

Towards Vaccinating The World

Landscape of Current COVID-19 Supply Chain and Manufacturing Capacity, Potential Challenges, Initial Responses, and Possible “Solution Space” - a Discussion Document

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Introduction

“I feel like I didn’t just get a vaccine, I got a shot of hope. It’s hope that this is the beginning of the end of this terrible pandemic.” – Dr Hagan, Frontline Worker¹

With over 2.6 million deaths as of 3rd March 2021,² and economic cost estimated at 5-14 trillion USD per year³ due to COVID-19, mitigating the pandemic is a paramount global priority and vaccines are a critical part of the solution.

Since the start of the COVID-19 pandemic, the world has seen **unprecedented progress** in vaccine development, manufacturing ramp-up, and deployment. Within a record time of less than a year, 11 vaccines are already in clinical use in the countries where they obtained approval (often with emergency/limited authorisation), more than 80 additional candidates are in clinical trials, and hundreds of candidates are in the pre-clinical phase. At the same time, vaccine manufacturers and suppliers of vaccine components are scaling up for COVID-19 vaccine production from zero to billions of doses, with an announced cumulative supply target of up to 14 billion doses by the end of 2021. This represents three to four times the pre-COVID-19 annual global demand for all vaccines of 3.5-5.5 billion.⁴ The impact of these efforts is starting to be seen, with over 270 million people globally vaccinated as of 3rd March 2021.⁵

The **increase in capacity** is remarkable because of the complexity of vaccine manufacturing processes that require specific know-how and equipment. It usually takes more than five years to build manufacturing capacity and 18-30 months to transfer production to other sites or manufacturers.⁶ The use of new technologies such as mRNA in response to COVID-19 poses additional challenges because no large-scale manufacturing capacity nor specific raw materials existed at the outset of the pandemic. COVID-19 vaccine manufacturers ramped up their own manufacturing in parallel to clinical development (“scale-up”) in response to this challenge. They also formed more than 150 partnerships⁷ with contract development and manufacturing organisations (CDMOs) and other multinational biopharmaceutical companies to transfer their technology and increase their overall production (“scale-out”). Notwithstanding these efforts, the strain on manufacturing capacities and capabilities is very high, in light of the immediacy and scale of the demand, which may be exacerbated further if a broader coverage of the population is needed and if boosters are needed due to waning efficacy and need to protect from new variants.

However, it has become apparent that many COVID-19 vaccine **input supplies** of raw and packaging materials, consumables and equipment are in short supply which may result in several COVID-19 vaccine manufactures not being able to **meet their current vaccine manufacturing commitments**. Such shortages will also impact the ability to manufacture other lifesaving vaccines and biologics. Mechanisms to ensure input supplies for current and increased manufacturing capacity intent need to be put in place with short, medium and long-term solutions.

The summit will evaluate all potential bottlenecks of supply chain for input supplies, from manufacturing, through procurement, export, delivery and use of the materials for COVID-19 vaccine manufacture. It is of paramount importance to anticipate, understand, and establish an open dialogue with all stakeholders to find and implement additional short-term and sustainable solutions to the inevitable supply chain challenges.

For this reason, Chatham House – with co-sponsorship from COVAX (CEPI, Gavi, WHO, UNICEF), IFPMA, BIO, and DCVMN – has convened the COVID-19 Vaccine Manufacturing and Supply Chain Summit with key public, private, and other vaccine stakeholders on 8th and 9th March 2021, to **explore the emerging input supply challenges in depth** and to start to work towards strategies to avoid or mitigate them. The main goals of the Summit are:

- Help to identify and define the most critical bottlenecks across the supply network for a diverse array of COVID-19 vaccines with an emphasis on input supply

- Provide a platform to explore a range of solutions to address bottlenecks.
- Lead to a series of recommendations, and ideally commitments, on the priority areas for monitoring and/or action.

Today, the only element that can be predicted about the future is its high degree of uncertainty. The objective of this document is to provide a structured fact base to serve as background for participants, not to attempt to predict any aspect of the future course of this pandemic. This fact base builds on perspectives and information developed and provided by Summit conveners and participants. Given the rapid pace of events in this space, it should be considered as a “best effort” guide towards a high-level analysis and assessment of the state of play today but it is unlikely to be complete and may have omissions. Any estimates should be validated before being used for decision-making. The discussion document should be viewed as a discussion guide for participants and is structured into the following sections:

1. Introduction to Vaccine Manufacturing and Supply Chain
2. COVID-19 Vaccine Supply and Demand Overview
3. Input Supply Challenges
4. Manufacturing Capacity and Interdependencies beyond COVID-19 Vaccine
5. Overview of Potential Solutions for Discussion
6. Moving to Action

In parallel to the Chatham House Summit, many discussions are ongoing on how further to increase available manufacturing capacity of vaccine drug substance/drug product and accelerate technology transfer.

