had produced ~40% of the world's COVID-19 vaccine exports.[32]

Despite this, there are a number of key manufacturing challenges impacting the attractiveness of the industry. Firstly, there is ***often limited funding support and effective engagement with public institutions*** – in particular, these institutions can be less willing to engage with industry stakeholders than in other jurisdictions. Currently, there are no specific EU funding mechanisms to support the development of manufacturing sites in Member States.[33] Related to this is the fact that there are minimal ***incentives for developing vaccine manufacturing infrastructure.*** Both of these challenges can prevent companies from improving or expanding their manufacturing capabilities which may be needed to produce innovative vaccines, meet public demand and prevent delays and shortages. To illustrate the difference between regions, we can look at evidence regarding the EU's post-COVID-19 budget for HERA. Unlike the US, where BARDA, the initiative supporting the development of medical countermeasures has seen its funding increase by 38% to $823m, HERA's budget has remained flat at $317m. This

30 Kamusheva et al (2022). Using real-world evidence in healthcare from Western to Central and Eastern Europe: a review of existing barriers. Available at: https://becarispublishing.com/doi/10.2217/cer-2022-0065

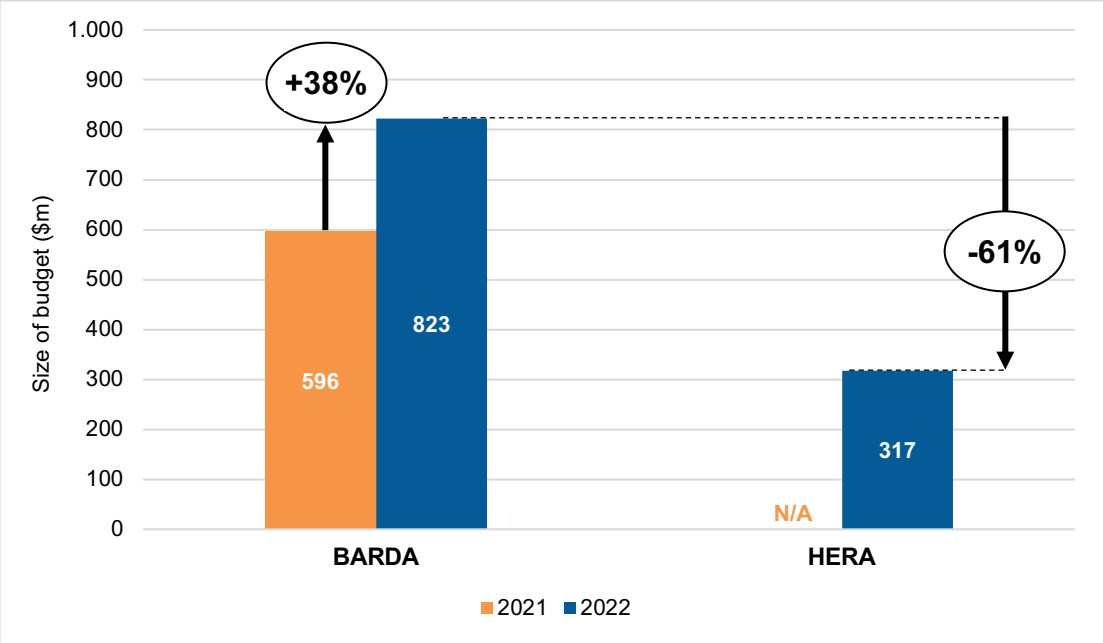
31 European Medicines Agency (2023). Overview of DARWIN EU. Available at: https://www.ema.europa.eu/en/about-us/how-we-work/big-data/data-analysis-real-world-interrogation-network-darwin-eu

32 European Federation of Pharmaceutical Industries and Associations (2022). Getting the world vaccinated against COVID-19 – version February 2022 Available at: https://efpia.eu/media/636690/efpia-vaccines-infographic-february-2022.pdf

33 CRA interview with VE members

represents a 61% smaller budget to fund related activities such as improving vaccine manufacturing (see Figure 4). However, it is worth highlighting that HERA is in its relative infancy given that it was only set up in 2021, and its introduction should be seen as a step in the right direction.

