STUDY

Requested by the COVI Committee

European Parliament

Mapping of long-term public and private investments in the development of COVID-19 vaccines

Policy Department for Economic, Scientific and Quality of Life Policies
Directorate-General for Internal Policies
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Mapping of long-term public and private investments in the development of COVID-19 vaccines

Abstract

This study provides a mapping of funds contributed by different actors for the R&D and the expansion of the production capacity of COVID-19 vaccines, with a focus on those authorised in the EU. Nine vaccines are examined. It is found that governments, mainly the US (with some not-for-profit entities) decisively supported corporate investments, either for R&D, manufacturing, or both, by nearly EUR 9 billion, i.e. on average EUR one billion of grants per vaccine, with, however, vast variance across companies. Moreover, almost EUR 21 billion was allocated to companies through Advance Purchase Agreements. While the EU and MS support through Advance Purchase Agreements was key to de-risk the production of vaccines, the role of EU and MS support in directly supporting R&D was marginal compared with the US federal government. The study assesses the necessity for continuing public support to R&D on vaccines for SARS-CoV-2 future variants of concern and possibly other coronaviruses. After highlighting current market failures, new incentive mechanisms in the public interest for vaccine R&D are suggested to grant equity and accessibility, as well as rewards in line with risks.

This document was requested by the European Parliament's Policy Department for Economic, Scientific and Quality of Life Policies to support the Special Committee "COVID-19 pandemic: lessons learned and recommendations for the future" (COVI).

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LIST OF ABBREVIATIONS

APAs	Advance Purchase Agreements
APERIM	Advanced Bioinformatics Platform for PERsonalised Cancer Immunotherapy
BARDA	Biomedical Advanced Research and Development Authority
CEPI	Coalition for Epidemic Preparedness Innovations
CERN	European Organization for Nuclear Research
CMO	Contract Manufacturing Organisations
CMMID	Centre for Mathematical Modelling of Infectious Diseases
COVAX	Covid-19 Vaccines Global Access
CoV	Corona Virus
COVI	European Parliament's Special Committee "COVID-19 pandemic: lessons learned and recommendations for the future"
COVID-19	COronaVIrus Disease 19/SARS-CoV-2
CRO	Contract research organisation
DG RTD	Directorate-General for Research and Innovation
DoD	Department of Defense
EC	European Commission
ECA	European Court of Auditors
ECDC	European Centre for Disease Prevention and Control
EDCTP	European and Developing Countries Clinical Trials Partnership
EEA	European Economic Area
EFSI	European Fund for Strategic Investments
EIB	European Investment Bank
EIC	European Innovation Council

EIT	European Institute of Innovation and Technology
EMA	European Medicines Agency
EMBL	European Molecular Biology Laboratory
EP	European Parliament
ESI	Emergency Support Instrument
EU	European Union
FDA	Food and Drug Administration
GAO	Government Accountability Office
GAVI	Global Alliance for Vaccines and Immunisation
H2020	Horizon 2020
HERA	European Health Emergency Preparedness and Response Authority
HHS	Health and Human Services
IACT	Immunostimulatory Against Antibodies for Cancer Therapy
IDFF	Infection Diseases Financial Facility
IPC	Infection Prevention and Control
IPR	Intellectual property rights
IRBM	Italian Biomedical Research Company
LSHTM	London School of Hygiene & Tropical Medicine
PI	Principal Investigator
MS	Member States
MERIT	Mutanome Engineered RNA Immuno-Therapy
MERS-CoV	Middle East Respiratory Syndrome Coronavirus Infection
mRNA	Messenger Ribonucleic Acid

NAIAD	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
NPI	Non-Pharmaceutical Interventions
OWS	Operation Warp Speed
RBD	Receptor-Binding Domain Fusion Heterodimer
R&D	Research and Development
SARS-CoV-1	Severe Acute Respiratory Syndrome Coronavirus 1
SARS-CoV-2	Severe Acute Respiratory Syndrome COronaVIrus 2 (*see also* COVID-19)
SUMMIT	Stepping Up mRNA Mutanome Immunotherapy
UN	United Nations
VC	Venture capital
WHO	World Health Organization

EXECUTIVE SUMMARY

Background

The COVID-19 pandemic posed a twofold challenge to governments and the pharmaceutical sector: to develop new vaccines for the novel threat and to produce billions of doses in a very short timespan. Thanks to a joint effort, both goals were reached. Although usually it takes a decade or longer, the first vaccines for the new diseases were developed in less than 12 months: as of February 3, 2021, there were 289 experimental COVID-19 vaccines in development, including 20 in phase 3 of clinical testing (Wouters, 2021). By March 2021, less than a year after the pandemic had hit European countries, more than 34 million doses had been administered in the European Union, with this number rapidly increasing over the next weeks (by the beginning of April 2021, 74 million doses were administered in the EU, and one year later more than 844 million doses).[1]

These extraordinary achievements were reached thanks to two decisive factors: a) more than two decades of basic research and, b) to huge investments in the pandemic period by a range of funders. For both these aspects a strong involvement of the public sector was key. Indeed, basic research and early-stage development are frequently supported by the public sector (see, among others, Galkina et al., 2018). During the pandemic an unprecedent amount of resources were also deployed for the financing of clinical trials and scaling-up manufacturing capabilities, and Advance Purchase Agreements (APAs).

However, **there is only limited understanding of the ultimate funding sources that were actually involved. A clear analysis of the funding for COVID-19 vaccines could provide critical insight for policy makers who need to address existing and future challenges relating to variants and R&D incentives.**

Against this background, the European Parliament's Policy Department for Economic, Scientific and Quality of Life Policies has requested this study to support the Special Committee "COVID-19 pandemic: lessons learned and recommendations for the future" (COVI) of the European Parliament (EP).

Aim and methodology

The main objectives of the study are (i) to map the funding for R&D and the expansion of the production capacity for the manufacturing of major COVID-19 vaccines in order to estimate the relative importance of funds by different actors and (ii) to ascertain the need for continuing support COVID-19 vaccines with public funds. This study focuses on funding allocated during the pandemic to the seven vaccines authorised for use in the EU (Comirnaty, from Pfizer and BioNTech; COVID-19 Vaccine Valneva; Nuvaxovid, from Novavax; Spikevax, from Moderna; Vaxzevria, from AstraZeneca; Jcovden, from Janssen; VidPrevtyn Beta, from Sanofi Pasteur), and also to COVID-19 Vaccine Hipra (currently under rolling review, it would be the only vaccine entirely developed and produced in Europe and for this reason it has been analysed in the report), and CVnCoV from CureVac (although it has been withdrawn from rolling review, it received important public financing, thus being relevant for our analysis). The study does not take into consideration funds previously invested in basic research or some relevant applications and subsequently exploited to develop the new vaccines, although this was very relevant for the rapid development of the vaccines and played a crucial role for some of them (notably, Comirnaty, Spikevax and Vaxzevria).

[1] https://ourworldindata.org/grapher/covid-vaccine-doses-by-manufacturer.

The methodology employed to draft the study combines desk research, statistical analysis and interviews involving 30 expert stakeholders, belonging to three groups: (1) representatives of pharmaceutical companies involved in the production of COVID-19 vaccines; (2) public health experts and scientists from the EU and the US; and (3) public decision makers and experts within institutions, both at the EU and national level, as well as from the US. The interviewees were selected through a combination of purposive and snowball sampling. The interviews took place between December 2022 and the first days of March 2023. Anonymity was ensured to the respondents' opinion and evidence provided, but the names of the interviewees are reported when we were authorised by them to do so.

In order to retrieve information on funding for R&D and extension of the production capacity for the manufacturing of vaccines, the first step was to investigate existing publicly available sources, such as public repositories, reports from the most relevant stakeholders, and scientific publications. This information was complemented and double-checked by interviews with relevant funders and pharmaceutical companies. Summary fiches summarising available data on funding associated with each vaccine were shared with the producers in order to give them the opportunity to amend them. Details about the feedback received by companies, if any, are reported.

The compiled data on funding must be considered a best estimate, since much information on public and private investments is kept confidential, and publicly available data are fragmented and different sources are often challenging to reconcile.

Key Findings

Collected evidence suggests that from 2020 to early 2022, combined support in various form by external funds (including mostly funds from governments, but also from some philanthropic entities, third private parties, international public-private partnerships and multilateral development banks) **for R&D and the expansion of production capacity for the nine vaccines included in the study were in the range of EUR 9 billion. Additionally, there were about EUR 21 billion of APAs. While the information about R&D expenditures sustained by companies for COVID-19 vaccines is not publicly available, our estimate is in the range of EUR 4-5 billion for the period 2020-2021**.

The governments and other public actors (hereafter also referred to as public sector) represent over 80% of the total external funds mapped. The public sector support took the form of grants, loans, and APAs, (each with a different incentive role) representing, respectively, 27%, 0.6% and 54% of total external funds mapped. The remaining funds were provided by philanthropic entities, third-party private companies, public-private partnerships, and the European Investment Bank (EIB). The share of public funding (i.e., provided by public entities at different governmental levels) over total funding strongly varies from company to company, going from zero for Pfizer (but the vaccine, Comirnaty, was co-developed with BioNTech, which received substantial public support, so that even Comirnaty was co-financed by the public sector), to 100% for Moderna. On average, public funding covered not less than 50% of cumulated R&D expenditures, which places governments as the principal partner in the development of COVID-19 vaccines.

Such direct and indirect public support to R&D and expansion of the production capacity considerably de-risked corporate investment in the development and manufacturing of vaccines, and consequently increased returns to investors particularly for those firms that did not claim to price the dose on a cost base. APAs, played an important de-risking role, shifting part of the risk from private firms to the public sector as these agreements were signed before vaccine approvals. Moreover, APAs allowed firms to better plan their production capacity and logistics. There is no evidence, however, that they incentivised R&D, which for most companies relied on earlier public sector grants.

Looking at funds tracked**, the role of the EU plus Member States in funding R&D was marginal compared to the US government** (respectively, 1% and 24.7% of total external funds mapped for R&D support only. If loans are also considered the respective shares are 2.8% and 24.3%). If external support granted for manufacturing vaccines is also considered, the role of the EU and Member States represents 10% versus 80% of the US. Adding loans, the respective shares become 11.9% and 78%. Indeed, the EIB played some role, mainly with a loan of EUR 100 million to BioNTech (preceded by another loan before the vaccine development), but also to other companies in the European vaccine arena. Such loans may have decreased the financing cost of R&D, manufacturing operations, and offered a credibility signal in the financial market for the companies.

EU role in supporting vaccine development revolved around APAs. Up to 2021, 8 APAs for 1.3 billion doses (excluding optional doses except for Sanofi-GSK) were signed by the EU and vaccine producers (including for the withdrawn vaccine CureVac). The cumulated value of such contracts is about EUR 6.8 billion, estimated with the leaked information from various sources on price per dose.

Looking into the future, according to experts, the SARS-CoV-2 virus is here to stay for at least the next ten years. Even in an optimistic scenario (where no new variant of concern or a new pandemic wave would emerge), rates of hospitalization and mortality remain non-negligible among the at-risk population, particularly the elderly and the fragile. Moreover, while existing vaccines offer a robust defence against severe illness, they suffer from some limitations, the most important ones being the declining immunity over a relatively short time span, and their limited resilience to virus mutations. Therefore, further R&D investments are needed to deal with COVID-19, its variants, and, possibly, other coronaviruses.

Scientific literature reviewed and experts interviewed for this study strongly suggest that R&D for COVID-19 vaccines should be sustained. Key research topics, according to some experts (but there is no consensus on all the items), include: (i) variant-proof SARS-CoV-2 vaccines; (ii) pan-sarbecovirus vaccines (i.e., against sarbecoviruses, the subgenus that includes all the SARS-like viruses); (iii) pan-betaCoV vaccines (i.e., against betacoronaviruses, which include sarbecoviruses, merbecoronaviruses like the one that causes Middle East Respiratory Syndrome (MERS), and two that now trigger the common cold); (iv) pan-CoV vaccines; v) needle-free vaccines. Beyond that, most experts mentioned the need to build a sophisticated monitoring system similar to that for influenza and to conduct studies to assess under-investigated topics on existing vaccines and comparative studies.

While there are market opportunities for both established pharmaceutical companies and newcomers, several of the research topics mentioned above would require R&D strategies that are not in the immediate interest of the industry to self-fund and perform due to high-risk and low returns. Hence, public support to R&D on COVID-19 vaccines, and possibly on other pandemic risks related to coronaviruses, is still needed. The crucial question is how this support should best be provided, in order to obtain adequate returns on investments for governments and taxpayers.

In this perspective, there are lessons to be learned from the recent experience in Europe, namely: (i) avoiding fragmentation and duplication of funding of R&D on COVID-19 vaccines; (ii) ensuring public support for clinical development of the next generation COVID-19 vaccines or vaccines protecting against unknown coronaviruses; (iii) creating a favourable regulatory and infrastructural environment for clinical trials in Europe; (iv) careful examination, in the public health interest, of the conditionalities of future R&D grants and de-risking mechanisms.

In conclusion, the study points out that action would be needed for the EU to have a prominent role in supporting the development of future coronavirus vaccines.

In the shorter term, a stable and clear legal EU framework for corporate R&D support on COVID-19 vaccines (and, more broadly, on vaccines for pathogens with pandemic potential) **should be designed**. This framework should include (a) an innovative template for IPR arrangements in the public interest when taxpayers' money supports R&D, (b) well-defined conditionalities on the location of production and logistics, and (c) fairer delivery arrangements and price affordability for European citizens and less-developed countries. Also, the role of HERA should be reconsidered. Indeed, the current design of HERA does not provide for the managerial and scientific strengths of the US Biomedical Advanced Research and Development Authority (BARDA) in the wider frame of the Administration for Strategic Preparedness and Response and cannot leverage on anything similar to the combined role of the NIH and BARDA (and other federal agencies) in the US.

In the long term, to radically change the EU approach to support frontier biomedical science, a previous study for the European Parliament (EP) (Florio et al. 2021) suggests exploring a more direct public intervention (as it was successfully implemented for space policy and other science-based sectors): **the creation of a pan-European R&D infrastructure and delivery organisation for medicines in certain critical areas, with the budgetary scale and scientific ambition comparable to the US NIH, combining EU and MS efforts.**

1. INTRODUCTION

This report at hands entitled "Mapping of Long-term Public and Private Investments in the Development of Covid-19 Vaccines" was requested by European Parliament's Policy Department for Economic, Scientific and Quality of Life Policies to support the Special Committee "COVID-19 pandemic: lessons learned and recommendations for the future" (COVI) of the European Parliament (EP).

1.1. Motivation of the study

At the end of 2019, a novel form of coronavirus disease, named COVID-19, caused by the SARS-CoV-2 virus, was first spotted in China. The virus proved to be highly contagious, and its initial strain was associated with a very high death toll. In early 2020, Italy was the first European country to be hit hard, followed by France and Spain, and eventually the virus spread to all EU countries and worldwide. The COVID-19 pandemic resulted in profound challenges to global public health.

In a race against time, a great number of research efforts were started with the aim of creating safe and effective vaccines. At the same time, production capacities had to be put into place to produce sufficient vaccine to inoculate a large part of the world population in a short time.

The development of a vaccine candidate usually requires considerable investments in research and development (R&D) and takes many years, most of which are spent in the three consecutive phases of clinical trials. In view of the urgency, a number of shortcuts were taken, such as carrying out parallel tests and using Emergency Use Authorization / Conditional Marketing Authorisation, while scaling up the manufacturing capacity already during the clinical tests. Unprecedented public and private financial investments were made, and scientific collaborations were put in place.

By the end of 2020, the first vaccines started to be used as part of a large-scale vaccination efforts and, according to the World Health Organization (WHO) vaccine tracker, as of December 2022, 50 vaccines have been approved for general or emergency use around the world and there were a further 230 vaccines in clinical or in pre-clinical development.

To accomplish these achievements, a massive amount of funding by a diversity of sources around the world was needed. Governments, international institutions, the private sector, research institutions and non-profits engaged in research activities, or their funding, and de-risking corporate investment.

However, there is only limited understanding of the funding sources committed and disbursed for the R&D and the investments to make the COVID-19 vaccines available. A clear analysis of the funding sources for COVID-19 vaccines could provide critical insight for policy makers who need to address existing and future challenges relating to SARS-Cov2 variants and R&D incentives. By "funding "we understand here a set of different mechanisms, each with a different role, which will be analysed in some detail.

1.2. Objective and scope of the study

The main objective of the study is to map investments both for the R&D and for the expansion of the production capacity for the manufacturing of selected major COVID-19 vaccines.[2] The list of vaccines which are considered in the study is shown in Table 1 below, and it includes the COVID-19 vaccines that were originally authorised and that can still be used in the EU. Moreover, information on two other

[2] In agreement with the European Parliament's Policy Department for Economic, Scientific and Quality of Life Policies, the study will not cover the mapping of semi-finished products and other linked products, such as syringes and vials.

interesting cases have been collected, i.e., CureVac and Hipra. The former, after having received support in various forms and from various bodies, including a loan from the European Investment Bank and an Advance Purchase Agreement signed with the European Commission (EC), has been withdrawn from rolling review.[3] Hipra, on the other side, is a vaccine currently under rolling review which was developed by a Spanish family-owned company. Hipra's COVID-19 vaccine is a bivalent vaccine based on an adjuvant recombinant protein. Despite its late arrival, the European Medicines Agency (EMA) decided to start the rolling review based on preliminary results from non-clinical data and clinical studies in adults which compared the immune response to the vaccine (measured by the level of antibodies against SARS-CoV-2) with that seen with the mRNA vaccine Comirnaty.

The study covers the following fields and answers the associated questions:

- **A mapping both of funding of R&D and the expansion of the production capacity for the manufacturing of COVID-19 vaccines, concentrating on the EU**. What was funded, and by whom? Where is the main research and development being performed, and what are the amounts involved? Which amounts were spent by firms, which by governments or other entities? How does this evolve with time?
- **The relative importance of funds invested into COVID-19 vaccines research by different actors**. What was the relative importance of funds invested into COVID-19 vaccines research by different actors, such as governments, international institutions, private sector, research institutions and non-profits?
- **The need for continuing support of COVID-19 vaccines with public funds**. Is there a need for further public support? Much of the current research seems to concentrate on adapting existing COVID-19 vaccines to the fast mutations of the virus. Which level of investment will be needed for this ongoing adaptation? Is there still a need for substantial public funding, as opposed to the availability of private funding?

In terms of geographical coverage, the focus of the study is mainly on the EU and, on the R&D public funding side, on the US, given their pivotal role. Most of public funding outside the US and the EU is not recorded, and most of the support at the level of individual countries is also not covered given the fragmentary nature of the evidence.

[3] A rolling review is a regulatory tool that EMA uses to speed up the assessment of a promising medicine or vaccine during a public health emergency. The rolling review continues until enough evidence is available for a formal marketing authorization application.

Table 1: The nine COVID-19 vaccines considered in the study

Vaccine	Platform	Use	Population				Phase achieved	Date of (conditional) authorization
			≥6 months	≥5 years	≥12 years	≥18 years		
Comirnaty (BioNTech and Pfizer)	mRNA	Primary vaccination	✓	✓	✓	✓	Authorised in EU	21/12/2020
		Booster		✓	✓	✓		
		Booster			✓	✓		
		Booster		✓	✓	✓		
Spikevax (Moderna)	mRNA	Primary vaccination	✓	✓	✓	✓	Authorised in EU	06/01/2021
		Booster			✓	✓		
		Booster			✓	✓		
		Booster			✓	✓		
Vaxzevria (AstraZeneca)	Adenoviral vector	Primary vaccination				✓	Authorised in EU	29/01/2021
		Booster				✓		
Jcovden (Janssen)	Adenoviral vector	Primary vaccination				✓	Authorised in EU	11/03/2021
		Booster				✓		
Nuvaxovid (Novavax)	Protein	Primary vaccination			✓	✓	Authorised in EU	20/12/2021
		Booster				✓		
COVID-19 Vaccine Valneva (Valneva)	Inactivated	Primary vaccination				✓ 18-50 years	Authorised in EU	24/06/2022
VidPrevtyn Beta (Sanofi Pasteur)	Protein	Booster				✓	Authorised in EU	10/11/2022
COVID-19 Vaccine HIPRA (HIPRA)	Recombinant Protein	Booster				✓ Adults fully vaccinated	Rolling review	/
CVnCoV (Curevac)	mRNA	Booster				✓	Withdrawn	/

Source: Authors, based on ECA (2022) and EMA website, last accessed February 9, 2023.

1.3. Structure of the study

The report is structured into three main sections. Section 2 presents the activities undertaken to conduct the study. It also discusses limitations of the research methodology. Section 3 discusses the findings of the research conducted and provides answers to the research questions by research topic. Section 4 presents the conclusions of the study. A set of Annexes complements the main body of the study. Annex I provides the list of relevant references and repositories consulted for the study. Annex II contains the interview questionnaires. Annex III contains the list of interviewees. Annex IV contains the summary fiches by company. Annex IV contains the list of projects funded through the first Horizon 2020 (H2020) emergency call.

2. METHODOLOGY & LIMITATIONS

This section presents the activities carried out to prepare the study, and its limitations.

2.1. Research methodology

The study has been carried out by combining three research methods, i.e., desk research, statistical analysis, and interviews. The table below shows how each method contributed to the three streams of research.

Table 2: Methods and research streams

	Q1 - Mapping of funding of R&D and the production of COVID-19 vaccines	Q2 - Relative importance of funds invested into COVID-19 vaccines R&D by different actors	Q3 - Need for continuing support COVID-19 vaccines with public funds
Desk research	✓		✓
Statistical analysis	✓	✓	
Interviews	✓		✓

Source: Authors' own elaboration.