The purpose of this Summit, and this discussion document, is not aimed to identify or assign responsibility. COVID-19 is an exceptional crisis with unforeseen and shifting challenges. The aim is to bring stakeholders together to understand and align on how to move forward together leveraging their combined capabilities to optimise access to vaccines against COVID-19 for good of the world.

1 Introduction to Vaccine Manufacturing and Supply Chain

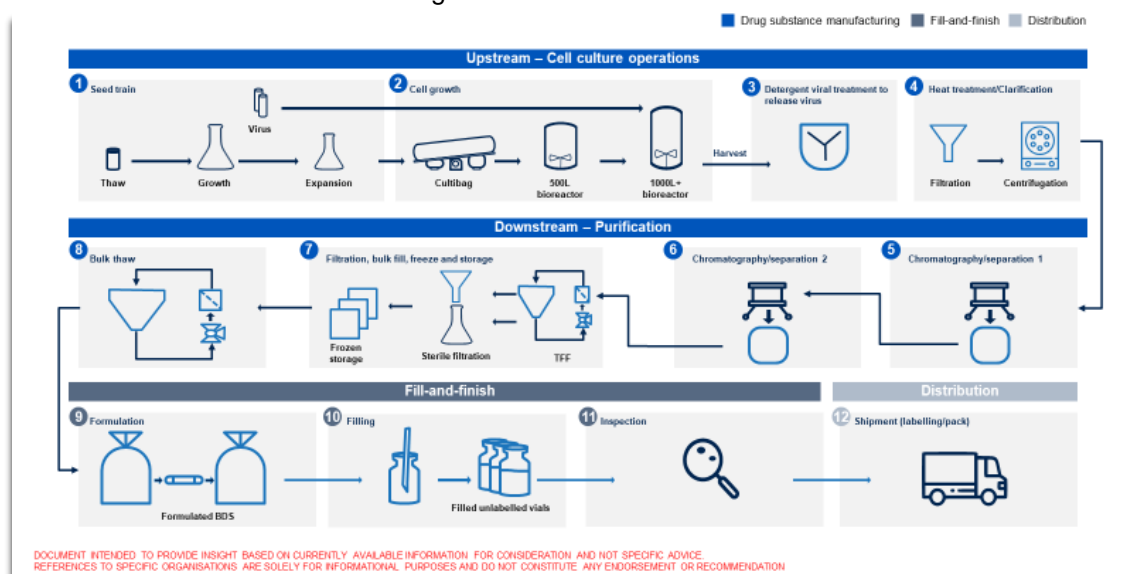
Key insights

- Vaccine manufacturing processes (*upstream, downstream, fill-and-finish*) are highly complex and characterised by cutting-edge science and technologies. Given this complexity, even the most advanced systems could experience challenges.
- Effective manufacturing needs to overcome major challenges, including the need for highly-specialised equipment and personnel, difficult and time-consuming technology transfers between partnering manufacturers, global supply, and manufacturing networks, and the need for on-time supply delivery of more than 100 components.
- Vaccine availability can reach its full potential only if both vaccine manufacturing capacity ramps-up reliably and a fully functional vaccine input supply chain continues to scale and deliver.

Vaccine manufacturing processes differ according to the type of vaccine.

The **biologic-derived vaccine manufacturing process** (e.g. viral vector, protein subunit, inactivated or attenuated viruses) can be divided into three core steps. In the first step (*upstream*), the cell culture is developed and cultivated, and is induced to produce the drug substance. In the second step (*downstream*), the cell culture harvest is purified via chromatography, filtration and other techniques to yield the purified drug substance. In the third and last step (*fill-and-finish*), the drug substance is formulated with other ingredients (or excipients) to enhance the immune response, where needed, and to ensure product stability, filled into vials, inspected, and packaged. The first and second step and the first two sub-steps of the third step (i.e. formulation and filling) must be conducted under stringent aseptic or sterile conditions. Manufacturing sub-steps in each of the three overarching steps differ significantly depending on the respective technology platform i.e. viral vector, protein subunits, and inactivated viruses. Exhibit 1 details the manufacturing process for viral vectors and Annex 1 covers protein subunit and inactivated virus.