Figure 4: Comparison of HERA and BARDA budgets post-COVID-19



Source: U.S. Department of Health & Human Services (2022). Budget in Brief - Strengthening Health and Opportunity for All Americans. Accessed at https://www.hhs.gov/sites/default/files/fy-2022-budget-in-brief.pdf

Another reported challenge affecting the industry is that ***manufacturing quality control processes and requirements are suboptimal and lack harmonisation.*** These processes are vital to ensure that vaccines are safe, effective and produced to a high standard. However, variations and complexity can lead to delays and/or shortages, as well as increased production costs and inefficiencies.[34] One example of the complexity of the EU manufacturing environment is that in order to meet EU packaging and language requirements, manufacturers have to develop up to 16 different packages – this contrasts to the US where only 1 type of pack can be used.[35]

Finally, it is reported that many ***national manufacturing infrastructures across the EU are suboptimal, with significant disparities between Member States in their manufacturing capabilities***. This suggests that the overall EU ecosystem is not well-placed to support manufacturing. This is demonstrated by a recent analysis by the European Commission

34 CRA interview with VE members

35 Pasté, M, et al (2022). Addressing vaccine supply challenges in Europe: expert industry perspective and recommendations. Health Policy 126.1

highlighting that there is a considerable concentration of manufacturing bases in a small number of countries across the EU such as Belgium, Germany and France.[36]

The implications of Manufacturing challenges affecting the attractiveness of the EU vaccines industry

- The limited availability of funding and other incentives to support manufacturing, alongside the lack of willingness of public institutions to engage with industry reduces the attractiveness of the EU as a region for manufacturing
- Challenges related to complex manufacturing requirements and suboptimal infrastructure can reduce the efficiency and sustainability of the EU's vaccine supply chain - this may limit the emergency response to vaccines shortages in the event of sudden outbreaks

3.4. Regulatory

The European Medicines Agency (EMA) is one of the leading health regulators in the world and plays a key role in ensuring the safety and effectiveness of vaccines in the EU. However, the EU's regulatory system has notable challenges which impact its ability to assess vaccines relative to other healthcare technologies. One of the key issues is the ***comparatively limited flexibility/utilisation of expedited regulatory pathways for vaccines relative to other regions.*** These pathways allow for vaccines (and other medicines) to move through the regulatory process in a timely manner, contributing to faster population access to innovative vaccines. Since 2015, the EMA has leveraged expedited pathways for ~17% of non-COVID-19 vaccines.[37] This is in stark contrast to the FDA, which has utilised these mechanisms for >65% of vaccines. According to our interviews there can be ***limited understanding/acceptance of vaccines that leverage next-generation platforms.*** Again, this acts as a considerable barrier to timely population access to innovative vaccines by slowing/hindering assessment timelines. Evidence of this can be seen in European regulatory assessments which have required vaccines using next-generation platforms to demonstrate higher efficacy and/or safety vs. existing vaccines.[38]

There also appears to a missed opportunity in terms of utilising the ***learnings from the COVID-19 pandemic.*** These have not yet translated into faster regulatory assessment post-pandemic. During the pandemic, median regulatory approval times for COVID-19 vaccines were less than 2 months – this was achieved by leveraging various regulatory procedures such as rolling reviews and by prioritising workforce resources. Despite these successes, approval timelines

36 European Commission. (2021). EU vaccines strategy: Ensuring access to safe vaccines against COVID-19. Available at: https://ec.europa.eu/info/live-work-travel-eu/coronavirus-response/public-health/eu-vaccines-strategy_en

37 CRA conducted a review of vaccines recently approved by EMA and the FDA to identify the extent of utilisation of expedited pathways for vaccines