2.1.1. Desk research

The **desk research** aimed at collecting and reviewing publicly available sources, including news, reports, academic articles, previous studies, and data repositories providing information on funding of R&D and the production of COVID-19 vaccines, as well as on the reasons (if any) for continuing support of these investments with public funds. A list of references and repositories consulted is included in Annex I, with the relevant web links. In order to guarantee that the identified sources cover the most relevant issues, we employ a systematic approach and methodology combining different strategies, which are laid out in the following:

- a list of the relevant keywords for online searching has been defined. The list has been enriched in an iterative process, where the results obtained from applying the search terms to the body of literature in scholarly databases such as REPEC and PUBMED or other repositories point to adding relevant keywords;
- publications by the most relevant stakeholders for contents relevant to the study topic have been screened. These include publications by the EC, the EP, the European Court of Auditors, ECDC, EMA, and other EU institutions, as well as some official publications by the governments of EU Member States. The reviewed literature also includes selected publications by international organisations, such as the Organisation for Economic Co-operation and Development (OECD) and the WHO, as well as relevant think-tanks and consultancies. The annual reports of pharmaceutical companies have also been reviewed, covering several years of reported R&D expenditures. To make sure that we include both official statements and innovative viewpoints, we also scan selected blog posts and conference proceedings relevant to the subject;

- additional references have been collected through advice from experts willing to share their knowledge with the principal investigator (PI) once informed about the study topic and/or interviewed as part of the study;
- once the relevant body of literature has been collected, the documents/publications have been classified by topics and keywords.

In order to retrieve information on funding for R&D and extension of the production for the vaccines listed in Table 1, the first step was to investigate existing databases such as those respectively provided by the Global Health Centre, G-FINDER, Policy Cures Research, Universities Allied for Essential Medicines (see Annex 1). The data collected were then supplemented with information made available in English by bodies directly involved in the funding (e.g. CEPI, BARDA, European Commission) and by the annual reports and balance sheets (retrieved from ORBIS database managed by Bureau Van Dijk[4]) of the individual pharmaceutical companies involved. It is still likely that data for some funders may be missing.

Where feasible, any repeated funding from/to the same entity has been tracked individually and aggregated only afterwards. Only funding with clear amounts and explicitly allocated to one of the vaccines considered has been included.

According to information available, the external funding mechanisms to incentivise the companies have been categorised as follow[5]:

- funds for research and development ("R&D only");
- funds for development and increasing production capacity ("R&D + manufacturing");
- Advance Purchase Agreements (APAs), i.e., dose purchases that were concluded before the vaccines received a recommendation for a conditional marketing authorisation.

Although APAs are not direct funding towards R&D, it is believed that they may have played a role in enabling pharmaceutical companies to de-risk the development and production of vaccines. On the other hand, purchases, in the strict sense, i.e., after marketing authorisation, were not included in the analysis, as they do not play a direct incentive role.

Moreover, it is also worth noting that:

- funds by public or not-for profit entities to support R&D or "R&D+manufacturing" may have taken the form of non-repayable support (i.e., grants) or repayable support (i.e., loans). Whenever possible and relevant we distinguish between these two forms of support. Conversely, private investments from third parties in the form of venture capital (VC) have not been considered (but they are briefly discussed);
- investments carried out by pharmaceutical companies for vaccine R&D and expansion of the production capacity have been collected as far as possible. However, they may often be estimations by the study team, because most companies have not disclosed specific figures regarding their investment;

[4] https://www.bvdinfo.com/en-gb/our-products/data/international/orbis?gclid=Cj0KCQiA3eGfBhCeARIsACpJNU_ISA2aPIY3hqoibD-7Z2Z7DR2h1pojB-gRsQPgx8DiESPXL9UVupQaAn-6EALw_wcB; see also the users' guide : https://www.wu.ac.at/fileadmin/wu/s/library/databases_info_image/ugorbisneo.pdf

[5] Due to the difficulty in finding transparent information and due to inconsistencies in the terminologies used by various institutions, in some cases the categorisation applied may be imprecise.

- public funds provided before the pandemic to conduct pathfinding research underpinning the vaccine development (e.g., decade long vaccine research at the National Institute of Allergy and Infectious Diseases at the US National Institutes of Health (NIH-NIAID); or research at the Oxford University on viral vectors) have not been considered;
- any transactions between partner industries (e.g., between BioNTech and Pfizer) as well as funds provided directly to licensees that produce and distribute vaccines on behalf of lead developers, or to contract development and manufacturing organisations that contribute to lead developers' vaccine production have not been considered.

The time frame covered by the desk-based research includes the years 2020, 2021 and 2022. Although information regarding the latter is incomplete due to the lack of official reports, it is reasonable to assume that for most vaccines the funds for R&D were allocated earlier (in 2020 and 2021), so any shortfall in 2022 should not significantly change the overall picture.

Based on information collected from publicly available sources and during the interviews with relevant funders and pharmaceutical companies (see section 2.1.3), a fiche summarising the fundings associated to each vaccine has been prepared and shared with the producers to get their feedback. The fiches are in Annex IV.

2.1.2. Statistical analysis

The data on funds for the different vaccines have been compiled in a database to allow for data analysis. Before aggregating data, when currency was not reported in EUR, it was converted according to the average exchange rate referring to the year of financing.

The **statistical analysis** consisted in analysing the data collected through the desk research and preparing descriptive statistics to show who has invested, how much, when, and where for both the R&D and the manufacturing of major COVID-19 vaccines. Visual aids have also been used to present the relative importance of funds invested into COVID-19 vaccines by different actors.

It is important to notice that the statistical analysis cannot be considered to globally cover all the funding mechanisms for the reasons presented in Section 2.2, particularly geographical coverage, hence it should be seen as an analysis on the sampled evidence.

2.1.3. Interviews

The **interviews** were aimed at collecting fresh evidence and opinions from three different groups of stakeholders, namely:

- representatives of pharmaceutical companies involved in the production of COVID-19 vaccines;
- selected public health experts and scientists from the EU and the US;
- selected public decision makers within institutions both at the EU and national level as well as from the US.

A total of 20 semi-structured online interviews involving 30 interviewees (see the list of interviewees in Annex III) have been conducted by the principal investigator, with the support of an assistant, between December 2022 and February 2023, following this protocol:

- sending an invitation email (with the Letter of recommendation from the Policy Department for Economic, Scientific and Quality of Life Policies enclosed) to potential interviewees to explain the topic of the study and requesting their availabilities for scheduling the interview.

- Upon showing interest to participate by replying to the invitation, each interviewee has been sent the interview guide. This allowed them to prepare their responses beforehand, which improved the overall flow of the interview session. The interview questionnaires are available in Annex II.
- Interviewees have been informed that their replies would be recorded but remain anonymous. Opinions or evidence arising from the interviews were usually needed to confirm or to suggest other sources, but in some cases provided unique evidence. These are reported simply in footnotes as "Source: personal communication to the principal investigator by an interviewee".

In addition, we received some answers or other contributions in written form. The usual disclaimer applies, meaning that the authors, and not the interviewees or any organisations, are responsible for the views presented in the study.

2.2. Limitations

Despite the possible inaccuracies in the estimates of funding, the resulting analysis combined with more qualitative information collected through interviews is considered robust enough to draw some policy recommendations. The main challenges in the data collection phase are listed below:

- **Availability of pharma companies**: All companies involved in the EMA-authorised COVID-19 vaccines, one under rolling review, and one withdrawn, were contacted by the study team starting December 2022 for an interview. An online interview (about one hour) was conducted by the PI with Pfizer, Sanofi, Hipra, and with Vaccines Europe, a specialized group within the European Federation of Pharmaceutical Industries and Associations (EFPIA). The above-mentioned three companies (Pfizer, Sanofi, Hipra) also sent written statements, and overall, they were willing to engage in a conversation about the study topics. Novavax sent a particularly detailed written response. AstraZeneca and GSK respectively replied with written statements. CureVac and Valneva declined the request, invoking confidentiality issues. Moderna replied that they could provide only information publicly available, and did not further contribute. BioNTech did not respond at all despite many solicitations. Different people of Janssen promised to respond, but to date did not. In mid-January, all contacted companies were asked to provide feedback on the accuracy and completeness of information included in the Summary Fiche prepared by the study team based on publicly available information (reported in the Annex IV for details). Feedback on the Summary Fiches was provided by three companies, i.e., Novavax, CureVac, and Hipra. Pfizer, Sanofi and GSK replied that they could not provide additional feedback due to confidentiality issues. The remaining companies did not respond. Overall, there were around 120 emails exchanged to achieve direct contacts with ten companies. The study team appreciates that five of them contributed more actively to the study: AstraZeneca, Hipra, Novavax, Pfizer, Sanofi.
- **Lack of official data sources**: Due to the difficulty in finding adequate and systematic information from official sources, the data was collected relying on a variety of publicly disclosed information. However, since many funding arrangements are confidential, details regarding the specific breakdown of spending are often unknown. In general, only funding for which there was evidence of their actual amount, and not merely an intention or announcement, were considered. Any APA for which only the number of doses (but not the relative disbursement) were available were not considered, given the impossibility of providing a reliable estimate of the transaction due to the differences in price per dose paid by the various governments. Therefore, funding estimates by this mechanism are likely to be underestimated, especially coming from some countries/institutions with less open disclosure approach.

- **Inconsistency of information:** The main limitation of the data collection concerns the inconsistency of information available across different sources. This is due to two issues: first, different institutions use different classification, so it is not always possible to clearly distinguish the type of funding or the purpose/destination of it. For example, the terms 'direct funding' or 'government grant', often found in contracts and reports, could indistinctly refer to funding for R&D, for increasing production capacity, or for a mix of both. Again, in the case of APAs, it is possible that part of the amount stipulated is to be attributed to the actual sale, while a portion is for the development of the vaccine itself. Second, inconsistencies spotted in different sources can be due to differences between announcements and actual commitments as well as the ongoing update of pre-existing agreements.

3. RESULTS

3.1. Mapping funding of R&D and extension of the production capacity for the manufacturing of COVID-19 vaccines

The COVID-19 pandemic posed a double challenge to governments and the pharmaceutical industry: to develop new vaccines for the novel threat and to produce billions of doses in a very short timespan. Thanks to a generalized effort, both goals were reached. **These extraordinary achievements were made possible by building upon more than two decades of basic research**. Basic research and early-stage development of vaccines are frequently supported by the public sector and charities (see, among others, Cross et al., 2021; Galkina et al., 2018). For instance, the ChAdOx vaccine platform underlying the Oxford–AstraZeneca COVID-19 vaccine relies on two decades of R&D by the Oxford Vaccine Group at the Jenner Institute, University of Oxford, led by Professor Sarah Gilbert and Professor Adrian Hill. According to Cross et al. (2021), the financing of such a vaccine platform was 97-99% public and charitable. See also Florio (2022) on the science behind the Moderna vaccine, particularly the research by Barney Graham and other scientists at the NIH-NIAID, and since 2005 by Drew Weissman and Katalin Karikò at the University of Pennsylvania. These are just examples of a wider and complex landscape not covered here.

During the pandemic, further efforts have been made by many diversified entities around the world to rapidly develop vaccines capable of preventing the spread of the SARS-CoV-2 virus. Resources have been invested in two directions: actual research and development, and funding to expand production capacity in order to be able to produce large numbers of doses quickly. Beyond that, advance purchase agreements were also offered by governments to producers. APAs are so-called 'pull' incentives, meant to de-risk companies' investments in order to encourage the development and manufacturing of products for which society has a need but for which the market does not provide enough 'pull' incentives to enlist a company to make the necessary investments (Boulet *et al*., 2021). APAs de-risks company investments in an often-costly research and development process, through upfront payments and through the promise to purchase products when they come to market. Many governments and international platforms used APAs to secure future vaccine supplies.

Based on the data collected (see Section 2.1.2 on sources and methodology), **from 2020 to early 2022, the combined support to companies by external funds** (including funds from governments, philanthropic entities, third private parties, international public-private partnerships and multilateral development banks) **for either R&D and the expansion of production capacity or both were in the range of EUR 9 billion for the nine vaccine here considered, and for the sources of funding included. The external incentives would jump to nearly EUR 30 billion if APAs are also considered**. Differentiating between types of funding, Table 3 shows the amounts of external funds received by the pharmaceutical companies involved in the production of COVID-19 vaccines in scope. The large figures for Moderna, Pfizer, and AstraZeneca, can be attributed to the following factors: the wide distribution worldwide, the earlier approval date compared to competitors, and the significant economic support from the US government (for Moderna). It is worth noting that although Pfizer did not receive any government R&D funding to develop its vaccine, its partner, BioNTech, did so.[6] According to data collected (see details in Annex IV), BioNTech received EUR 584.5 million in funding from the German government to assist with COVID-19 vaccine development and a loan of EUR 100

[6] Moreover, even Pfizer benefited from past NIH research.

million by the European Investment Bank (EIB), which also assisted the company before the pandemic with an earlier significant loan.

Table 3: Amount of external support funds received by entity and by type (EUR million)

	R&D only		R&D + manufacturing		APAs***
	Grant*	Loan**	Grant*	Loan**	
Moderna	123.8		838.0		8,974.8
Pfizer					5,929.8
AstraZeneca	336.8		1,403.5		1,993.7
Novavax			1,982.0		
Sanofi			2,185.9		607.2
Janssen	46.8		780.6		2,445.0
BioNTech	118.4		584.6	100.0	
Valneva	15.2				489.5
Oxford University	19.8		57.5		
CureVac	15.6		291.9	25.0	450.0
Hipra	6.6	12.9		45.0	
TOTAL	683,0	12.9	8,124.0	170.0	20,890

Note: CureVac and Hipra are not part of the vaccines authorised by EMA. * Grant is non-repayable support provided either by the public sector or other private companies. ** Loan is repayable finance provided either by the European Investment Bank or national public entities. *** The APA volume considered is the total volume of the contract for the purchase of doses (excluding optional ones) foreseen in the contract. The amount may or may not include a down payment. APA volumes for BioNTech, and Oxford University are nil because marketing authorization for the vaccines they have developed is held respectively by Pfizer, and AstraZeneca.

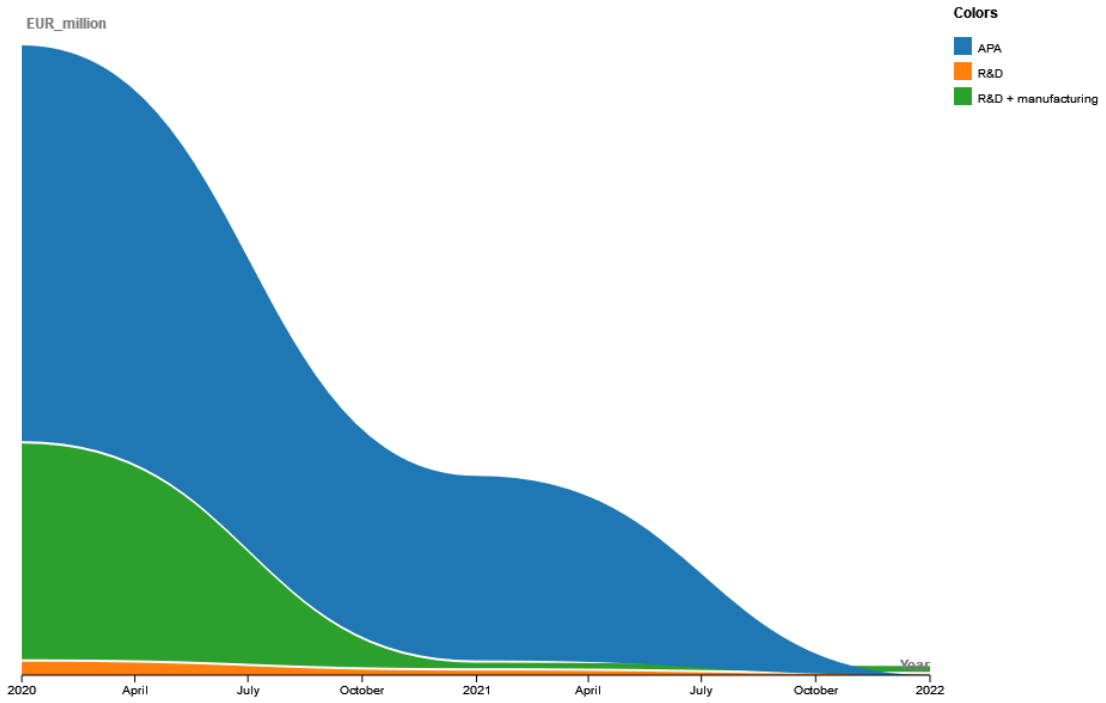
Source: Authors, see details and sources in Annex IV.

Mapping the dynamics over time, it emerges that **during 2020 and for the first part of 2021, all types of support** (grants/loans exclusively for R&D, for both R&D and manufacturing, and APAs) **were provided** (see Figure 1). In 2021, as the conditional marketing authorisation of the vaccines started to be released, various institutions started to purchase doses, causing expenditure on purchases to soar. In 2022, the external funding for R&D, for both R&D and manufacturing, and APAs was clearly lower[7], as effective vaccines were already available. It is also worth noting that vaccines that started the EMA's rolling review at the end of 2021 or 2022, such as Valneva and Hipra, received relatively less funds than first comers did. For instance, Hipra could not sign an APA because there were too many doses available in Europe when they approached the EC. Nevertheless, in August 2022, a joint procurement agreement was signed between Hipra and European Health Emergency Preparedness and Response Authority (HERA) to ensure wider preparedness.[8] This agreement is not a commitment but rather a right for the 14 participating countries to purchase up to 250 million doses once the vaccine receives a positive assessment by the EMA.

[7] It is also worth noting that at the time of writing reliable data on the year just ended (2022) were more difficult to found.

[8] https://ec.europa.eu/commission/presscorner/detail/en/IP_22_4782.

Figure 1: External funding over time



Source: Authors' own elaboration.

The evidence of direct corporate investments in vaccine R&D and expansion of the production capacity is scant. Only a few companies have provided information in this regard for this study (see Box 1), which prevents making consistent comparisons between vaccines.

Box 1: Three examples of direct corporate investment

The evidence of direct corporate investments in vaccine R&D and expansion of the production capacity were provided by three companies, Pfizer, Novavax, and Hipra, namely:

- According to information disclosed by Pfizer, the company invested globally at risk over USD 2 billion with over USD 1 billion into the European manufacturing and logistics network across 12 EU Members States and hired more than 1500 employees. In early December 2022, Pfizer announced a USD 2.4 billion investment in two European manufacturing sites, Grange Castle in Dublin and Puurs in Belgium, creating approximately 750 Full Time Equivalent across the sites – and securing mRNA manufacturing in Europe.
- According to information provided by Novavax, their research and development expenses increased to approximately USD 2.5 billion in 2021 as compared to USD 747 million in 2020, an increase of USD 1.8 billion due to the cost of developing activities relating to NVX-CoV2373. Moreover, according to Novavax's communication to the PI, during 2020, the company's investing activities primarily consisted of capital expenditures, advanced purchases of raw materials and equipment, and acquisition of Novavax CZ, i.e., the Czech site. Capital expenditures for 2021 and 2020 were USD 57.5 million and USD 54.6 million, respectively. Official figures for 2022 are not available yet. However, Novavax claims to have expended significant capital for further development activities related to the NVX-CoV2373 program, including the additional build-up of research and development and manufacturing facilities and related equipment.
- According to information provided by Hipra's representatives, their vaccine has been 70% self-financed. Debt finance represents 27% and grants 3%. In particular, Hipra's total R&D expenditure directly related to the COVID-19 vaccine amounted to EUR 9,6 million in 2021 and EUR 28,4 million in 2022. However, these amounts do not include the following: expenses associated with registration, promotion, and production activities; capital investments; use of pre-existing equipment/facilities; and stock investment.

Source: Authors, based on information provided by cited companies for this study.

Data in Table 4 come from company reports and are relative to total corporate R&D expenditures. For most of the companies, the study has considered as attributable to COVID-19 vaccines the increase of total R&D expenses of 2020 (upper bound estimate), after making some adjustments to account for the R&D trends of the two years before the pandemic. R&D expenses of 2021 were included only for companies whose vaccines was authorised in late 2021 or 2022. For Pfizer and Novavax the study relies on figures directly provided by the companies, summing to USD 3.8 billion. On the one side, it is possible that some R&D expenditures were not reported by companies in their reports for the fiscal year 2020 and are, to a certain extent, included in the fiscal year 2021. On the other side, the companies manage a wide portfolio of projects; hence they may have increased their R&D outside the COVID-19 vaccines. This study does not extend to further post-authorisation corporate R&D, for example, on adapted vaccines or new projects related to COVID-19.

Summing up the figures, **the cumulated volume of corporate R&D expenditure incurred by producers** (of the seven authorised vaccines only) **somehow attributable to COVID-19 vaccines is** in the range EUR 4-5 billion of corporate R&D. In the rest of the study, we shall use this range, in order to match it with the external support provided in years 2020 and 2021, which, as mentioned, is about EUR 9 billion (for nine vaccines, out of which about EUR 8 billion is provided by public sector). The EUR 9

billion figure (mostly in the form of grants), however, includes support to increasing production capacity. This does not consider additional funding, particularly by BARDA to suppliers (such as Merck) related products, such as vials, biocontainers, needles, syringes, etc.[9]

Table 4: Total corporate R&D expenditure (million), nine companies, 2018-21

Company		2018	2019	2020	2021	Note
Pfizer	USD	7,760	8,385	9,393	13,829	Conditional marketing authorisation issued: 21/12/2020.
Novavax	USD			609	2,246	Figures specific for Nuvaxovid. Conditional marketing authorisation issued: 20/12/2021.
Janssen	USD	8,446	8,834	9,563	11,882	Figures specific for "pharmaceutical". Conditional marketing authorisation issued: 11/03/2021.
Sanofi	EUR	5,894	6,018	5,530	5,692	Marketing authorisation issued: 10/11/2022.
Moderna	USD	454	496	1,370	1,991	Conditional marketing authorisation issued: 06/01/2021.
Valneva	EUR			19.0	113.9	Figures specific for COVID-19. Marketing authorisation issued: 24/06/2022.
AstraZeneca	USD	5,932	6,059	5,991	9,736	Conditional marketing authorisation issued: 29/01/2021.
BioNTech	EUR	n.a.	226.5	645	949	See Pfizer for the authorization date.
GSK	GBP	3,893	4,568	5,098	5,278	See Sanofi for the authorization date.