Exhibit 1 – Viral Vector Manufacturing Process



The production process of **mRNA vaccines is largely chemical** in nature rather than biological. First, a plasmid DNA template for the mRNA drug substance is produced via biological fermentation, and then an enzyme-catalysed in-vitro transcription process produces the mRNA drug substance that codes for the desired protein, in this case the spike protein. The raw mRNA undergoes chemical reactions of capping and stabilisation to render it biologically active, and is then formulated in lipid nanoparticles (LNPs). LNPs are formed by subjecting a blend of lipids, including cholesterol and cationic or PEGylated lipids, to a microfluidic or nanofluidic mixing operation. Once the mRNA drug substance is formulated into LNPs, it undergoes fill-and-finish as well as quality assurance and quality control in the same manner as the other vaccines (see Annex 1).

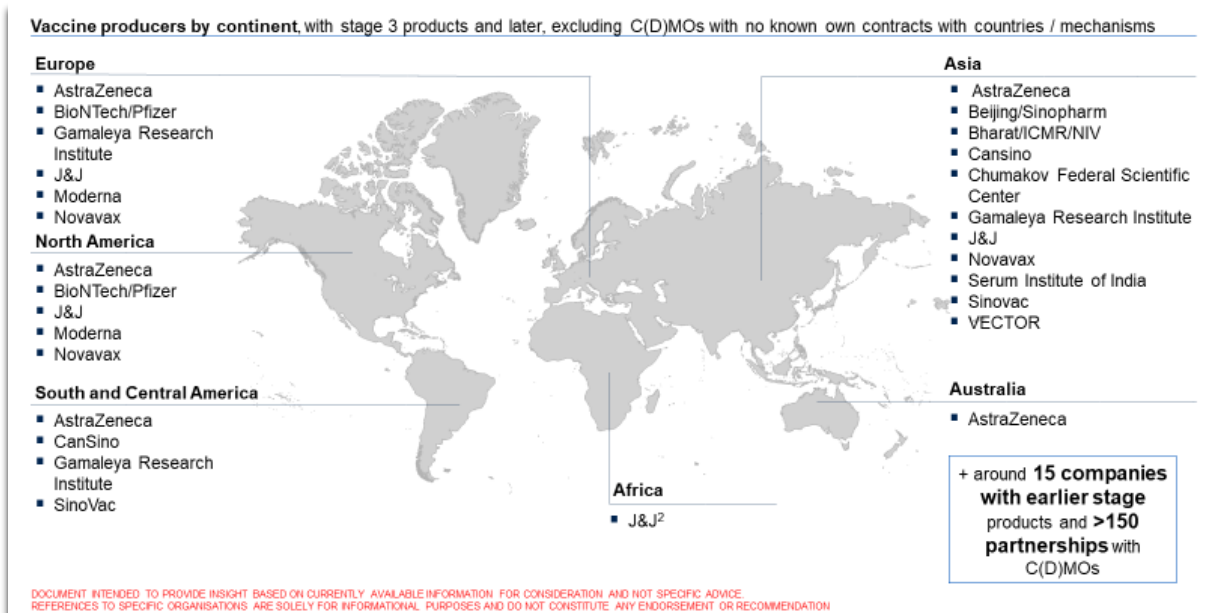
The complexity of the processes described above and the biological nature of critical steps makes vaccine manufacturing at times unpredictable, and even the most advanced production systems can experience failure. Quality control and quality management are therefore highly sophisticated and a critical component of every vaccine production system.