38 EU Vaccine Industry Roundtable 2019. Available at: https://irp-cdn.multiscreensite.com/4b9fd501/files/uploaded/kENUP%20Vaccine%20Roundtable%20Findings%207-Sep-2019%20WEB.pdf

post-pandemic have not shortened compared to before the pandemic, with the median time to approval still ~11 months.[39] The current inability to translate the learnings from the pandemic is likely hindering population access to innovative vaccines. However, as part of the EC's revision of the General Pharmaceutical Legislation, measures to reduce regulatory assessment timelines, such as the increased use of rolling reviews and temporary marketing authorisations, have been proposed.[40]

The implications of Regulatory challenges affecting the attractiveness of the EU vaccines industry

- Comparatively limited regulatory flexibility may lead to developers prioritising approval in other countries and regions, which in turn can result in slower access to innovative vaccines
- Lack of familiarity with new platforms can lead to higher evidence thresholds for assessing safety and efficacy; this acts as a barrier to timely regulatory approval
- Failure to improve regulatory resources and efficiency to ensure timely approval of innovative vaccines risks their timely access

3.5. Access

The access environment for vaccines (and other health technologies) is a Member State competency, but the EU can play a supporting role in improving vaccine uptake and equity. Currently, the EU market access environment for vaccines is fragmented. A key issue is that ***national vaccine committees are slow to make recommendations contributing to significant disparities in reimbursement timelines across Member States***. Evidence for this demonstrates that in 30% of EU countries, it often takes 6+ years for a new vaccine to be reimbursed.[41] This also highlights that immunisation programs are slow and lack dynamicity to adopt innovative vaccines, resulting in considerable delays to population access. Another challenge relates to the ***budget setting process for vaccines and vaccinations, combined with tendering practices that can be highly punitive.*** Currently, 77% of Member States spend less than 0.5% of their healthcare budget on immunisation, highlighting the relatively low prioritisation vaccines are given in health expenditure.[42] These funding challenges create uncertainty for developers of innovative vaccines and can disincentivise future research.

Across the EU, ***vaccine hesitancy continues to be an issue post-COVID-19***, with a recent survey finding that some countries such as Poland, now have notably higher hesitancy levels

39 CRA conducted a review of vaccine approval timelines (measured as the length of time between application date and approval) before, during and after the pandemic for both the EMA and FDA

40 European Commission (2023). Reform of the EU pharmaceutical legislation. Available at: https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe/reform-eu-pharmaceutical-legislation_en#:~:text=The%20revision%20aims%20to%20achieve,they%20live%20in%20the%20EU

41 Laigle, V, et al. (2021). Vaccine market access pathways in the EU27 and the United Kingdom− analysis and recommendations for improvements. Vaccine 39.39

42 Faivre, P, et al. (2021). Immunization funding across 28 European countries. Expert review of vaccines 20.6

than global averages.[43] This has a negative impact on vaccine uptake and similarly to the aforementioned funding challenges can reduce the incentive for companies to develop new vaccines.

Finally, there are ***considerable disparities in vaccine monitoring infrastructure across Member States***, with significant heterogeneity in monitoring policies and limited guidance at the EU level.[44] Vaccine monitoring can play a key role in capturing information that can be used by a range of stakeholders to improve public health. This includes tracking the effectiveness of vaccines e.g., in different segment populations, identifying whether vaccine coverage targets have been met, and supporting demand forecasting.

The implications of Access challenges affecting the attractiveness of the EU industry