Source: Authors, based on companies' annual reports.

As the corresponding expenditures in the increased production capacity by firms is not available for most of the companies, one cannot properly compare the total public and private investment. While for two companies (Pfizer and Novavax) we were directly provided some figures by the interviewees, for all the companies involved in the development of authorised vaccines we recur to an indirect approach: we have collected the data on total fixed assets in the years before and after the (conditional) marketing authorisation.

While any production increase may be supported by changes in the purchase of components, in the size of employment, or in procurement contracts with suppliers, some changes in fixed assets should be expected as well. In fact, fixed assets as for the usual accountancy conventions are defined as follows: «*Fixed assets are physical or tangible items that a company owns and uses in its business operations to provide services and goods to its customers … When a business acquires a fixed asset, it is recorded on the balance sheet - usually as property, plant and equipment … Common examples of fixed assets include: computer equipment; vehicles; machinery; tools; land; buildings, furniture. Intellectual property, like patents, copyrights and trademarks, can also be considered fixed assets. While they are not physical assets, they are intended to help generate revenue*»[10] We also checked the intangible fixed assets component in

[9] https://medicalcountermeasures.gov/barda/influenza-and-emerging-infectious-diseases/coronavirus/pharmaceutical-manufacturing-in-america/?filter=all

[10] Source: https://tax.thomsonreuters.com/en/glossary/fixed-assets#one.

order to guess the change in production assets. It is important to consider that in the pharmaceutical industry, intangible assets, such as patents, are often a major component of total assets.

To fetch the data in a comparable way, we have used the largest repository of corporate account data, the ORBIS database, and extracted the information available on total fixed assets for the nine companies, in the years 2018 and 2019, before the pandemic and 2020 and 2021, after it. Table 5 reports such data. Balance sheets, however, do not usually specify the amount of investment, i.e. change in fixed assets, related to a specific product, such as a vaccine. Hence the data must be interpreted with caution, as they can refer to a range of different products, and not just the COVID-19 vaccines.

Our guess is that **the cumulative production investments of the nine companies in 2020-2021 may be in the range of EUR 11 +/- 3 billion,** mostly depending on the missing data about Pfizer investments outside Europe, about AstraZeneca worldwide, and how to interpret the total asset increase of some other companies, particularly the very high fixed investment of Moderna.

Table 5: Total corporate fixed assets (EUR million), nine companies, 2018-21

Company	2018	2019	2020	2021	Note
Pfizer	95,630	119,985	97,109	107,525	Conditional marketing authorisation issued: 21/12/2020.
Novavax	77	67	272	372	Conditional marketing authorisation issued: 20/12/2021.
Janssen Pharmaceutica	9,926	9,712	10,110	n.a.	Conditional marketing authorisation issued: 11/03/2021.
Sanofi	1,636	1,583	n.a.	1,490	Marketing authorisation issued: 10/11/2022.
Moderna	349	410	847	7,591	Conditional marketing authorisation issued: 06/01/2021.
Valneva	104	136	141	232	Marketing authorisation issued: 24/06/2022.
AstraZeneca	39,354	40,782	38,452	69,856	Conditional marketing authorisation issued: 29/01/2021.
BioNTech	n.a.	237	651	759	See Pfizer for the authorization date.
GSK	45,896	70,758	65,915	71,676	See Sanofi for the authorization date.

Source: Authors based on Orbis data.

Given the evidence, **we can confidently conclude that – albeit with significant differences across companies – US taxpayers were major funders of corporate R&D and productive investment on most of the nine COVID-19 vaccines considered.** The incentive in grant form was about one billion per vaccine on average (including one withdrawn), but with a very wide variance across the considered vaccines and companies. **Moreover, some of these incentives and the almost EUR 21 billion of APAs that we have been able to track may have also contributed to de-risking around EUR 11 billion of corporate investment for the production capacity of vaccines until 2021.**

One issue this study has not examined is the potential role of venture capital in the EU and more in general of a Capital Markets Union (CMU)[11] in the support of R&D for vaccines. While a full treatment of

[11] https://finance.ec.europa.eu/capital-markets-union-and-financial-markets/capital-markets-union/what-capital-markets-union_en

this topic is beyond the scope of our analysis, the box below briefly discusses some facts and their implications. Based on that it is possible to conclude that VC probably made a little difference in the development of COVID-19 vaccines, compared with the critically important role of government emergency funds through BARDA in the US, but also, to a certain extent, with the role played by the EIB to support BioNTech, CureVac, and others. Even in the US context, despite its VC availability, leading economists (Athey *et al*. 2022b) argue that "*there is a strong economic case for continued federal investment in COVID-19 vaccines and therapeutics. In brief, the private sector on its own will invest too little because COVID-19 vaccines and therapeutics generate enormous benefits for public health and the macroeconomy that private firms can only very partially capture*." The bottom line is that while VC has played a role in the biotech landscape worldwide, it cannot remedy the market failures in the vaccine sector because, after all, the objective of VC is to identify potential high returns for their investors from early-stage projects, and not to select those projects based on public health needs per se, when financial returns are unclear.

Box 2: Capital markets and COVID-19 vaccines

The CMU was launched in 2014 by President Juncker and was restated by president Von der Leyen in 2019 in her Agenda for Europe. Several actions have been proposed to achieve a CMU. The question in our context is whether the structural problems of the EU capital markets may have contributed in the past and may risk in the future to slow down the development of vaccines (and more in general biomedical innovation) by European companies.

If one focuses on how Venture Capital players reacted to the pandemic in the early months of 2020, when risk and potential reward of investment on vaccines (in general) were probably higher, the following data emerge: there were USD 2.3 billion of VC (until end of August 2020) going to vaccine companies worldwide, doubling the share of total VC funds from 0.6% (2015-2019) to 1.2%. US-located companies raised nearly USD 1 billion, German companies over USD 800 million, France close to USD 50 million, and no transaction were recorded in other EU countries (Savills Research, 2020) The difference between the role of VC in the US, where the sector is largely developed, and in the EU, where it is often considered lagging behind, does not seem significant.

Moreover, there is strong evidence that VC in general has not been resilient to the pandemic, as it rather decreased its operations, see Bellavitis and others (2022). Using a dataset of 39,527 funding rounds occurring before and during the pandemic in 130 countries, these authors show that the effect of COVID-19 pandemic on VC was "*a significant decline in investments … this decline is more pronounced for investments characterized by higher uncertainty, namely investments in seed-stage ventures, industries affected more heavily by the COVID-19 crisis, international investments, and non-syndicated investments. Investor prominence partially moderates these effects*."

On the other side a JRC paper by Bellucci et al. (2020) suggests that there was some reallocation of VC towards deals in pandemic-related categories. Using Zephyr database, the authors looked for deals where five words were mentioned in the descriptions: biology, pharmaceutical, medicine, health, and supply chain, and found a positive empirical relationship between the spread of COVID-19 and VC investment in pandemic-related deals, in terms of invested amount and number of transactions. Again, these transactions are mostly unrelated to vaccines and high-risk R&D on infectious diseases. There is no evidence that VC made a difference in COVID-19 vaccine development.

Source: Authors, based on cited sources.

3.2. The relative importance of funds invested into COVID-19 vaccines by different actors

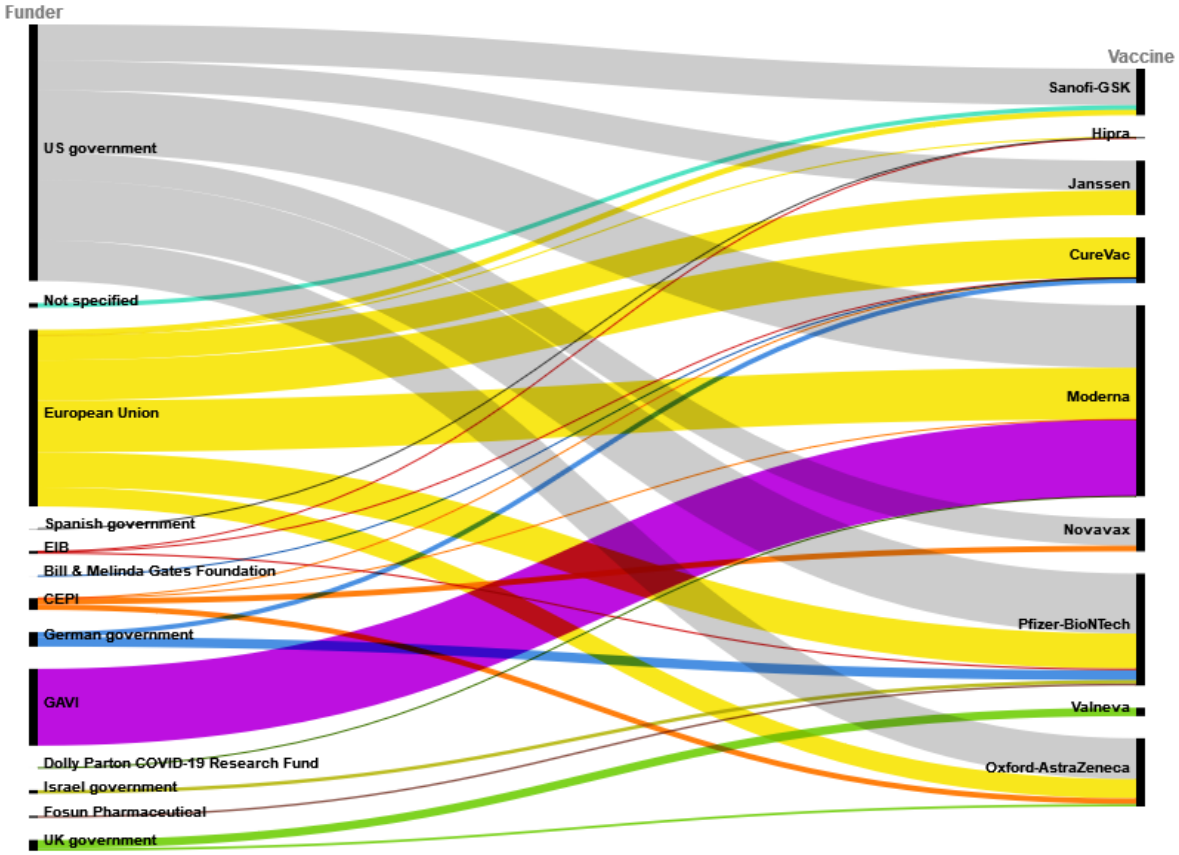
Shifting the focus from recipients to funders, Figure 2 shows the entities that contributed to the cumulated funding (for "R&D only", "R&D + manufacturing" and "APAs") of each vaccine. **The most prominent** among them **are the US government,** with EUR 15.4 billion (51.6% of total tracked funding), **the European Union**[12]**,** with EUR 7.9 billion (26.3% of total tracked funding), **and the Global Alliance for Vaccines and Immunisation** (GAVI), with EUR 4.6 billion (15.5% of total tracked funding). Most of the funds mapped for the US came from the US BARDA. The European Union stream includes the funding provided by the EU budget as well as Member States through six APA contracts, the only ones for which the funding amount has been disclosed.[13] These figures do not include other types of procurement contracts after marketing authorisation.

Altogether, governments and other public actors contributed by means of grants (27%), loans (0.6%), and APAs (54%), representing over 80% of the total external funds mapped. The remaining funds were provided by philanthropic entities, third-party private companies, public-private partnerships, and the European Investment Bank (EIB).

[12] Including support provided by the EU, EIB, and MS tracked.

[13] The cost per dose for Oxford-AstraZeneca and Moderna was retrieved directly from contracts that have been made available in full, notably thanks to the work of Italian investigative journalists working for the RAI, the public television. For CureVac the APA volume was retrieved by the company annual report and confirmed by the company's representative. For Janssen, Sanofi/GSK, and Pfizer/BioNTech, the price list revealed by a Belgian minister was used to calculate the volumes of APAs. If the weighted average cost per dose calculated by the European Court of Auditor that is EUR 15 is applied (ECA, 2022) to all doses purchased through APAs regardless the producers, the EU funding would jump to EUR 16.9 billion. However, this amount would be overestimated because such a weighted average cost per dose was calculated including also the volumes of three purchase agreements.

Figure 2: Sources of cumulated funding for "R&D only", "R&D + manufacturing" and "APAs") of COVID-19 vaccines by funder

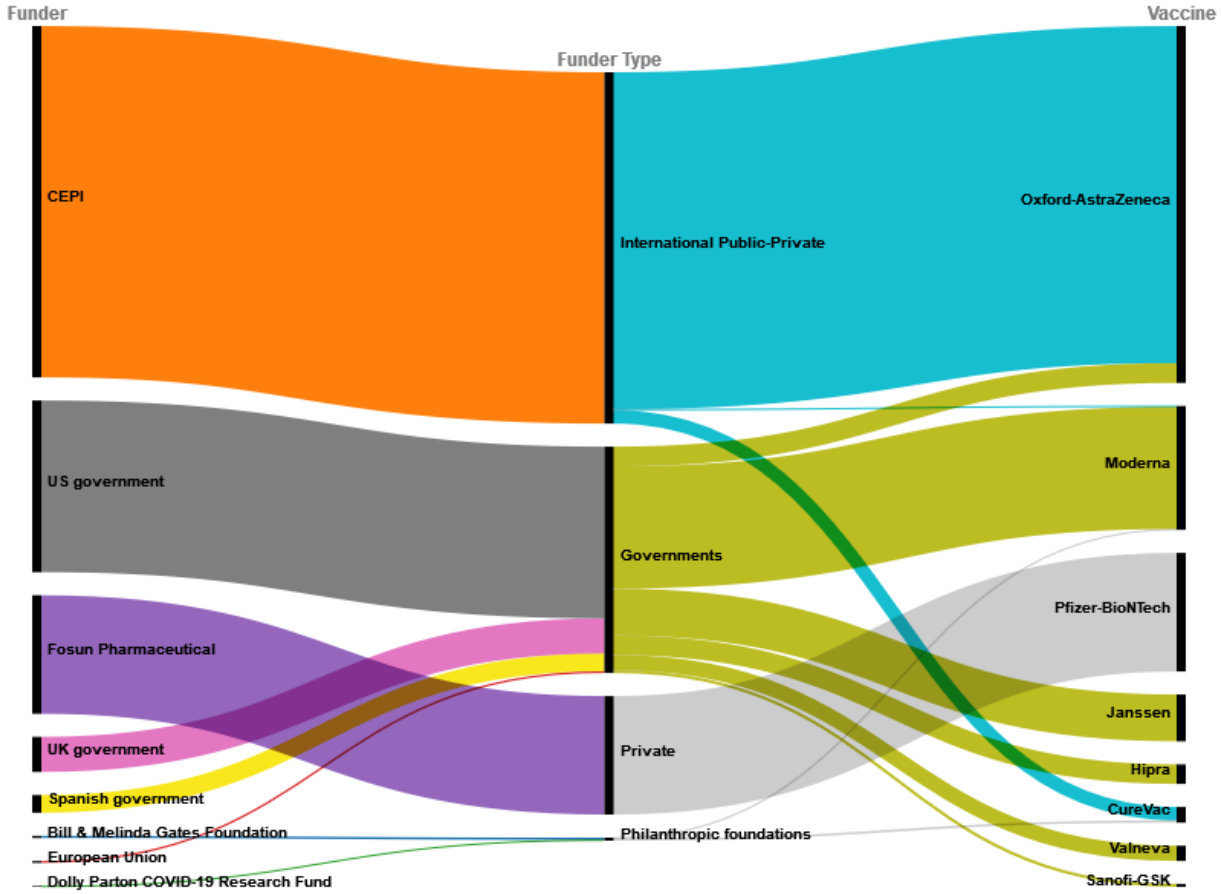


Source: Authors' own elaboration.

Focusing only on the grants that were explicitly directed at the R&D on vaccines (see Figure 3), **with a total of EUR 19.5 million the share of funds coming from EU and MS is marginal** compared to total funds mapped. As reported in Section 3.2.2, the EC provided EUR 350 million to support coronavirus vaccine development, however, these funds did not directly contribute to the development of one of the vaccines under the scope in this study. The US government and Coalition for Epidemic Preparedness Innovations (CEPI)[14] are by far the largest funders with, respectively, EUR 168.8 million and EUR 351.1 million. Together they cover 75% of total support funds for "R&D only". They are followed by Fosun Pharmaceutical, a Chinese company, with EUR 118.4 million, the UK government with EUR 35.1, the US philanthropic foundations Dolly Parton COVID-19 Research Fund and the Bill & Melinda Gates Foundation (respectively EUR 0.9 and EUR 2.2 million). There may be other funding by these or other entities that we have been unable to confirm in spite of press releases not always followed by evidence.

[14] It is worth noting that CEPI has secured financial support from many governments worldwide, private investors & philanthropies. The EC also provides contribution to CEPI. Source: https://cepi.net/about/whoweare/.

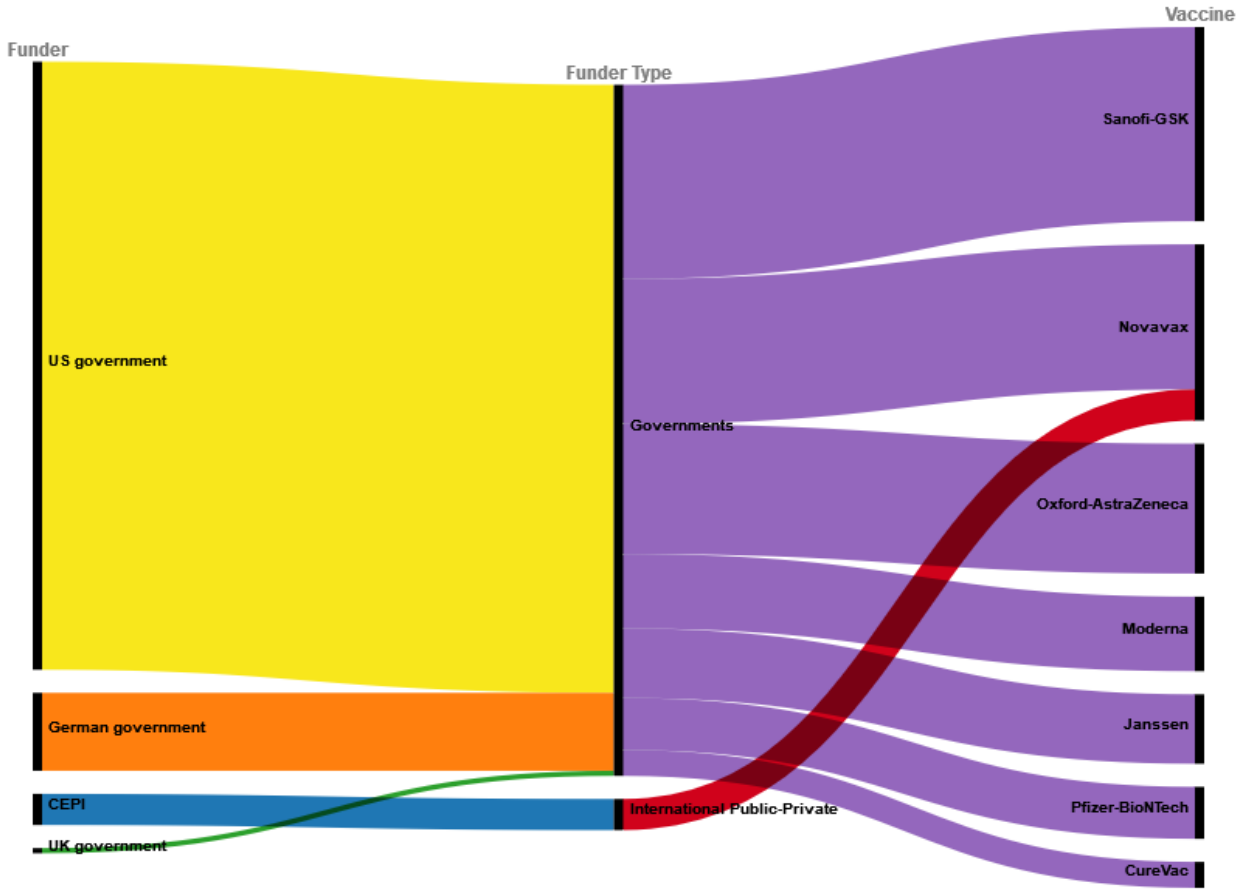
Figure 3: Sources of grants for COVID-19 vaccine "R&D only" by funder



Source: Authors' own elaboration.

Concerning the grants provided to support development and the extension of the production capacity, the US government is the major funder, with EUR 6.8 billion, representing 82% of the total funding (see Figure 4). It is followed by the German government (EUR 876.5 million) and CEPI (EUR 350.4 million). According to one of the interviewed companies, the funding received from the US Government and CEPI were key to support the company's ability to expedite the clinical development and production of the vaccine, including at their facility in Europe.