Independently of the type of vaccine, achieving this complex manufacturing process without compromising on quality comes with several operational challenges, including:

- **Highly-specialised equipment and personnel:** cutting-edge medical science and advanced manufacturing technologies have led to highly sophisticated vaccines, but with that the need for highly-specialised equipment and personnel, which represented a challenge even before COVID-19.
- **Manufacturing consistency and control to guarantee the quality and safety of each vaccine:** quality, efficacy, and safety are paramount to vaccines. To ensure that vaccines are of the highest quality, manufacturers much ensure that each individual manufacturing and control step is conducted consistently with the defined process. Manufacturing and quality assurance teams are accountable for ensuring that each manufacturing and control sub-step is duly conducted, and that any deviation is investigated and leads to corrective and preventative actions. Somewhere between 100 and 1,000 quality controls are performed at each step of the manufacturing process. Furthermore, external regulatory authorities assure some of these quality controls and review the batch summary protocol before releasing each individual batch for use.
- **Lengthy capacity ramp-up and technology transfer timelines:** new biopharmaceutical manufacturing technologies require a ramp-up period as the processes are stabilised, refined, and optimised, which typically takes a course of years. For mRNA vaccine production, as one example, the entire supply chain has to be built from scratch. Given the demands of COVID-19 vaccine supply, there has been limited time to scale and optimise manufacturing processes and prepare technology transfer between partnering manufacturers.
- **Global manufacturing network:** given the specialisation need as well as the high demands induced by COVID-19, the vaccine manufacturing networks are in general global and have been built by collaborations with contract development and manufacturing organisations (CDMOs). Currently, around 55% of capacity is located in East Asia, 40% in Europe and North America, and less than 5% in Africa and South America.
- **Lengthy manufacturing times:** today, on average 90 to 120 days are needed for the manufacturing and control of a single batch of COVID-19 vaccine, whatever the technology - mRNA, viral vector, or recombinant protein. In some cases, initiatives to reduce production lead times have been announced. For example, Pfizer-BioNTech has launched 'Project Light Speed' to reduce production time of its mRNA vaccine from 110 days to 60.

- **On-time input supply delivery for more than 100 components:** as vaccine manufacturing must run 24/7 and is time-sensitive, all input materials and consumables need to be available when required. Lack of availability of a single component could halt the entire production process and may force the scrapping of a batch that might already have been in production for several weeks.⁸

Exhibit 2 – Vaccine producers by continent, with stage 3 products and later, excluding C(D)MOs with no known own contracts with countries / mechanisms



To ensure the availability of **manufacturing capacity** for the required COVID-19 vaccine doses, COVID-19 vaccine manufacturers have ramped up their own manufacturing in parallel to clinical material development (“scale-up”) and formed more than 150 partnerships⁹ with CDMOs and a range of other vaccine manufacturers across the world, including capacity on each continent (“scale-out” through licensing agreements). Billions of dollars have been invested by governments and manufacturers at risk to support vaccine manufacturing capacity expansion.

In addition to the availability of capacity, the **vaccine input supply chain** is of utmost importance. The manufacturing of vaccine relies on crucial input in the form of raw materials, consumables and equipment across the value chain (upstream, downstream, fill-and-finish). Some of this input is common to all types of vaccines (and even to other biologics), and some very specific to each technology platform. This supply base for vaccine inputs is global and in certain cases potentially limited. Moreover, for selected materials such as glass vials, significant risks exist in the upstream supply chain e.g. boric acid constraints. These vaccine supply chain characteristics pose challenges that need to be addressed to ensure continuous vaccine manufacturing. In the following chapters, these are detailed for the COVID-19 vaccine input supply.

Despite major efforts to date, new challenges will continue to arise and need to be considered. Some of them are also detailed in the following chapters.

2 COVID-19 Vaccine Supply and Demand Overview

Key insights

- Global demand for COVID-19 vaccines could range from ~10-14 billion doses in 2021 depending on the final aspired coverage rate, need for re-vaccination and boosters. There is currently large geographic variability in announced deals and demand. Estimates of the percentage of the population required to meet herd immunity vary, but a working estimate is 70%, or about 5.5 billion people worldwide, thus requiring 11 billion doses of a two-dose regimen (subject to change if new variants are more transmissible).
- Manufacturers have announced a supply target of up to 14 billion doses – this would triple previous annual vaccine output.
- The degree to which disparities between supply and demand will continue depends on future developments, including approval of late-stage candidates, optimisation and ramp-up of manufacturing processes in line with plans, input supply challenges (e.g. bioreactor bags, filters), and the impact of variants
 - Even if these developments turn out favourably, disparity will persist in the majority of 2021 in any scenario but most demand could be met by the end of 2021.
 - If these developments turn out less favourably, disparity could persist for much longer.
- Finally, there are significant geographical demand and supply imbalances.