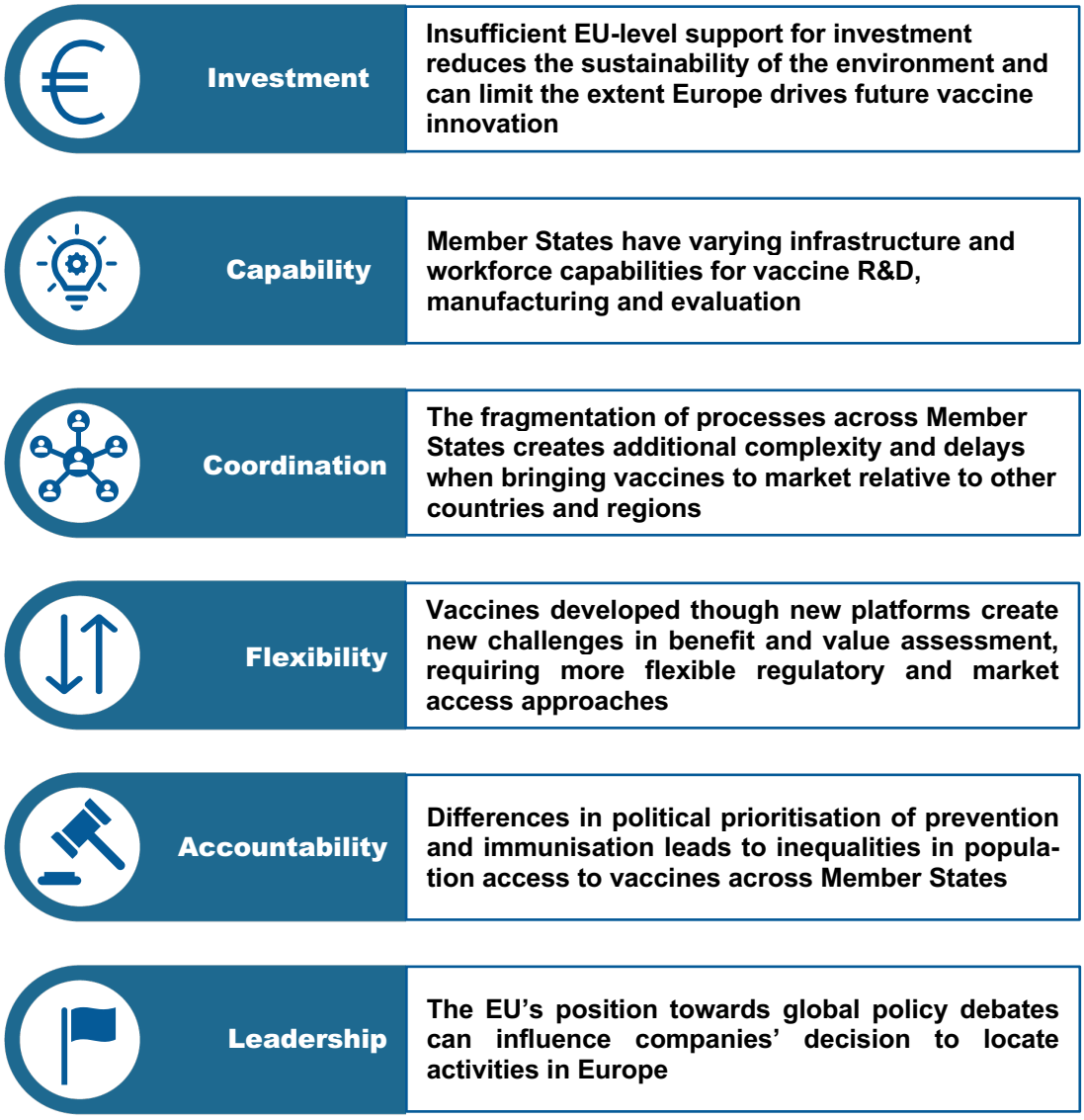
- The access environment for vaccines in the EU is highly fragmented and introducing uncertainties for vaccine manufacturers
- Slow recommendation and funding timelines delay population access to innovative vaccines and low vaccine uptake may reduce incentive to research and develop new vaccines
- Suboptimal vaccine monitoring infrastructure prevents EU/MS from identifying whether vaccine coverage rates are met, with implications on demand forecasting

3.6. Summary

In summary, from the investment drivers and the key challenges in each phase of the value chain there are several factors which impact the attractiveness of the EU's vaccine industry. Due to the nature and structure of the EU healthcare policy environment, they can also be grouped into thematic cross-cutting challenges that affect the health and attractiveness of the EU ecosystem and impact multiple aspects of the vaccine value chain. We have set out these thematic challenges below.