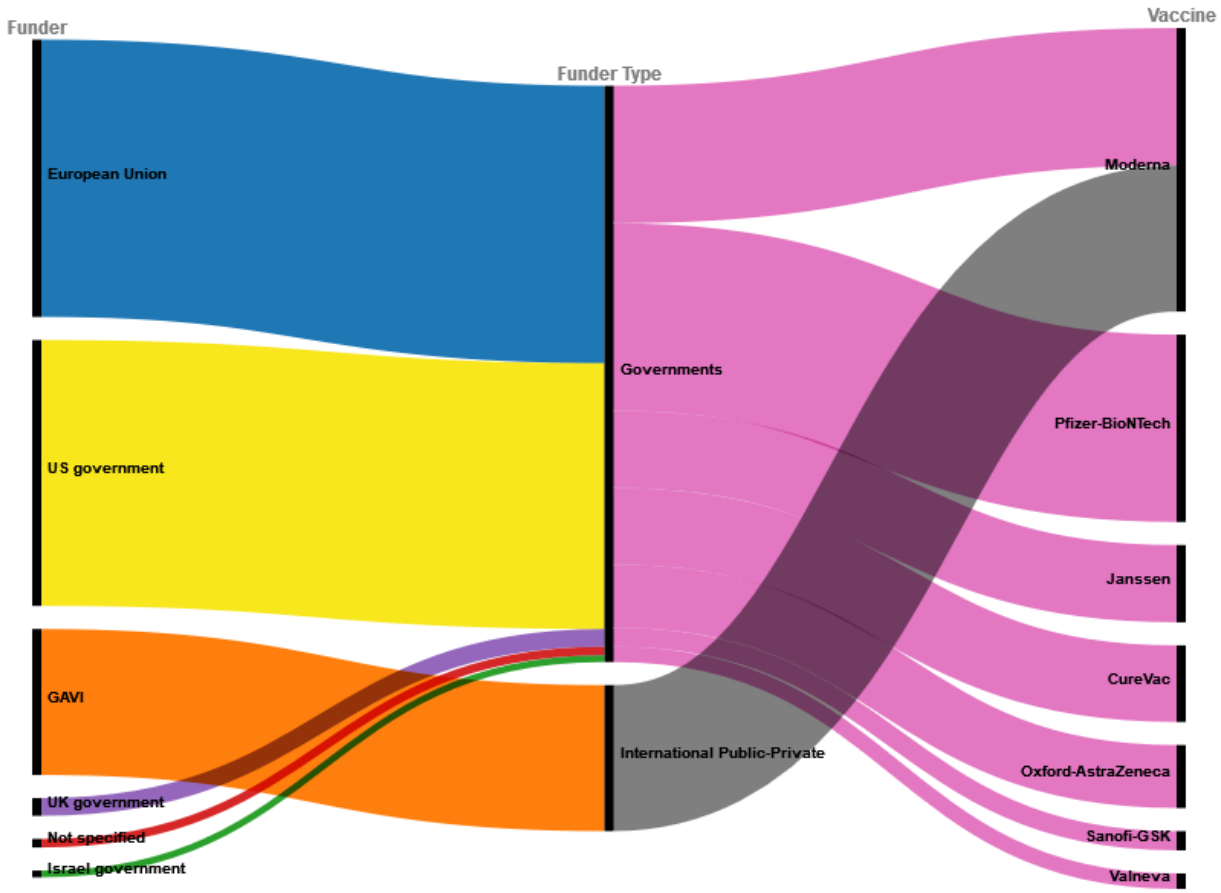
Figure 4: Sources of grants for COVID-19 vaccine "R&D + manufacturing" by funder



Source: Authors' own elaboration.

When APAs are considered, the US government and the EU are by far the largest funders among those mapped (Figure 5). According to data collected, the US and EU together represent 73% of the total APAs whose amount has been disclosed. The other entities that used this type of funding are GAVI (EUR 4.6 billion), the UK government (EUR 560.5 million), and the Israel government (EUR 214.9 million). According to interviewed companies, APAs helped to rapidly produce and distribute COVID-19 vaccines amid the public health emergency by providing them with an efficient contracting process, funding for manufacturing scale-up, and predictable product demand. There is no evidence that APAs incentivised R&D.

Figure 5: Sources of COVID-19 vaccine APAs by funder



Source: Authors' own elaboration.

Primarily with Operation Warp Speed (see Box below), **the US government contributed to all investment types for vaccines from R&D to APAs. Conversely, the EU and MS funds were mainly concentrated on APAs.** Some companies explained that while the US financed the bulk of R&D and industrial scale-up on the US soil, the EC was relatively quick in sending teams to negotiate APA contracts. These have been instrumental in helping companies set up or expand their production capacity in the EU.

The next sections discuss, respectively, the EC COVID-19 vaccine strategy and the EC and EIB support for R&D and manufacturing of COVID-19 vaccines.

Box 3: US Operation Warp Speed

Operation Warp Speed (OWS) was an interagency partnership among components of the Department of Health and Human Services (HHS), including the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the National Institutes of Health (NIH), and the Biomedical Advanced Research and Development Authority (BARDA), and the Department of Defense (DoD). OWS engaged with private firms and other federal agencies, including the Department of Agriculture, the Department of Energy, and the Department of Veterans Affairs.

The initiative was launched in May 2020 by the Trump Administration to coordinate the efforts of agencies to respond to the COVID-19 emergency by accelerating the development, manufacturing, and distribution of COVID-19 vaccines, therapeutics, and diagnostics.

Initially, the US Congress directed almost USD 10 billion to this initiative through supplemental funding, including the CARES Act. The USD 10 billion included more than USD 6.5 billion designated for countermeasure development through BARDA and USD 3 billion for NIH research. Funding was then increased to about USD 18 billion by October 2020. Out of this, over USD 12 billion had been invested in vaccine-related contracts.

Source: Authors, based on HHS (2020), Siddalingaiah (2021); Baker and Koons (2020), Lancet (2021).

3.2.1. COVID-19 vaccines strategy by the EC

The EC effort to secure vaccines for EU citizens focused on creating an ad-hoc and tailor-made procurement system. However, the EC action on procurement started later than the UK and US ones (ECA, 2022; Deters and Zardo, 2022). Initially, France and Germany took the matter into their hands and launched an initiative for joint procurement in April 2020. They contacted pharma companies and invited Italy and the Netherlands to join what became the 'Inclusive Vaccine Alliance'. However, after ample political debate, it was decided to adopt an EU-wide approach, to be carried out by the European Commission on behalf of the Member States.[15]

Only on 17 June 2020, the EC published its COVID-19 vaccines strategy, which focuses on a centralised EU procurement process, and revolves around two pillars: i) securing sufficient production of vaccines in the EU and thereby sufficient supplies for its Member States; and ii) adapting the EU's regulatory framework to the current urgency and making use of existing regulatory flexibility.

In parallel with the publication of its COVID-19 vaccine strategy, **the EC signed an agreement with the 27 Member States, allowing it to conclude APAs with COVID-19 vaccine manufacturers on their behalf**.[16] With these contracts, the Commission secured Member States' the right to buy a specified number of vaccine doses in a given timeframe and at a given price. In return, part of the development costs faced by vaccine manufacturers was financed by down payments from the EU budget. As soon as a vaccine candidate is authorised by EMA, the down payments are used against purchases of the vaccine by the Member States. In case the vaccine is not authorised, these payments may not always be fully recovered (ECA, 2022).

According to the European Court of Auditors (ECA, 2022), **between August 2020 and November 2021, the Commission signed 8 APA contracts** with vaccine manufacturers (see Table 6). These

[15] https://www.consilium.europa.eu/en/meetings/epsco/2020/06/12/

[16] Commission Decision of 18 June 2020, C(2020) 4192 and its subsequent approval by each Member State.

contracts were concluded before the vaccines received a recommendation for a conditional marketing authorisation from the EMA and were financed through the Emergency Support Instrument (ESI), a financing instrument directly managed by the EC that allows it to provide support within the EU in case of disasters. In the same period, three purchase agreements were signed (with Pfizer/BioNTech and Moderna) for vaccines having already received an EU conditional marketing authorization. These contracts do not include any down payment from the EU budget, though Moderna required a down payment from the Member States.

Table 6: Potential COVID-19 vaccine doses secured by the EU up to the end of 2021 through 8 APA contracts

Vaccine by	Contract signature	Number of contracted doses (million)	Number of optional/additional doses (million)	Total number of doses (million)
AstraZeneca	August 2020	300	100	400
Sanofi/GSK	September 2020	-	300*	300
Janssen**	October 2020	200	200	400
Curevac	November 2020	225	180	405
Pfizer/BioNTech	November 2020	200	100	300
Moderna	December 2020	80	80	160
Novavax	August 2021	100	100	200
Valneva	November 2021	24	36	60

Note: *The Sanofi/GSK contract is an options contract with no obligation on the MS to purchase any doses. Sanofi/GSK received a down payment. **Janssen Pharmaceutica NV is an affiliate of Johnson & Johnson.

Source: Authors, based on ECA (2022).

It is worth noting that down-payments represent only a share of the total value of the APAs. According to ECA (2022), the EC paid more than EUR 2.55 billion in down-payments to vaccine manufacturers. See box 4 for details on down-payments and total volumes of Moderna and AstraZeneca APAs. These are the only contracts that, as far as we know, have been made available in full, notably thanks to the work of Italian investigative journalists working for the RAI, the Italian public television company.[17]

[17] For the AstraZeneca, see unredacted version of the APA's here: https://www.rai.it/dl/doc/2021/02/19/1613725900577_AZ_FIRMATO_REPORT.pdf and for Moderna here: https://www.rai.it/dl/doc/2021/04/17/1618676613043_APA%20Moderna__.pdf.

Box 4: APAs and down payments: two cases

EU-Moderna APA: This is an Advanced Purchase Agreement for the procurement of 80 million vaccine doses, with an option to order 80 million more. The agreement states a price of USD 22.90/dose.

The agreement also specifies the calculation method for the down payment that is meant to cover the financing of the following activities: raw material (USD 84 million), technological transfer (USD 4 million), facility investments (USD 173 million), fill finish (USD 57 million), pharmacovigilance and regulatory/medical affairs (USD 37 million), shipping/warehousing (USD 10.4 million).

Moderna	Number of doses	Price	Total
Total APA	80,000,000 (+80,000,000 optional)	USD 22.5	USD 1.8 billion (+ USD 1.8 billion optional)
Down payment	20% out of 80,000,000	USD 22.5	USD 360 million (318,471,338 €)

EU-AstraZeneca: This is an Advanced Purchase Agreement for the production, purchase, and supply of 300 million doses of a vaccine for distribution within the EU by end June 2021, with an option to order an additional 100 million. The agreement states that the price is set at EUR 2.90/dose.

The agreement also specifies the calculation method for the initial payment that is meant to cover the financing of the following activities: technological transfer & tech support (EUR 41 million), procurement of critical material (EUR 41 million), drug product & packaging reservation fee (EUR 49 million), drug substance CMO capacity reservation fee, raw materials, and resins (EUR 205 million).

AstraZeneca	Number of doses	Price	Total
Total APA	300,000,000 (+100,000,000 optional)	2.9 EUR	EUR 870 million (+ EUR 290 million optional)
Initial payment		Lump-sum	EUR 336 million

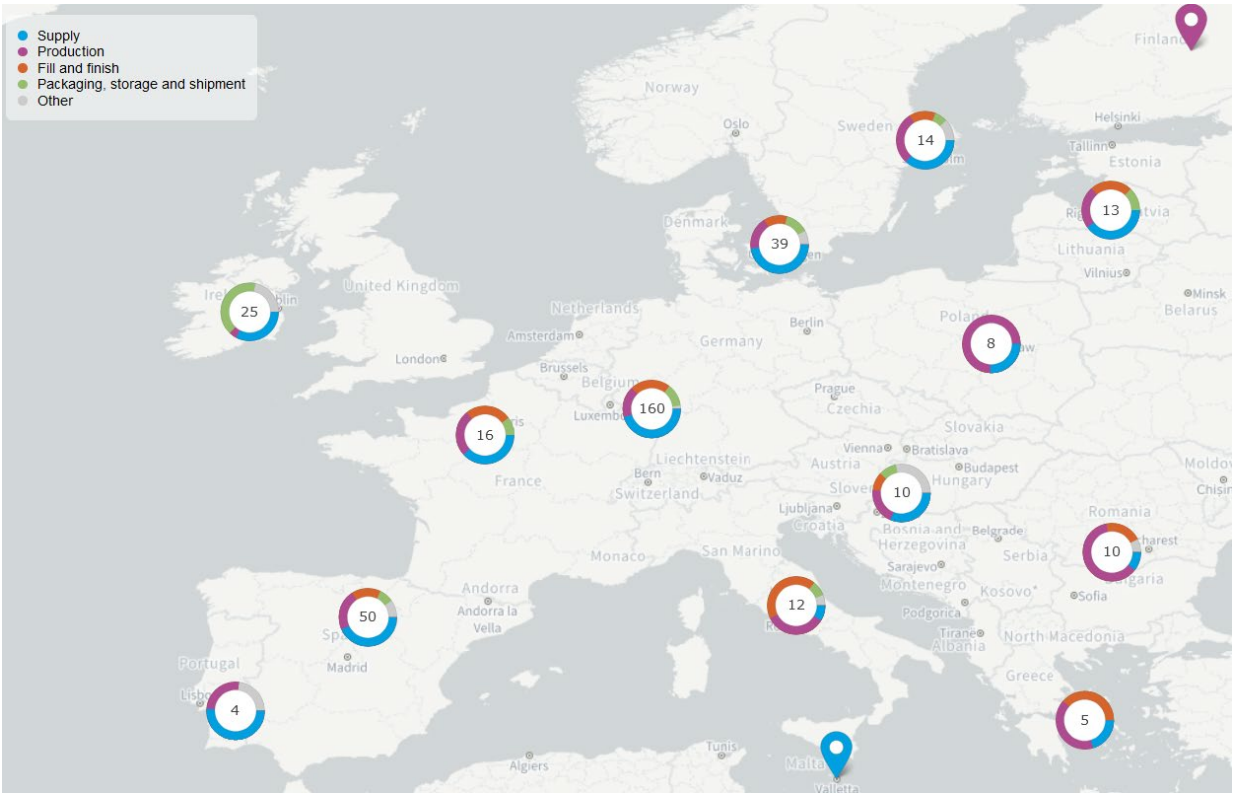
Source: Authors, based on contracts in the public domain, see footnote 10.

According to ECA (2022), all 11 contracts signed between August 2020 and November 2021 **include a clause on the location of vaccine production**. Six contracts allow the contractors to use facilities in the US, Switzerland, the UK or the European Economic Area (EEA). Four contracts specify that the contractors need to inform the Commission if they intend to use additional facilities located outside the EU. In four other cases, the contractor needs to obtain the Commission's prior consent to use facilities outside the EU, UK, EEA or Switzerland.

Although the EC strategy aimed at a sufficient production of vaccines in the EU to ensure supply security, given the structure of the global supply and production chains, **it had limited leverage to prevent production steps to take place in non-EU locations** and overcome supply challenges. The EC only set up a task force to support manufacturing and supply chains in February 2021. By comparison, the US and the UK anticipated manufacturing and supply problems earlier in the process, either by funding the development of industrial capacity or by actively monitoring and supporting the production efforts of companies (GAO 2021a; GAO 2021b; and UK National Audit Office, 2020).

In 2021, the task force mapped vaccine production capacity in the EU, throughout the supply chain that includes the following steps: supply (production/supply of raw materials, consumables, disposables, equipment); production (manufacturing and formulation); fill & finish, packaging; storage & shipment; other activities such as process development of vaccines, R&D, clinical trial management services. The result of such mapping is publicly accessible, the figure below provides the map available on the EC website.

Figure 6: Map of the production capacity in the EU (2021)



Source: https://single-market-economy.ec.europa.eu/coronavirus-response/task-force-industrial-scale-covid-19-vaccines_en.

The box below reports more detailed information on vaccine production in the EU provided by three of the contacted companies.

Box 5: Vaccine production in the EU: some cases

- Sanofi-GSK: the production of VidPrevtyn Beta leverages the EU manufacturing footprint of Sanofi and GSK (for the adjuvant) with production sites based in France, Italy, Belgium and Germany, covering the full value chain from drug substance to drug product.
- Novavax stated that much of its supply chain is based in Europe. They acquired a state-of-the-art vaccine manufacturing facility in Czechia, in which they invested significantly to produce the antigen, and they have significantly expanded the facility in Sweden where they produce the adjuvant. The Czech and Swedish sites collectively employ more than 650 people. Novavax also partnered with organisations in Germany, Ireland, Belgium, Spain, Poland, and the Netherlands that produce the final packaged product for European and global use. Beyond Europe, Novavax partnered with manufacturers around the world, including SK bioscience in the Republic of Korea, Takeda in Japan, and the Serum Institute of India.
- Pfizer claimed to have invested USD 1 billion into their European manufacturing and logistics network across 12 EU Members States and hired more than 1500 employees. Comirnaty is not only made in Europe as a finished product, but all the key components required to manufacture the vaccine are sourced in Europe. During the peak of the pandemic, Pfizer's European manufacturing network spanned 19 sites, including 12 contract manufacturing partners. Moreover, 235 components of the vaccine were sourced in Europe across 12 Member States and about 35 suppliers.

Source: Authors, based on exchanges between the PI and the mentioned companies.

When the COVID-19 outbreak reached Europe in March 2020, **some funding opportunities were created by the EC to support clinical research projects on COVID-19**. The Commission pledged EUR 1.4 billion under the Coronavirus Global Response initiative, of which about EUR 1 billion comes from Horizon 2020 Framework Programme for Research and Innovation (Annex 3 gives an overview of funding mobilised under Horizon 2020 (H2020) to contribute to the Coronavirus Global Response). Out of this, only EUR 350 million are dedicated to support coronavirus vaccine development though not directly targeting the vaccine producers.[18] Prior to the COVID-19-specific investments, however, the EC claims to have invested over EUR 650 million through H2020 (2014-2020) in vaccine and vaccination research and innovation (see, for instance, the case of BioNTech in box 6).

[18] https://research-and-innovation.ec.europa.eu/research-area/health/coronavirus/vaccines_en and material shared by Directorate General for Research and Innovation.

Box 6: EU research and innovation grants to BioNTech

The EC has been supporting BioNTech and its founders for many years with major research and innovation grants both for its work on therapeutic antibodies and on mRNA. Before COVID-19 hit, BioNTech or researchers' academic affiliation have received EU funding through these projects: MERIT - Mutanome Engineered RNA Immuno-Therapy (FP7); IACT - Immunostimulatory against antibodies for cancer therapy (FP7); APERIM - Advanced bioinformatics platform for PERsonalised cancer Immunotherapy (H2020); and SUMMIT - Stepping Up mRNA Mutanome Immunotherapy (H2020).

According to co-founders of Germany's BioNTech, "*the continuous EU funding, and also the funding of the German government allowed them to generate deep scientific understanding of the immune recognition of cancer. The funding has also supported the early stages of our mRNA vaccine research. It helped them to improve the vaccines and generate preclinical and early clinical data for their individualised mRNA cancer vaccine approach*."

Source: Authors, based on https://research-and-innovation.ec.europa.eu/research-area/health/coronavirus/vaccines_en, and https://ec.europa.eu/research-and-innovation/en/horizon-magazine/qa-biontech-vaccine-only-mrna-10-just-beginning-say-co-founders.

In January 2020, the Commission launched the first H2020 emergency call for expressions of interest entitled "SC1-PHE-CORONAVIRUS-2020: Advancing knowledge for the clinical and public health response to the [COVID-19] epidemic" with a budget of EUR 10 million subsequently increased up to EUR 48.5 million. The Commission received 91 proposals within the very short two-week deadline. In total, EUR 48.2 million was awarded to 18 projects improving preparedness and response to outbreaks, rapid diagnostic tests, new treatments and new vaccines. Among these, 2 projects received EUR 5.7 million to develop safe and effective vaccines. These 2 projects are briefly presented in table 7.

Table 7: H2020 vaccine projects

	Objective	Leader	Partners	EU funding
OPENCORONA Rapid therapy development through Open Coronavirus Vaccine Platform	The project will use DNA vaccine technology to develop a vaccine that can also be used as a therapy against the virus.	Karolinska Institutet (SE)	7 partners: DE (1), IT (1), SE (5)	EUR 3,000,000
Prevent-nCoV Prevention of 2019 nCoV infection through development and clinical testing of a novel Virus Like Particle (VLP) vaccine	To develop and evaluate a potential vaccine that uses Virus Like Particle to expose coronavirus proteins to the immune system.	Københavns Universitet (DK)	6 partners: DE (1), DK (3), NL (2)	EUR 2,728,340

Source: Authors, based on https://cordis.europa.eu/project/id/101003666 and https://cordis.europa.eu/project/id/101003608.

Moreover, EUR 100 million of the first emergency call was awarded to CEPI to support the rapid development of COVID-19 vaccines. The bulk of this grant has been used for CEPI's partnership with SK

Bioscience to develop a variant-proof vaccine against SARS-CoV-2. The list of projects funded through the first H2020 emergency call is in Annex V.

On 3 March 2020, the Innovative Medicines Initiative (IMI), supported through the EC's H2020, launched a special fast-track call for the "Development of therapeutics and diagnostics combatting coronavirus infections" with an EU contribution of EUR 45 million, which was subsequently increased to EUR 72 million.[19] 8 projects were short-listed for funding. On 19 May 2020, the EC launched a second request for expressions of interest for innovative and rapid health-related approaches to respond to COVID-19 and to deliver quick results for society for a higher level of preparedness of health systems (SC1-PHE-CORONAVIRUS-2020-2) with a budget of EUR 129.5 million. 23 projects were short-listed for funding with a total of EUR 128.2 million. **However, none of the projects awarded in the context of these two calls involves funding for vaccines R&D**.

The EC also invested in developing clinical networks and research infrastructures to ensure preparedness to deliver clinical research. With nearly EUR 26.5 million coming from H2020, the EC funded the VACCELERATE project[20]. VACCELERATE platform acts as a single-entry point for vaccine developers that are interested in doing vaccine trials in Europe, maps clinical trial and laboratory sites across Europe and identifies the best locations for conducting Phase 2 and 3 vaccine trials. The project was launched at the beginning of 2021, nearly a year after the start of the crisis. It then took another year to develop a protocol. Hence, the platform started to operate in 2022 when the situation was completely changed with respect to 2020. VACCELERATE currently implements three trials. The first trial studies the immune response of a second booster vaccine in the elderly (over 75 years old), the second trial studies the immune response of a second booster vaccine in the general adult population, and the third trial evaluates regimens of reduced-dose vaccination in children.[21] VACCELERATE has been conceived as a pilot project, ending in 2024, but the idea is to scale it up to serve other diseases. It will be part of the preparedness initiative for the next pandemic. In principle, the platform could also serve pharmaceutical companies. However, since big pharma usually works with global contract research organisations (CROs), the platform is expected to mainly serve universities, research institutes and SMEs. Some related bibliography is presented in Annex 1.

3.2.2. EIB support for vaccines R&D and manufacturing

The European Investment Bank (EIB), working in collaboration with the European Commission, **has supported the development of vaccines and the expansion of manufacturing.** Loans are provided under the InnovFin Infectious Diseases Finance Facility, backed by Horizon 2020[22]. Specifically:

- On 11 June 2020, the EIB and BioNTech signed a EUR 100 million loan agreement[23] for the development and large-scale production of portfolio of vaccines, including a vaccine candidate against SARS-CoV-2. The deal also allowed the company to expand its manufacturing capacity in order to supply the vaccine worldwide quickly in response to the pandemic. BioNTech was not a new client for the Bank. In 2019, the EIB supported the company with a EUR 50 million loan agreement under the European Growth Finance Facility for BioNTech's personalised cancer

[19] https://research-and-innovation.ec.europa.eu/news/all-research-and-innovation-news/covid-19-horizon-2020-partly-funding-innovative-medicines-initiative-fast-track-call-2020-03-03_en.

[20] https://cordis.europa.eu/project/id/101037867/it.

[21] https://vaccelerate.eu/experts/.

[22] https://www.eib.org/en/products/mandates-partnerships/innovfin/products/infectious-diseases.htm.

[23] https://www.eib.org/en/press/all/2020-144-eib-to-provide-biontech-with-up-to-eur-100-million-in-debt-financing-for-covid-19-vaccine-development-and-manufacturing.

immunotherapy programme. Although the company – which was not revenue generating at the time - would have been able to raise the money needed even without the EIB loan, thanks to the high capitalisation and to the numerous partnerships in place, the support of the EIB offered the advantage to be immediate.

- In July 2020, the EIB and CureVac signed a EUR 75 million loan agreement for the development and large-scale production of vaccines, including CureVac's vaccine candidate against SARS-CoV-2.[24] In addition, the loan was supposed to support the company's efforts to expand its existing Good Manufacturing Practice certified production capabilities and accelerate the completion of its fourth production site in Tübingen, Germany.
- In June 2021, the EIB and Univercells signed a EUR 30 million loan agreement to enable the production of large volumes of COVID-19 vaccines in a new facility and to co-develop a pipeline of COVID-19 vaccines.[25]
- On 19 October 2021, the EIB and Hipra signed a loan agreement worth EUR 45 million to support the development of a new COVID-19 vaccine.[26] More specifically, the agreement covers R&D and manufacturing investments required to bring the vaccine to the market.
- In April 2022, the EIB signed a EUR 15 million loan with the Italian Biomedical Research Company (IRBM) to expand the capacity to make vaccines and increase research into the coronavirus and other diseases.[27]

The EIB, alongside the EC, also contributed to the global vaccine initiative COVAX, the international facility to ensure fair and universal access to COVID-19 vaccines. In December 2020, the Bank contributed EUR 400 million of financing to support the COVAX initiative to provide 1 billion doses for low- and middle-income countries. The EIB loan complemented a EUR 100 million EU grant to Gavi, the vaccine alliance, that administers the COVAX Facility.[28] Up to March 2022, COVAX has received a total of EUR 900 million from the EIB. In April 2022, The EIB pledged an additional EUR 1 billion to support COVAX.

3.3. The need for continuing supporting COVID-19 vaccines with public funds

The previous sections have presented some evidence on the role of private investors, governments, and NGOs in the funding of R&D and production of COVID-19 vaccines. This section discusses whether and to what extent it can be warranted to deploy such financial efforts in the future, focusing on the potential role of the EU and its Members States, and provides some policy recommendations. It does so after having presented the pandemic scenario for the next years, the R&D needs in such a future scenario, and current market failures.

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24 https://www.eib.org/en/press/all/2020-181-germany-eib-and-european-commission-provide-curevac-with-a-eur75-million-financing-for-vaccine-development-and-expansion-of-manufacturing.

25 https://www.eib.org/en/press/all/2021-243-belgium-eib-boosts-innovative-biotech-company-univercells-with-eur30-million-of-european-financing-to-support-covid-19-related-projects.

26 https://www.eib.org/en/press/all/2021-345-eib-helps-hipra-to-develop-a-covid-19-vaccine.

27 https://www.eib.org/en/press/all/2022-201-italy-eib-provides-eur15-million-to-fund-coronavirus-research-at-irbm.

28 https://www.eib.org/en/press/all/2020-366-team-europe-contributes-eur500-million-to-covax-initiative-to-provide-one-billion-covid-19-vaccine-doses-for-low-and-middle-income-countries.htm.

3.3.1. Pandemic or endemic COVID-19 in the next years?

Forecasting the evolution of the pandemic is not an easy task, given the unpredictable mutations of the virus, the possible changes in socio-economic conditions across the globe, and the transformation of policy responses. A notable example is the unexpected and sudden transition of China from a 'zero Covid' policy to one much more relaxed, with huge implications in terms of infection surges.[29]

The European Centre for Disease Prevention and Control (ECDC) has developed several models (see ECDC 2022b) to forecast how the COVID-19 pandemic may evolve in terms of cases, hospitalisations and deaths.[30] Most of the existing models focus on a time horizon of 9-12 months, which is not particularly helpful to decision-making on vaccine R&D, which may take years to deliver a viable innovation. Several reviewed papers tend to align with statements such as the following one by Reiner et al. (2022):

"As infection-derived and conferred protection wanes, we expect infections to rise, but given the large proportion of the population that had some level of immunity to SARS-CoV-2 as of June 1, 2022, all but the most pessimistic forecasts in this analysis do not predict a massive global surge by November 30, 2022. All signs point towards COVID-19 transitioning into a more endemic transmission regime (lower, but sustained disease burden), and with the introduction and proliferation of novel therapeutic interventions expected in mid- to late 2022, the likelihood of returning to past levels of COVID-19 mortality is low. The characteristics of future COVID-19 variants are difficult to predict, and our forecasts do show some considerable variation in outcomes as a function of variant properties."

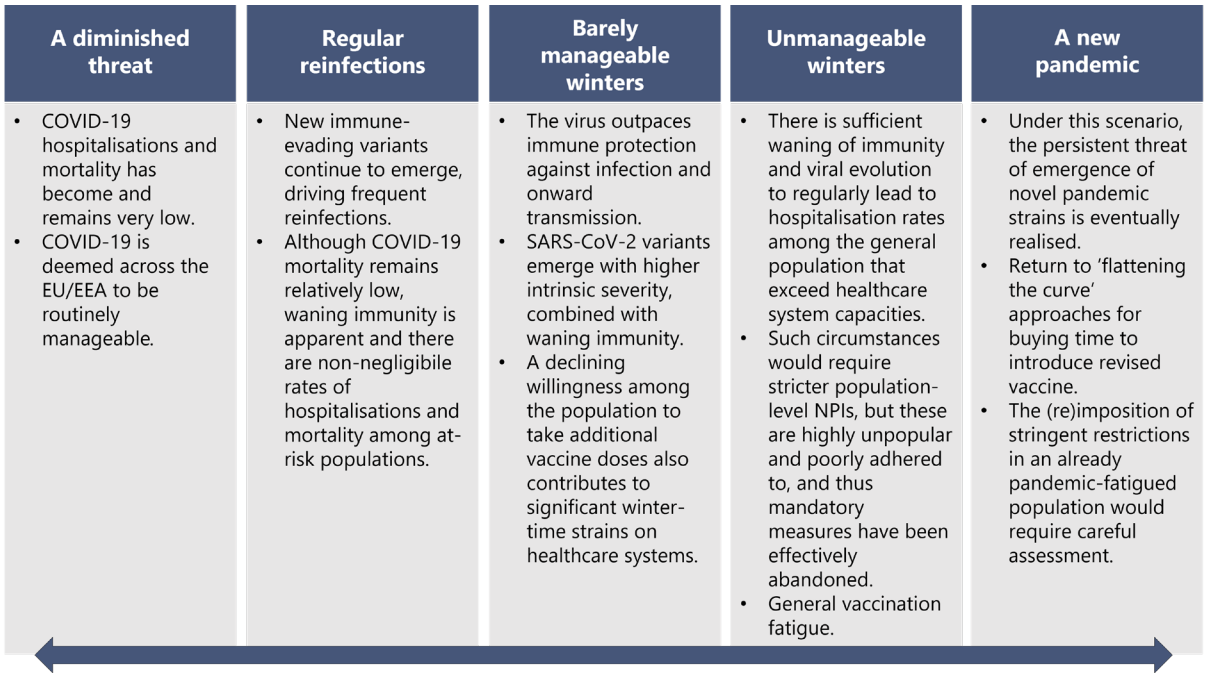
However, **the ECDC (2022a) has provided some qualitative scenarios to 2032**, summarised in Figure 7, which shows a range of possible outcomes from a 'diminished threat' to 'a new pandemic', with intermediate cases, depending upon different combinations of factors such as:

- viral properties, including viral evolution, growth rate, disease severity (intrinsic), seasonality;
- immunology, including immune protection from severe outcomes, duration of protection;
- societal factors, including societal tolerance for non-pharmaceutical interventions (NPI) and infection prevention and control (IPC) measures, societal tolerance for the residual risks of COVID-19, vaccination acceptance, healthcare system capacities;
- medical interventions including vaccines, antiviral medications, diagnostics.

[29] See Nixon et al. (2022) on the conceptual and technical issues involved.

[30] See the European COVID-19 Scenario Hub launched in May 2022. It will serve as a resource for Member States in their pandemic planning and inform decisions aimed at minimising the expected burden caused by COVID-19 under different scenarios. The hub is developed and run by the European Centre for Disease Prevention and Control (ECDC) in co-operation with the Centre for Mathematical Modelling of Infectious Diseases (CMMID) at the London School of Hygiene & Tropical Medicine (LSHTM).

Figure 7: Qualitative long-term scenarios



Source: Authors, based on ECDC (2022).

The ECDC (2022a) concludes that:

"Given the number of uncertainties surrounding possible trajectories for the COVID-19 pandemic, particularly in light of the continued high levels of viral transmission globally, and the possibility that new variants of concern may arise, ***it seems clear that SARS-CoV-2 is here to stay****. As such, public health systems, clinical services and society in general will need to adapt to the fluctuating levels of threat that this virus is likely to present in the coming years. [...]* ***Common to all scenarios is the perpetual risk posed by new SARS-CoV-2 variants****. A key message is that even when or where current scenarios appear to be less severe, adequate surveillance and monitoring systems need to be in place to detect changes in the level of threat posed by SARS-CoV-2, and preparedness must be strengthened in order to mount an effective and proportionate response to rapidly deteriorating situations."*

The experts consulted for the present study broadly concur with this view. The following statements have some implications for R&D needs discussed in the next section:

- "SARS-Cov-2 is here to stay".
- "Variants of concern may arise".
- "A new pandemiccannot be excluded".

3.3.2. R&D needs

The scientific knowledge about how to design COVID-19 vaccines has made significant progress in the last three years, but it is far from having achieved a steady state. According to the dashboard made available from the Covid-19 - living NMA initiative, on January 20, 2023, there were 932 ongoing clinical studies from phase 1 to 4 covering a range of technologies: RNA based vaccine (27%); Protein subunit (25%); Non replicating viral vector (17%); Inactivated virus (16%); Others (15%). The latter are studies on other technologies, classified as: DNA based vaccine, virus-like particle, replicating viral vector, viral vector (non-replicating)/APC (antigen presenting cell) and others. Several studies are of

comparative nature and may cover the efficacy of different technologies. Overall, about 4,4 million patients were involved in clinical studies (as of 5 January 2023).

Concerning the sponsor/funder of the studies, it is interesting to observe that along with major companies, many studies are supported by public sector organisations, universities, and not-for-profit entities. For example, just considering RNA based vaccines (all phases, totaling to 255 studies as of 20 January 2023), along with companies such as BioNTech (20 studies), Moderna (14 studies), CureVac (6 studies), AIM Vaccine (5 studies), Sinocelltech (4 studies), CanSino (3 studies), GSK (3 studies), there are a large number of studies registered by such entities as National Institute of Health-National Institute of Allergy and Infectious Diseases NIH-NAIAD (14 studies), Thai National Vaccine Institute, Murdoch Children's Research Institute, University Medical Center Utrecht (with 5 studies each), University of Cologne, Chulalongkorn University, University College Dublin (with 4 studies each). Focusing only on the 41 studies at Phase 3 (as of 20 January 2023), 17 are registered by companies and the remaining 24 by a mix of public / not-for-profit entities. A similar pattern of industry and public sector sponsored studies can be observed for the other vaccine technologies, with public and private sector sponsored studies registered for phase 1 and phase 2 having similar shares.

Consensus exists on continuing support of COVID-19 vaccines adopting a portfolio strategy. The fact that so many studies are going on worldwide, with so many research teams involved, indicates that several research questions are still not answered. Looking at the literature (drawing also from Remuzzi and Florio, forthcoming 2023) and based on interviews with experts, including particularly Prof. Oliver A. Cornely (University of Cologne), Dr. Gary L. Disbrow (BARDA), Dr. Emily Erbelding (NIH), Dr. Christiane Gerke (Institute Pasteur), Prof. Andrew Pollard (Oxford), Prof. Giuseppe Remuzzi (Mario Negri Institute), and with some company representatives, the potential avenue of public support is many-fold:

- **Developing a novel vaccine platform to target some more stable features of the virus in order to induce durable sterilising immunity.** For the COVID-19 mRNA vaccine, data suggest that protection to viral infection may last 3 months or shorter, despite a remarkable and durable protection against hospitalization, severe disease and death. To overcome this limitation and to keep up with mutations, multiple booster shots have been authorised to restore antibody waning and confer additional protection. However, recent data suggest that the efficacy of updated bivalent vaccine boosters may not be as effective in preventing viral infection against different variants. This finding could be explained by the so called 'immune imprinting': an initial exposure to a virus limits a person's future immune response against different variants by triggering the antibody response against the initial viral strain encountered during vaccination or infection (Brazil, 2023). Therefore, according to some experts' opinion[31], R&D should focus at developing novel vaccine platform to target some more stable features of the virus in order to induce durable sterilizing immunity (see box below).

[31] Source: interview with Professor G. Remuzzi by the PI.

Box 7: Novel vaccine platform: approaches

The approaches to develop novel vaccine platform to target some more stable features of the virus in order to induce durable sterilizing immunity might include, among many other methods, targeting S protein viral sequences that are immutable, immunogenic, and accessible to neutralizing antibodies; including other targets from the virus such as portions of the membrane, envelope, or nucleocapsid proteins; targeting conserved or occluded (structurally hidden) epitopes using nanoparticles of randomly arrayed receptor binding domains; and developing vaccines based on T-cell receptor constructs that specifically recognize the SARS-CoV-2 RNA-dependent RNA polymerase (Marks et al., 2023).

Source: Remuzzi and Florio, forthcoming 2023.

- **Investing in the so-called next/new/second generation COVID-19 vaccines**, i.e., vaccines that offer a longer protection and/or a broader range of protection, meaning they are multi-balanced (Marks et al., 2023). With a new-generation SARS-CoV-2 vaccine, it would not be necessary to modify the vaccine every time a variant comes up and to have a booster shot to restore protection. Possible approaches to achieve more durable SARS-CoV-2 vaccine immunity include the followings: (i) variant-proof SARS-CoV-2 vaccines; (ii) pan-sarbecovirus vaccines (i.e., against sarbecoviruses, the subgenus that includes all the SARS-like viruses); (iii) pan-betacoronavirus vaccines; (iv) pan-coronavirus vaccines. Regarding variant-proof SARS-CoV-2 vaccines, different approaches are possible (see box below). Other strategies seek to cover incrementally broader Corona Virus (CoV) space. A strategy seeking to confer pan-sarbecovirus coverage is the nanoparticle vaccine (Mosaic-8b) developed by Cohen and colleagues (Cohen et al., 2022). For the other two approaches, see the next bullet point. Among others, CEPI invests in exploring a distinct way of designing a shot that will be broadly protective against one or more coronaviruses.[32] Since it is not known yet which scientific approaches will work, CEPI considers having a portfolio of options to maximise the chances of success – just as it was done with first generation COVID-19 vaccine development. CEPI's approach is considered promising by all the interviewed experts.

Box 8: Variant-proof SARS-CoV-2 vaccines: approaches

Approaches include: multivalent platforms or formulations with distinct variants (with or without the ancestral SARS-CoV-2 Spike strain); inserts designed to elicit cellular responses (such as Nucleocapsid, that is an internal RNA-binding protein which has long been viewed as an important target for T-cell response, that may eventually confer broad protection); or the ancestral SARS-CoV-2 Spike strain in a platform deemed to elicit broader and more potent immunity. It is important to note that these variant-proof strategies do not necessarily include distinct variant sequences, because it is argued that a given vaccine candidate based on the ancestral SARS-CoV-2 antigen could offer superior immune responses that would cover a broad array of viruses. In this regard, researchers at Duke University have developed a vaccine candidate based on the ancestral SARS-CoV-2 strain and aimed to be variant-proof (Li D et al., 2022).

Source: Remuzzi and Florio, forthcoming 2023.

[32] https://cepi.net/news_cepi/the-race-to-future-proof-coronavirus-vaccines/.

- **Investing in the fundamental research for the so-called universal coronavirus vaccines, or at least a pan-betacoronaviruses vaccine**.[33] This avenue of research, which is, for instance, in the NIH-NIAID agenda[34], is the most ambitious and risky. Anthony Fauci, former director of the NIAID, called the development of universal coronavirus vaccines an "urgent need".[35] He argued that more resources are needed to continue the fight, and he has been publicly lobbying lawmakers to allocate them. However, other experts are more sceptical, and point out at the experience with influenza for which, despite decades of research, such a next-generation vaccine has not been developed yet. Hence, they suggest to invest on monitoring, adaptation, and periodic boosters rather than on R&D on a pancoronavirus vaccine.
- In fact, because COVID-19 might become endemic and because the possibility to develop a universal vaccine is highly uncertain, it is also considered necessary to **continue investing in a sophisticated monitoring system** similar to what governments have put in place for influenza. Indeed, the influenza vaccine composition is reviewed before every flu season because influenza viruses constantly evolve through antigenic changes. To inform vaccine updates, laboratories that contribute to the World Health Organization Global Influenza Surveillance and Response System monitor the antigenic phenotypes of circulating viruses all year round. Vaccine strains are selected in anticipation of the upcoming influenza season to allow adequate time for production.
- Since booster doses of existing vaccines are still needed, **studies on under-investigated topics on existing vaccines** are necessary, including: 1) studies on the vaccines for children and their dose (some experts do not see this as a critically important issue, except as an indirect way to protect elderly patients through increased vaccination of the children); 2) real-life studies to determine effectiveness of vaccines with updated composition and according to different platform technologies over time and across target populations; 3) studies to investigate more in-depth the differences of responses to vaccines for specific immunocompromised populations in order to adjust vaccine schedules. Since activation of innate and adaptive immunity by SARS-CoV-2 vaccines is essential for triggering host immune response, immunosuppressive agents given chronically to these patients might restrict such response, eventually reducing the efficacy of the vaccine. An example is the case of people with multiple sclerosis who are considered at high risk for COVID-19-related complications and at increased risk of disease relapse induced by the infection (Capone et al., 2023).
- **Needle-free vaccines**. Most people dislike getting a needle in their arm, so the idea of getting a vaccine in a puff of nasal spray sounds attractive in terms of social acceptance, particularly for children. Beyond this, there are signs (Tang et al., 2022; Mao et al., 2022) that intranasal vaccines may be better than ordinary vaccines at preventing respiratory viruses from spreading between people because they induce an immune response concentrated in the mucosal tissues of the airways, where the COVID-19 virus enters the body. According to an expert opinion[36], there are at least 12 nasal vaccines that are in clinical development, and 4 have reached phase 3 randomised, placebo-controlled trials, with promising results. However, while for an intramuscular COVID-19

[33] A pan-betacoronaviruses vaccine would be against betacoronaviruses that includes the original SARS-CoV-1, and MERS-CoV, as well as the pandemic SARS-CoV-2, some of the seasonal coronaviruses that cause common colds in people, and several other coronaviruses that circulate widely in bats. There are ongoing studies testing pan-betaCoV vaccines, but details on the vaccine inserts are not available (Dolgin, 2022).

[34] https://www.niaid.nih.gov/news-events/niaid-issues-further-awards-pancoronavirus-vaccine-development.

[35] Morens, M.D., Taubenberger, J.K., and Fauci, A.S. 2022. Universal Coronavirus Vaccines — An Urgent Need, New England Journal of Medicine 386: 297-299. Available at: https://www.nejm.org/doi/full/10.1056/nejmp2118468.

[36] Source: interview with Prof. G. Remuzzi by the PI.

vaccine it is easier to assess the effectiveness, measuring the neutralizing-antibody levels circulating in the blood, for mucosal vaccines the measuring of immune responses is not straightforward (Waltz, 2022; Topol and Iwasaki, 2022). Nasal vaccine technology is still relatively new and, therefore, further trials to study the immune response of such vaccines and their overall effectiveness are needed.