43 Lazarus, Jeffrey V., et al. (2023). A survey of COVID-19 vaccine acceptance across 23 countries in 2022. Nature Medicine

44 Díez-Domingo, Javier, et al. (2022). The value of public-private collaborative Real-World Evidence platforms to monitor vaccine performance post-authorization: DRIVE-a European initiative. Expert Review of Vaccines 21.12



4. Recommendations to improve attractiveness and improve the vaccines ecosystem in the EU

4.1. Policy priorities and asks

Based on the key findings and supporting evidence identified throughout the research and the input from the industry interviews, we developed policy priorities corresponding to the cross-cutting challenges, to improve the attractiveness of the vaccines industry in the EU. Each of these objectives is associated with specific policy asks, as set out in Table 2.

Table 2: Policy asks to improve the attractiveness of the EU's vaccines industry

Challenge	Objective	Policy asks
Investment	There is **sufficient levels of funding and investment** to sustainably support vaccine innovation	• **Greater adoption of innovative financing mechanisms** and simplified funding pathways to support developers • Commitments to **increase HERA's budget and greater availability of incentives** to support vaccine R&D and manufacturing, and ensure diversification of future innovation given the risk/complexity of industry business model • Reposition funding immunisation as a **healthcare investment and set/implement targets for vaccination coverage**
Capability	There is a need for investment in the **appropriate infrastructure and skilled workforce** for vaccine R&D, manufacturing and assessment	• EU-level funding dedicated to **developing the digital environment** for clinical trials and manufacturing across MS • Support MS investment in developing **infrastructure in RWE collection and immunisation monitoring** • Facilitate best-practice sharing aimed at **upskilling EU vaccine workforce** and provide greater support to MS (e.g., GMP training) to improve R&D and manufacturing capabilities through green/digital transition. Greater European focus on the **benefits of an innovation hub model is needed**
Coordination	Ensure **processes are streamlined and harmonised**, where possible, to provide more timely population access to innovative vaccines	• **Streamlining of packaging regulation**, i.e., single package across the EU, and the leverage electronic Product Information Leaflet (e-PIL) • Develop **demand forecasting mechanisms** to enable manufacturers to better plan and encourage investment to optimise sustainable vaccine supply • Enable faster and more equitable access to vaccines across the EU through reducing **disparities in HTA assessment, NITAG review timelines and recommendations**

Flexibility	The **regulatory and access environment has the necessary flexibility** to support the assessment of innovative vaccines	• Greater flexibility in regulatory assessment and **availability of alternative approval pathways** • Greater adoption of **expedited regulatory pathways** in non-emergency contexts to facilitate faster access to innovation
Accountability	EU-wide policy **prioritisation of prevention and immunisation** to ensure greater equality in population access to vaccines	• EU to play a greater role in initiatives to **reduce vaccine hesitancy rates** and improving vaccine coverage • **Greater MS accountability in vaccine-preventable diseases & immunisation** • EU and MS should **ensure the necessary regulatory & NITAG expertise and resources are in place** to support vaccine assessment; furthermore, there should also be greater transparency in the decision-making process
Leadership	The EU **demonstrates consistent support of the EU vaccines industry** in global policy debates	• **Ensure policy prioritisation for immunisation,** recognising the benefits of vaccination throughout the life-course • Greater recognition of the **strategic value of the vaccine sector** in the EU, ensuring that the EU plays a stronger and more supportive role in global policy debates

4.2. Conclusion

The objective of this report was to consolidate views on the key drivers of vaccine investment, assess the current attractiveness of the EU vaccines industry and develop policy priorities to support improvements in the industry's attractiveness. Both supply-side and demand-side factors play a critical role in driving vaccine investment. Greater recognition of these factors in policy decision-making would improve the overall health of the vaccine ecosystem in the EU.

While the EU vaccine industry has notable strengths, there is some evidence of its comparative decline and reduced attractiveness across the vaccine value chain. This includes a reduction in global vaccine clinical trials being conducted in the region and a lack of understanding regarding new platforms. Furthermore, we find that there are a number of cross-cutting challenges, including investment, capability and flexibility that negatively impact the attractiveness of the industry.

If these challenges are recognised, and appropriate policies are prioritised, the EU will continue to be a global leader in the development of innovative vaccines to the benefit European citizens and the economy.