- **Comparative studies:** Safety of vaccines approved by the major agencies is overall good, and adverse events are rare and, in most cases, allow full recovery. However, since not all platforms cause the same reactions, a better understanding of the underlying mechanisms according to which the vaccines cause side effects, in conjunction with the identification of the vaccine components and/or platforms that are responsible of these reactions in terms of pharmacovigilance, could probably enable the improvement of future vaccines against COVID-19 and/or even other pathological conditions, as highlighted by one of the interviewed experts.
- **Stabilisation of vaccines:** the cold chain particularly for mRNA vaccines preservation is challenging, particularly in countries with frequent electricity interruptions. CEPI has launched a call for new ways to preserve the vaccines[37].

The list is not exhaustive but representative of the open research questions.

3.3.3. Market mechanisms and possible failures

Several of the above-mentioned issues would require R&D strategies that are not in the immediate interest of the industry to self-fund and perform. A previous study for the European Parliament (Florio *et al*., 2021; Florio and Gamba, 2021) has identified six structural market and policy failures in pharmaceutical R&D. They are briefly recalled below, where it is also argued why they are relevant to COVID-19 vaccines.

- **Disconnection between corporate R&D choices and public health priorities**: The industry has been successful in providing a portfolio of vaccines against SARS-CoV-2 in a very short time. This result stands on the shoulders of more than two decades of substantial intellectual contributions by public and not-for-profit entities. Concerning the mRNA technology, the public contribution includes specific intramural and extramural programs of the NIH-NIAID, and discoveries at the University of Pennsylvania, which were instrumental to the development of both the Moderna and Pfizer-BioNTech vaccines (see Lalani et al. (2021) and Florio (2022)). For the viral vector-based vaccines, previous research conducted at the University of Oxford was, for instance, essential to developing the Oxford-AstraZeneca vaccine. Moreover, several more traditional inactivated virus vaccines worldwide were developed by scientists in public research institutes and only later produced and distributed by companies (Wouters et al., 2021). In fact, most established companies have divested R&D on vaccines and infectious diseases in the last decades (Taghreed et al., 2019; PharmaProjects, 2020) and they rushed on the COVID-19 arena when the business case became highly favorable. Even such rush was sustained by exceptional disbursement of public money in various forms and other de-risking mechanisms, as documented in the previous sections. Hence, with only a small number of exceptions (an example is the vaccine candidate by Hipra, a Spanish 'outsider' company specializing in veterinary medicine), established companies were substantially incentivised to deliver vaccines by governments, international institutions, and not-for-profit entities.

[37] https://cepi.net/news_cepi/cepi-opens-call-to-develop-heat-stable-vaccine-tech-for-use-against-epidemic-and-pandemic-threats/

- **Mismatch between open science in the public sector and patents protecting the investors**: The business model of the pharmaceutical industry for COVID-19 vaccines heavily relies on the 'legal monopoly' provided by filing a patent or family of patents. The traditional aim of patent legislation is to counterbalance the private incentives of legal monopoly with an obligation to publicly disclose information on inventions in the patent files. This disclosure in principle would create a positive externality, as the social value of a patent would be greater than its private value because third parties would benefit from such public information. However, this disclosure mechanism has limited scope because trade secrets remain de facto undisclosed. This fact was evident in the case of the Moderna vaccine. Moderna announced it would not start legal actions against imitators of its vaccine, but refused to collaborate with the mRNA hub that the WHO has established in South Africa.[38] The intellectual property model adopted by pharmaceutical companies has contributed to inequitable access to COVID-19 vaccines and has created a public debate about the need for a COVID-19 intellectual property waiver, a view shared by the majority vote of the European Parliament[39], and by initiatives supported by over one hundred countries at the WTO (Foss-Solbrekk, 2021).

  The protection granted by patents is even more disproportionate considering the increasing diffusion of open science practices in fundamental research, primarily funded by public money, providing free access to a wealth of scientific results to private companies. An example is the immediate availability of the SARS-CoV-2 genome in the public domain after its sequencing in China and deposit to the GenBank (Wu et al., 2020). In the legislation or actual practice, there is no systematic policy frameworks to deal with the protection of the public interest when a combination of open science upstream, government subsidies to R&D, patents, and market authorization leads to unaffordable prices and scarcity of medicines in specific fields.

- **Excessive rents for financial investors in the industry.** The issue of expensive drugs and high profitability of the pharmaceutical industry has attracted the attention for example by the US Government Accountability Office (GAO, 2017) and others respected economic analysts (see, e.g., Ledley et al., 2020; The Economist, 2019). Even after discounting for R&D expenditures and risks, the return on sales and other financial performance indicators from official company reports signal that the pharma industry is highly profitable. Negotiated prices for COVID-19 vaccines are, in most cases, unknown, as well as the marginal cost and the average cost per dose. Thus, income earned by sales of COVID-19 vaccines is also unknown, but a back of the envelope calculation suggests it is extremely high. According to the ECA (2022), the average price of COVID-19 vaccine doses acquired by the European Commission until December 2021 was EUR 15. The first APA between the EU and Moderna and the EU and AstraZeneca mention a price of EUR 2.90/dose for the latter company, and at USD 22.90/dose for the former.[40] Kates et al. (2022) estimates the US federal government has paid Pfizer and Moderna USD 19.50 per dose and USD 15.25 per dose, respectively. Concerning the average cost per dose, the Imperial College researchers (Kis and Rizvi, 2021) estimate the cost per dose for mRNA vaccines to be about USD 1.18 for Pfizer/BioNTech and USD 2.85 for Moderna[41], which would generate huge profits if compared with these prices per dose.

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38 https://healthpolicy-watch.news/moderna-waives-its-covid-patent-permanently-but-wont-share-tech-with-mrna-hub/.

39 https://www.europarl.europa.eu/doceo/document/A-9-2021-0284_EN.html.

40 For the AstraZeneca, see unredacted version of the APA's here: https://www.rai.it/dl/doc/2021/02/19/1613725900577_AZ_FIRMATO_REPORT.pdf and for Moderna here: https://www.rai.it/dl/doc/2021/04/17/1618676613043_APA%20Moderna__.pdf.

41 The report from People's Vaccine Alliance provides example of prices charged by different companies to different countries. Pfizer/ BioNTech is said to charge the lowest price of USD 6.75 to the African Union and the highest price of USD 28 a dose to Israel. Moderna

Given the total EC purchase expenditure of EUR 71 billion reported by the European Court of Auditors (ECA) at EUR 15 average price per dose, income of the order of tens of billions have been earned by investors and extracted from European taxpayers in less than two years. Corporate taxation may have recouped ex-post some extra-profits, but to a limited extent and not mainly for the EU taxpayers, given that US-based companies had the lions' share in the market, and consequently in the income earned from the contracts. Private profits may further increase since, following the Biden Administration announcement to prepare for the transition of COVID-19 vaccines to the commercial market, some companies have indicated a prospect price increase up to 130 USD per dose without evidence of corresponding increased costs.[42]

- **Oligopolistic market power on the supply side, and issues of access and affordability**. The current market landscape of approved COVID-19 vaccines shows a highly skewed distribution: an oligopolistic core with a fringe of companies. This market structure may contribute in the future to high vaccine prices, which, in turn, may create affordability problems for patients and sustainability of healthcare systems, particularly, but not only, in less developed economies. To the best of our knowledge, no competitive mechanism has been put in place. For example, we have not been able to spot any intention by governments and international authorities to recur to competitive bids for procurement[43], even among those COVID-19 vaccines that are based on similar technologies or when the effectiveness varies from vaccine to vaccine. Cost-effectiveness of vaccines is something which deserves attention. The price of vaccines per dose differs by orders of magnitude, from USD 3-4 for Oxford-AstraZeneca vaccines to over USD 100 USD according to Pfizer communication to investors for future sales. Hence, the implied cost-effectiveness, e.g., the deaths avoided per Euro spent across available vaccines, also varies hugely.
- **Inadequate optimisation studies after market authorisation.** While companies have the incentives to invest money in preparing clinical trials and other studies to support their applications for marketing authorisations, they have no incentive to perform comparative clinical trials and 'real life' studies after a drug has been authorised (Lacombe *et al*., 2019), especially if they include post-authorisation comparisons across medicines, including those of competitors. Since these aspects are relevant in a public health perspective, regulators may try to convince companies to perform long-term studies, or they can commission such studies from third parties. The first approach may not be successful for lack of incentives. The second approach has been implemented, so far, only in a non-systematic and often voluntary manner by non-commercial entities, as suggested by the analysis of existing clinical trials for COVID-19 vaccines.[44] Clearly, there are statistical difficulties in

offered South Africa a price between USD 30-42 a dose. Colombia has paid twice the price paid by the US for Moderna vaccines. Senegal said it paid around USD 20 a dose for Sinopharm vaccines.

42 Pfizer indicated that the expected commercial price per dose for its vaccine is in the range of USD 110-130: https://s28.q4cdn.com/781576035/files/doc_downloads/2022/10/IDWeek22/PFE-USQ_Transcript_2022-10-20.pdf, while Moderna has suggested a commercial price between USD 82 and USD 100 per dose: https://s29.q4cdn.com/435878511/files/doc_presentations/2022/09/Moderna-Final-R-D-Day-Slides_PDF-(09.08.22).pdf.

43 While negotiated procedures can be inevitable in case of extreme urgency, in normal times, competitive bids for procurement help governments spur competition, which is a crucial element in price setting since it naturally leads to price decreases. The objective of international competitive bidding, or open tendering, is to provide potential bidders an equal opportunity to participate in the tender procurement system. Awards should be based on the most attractive offer from suppliers who meet the tender provisions regarding quality, price, and additional supplier services (e.g. speed, cold chain logistics, and supply security). If the creation of a competitive environment for procurement next-generation COVID-19 vaccines seem too far-fetched, pull mechanisms in the form of Advance Market Commitments should at least be considered. These are commitments to suppliers as a group rather than bilateral contracts with individual firms (such as APA). They aim to incentivize suppliers by promising to buy an agreed quantity of qualifying products at a fixed price without committing specific volumes to particular suppliers (for a discussion see e.g. Towse et al., 2021; Thornton et al. 2020). In principle, Advance Market Commitments can also differentiate the reward to reflect quality differences between products (see for instance the proposal of Chalkidou et al., 2020).

44 Available at: https://Covid-19 - living NMA initiative.

performing observational studies or randomised trials after three years of the pandemic, with billions of people vaccinated and /or exposed to the virus in one or more of its variants.

- **Information asymmetries in the public procurement**. Pharmaceutical companies have no interest in sharing information on the cost structure of R&D, or the production and distribution cost. Hence, most public authorities have limited data to ascertain whether their public procurement arrangements, including the long-term resilience of production capacity in a country, are efficient. The pandemic has revealed and confirmed some structural failures of market arrangements and current policies in this area. New policy options should be considered for the future.

3.3.4. Policy options

Betting on a benign evolution of the COVID-19 pandemic does not seem in compliance with a precautionary principle from a health policy perspective. In spite of the current global data pointing to endemic disease with low fatality rate (worldwide 1% deaths out of confirmed infections, seven times less than at peak in March 2020[45]), four out of five ECDC scenarios suggest that the future impact of COVID-19 will be non-negligible in terms of stress on the health system because of hospitalisations, vaccination demand, and medical assistance demand, particularly for the elderly and other patients at risk. Given the demographic structure of the EU in the next decade, this is not a minor challenge. According to Eurostat data, in early 2018, there were 101.1 million older people (aged 65 years or more) living in the 28 EU countries, which is 19.7% of the total population (Eurostat, 2019). According to latest data, in 2021, more than one-fifth (20.8 %) of the EU population was aged 65 or more and the share of people aged 80 years or above in the EU's population is projected to have a two and a half fold increase between 2021 and 2100, from 6.0 % to 14.6 %.[46]

Hence, even in the more limited perspective of health threats for the higher-risk population, **the forecast that SARS-CoV-2 will be around for at least the next ten years calls for sustained attention**. Particularly for vaccination, given that, until now, other medical remedies, including antiviral drugs, played a limited role. Moreover, even in the endemic scenario, the impact of a pathology, year by year affecting a non-negligible part of the population, has socio-economic consequences in terms of absence from work and assistance to relatives. In this regard, the global burden of pediatric COVID-19 is potentially not insignificant as well (Kaslow et al., 2022).

The crucial question is, therefore, whether, in a scenario of the continued need for vaccinations globally with high priority for older people and those with co-morbidity, **there is a need for further R&D on COVID-19 vaccines**.

The currently available vaccine portfolio has limitations that cannot be ignored. The most important one is the drop of antibodies over a relatively short time and their limited resilience to virus mutations, particularly those mutations changing the spike glycoprotein (since most existing vaccines activate the immune system with the spike glycoprotein as the target). By looking at the clinical trials submitted for registration by current and potential new players, **it seems clear that the industry will continue to invest in the R&D of adapted vaccines**. Nowadays, the size and profitability of the COVID-19 vaccine market are considerable (even if not without risk for some companies). Hence, most experts do not

[45] see https://ourworldindata.org/mortality-risk-covid

[46] https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Population_structure_and_ageing.

expect a need for a new "Warp Speed" size operation in the range of billions of Euros of subsidies to the industry to push it to invest in R&D and new production capacity.

However, the industry is unlikely to deploy the effort needed on all or most of the research avenues previously discussed (see section 3.3.2), particularly if this would imply abandoning previous corporate investment when new solutions may risk crowding out established market dominance. After all, one can assume that a company would develop selected projects based on its business case and not mainly on public health considerations.

Moreover, **there are lessons to be learned** from the recent past for what concerns the European scenario. Namely:

- **avoid fragmentation and duplication of funding of R&D on COVID-19 vaccines**. In the US, the yearly budget of NIH in 2021 was USD 43 billion[47] (Sekar, 2022), while the budget of BARDA[48] for pandemic preparedness in normal times is USD 1.5-2 billion per year, out of which about USD 550 million for advanced research and development and USD 300 million for pandemic, and this is part of wider HHS department frame.[49] In Europe, the lack of a pan-European major public research institute has the undesirable consequence that for vaccine science (as for the rest of biomedical research), grants of relatively small size are disbursed by several players with very limited coordination among them, both at EU[50] and at the level of the Member States.[51] Thus, there is the risk that no program reaches the necessary critical mass to orientate private R&D investments. With the launch of HERA and the forthcoming Strategic Research and Innovation Agenda[52] for pandemic preparedness, the situation may improve, but probably not dramatically. Indeed, HERA's funding mechanisms suffer significant vulnerabilities (see box 9).

[47] From FY2016 through FY2022, NIH has seen funding increases each year. In 2016 the budget was USD 32.3 billion, in 2022 USD 46.1 billion (Congressional Research Services. 2022. National Institutes of Health (NIH) Funding: FY1996-FY2023).

[48] It is within the Administration for Strategic Preparedness and Response in the U.S. Department of Health and Human Services.

[49] https://aspr.hhs.gov/AboutASPR/BudgetandFunding/Pages/BudgetandFundingFY2021.aspx.

[50] One cluster out of six of the EU Research Framework Programme for 2021-2027 is specifically dedicated to health. Such cluster also support the Innovative Health Initiative, a public-private partnership aimed at supporting pre-competitive research for products or solutions that respond to unmet public health needs and that can be implemented into healthcare systems. The resources available to IHI are up to EUR 1.2 billion provided by the Horizon Europe Health Cluster, at least EUR 1.0 billion provided by the member industry associations, and up to EUR 200 million from Contributing Partners (source: Innovative Health Initiative, 2022). The work programme for 2023 of the EU4Health Programme provides EUR 100 million to Thematic Innovation - Research, Innovation and Digitalisation Window financial product (more specifically, in the policy area '1.1 Health innovation investment') implemented by the EIB under the InvestEU Fund. The aim is to support investments into R&D of medical countermeasures for pandemic preparedness, in particular into vaccines and other preventive interventions, therapeutics, and diagnostics. HERA will cooperate with EIB for the successful implementation of the action. The work programme for 2023 of the EU4Health Programme also provides EUR 84 million to support HERA to speed up the development of, access to and/or uptake of innovative technologies and critical medicines.

[51] The fragmentation of the health research system is also recognised in the by the Innovative Health Initiative (see IHI, 2022).

[52] In 2023, HERA, together with other Commission's services and in cooperation with Member States, will be involved in the preparatory phase of the EU Partnership on Pandemic Preparedness, which intends to develop a Strategic Research and Innovation Agenda for pandemic preparedness by 2024.

Box 9: The HERA arrangements in the domain of R&D promotion and funding: some issues

The total budget of HERA for 2022 amounted to EUR 1.3 billion. Out of this, EUR 306.8 million were dedicated to promoting R&D (EC, 2022). In 2023, the total HERA's budget is 1.267,6 million and includes contributions from EU4Health (EUR 242,75 million), Horizon Europe (EUR 389 million) and UCPM/rescEU (EUR 636 million) Programmes. Out of this, EUR 474.6 million (of which about EUR 390 comes from Horizon Europe) are dedicated to promoting advanced R&D of medical countermeasures and related technologies (EC, 2023). HERA's activities in promoting R&D for medical countermeasures are mainly implemented via calls under Horizon Europe. The limited funding and the reliance on Horizon Europe calls generate some weaknesses. First, Horizon Europe calls have a fairly limited duration of funding, i.e. 3 to 5 years. They are mainly focused on comparatively short-term impacts (diagnostic devices, etc.), rather than on urgently needed horizon-scanning activities or on the long process of developing medical countermeasures. Second, HERA's R&D funding is constrained by Horizon Europe rules (e.g. consortia must usually be composed of at least three organisations, funding is allocated via open competitive calls, priorities are defined in biannual programmes agreed through the comitology procedure and there are geographical limitations to projects). Third, HERA's ability to allocate funding more flexibly and in fast-track when needed is strongly limited (e.g., in comparison with BARDA). Allocating larger sums of money in a single call or grant, or focusing the scope of calls on certain technologies or research areas will therefore be difficult for HERA. Fourth, the scientific independence to set the priorities of the research agenda, activities, and outputs might not be guaranteed, since HERA currently relies on an external advisory forum composed of experts that can provide scientific advice, when needed (a strategic agenda for research and innovation needs and gaps for pandemic preparedness will be ready for 2024). The current arrangement is different from a governance where the scientific community is empowered of a co-decision process. Finally, the scale of funding provided altogether by Horizon Europe calls and EU4Health programmes to HERA does not match the funding needs required to support R&D for a new vaccine, a new drug or a new technology (on average may require EUR 1 billion per each project).

Source: Authors, based on EC (2022), EC (2023); EP (2021), and Renda *et al*. (2023).

- In a previous study for the EP (2021), the **creation of a European R&D infrastructure and delivery organisation for medicines** was suggested. One of the options considered is to set up such infrastructure with a focus on infectious diseases at the scale, for example, of the European Space Agency (around EUR 7 billion in 2022[53], including contributions to specific missions by some participants), and with independent governance delegated to the scientific community. This action would close the gap with the US in this area and terminate the current fragmented situation, by achieving over one hundred innovative products in 30 years in areas neglected by industry or where there are social affordability concerns because of high prices.

[53] https://www.esa.int/ESA_Multimedia/Images/2022/01/ESA_budget_2022.

Box 10: Portfolio approach

A possible criticism of the proposal to create a European public infrastructure for biomedical R&D is that the pandemic has shown the difficulty of determining in advance which vaccine would be the most effective and timely. The US BARDA and the German government are two cases in point. For example, BARDA's COVID-19 medical countermeasure portfolio includes 105 products, of which eight were vaccines. Among others, they supported the Sanofi-GSK recombinant protein vaccine, which was initially unsuccessful, and the Merck-IAVI vaccine project, which was then cancelled. Another example is the German government's decision to initially support BioNTech and CureVac vaccines. The latter was then withdrawn. In 2022, the German Government reinforced its partnership with five companies (BioNTech; CureVac/GSK; Wacker/CordenPharma; Celonic; and IDT Dessau) in the form of a fee for production capacity until 2029 possibly also for new pandemic episodes, with a contract of EUR 2.861 billion. Hence, the German government is betting on different players for the next generation vaccines. The lesson to be learned from the BARDA and German government story of support to vaccine R&D is that failures are part of the scientific landscape and, therefore, public support, in whatever form, cannot focus just one project, or even to avoid any support to R&D because of the risk of failure. Thus, should European institutions take the bold step to create a European R&D infrastructure and delivery organisation for medicines, a portfolio approach with competing candidates screened and recommended by the scientific community could be developed under one roof. A portfolio approach is different from duplications and fragmentation of resources that we have noticed in the current EU context, where a plethora or relatively small projects are funded with public money, either by the Member States or by EC managed programs, without a unique place where a comparative appraisal of scientific merits is done by an expert body empowered to do so, as, by comparison happens at CERN or EMBL.

Source: Authors based on BARDA's Expanding, COVID-19 Medical Countermeasure Portfolio and Bundesministerium für Gesundheit, 2022.

Even if initiated soon, the creation of such infrastructure would require several years to reach a consensus among Member States and possibly some non-EU partners. Hence, in **the short term, the design of the current R&D funding mechanisms for coronavirus in the EU and the role of HERA should be reconsidered**. The latter should evolve into an autonomous science-based agency - without the constraint to leverage on different funds - with, among others, the potential to drive the COVID-19 vaccine landscape. Currently, in fact, the funding of future R&D on COVID-19 vaccines remains disbursed by different actors and programs[54], that evolve along different legal basis, management styles, and timing.

- **Ensure public support for late development of the next generation COVID-19 vaccines or vaccines protecting against unknown coronaviruses**. While in the first two phases of vaccine development the financing is well covered by governments and investors such as CEPI, some private foundation, PATHS and others, in the third stage, which actually accounts for about 70% of total development costs, there is a big gap in financing (Yamey *et al*., 2020). It cannot be expected that private companies alone invest in late development, especially when there is not a clear market to serve. Previous own negative experience on vaccines may also determine the reluctance of some pharmaceutical companies to join the race of new vaccine developments. Therefore,

[54] See footnote 51.

ensuring consistent funding during the whole process of vaccine development is essential. In the US, NIH supports basic research and potentially phase 1 of clinical trials, then BARDA carries out phase 2, and if possible, phase 3. BARDA also supports the scale up and manufacturing process. Current HERA arrangements miss a solid and agile mechanism to ensure interaction with research institutes and the private sector, an element that proved essential, inter alia, for BARDA's successful handling of R&D during the COVID-19 pandemic (Renda *et al*., 2023). Should the European Union want to have a prominent role in supporting the development of future coronavirus vaccines, as well as to fill existing gaps in unmet clinical needs, and be prepared for high-impact health threats,[55] it should invest reasonable funding to directly address areas where the disconnection between corporate R&D and public health needs is larger. According to interviewed experts, investments on the scale of EUR hundreds of millions would be needed to support phase 2 and phase 3 studies (and billions for a portfolio approach of vaccines and medical countermeasures on selected pathogens).

- **Create a favorable regulatory and infrastructural environment for clinical trials in Europe.** Another peculiarity of Europe is the difficulty to conduct clinical trials. The difficulty has three roots. First, volunteers are needed for conducting trials, and these volunteers should be preferably naïve[56], which is almost impossible to find in Europe. The second difficulty has a regulatory nature. Until 2022, each clinical trial had to be approved by each Member State. This creates a very cumbersome and lengthy process. In 2014, a new Regulation on clinical trials[57] was adopted to introduce a coordinated approval, but its application only started in January 2023 due to technical difficulties with the development of the IT systems. The Regulation introduces an authorisation procedure based on a single submission via a single EU portal, an assessment procedure leading to a single decision, rules on the protection of subjects and informed consent, and transparency requirements. The new Regulation will make it easier for pharmaceutical companies and scientists to conduct multinational clinical trials, which should increase the number of studies conducted within the EU. The ethical review of the trial remains a separate process to be conducted by each country in accordance with its laws. However, a time limit of 60 days has been introduced for the ethics committees to express their opinion; after that, the trial is considered approved. Although the Regulation is expected to overcome some of the bottlenecks experienced in the past, the interviewed stakeholders expressed concerns about the functioning of the Clinical Trial Information System[58] and the limits imposed on the use of individual patient data. The third difficulty relates to rivalry to perform clinical trials between universities and hospitals and among hospitals, since in some countries the Ministry of Health grants extra money based on the research activity. Such a system disincentivises collaboration. The incentive provided by the EU Research Framework Programme to run multinational clinical trials does not help since the funding is in the range of EUR 100 million per year. Although funding for VACCELERATE platform will be ensured in the next years, the difficulty of conducting clinical trials will not be settled unless action is taken to address its three roots.

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55 The Intelligence Gathering and Threat Assessment Medical Countermeasures Intelligence Platform will establish and regularly update a list of high-impact health threats requiring medical countermeasures preparedness and map and analyse existing and developing medical countermeasures, and remaining gaps.

56 A naïve volunteer is someone who has been neither exposed to the virus nor to the vaccine.

57 REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.

58 It has been explained that the system does not allow for more than one amendment of the trial at a time. Since it takes two months to get an approval for a new amendment, it means that it is possible to make one amendment every two or three months.

- **Careful examination, in the public health interest, of the conditionalities of future R&D grants and de-risk mechanisms.** A new policy framework is needed to avoid future vaccine science supported by the taxpayer will be fully privatised without any guarantees concerning intellectual property rights (IPR), equitable distribution, and affordable prices. During the pandemic the negotiations were conducted under pressure and in a context of asymmetric information. The current landscape would instead allow fairer arrangements between funds' providers and beneficiaries, including the possibility that IPR and licensing power are attributed, fully or partly, to public institutions that supported R&D. The agreements with companies should be done in much more transparent way, in more stable legal framework, in order to offer clear guidelines to the stakeholders and accountability to citizens.

4. CONCLUSIONS

Although information on public funding for R&D and the expansion of the production capacity for the manufacturing of COVID-19 vaccines is generally publicly available, this is, by nature, very fragmented. Indeed, a large number of different actors took part in the generalised effort to develop new vaccines for the novel threat and to produce billions of doses in a very short time span. On the other side, almost all pharmaceutical companies have not disclosed figures regarding corporate R&D investments for COVID-19 vaccines since these data are considered confidential.

However, information on the source of funding for COVID-19 vaccines, the amount of funds, and their timing is crucial to understand where the stimulus to innovation came from, as well as the distribution of risks. This, in theory, should have important implications in terms of accessibility to vaccines and redistribution of the returns, as well as equity. Moreover, it is strongly relevant to design informed policies for the development of, and access to, new medical countermeasures in the future, especially in the area of unmet clinical needs (including, among others, antimicrobials and drugs for rare diseases).[59] Lastly, it is important in order to grant transparency and to account for public expenditures to taxpayers.

For these reasons, this study attempts to provide a clearer picture of the funding for the development and the expansion of production capacities granted to a sample of COVID-19 vaccines, and in particular to shed light on the role of the European Union. It does so for the seven vaccines authorised for use in the EU (Comirnaty, from Pfizer and BioNTech; COVID-19 Vaccine Valneva; Nuvaxovid, from Novavax; Spikevax, from Moderna; Vaxzevria, from AstraZeneca; Jcovden, from Janssen; VidPrevtyn Beta, from Sanofi Pasteur), while providing information also for COVID-19 Vaccine Hipra (currently under rolling review, it would be the only vaccine entirely developed and produced in Europe and for this reason it has been analysed in the study), and CVnCoV from CureVac (although it has been withdrawn from rolling review, it received important public financing, thus being relevant for the analysis).

To reach this goal, data from different publicly available sources were gathered through desk research and were subsequently complemented and double-checked through 20 interviews involving 30 expert stakeholders: representatives of pharmaceutical companies; public health experts and scientists from the EU and the US; and public institutions. Importantly, data presented may be incomplete or contain inaccuracies due to the lack of official data (mainly on corporate investments) and inconsistency among sources; for these reasons, results should be considered a best-attempt estimate.

Our results point out that, although revenues from COVID-19 vaccines were fully privatised, external funds provided during the pandemic were critically important, with grants per vaccine of about EUR one billion, with a surprisingly high variance across companies. **If,** in addition to funding for R&D and the expansion of production capacities, **also APAs are considered as an incentive, the role of external funds becomes even more significant (nearly EUR 30 billion).** This result is further reinforced if previous funding for basic research subsequently exploited to develop the vaccines (not considered in this study) would be taken into account.

[59] Several public incentives have been proposed to stimulate R&D in this area, and in particular for antimicrobials, whose development represents the next challenge for the public sector (given the low profitability of these drugs for firms, and their importance for public health). In this context, HERA has commissioned further analysis of an annual revenue guarantee to stimulate antibiotic innovation, while the EC is expected to include transferable exclusivity vouchers in the proposed revision of the pharmaceutical legislation, expected in March 2023 (Ardal et al., 2023). The evaluation of each incentive scheme should consider its cost for the public sector, as well as its impact on innovation, accessibility, the market of generics and biosimilars, and the sustainability for health care systems.

External funds are mainly provided by the public sector (over 80%), through grants, loans and APAs, while the remaining part is financed by philanthropic entities, third party private companies (to be noted that private investments from third parties in the form of venture capital have not been considered), public-private partnerships and the EIB. This implies that **governments played a central role as a major partner of private firms in the development of vaccines,** although the amount of public fundings, the type of funds, as well as the share of public funding over corporate ones, strongly vary from company to company.

Among governments, the US and the UK ones are by far the largest funders of vaccines' R&D (not considering China, Russia and other countries). The role of the EU and its Member States was overall marginal to support R&D. If also funds for the extension of the production capacity are considered, the share of cumulated funding provided by the EU and its Member States increase thanks to the German support to BioNTech. EIB also granted some loans for R&D and extension of the production capacity. If also APAs are considered, the US government and the EU lead public financing for the vaccines we have considered in our sample of evidence, since they account for the majority of the tracked APAs funding in developed economies. While the US government extensively used all financing incentives to support vaccine development, the EU mainly contributed through APAs, signed on behalf of Member States. The EU strategy secured enough vaccines for the EU citizens and fair distribution of vaccines within the EU (at high price relative to marginal cost), and to a certain extent contributed to vaccination efforts in low- middle- income countries.

External funds to R&D and manufacturing, as well as APAs, were very salient in 2020, decreasing in 2021.

These results highlight that external funding played a fundamental role in the development and manufacturing of COVID-19 vaccines. This should not surprise: given their low returns in the past and the high risk associated with their development, vaccines (as well as other areas of research sharing the same characteristics, such as orphan drugs) often suffer from underinvestment from the pharmaceutical industry. External funds and the tools implemented to finance R&D and manufacturing played an important de-risking role, shifting part of the risk from private firms to the public sector, consequently increasing the returns for the pharmaceutical companies. **According to interviewed experts, COVID-19 is here to stay, and further R&D is required in order to improve vaccines for what concerns the resilience to virus mutations and more durable immunity.** Further studies on under-investigated topics on existing vaccines, as well as comparative studies, are also needed. Since, as mentioned above, vaccines represent a salient example of the mismatch between corporate R&D choices and public health priorities, and comparative studies hold no interest for pharmaceutical companies, public intervention will still be needed in these areas of research (as well as on other pandemic risks), as confirmed by the experts.

In this context, to ensure that health challenges are tackled equitably, and that rewards are in line with the distribution of risks, conditionalities of future R&D grants and de-risking mechanisms should be scrupulously detailed. **IPR arrangements should take into account the role of public funds, and pricing policies should reflect previous public R&D investments and support. Similarly, clauses to ensure supply security should be carefully listed. A stable legal environment is also in the long-term interest of the competitiveness of the European industry.**

If the EU wants to play a prominent role in supporting the development of future coronavirus vaccines, **fragmentation and duplication of funding should be avoided**. Moreover, as mentioned, a stable and clear legal EU framework for corporate R&D support on COVID-19 vaccines (and more broadly on vaccines for pathogens with pandemic potential) should be designed and a favorable regulatory and

infrastructural environment for conducted clinical trials within the EU should be pursued. **In the short term, the design and role of HERA should be revised** to ensure it possibly becomes an autonomous entity with its own budget. HERA is burdened with being the flagship of the EU's capacity to react to future pandemics. Still, its leverage in terms of legal instruments, political consensus, and funding is not yet proportionate to its ambition. As suggested by a STOA study (Florio *et al*., 2021), **in the long run, the creation of a pan-European R&D infrastructure and delivery organisation focusing on threats and areas of research and development that are underinvested under the current business model should be considered.** The infrastructure should have the budgetary scale and scientific ambition of the US NIH, and be equipped with home-grown research and development capacity, with a combined effort of the EU institutions and the Member States.

ANNEX 1. REFERENCES & REPOSITORIES

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c. REPOSITORIES

Global Health Centre. The data collected show R&D investments and/or commitments to invest, but not the actual disbursements of funding. Moreover, they do not distinguish between grants, loans or other types of financing arrangements. Note that many journalistic articles report this data but it is only the announcements.

G-FINDER. The repository contains funding figures by disease (including COVID-19). Funding data is gathered on an annual basis via the G-FINDER survey while the R&D pipeline tracker is updated at regular intervals throughout the year.

Policy Cures Research: COVID-19 R&D tracker. It tracks global funding commitments for COVID-19 R&D since 1 January 2020. It covers public, philanthropic & industry funding commitments. The data is available in an interactive dashboard and allows exploring data by funder, product developer and/or product.

Universities Allied for Essential Medicines: COVID Mapping. It maps public investment in International COVID-19 R&D. Data on investments in COVID-19 medicines, vaccines and diagnostics are summarized in an interactive dashboard. It can also be downloaded in various formats.

CEPI. It contains CEPI data about their financing portfolio.

Medical Countermeasures. The website includes US BARDA's investments in COVID-19 Medical Countermeasure Portfolio.

ANNEX 2. INTERVIEW QUESTIONNAIRES

Questionnaire for companies

1 Did your company has received funds in the form of grants to support R&D for Covid-19 vaccine from the following entities:

- European Commission
- One or more EU Member States
- One or more non-EU Member States
- Other entities, such as charities, international bodies (such as CEPI and IVI)

For each entity, please specify donating body, time and amount.

2 Please describe the conditions attached to such grants and problems if any encountered in the process, such as 'red-tape' issues.

3 Would you say that such support to R&D was critically important?

4 Did your company enter in an Advance Purchase Agreement (APA) with the European Commission and/or with an EU Member State? Please describe the conditions attached to such APAs and problems if any encountered in the process, such as 'red-tape' issues.

5 Would you say that such APAs were critically important to speed up R&D or production of vaccines?

6 Did your company receive loans or other form of support from European Investment Bank (EIB) or other multilateral development banks? How would you describe the impact of these financial mechanisms in the perspective of accelerating R&D and production of vaccines?

7 What is the total amount of R&D expenditure by year on Covid-19 vaccines by your company?

8 In which countries is the main intramural research and development of Covid-19 vaccines being performed by your company? How many researchers are involved within the company respectively in the EU and outside? Do you perform extramural R&D in the EU with Universities, CROs, other companies and institutes?

9 Similarly, in which countries is the majority of the respectively past and current investments in Covid-19 vaccines production capacities being made?

10 How much was invested, and how much continues to be invested by your company overall for Covid-19 vaccines?

11 Much of the current research seems to concentrate on adapting existing COVID-19 vaccines to the fast mutations of the virus. Which level of investment will be needed for this ongoing adaptation?

12 Is there still a need for substantial public funding for R&D of Covid-19 vaccines?

Questionnaire for experts & decision makers

1 Several companies received funds to support R&D on Covid-19 vaccines by European Commission (EC), one or more EU Member States, one or more non-EU Member States, other entities (e.g. charities, international bodies such as CEPI and IVI). Would you say that such

support to R&D was critically important to increase speed and effectiveness of vaccine discovery?

2 What are (if any) the lessons learned from public funding of Covid-19 vaccines R&D? Should conditions on patents, prices, delivery mechanisms have been attached to public support of R&D?

3 Some companies entered in an Advance Purchase Agreement (APA) with the European Commission and/or with an EU Member State. Would you say that such APAs were critically important to speed up R&D or production of vaccines? Should better conditions have been negotiated?

4 Do you evaluate that the amount and mechanisms of public support to the development of Covid-19 vaccines was overall adequate in terms of proportionality with the outcome? Too much tax-payers money or too little?

5 Much of the current research seems to concentrate on adapting existing COVID-19 vaccines to the fast mutations of the virus. Do you think that the current R&D landscape is adequate to manage future challenges or that radically innovative R&D avenues are needed?

6 Is there still a need for substantial public funding for R&D of Covid-19 vaccines or companies have already sufficient market incentives?

7 Do you have further advice on public support to R&D on Covid-19 vaccines looking at the future of the pandemic?

ANNEX 3. LIST OF INTERVIEWEES

EXPERTS		
CONTACT POINT	AFFILIATION/POSITION	DATE OF THE INTERVIEW
Jacques Demotes	Director General - European Clinical Research Infrastructure Network (ECRIN)	02 December 2022
Emily Erbelding	Director - Division of Microbiology and Infectious Diseases NIAID/NIH	12 December 2022
Gary L. Disbrow	Director - Biomedical Advanced Research and Development Authority (BARDA)	19 December 2022
Christiane Gerke	Head of Vaccine Programs/Head of Vaccine Innovation Development - Institut Pasteur	17 January 2023
Andrew Pollard	Ashall Professor of Infection & Immunity, Director - Oxford Vaccine Group, Department of Paediatrics at the University of Oxford	02 February 2023
Giuseppe Remuzzi	Scientific Director - "Mario Negri" Institute for Pharmacological Research and Professor of Nephrology - University of Milan	Written contribution: 24 January 2023
Oliver A. Cornely	Director - Institute of Translational Research, CECAD Cluster of Excellence, University of Cologne and Coordinator - VACCELERATE Consortium	08 February 2023
Rosa Castro	Senior Policy Manager for Healthcare Delivery & EPHA Networks Coordinator, European Public Health Alliance	06 March 2023

INSTITUTIONS		
CONTACT POINT	AFFILIATION/POSITION	DATE OF THE INTERVIEW
Slovenian Medicines and Medical Devices Agency (JAZMP)		
Momir Radulovic	Executive Director - Slovenian Medicines and Medical Devices Agency	19 December 2022
European Court of auditors (ECA)		
Nicholas Edwards	Auditor - ECA	16 January 2023
Paul Stafford	Head of Unit - ECA	16 January 2023
European Investment Bank (EIB)		

Cristina Niculescu	Life Sciences Specialist, Innovation & Competitiveness Department, Projects Directorate	14 December 2022
Valeria Iansante	Life Sciences Specialist, Life Sciences & Health Division, Innovation & Competitiveness Department, Projects Directorate	14 December 2022
European Medicines Agency (EMA)		
Marco Cavaleri	Head of Health Threats and Vaccine Strategy and Chair of Emergency task Force	30 November 2022
Directorate-General for Research and Innovation (RTD) – European Commission		
Undisclosed	Undisclosed	20 December 2022
Health Emergency Preparedness and Response Authority (HERA)		
Undisclosed	Undisclosed	20 January 2023 02 March 2023
Undisclosed	Undisclosed	01 February 2023

COMPANIES		
CONTACT POINT	AFFILIATION/POSITION	DATE OF THE INTERVIEW
AstraZeneca		
Violeta Georgieva-Koleva	EU Government Affairs Senior Manager	Written contribution: 31 January 2023
Hipra		
Elia Torroella Busquets	Executive Vice-President R&D and Regulatory Affairs	13 January 2023
David Alonso Raluy	Director, Finance	13 January 2023
Novavax		
Andrea Corazza	Senior Director, Policy & Government Affairs, Europe	Written contribution: 04 February 2023
Pfizer		
Aylin Tuzel	mRNA Commercial Lead	Written contribution: 22 December 2022

Andrea Chiarello	Director, Head of EU Government Affairs -	03 February 2023 and written contribution: 22 December 2022
Diane Thomson	Senior Director, Global Vaccines Public Affairs	03 February 2023
Sanofi		
Francois Sandre	Head, Europe Commercial operations for Sanofi Vaccines	25 January 2023
Corinne Bardone	Head, Vaccines Public Affairs Europe	25 January 2023
Vaccines Europe		
Sibilia Quilici	Executive Director - Vaccines Europe and EPFIA	30 January 2023

ANNEX 4. SUMMARY FICHES

SUMMARY FICHE

ASTRAZENECA

The company has preferred not to comment on this Fiche or on information from the public domain

1. KEY INFO

Name	AstraZeneca plc
Headquarters	Cambridge, England, UK
Year of foundation	1999
Type of firm	Public limited company
Listed	LSE: AZN

2. PRODUCTS AND TURNOVER (£ MILLIONS)

Product portfolio	Oncology, biopharmaceuticals, cardiovascular, renal, metabolism, respiratory and immunology, vaccines, rare diseases	Website
Revenue (Net income) 2019	19114 (+1046)	Financial Report
Revenue (Net income) 2020	21518 (+2492)	Financial Report
Revenue (Net income) 2021	27509 (+81)	Financial Report

3. COVID-19 VACCINE

Name	Vaxzevria or COVID-19 Vaccine AstraZeneca
Type	Viral vector
EMA status	Approved
Date of the authorization request	01/2021
Date of EMA conditional marketing authorization	29/01/2021
Date of EMA standard marketing authorisation	31/10/2022
Date of FDA marketing authorization	/

4. EXTERNAL FUNDING SOURCES

FUNDING FOR R&D + MANUFACTURING CAPACITY				
Date	Funder	Amount ($ Millions)	Typology	Source

04/2020	CEPI	384	Funding for R&D	CEPI-Portfolio
10/2020	US government	1600	Direct funding (R&D+ manufacturing)	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio

Note: The table does not include the funding provided to Oxford University by the UK government, totalling about EUR 77 million.

ADVANCE PURCHASE AGREEMENTS (APA)						
Date	Funder	Number of doses	Price per dose	Amount (Millions)	Typology	Source
08/2020	US government	missing	Missing	1200 $	APA	Guarascio, 2020, EU pays 336 million euros to secure AstraZeneca's potential COVID-19 vaccine
08/2020	UK government	missing	Missing	65.5 £	APA	Guarascio, 2020, EU pays 336 million euros to secure AstraZeneca's potential COVID-19 vaccine
2020	EU	300 million	EUR 2.90	870 EUR	APA	Advanced Purchase Agreements for Covid-19 vaccines

SUMMARY FICHE
BIONTECH

The company never replied to principal investigator's requests of contact.

1. KEY INFO

Name	BioNTech SE
Headquarters	Mainz, Germany
Year of foundation	2008
Type of firm	Public company
Listed	Nasdaq: BNTX

2. PRODUCTS AND TURNOVER ($ MILLIONS)

Product portfolio	Immunotherapies for oncology and infectious diseases	Website
Revenue (Net income) 2019	122 (-200)	Financial Report
Revenue (Net income) 2020	550 (+17)	Financial Report
Revenue (Net income) 2021	22430 (+12166)	Financial Report

3. COVID-19 VACCINE

Name	Cominarty or Pfizer–BioNTech COVID-19 vaccine
Type	mRNA
EMA Status	Approved
Date of the authorization request to EMA	12/2020
Date of EMA conditional marketing authorisation	21/12/2020
Date of EMA standard marketing authorisation	10/10/2022
Date of FDA marketing authorisation	12/2020, then approved in 08/2021

4. EXTERNAL FUNDING SOURCES

FUNDING FOR R&D + MANUFACTURING CAPACITY				
Date	Funder	Amount (Millions)	Typology	Source
03/20	Fosun Pharmaceutical	135 $	Funding for R&D	https://www.ft.com/content/271ee270-6796-11ea-800d-da70cff6e4d3

06/20	EIB	100 EUR	Loan for R&D and manufacturing	European Investment Bank, 2020, "Germany: Investment Plan for Europe - EIB to provide BioNTech with up to €100 million in debt financing for COVID-19 vaccine development and manufacturing"
09/20	German government	375 EUR	Direct funding (R&D+ manufacturing)	Staff R., 2020, "BioNTech wins $445 million German grant for COVID-19 vaccine", Reuters BioNTech press
2020	German government	238.9 $	Direct funding (R&D + manufacturing)	Annual Report Pursuant to Section 13 Or 15(d) of the Securities Exchange Act of 1934, 2020, BioNTech

Note: the APAs supporting the production of Cominarty are not included here because they were reported under the Summary Sheet of Pfizer.

SUMMARY FICHE
CUREVAC

The fiche has been read and validated by CureVac's representative.

1. KEY INFO

Name	CureVac
Headquarters	Tübingen, Germany
Year of foundation	2000
Type of firm	Public company
Listed	Nasdaq: CVAC

2. PRODUCTS AND TURNOVER ($ MILLIONS)

Product portfolio	Therapies using messenger RNA technology, focusing on three therapeutic areas: prophylactic vaccines, cancer immunotherapies and molecular therapies	Website
Revenue (Net income) 2019	19 (-112)	Financial Report
Revenue (Net income) 2020	56 (-147)	Financial Report
Revenue (Net income) 2021	122 (-487)	Financial Report

3. COVID-19 VACCINE

Name	(CVnCoV))
Type	mRNA
EMA Status	Withdrawn[60]
Date of the authorization request to EMA	02/2021

4. EXTERNAL FUNDING SOURCES

FUNDING FOR R&D + MANUFACTURING CAPACITY				
Date	Funder	Amount (Millions)	Typology	Source
07/2020	EIB	25 EUR already returned in 2021 (the other 50 cancelled)	Loan for (R&D+ manufacturing)	Report of Foreign Private Issuer on Form 6-K, CureVac
01/2020	CEPI	7 $	Funding for R&D	Cepi, Portfolio
01/2020	CEPI	8.3 $	Funding for R&D	Cepi, Portfolio

[60] https://www.ema.europa.eu/en/news/ema-ends-rolling-review-cvncov-covid-19-vaccine-following-withdrawal-curevac-ag.

09/2020	German government	292 EUR	Direct funding (RD+ manufacturing)	Busvine D., 2020, "Curevac gets $300 million grant to hurry up COVID-19 vaccine", Reuters
2020	Gates foundation	2.16 EUR	Funding for R&D	Report of Foreign Private Issuer on Form 6-K, CureVac

ADVANCE PURCHASE AGREEMENTS (APA)						
Date	Funder	Number of doses	Pirce/dose	Amount (Millions)	Typology	Source
2021	EU	Missing	Missing	450 EUR	APA	Report of Foreign Private Issuer on Form 6-K, CureVac

SUMMARY FICHE

GSK

The company stated in writing that GSK did not receive direct public funding related to the vaccine, while Sanofi, which is the marketing authorisation holder and developed the antigen, was the recipient of some support.

1. KEY INFO

Name	GSK plc
Headquarters	London, England, UK
Year of foundation	2000
Type of firm	Public limited company
Listed	LSE: GSK

2. PRODUCTS AND TURNOVER (£ MILLIONS)

Product portfolio	Infectious diseases, HIV, oncology, and immunology	Website
Revenue (Net income) 2019	33754 (+4645)	Financial Report
Revenue (Net income) 2020	34099 (+5749)	Financial Report
Revenue (Net income) 2021	34114 (+4385)	Financial Report

3. COVID-19 VACCINE

Name	VidPrevtyn Beta
Type	Subunit (adjuvanted recombinant)
EMA Status	Approved
Date of the authorization request	07/2021
Date of EMA marketing authorization	10/11/2022
Date of FDA marketing authorization	/

SUMMARY FICHE
HIPRA

This fiche includes the feedback received by Hipra's representatives.

1. KEY INFO

Name	Hipra
Headquarters	Amer, Girona, Spain
Year of foundation	1954
Type of firm	Biotechnological pharmaceutical company
Listed	No

2. PRODUCTS AND TURNOVER (EUR MILLIONS)

Product portfolio	Prevention for animal and human health, with a broad range of highly innovative vaccines and an advanced diagnostic service	Website
Revenue (Net income) 2019	40,1	
Revenue (Net income) 2020	48,7	
Revenue (Net income) 2021	50,1	

3. COVID-19 VACCINE

Name	COVID-19 Vaccine HIPRA (PHH-1V)
Type	Recombinant protein
Status	EMA: rolling review
Date of the authorization request	03/2022

4. EXTERNAL FUNDING SOURCES

FUNDING FOR R&D + MANUFACTURING CAPACITY				
Date	Funder	Amount (EUR Millions)	Typology	Source
04/2021	Spanish government (Centro para el Desarrollo Tecnológico Industrial)	2.9	Loan + direct funding for R&D[61]	Interview with Hipra's representatives

[61] EUR 2.9 million loan of which EUR 0.9 million of non-refundable (Grant). The project duration 15 months (ending May 2022).

10/2021	EIB	45[62]	Loan for R&D + manufacturing	European Investment Bank, 2021, "Spain: EIB helps HIPRA to develop a COVID-19 vaccine"
11/2021	EU (European Health and Digital Executive Agency)	1.8	Direct funding for R&D	Interview with Hipra's representatives
12/2021	Spanish government (Centro para el Desarrollo Tecnológico Industrial)	14.8	Loan + direct funding for R&D[63]	Interview with Hipra's representatives
08/2022	EU (HERA)	Financial amount missing, 250 million doses[64]	Joint procurement contract[65]	Reuters, 2022, "EU signs joint procurement deal with Spain's HIPRA for COVID vaccines" Interview with Hipra's representatives

[62] Three disbursements have already been made, covering 100% of the loan granted.

[63] EUR 14.8 million Loan of which EUR 3.9 million of non-refundable support (Grant). The project duration is 17 months (ending January 2023).

[64] 250 million doses in EU's portfolio https://commission.europa.eu/strategy-and-policy/coronavirus-response/safe-covid-19-vaccines-europeans_en#eus-vaccine-portfolio.

[65] It does not represent a firm purchase commitment.

SUMMARY FICHE
JANSSEN

After an initial contact with a senior representative, the company never provided a feedback.

1. KEY INFO

Name	Janssen Pharmaceuticals
Headquarters	Beerse, Belgium
Year of foundation	1953 (from 1961 part of J&J)
Type of firm	Pharmaceutical company
Listed	No (but Johnson & Johnson is listed)

2. PRODUCTS AND TURNOVER ($ MILLIONS)

Product portfolio	Cardiovascular, Immunology, Infectious Diseases, …	Website
Revenue (Net income) 2019	82059 (+15119)	Financial Report
Revenue (Net income) 2020	82584 (+14714)	Financial Report
Revenue (Net income) 2021	93775 (+20878)	Financial Report

3. COVID-19 VACCINE

Name	Jcovden or COVID-19 Vaccine Janssen (Ad26.COV2.S)
Type	Viral vector
EMA Status	Approved
Date of the authorization request	02/2021
Date of EMA conditional marketing authorisation	11/03/2021
Date of EMA standard marketing authorisation	10/01/2023
Date of FDA marketing authorisation	02/2021

4. EXTERNAL FUNDING SOURCES

FUNDING FOR R&D + MANUFACTURING CAPACITY				
Date	Funder	Amount ($ Millions)	Typology	Source
02/2020	US government	20.6	Direct funding for R&D	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio

03/2020	US government	435.6	Direct funding (R&D + manufacturing)	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio
03/2021	US government	32	Funding for R&D	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio
11/2020	US government	454.3	Direct funding (R&D+ manufacturing)	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio

ADVANCE PURCHASE AGREEMENTS (APA)						
Date	Funder	Number of doses	Price/dose	Amount ($ Millions)	Typology	Source
08/2020	US government	100 million	missing	85.3	APA	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio
08/2020	US government	100 million	missing	1002	APA	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio
08/2020	African union	400 million	missing	missing	APA	Janssen Pharmaceutical Companies of Johnson & Johnson, 2021, "Johnson & Johnson Announces Advance Purchase Agreement with the African Vaccine Acquisition Trust for the Company's COVID-19 Vaccine Candidate"
10/2020	EU	200 (+200 Million optional)[66]	8.5 $	1700	APA	Elvinger, J., et al., 2022, "EU COVID-19 vaccine procurement", European Court of Auditors Special Report Price per dose revealed by the Belgian Minister on Twitter

[66] 400 million doses in EU's portfolio https://commission.europa.eu/strategy-and-policy/coronavirus-response/safe-covid-19-vaccines-europeans_en#eus-vaccine-portfolio.

SUMMARY FICHE
MODERNA

No feedback was provided on this fiche by the company due to their confidentiality policy.

1. KEY INFO

Name	Moderna
Headquarters	Cambridge, Massachusetts, U.S.
Year of foundation	2010
Type of firm	Public company
Listed	Nasdaq: MRNA

2. PRODUCTS AND TURNOVER ($ MILLIONS)

Product portfolio	Therapies using messenger RNA technology, such as for infectious, immuno-oncology, and cardiovascular diseases	Website
Revenue (Net income) 2019	60 (-514)	Financial Report
Revenue (Net income) 2020	803 (-747)	Financial Report
Revenue (Net income) 2021	18413 (+12202)	Financial Report

3. COVID-19 VACCINE

Name	Spikevax or COVID-19 Vaccine Moderna (mRNA-1273)
Type	mRNA
EMA Status	Approved
Date of the authorization request to EMA	11/2020
Date of EMA conditional marketing authorisation	06/01/2021
Date of EMA standard marketing authorisation	03/10/2022
Date of FDA marketing authorisation	12/2020

4. EXTERNAL FUNDING SOURCES

FUNDING FOR R&D + MANUFACTURING CAPACITY				
Date	Funder	Amount ($ Millions)	Typology	Source
16/04/2020	US government	430	Direct funding (RD + manufacturing)	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio

05/2020	US government	53	Direct funding (manufacturing)	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio
07/2020	US government	472	Direct funding (RD + manufacturing)	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio
01/2020	CEPI	1	Funding for R&D	Cepi, Portfolio
11/2020	Dolly Parton COVID-19 Research Fund	1	Funding for R&D	Andrew S., 2020, "Dolly Parton helped fund Moderna's Covid-19 vaccine research", CNN
06/21	US government	144	Funding for R&D	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio

ADVANCE PURCHASE AGREEMENTS (APA)						
Date	Funder	Number of doses	Price/dose	Amount ($ Millions)	Typology	Source
08/20	US government	100 million	$ 15.25	1525	APA	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio
12/20	US government	100 million	$ 16.67	1667	APA	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio
2020	GAVI/COVAX	Missing	Missing	6	APA	Moderna, 2022, Proxy Statement
2020	EU	80 million doses	$ 22.9	1832	APA	Advanced Purchase Agreements for Covid-19 vaccines
05/21	GAVI/COVAX	650 million doses	$7.00 per 100 µg dose	5448	APA	Moderna, 2022, Proxy Statement

SUMMARY FICHE
NOVAVAX

This fiche includes the feedback received by Novavax's representative.

1. KEY INFO

Name	Novavax
Headquarters	Gaithersburg, Maryland, U.S.
Year of foundation	1987
Type of firm	Public company
Listed	Nasdaq: NVAX

2. PRODUCTS AND TURNOVER ($ MILLIONS)

Product portfolio	Transformational vaccines	Website
Revenue (Net income) 2019	19 (-133)	Financial Report
Revenue (Net income) 2020	476 (-418)	Financial Report
Revenue (Net income) 2021	1146 (-1744)	Financial Report

3. COVID-19 VACCINE

Name	Nuvaxovid and Covovax (NVX-CoV2373)
Type	Subunit (adjuvanted recombinant)
EMA Status	Authorised
Date of the authorization request to EMA	02/2021
Date of EMA conditional marketing authorisation	20/12/2021
Date of FDA marketing authorisation	07/2021

4. EXTERNAL FUNDING SOURCES

FUNDING FOR R&D + MANUFACTURING CAPACITY				
Date	Funder	Amount ($ Millions)	Typology	Source
2020	US government	60	Direct funding (RD+ manufacturing)	Novavax, 2021, "A New Era Has Begun", Annual Report.
07/2020	US government	1800	Direct funding (RD+ manufacturing)	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio

Until 2021	CEPI	399.5	Direct funding (RD+ manufacturing)	Novavax, 2021, "A New Era Has Begun", Annual Report. CEPI portfolio.

ADVANCE PURCHASE AGREEMENTS (APA)						
Date	Funder	Number of doses	Price/dose	Amount ($ Millions)	Typology	Source
2021	Gavi	300	missing	missing	APA	Novavax, 2021, "A New Era Has Begun", Annual Report.
2021	EU	100 million doses for 2021[67]	missing	missing	APA	Novavax, Inc., 2021, "Novavax and European Commission Finalize Advance Purchase Agreement for up to 200 million doses of COVID-19 Vaccine", PRNewswire

[67] Commitment to buy 20 million doses. The other 80 million does are optional.

SUMMARY FICHE
PFIZER

No comment on this fiche was provided by the company due to their confidentiality policy

1. KEY INFO

Name	Pfizer
Headquarters	New York City, New York, U.S.
Year of foundation	1849
Type of firm	Public company
Listed	NYSE: PFE

2. PRODUCTS AND TURNOVER ($ MILLIONS)

Product portfolio	Largest drug company (cardiovascular, vaccines, antidepressants, …)	Website
Revenue (Net income) 2019	41172 (+10838)	Financial Report
Revenue (Net income) 2020	41651 (+6630)	Financial Report
Revenue (Net income) 2021	81288 (+22415)	Financial Report

3. COVID-19 VACCINE

Name	Cominarty or Pfizer–BioNTech COVID-19 vaccine
Type	mRNA
EMA Status	Approved
Date of the authorization request to EMA	12/2020
Date of EMA conditional marketing authorisation	21/12/2020
Date of EMA standard marketing authorisation	10/10/2022
Date of FDA marketing authorisation	12/2020, then approved in 08/2021

4. EXTERNAL FUNDING SOURCES

FUNDING FOR R&D + MANUFACTURING CAPACITY						
Date	Funder	Number of doses	Price/dose	Amount ($ Millions)	Typology	Source
07/20	US government	100 million	missing	1950	APA	BARDA's Expanding ermeasure Portfolio
12/2020	US government	100 million	missing	2011	APA	BARDA's Expanding

						COVID-19 Medical Countermeasure Portfolio
11/2020	EU	200 million	$ 12	2400	APA	Elvinger, J., et al., 2022, "EU COVID-19 vaccine procurement", European Court of Auditors Special Report
11/2020	Israel	Missing	missing	245	APA	Winer S., 2021, "Israel said to be paying average of $47 per person for Pfizer, Moderna vaccines", The Times of Israel
2020	United States	Missing	missing	154	APA	Annual Report Pursuant to Section 13 Or 15(d) of the Securities Exchange Act of 1934, 2021, Pfizer

SUMMARY FICHE
SANOFI

The company has declined to comment on this Fiche and stated that information linked to the APA are proprietary or from external sources.

1. KEY INFO

Name	Sanofi Pasteur
Headquarters	Lyon, France
Year of foundation	2004
Type of firm	Vaccines division of Sanofi
Listed	No (but Sanofi S.A. is listed, Euronext Paris: SAN)

2. PRODUCTS AND TURNOVER (EUR MILLIONS)

Product portfolio	Vaccines	Website
Revenue (Net income) 2019	36126 (+2907)	Financial Report
Revenue (Net income) 2020	36041 (+12294)	Financial Report
Revenue (Net income) 2021	37761 (+6223)	Financial Report

3. COVID-19 VACCINE

Name	VidPrevtyn Beta
Type	Subunit (adjuvanted recombinant)
EMA Status	Approved
Date of the authorization request	07/2021
Date of EMA marketing authorization	10/11/2022
Date of FDA marketing authorization	/

4. EXTERNAL FUNDING SOURCES

FUNDING FOR R&D + MANUFACTURING CAPACITY				
Date	Funder	Amount (Millions)	Typology	Source
04/2020	US government	30.8 $	Direct funding for R&D	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio
07/2020	US government	2042 $	Direct funding (R&D+ manufacturing)	BARDA's Expanding

				COVID-19 Medical Countermeasure Portfolio
08/2021	US government	6.7 $	Direct funding (R&D+ manufacturing)	BARDA's Expanding COVID-19 Medical Countermeasure Portfolio
2021	US government	147 EUR	Direct funding (R&D+ manufacturing)	Sanofi, 2022, Half-Year Financial Report
2022	US government	215 EUR	Direct funding (R&D+ manufacturing)	ıancial Report

ADVANCE PURCHASE AGREEMENTS (APA)						
Date	Funder	Number of doses	Price/dose	Amount ($ Millions)	Typology	Source
2020	EU	300 milion[68]	missing	384	APA	Blenkinsop P. and Blamont M., 2020, "EU pays $384 million for Sanofi-GSK COVID vaccine as WHO scheme deadline looms", Reuters
2020	UK + EU + Canada + USA	Missing	missing	319	APA	Annual Report Pursuant to Section 13 Or 15(d) of the Securities Exchange Act of 1934, 2021, Sanofi

Note: the fiche does not include the financial support provided to GSK for the development of the VidPrevtyn Beta.

[68] 300 million doses in EU's portfolio https://commission.europa.eu/strategy-and-policy/coronavirus-response/safe-covid-19-vaccines-europeans_en#eus-vaccine-portfolio.

SUMMARY FICHE
VALNEVA

The company declined the participation in the study, as for communication to Vaccine Europe, due to the fact they are under confidentiality with some governments

1. KEY INFO

Name	Valneva SE
Headquarters	Saint-Herblain, France
Year of foundation	2013
Type of firm	Public company
Listed	Euronext Paris: VLA

2. PRODUCTS AND TURNOVER (EUR MILLIONS)

Product portfolio	Vaccines	Website
Revenue (Net income) 2019	126 (-2)	Financial Report
Revenue (Net income) 2020	110 (-64)	Financial Report
Revenue (Net income) 2021	348 (-73)	Financial Report

3. COVID-19 VACCINE

Name	Valneva COVID-19 vaccine
Type	Inactivated
EMA Status	Approved
Date of the authorization request to EMA	05/2022
Date of FDA marketing authorization	/
Date of EMA marketing authorization	24/06/2022

4. FUNDING SOURCES

FUNDING FOR R&D + MANUFACTURING CAPACITY				
Date	Funder	Amount (EUR Millions)	Typology	Source
09/2020	UK government	558	APA (five-year supply)	Blankenship K., 2020, "Valneva signs $1.6B supply, development agreement with U.K. for coronavirus vaccine hopeful", FiercePharma

11/2021	EU	Missing	APA	Elvinger, J., et al., 2022, "EU COVID-19 vaccine procurement", European Court of Auditors Special Report
02/2022	Scotland's national economic development agency	16	Direct funding for R&D	Valneva, 2022, Half-Year Financial Report: January 1 to June 30 2022

ANNEX 5. H2020 SUPPORT TO CORONAVIRUS GLOBAL RESPONSE

Object	EUR Millions
Societal Challenge 1 (Health) - First dedicated call (March 2020) for research & innovation to develop diagnostics, treatments and vaccines - 18 projects	48.2
Innovative Medicines Initiative (IMI) Public-Private Partnership between the EU and the pharmaceutical industry	72
Contribution to Coalition for Epidemic Preparedness Innovations (CEPI) (EUR 50 million were mobilised + EUR 50 million in the final approval process)	100
European and Developing Countries Clinical Trials Partnership (EDCTP) Public-Private Partnership focusing on infectious diseases research in sub-Saharan Africa	25.25
European Institute of Innovation and Technology (EIT) Health 2020 COVID-19 Rapid Response Call and Extension for Headstart Call with focus on Digital Health solutions with a minimum TRL of 8 and direct impact on the current crisis	6
European Innovation Council (EIC) Accelerator pilot Start-up companies and SMEs with relevant innovations had been alerted to the possibility of applying to the March bottom-up call for proposals. Additional budget of EUR 150 million (from internal redeployment) specifically allocated for the best COVID-19 related proposals	165.63
Societal Challenge 1 (Health) - Second call for Expression of Interests - complements earlier actions by strengthening capacity to manufacture and deploying readily available solutions, including understanding of the behavioural and socio-economic impacts – 24 projects	133.4
Reinforcement of InnovFin Infection Diseases Financial Facility (IDFF): EUR 75 million to CureVac; EUR 30 million credit enhancement via Horizon 2020 InnovFin financing mechanism to BioNTech (which allowed the EIB to provide EUR 100 million loan through the European Fund for Strategic Investments EFSI), EUR 10 million to Scope Fluidics, EUR 24 million to Atriva, EUR 24.5 million to Immunic, EUR 15 million to AB Science, EUR 20 million to the AMR Action Fund, EUR 20 million to Bioversys and EUR 30 million to Univercells	248.5
Societal Challenge 1 (Health) Extension activities COVID-19 related projects including clinical trial	54.2
Infrastructure and Data sharing EU COVID-19 platform (extension activities and re-orientation of on-going grants) Public Health Information Research Infrastructure	15.5
Leadership in Enabling and Industrial Technologies - ICT Support for the deployment of innovative robotics solutions in healthcare to the DIH-HERO project	3.5
Total mobilised	**872.18**
Reinforcement of InnovFin Infection Diseases Financial Facility (IDFF)	151.6
Grand total	**1,023.78**

Source: https://research-and-innovation.ec.europa.eu/research-area/health/coronavirus/eu-funding_en, Last update 5 July 2021.

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