2.1 COVID-19 Vaccine Demand Overview

Many demand calculations and scenarios exist, but they all conclude that demand is high and immediate. COVID-19 vaccines are one of the core pillars to accelerate the end of the pandemic and protect lives and livelihoods, and all economies are pursuing broad vaccine coverage as fast as possible. As of late February 2021, countries, regional and global mechanisms such as COVAX have announced secured doses of ~9-11 billion for 2021.¹⁰ Of these, ~5 billion doses are for high-income countries (HICs), ~2-3 billion doses for upper-middle income countries (UMICs), and ~2-3 billion for the 92 low and middle-income countries that include COVAX Advance Market Commitments (the “AMC countries”). See Exhibit 3.

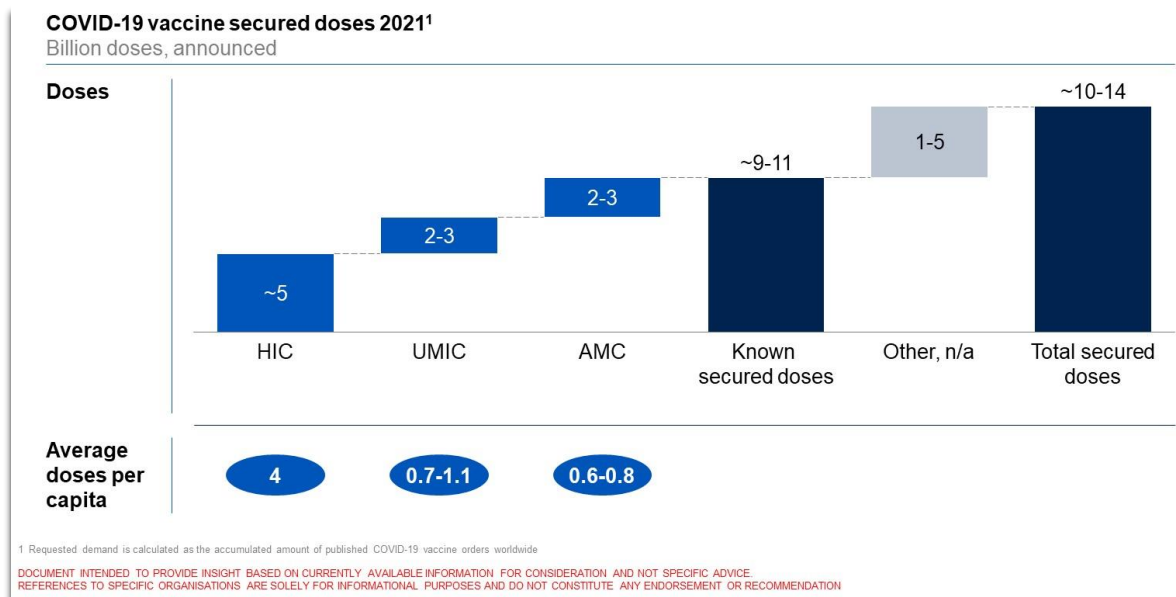
Within these three country groups, different patterns have emerged. HICs have agreed to buy the greatest number, proportional to their populations, and would theoretically be able to vaccinate their populations twice over if all vaccine candidates succeed and all volume come through. UMICs could vaccinate ~35%-52% of their population depending on the country, and AMC countries ~28%-42% of their population (with ~70% of vaccines provided through the COVAX facility).^{*} While limited coverage can stand in the way of effective immunisation programmes, expansive ordering could, if not adequately managed (for example through donations or dose exchange), also entail challenges, such as risks of write-offs of finished products (e.g. for vaccine expiry and/or for misfit due to epidemiology evolution) and wastage of raw materials, putting even more pressure on the whole supply chain.

* Assuming dosing as per the respective regulatory approval

Beyond known requested demand there are up to 5 billion of additional demand. While these volumes are not clearly attributable, markets seem to clear immediately: additional volume commitments are usually directly absorbed by demand. It is therefore likely to be adequate to assume that all volume commitments of up to 14 billions correspond to actual demand in 2021.

Demand beyond 2021 is even less certain and depends on a wide range of assumptions, including but not limited to epidemiology, financing, remaining base-immunisation to be achieved, as well as both roll-out and absorptive capacity of vaccination programmes. Despite the uncertainty, the demand for 2022/23 is not expected to be higher than the 2021 demand.

Exhibit 3 – COVID-19 Vaccine Demand 2021



Overall, at least five questions remain regarding COVID-19 vaccine demand:

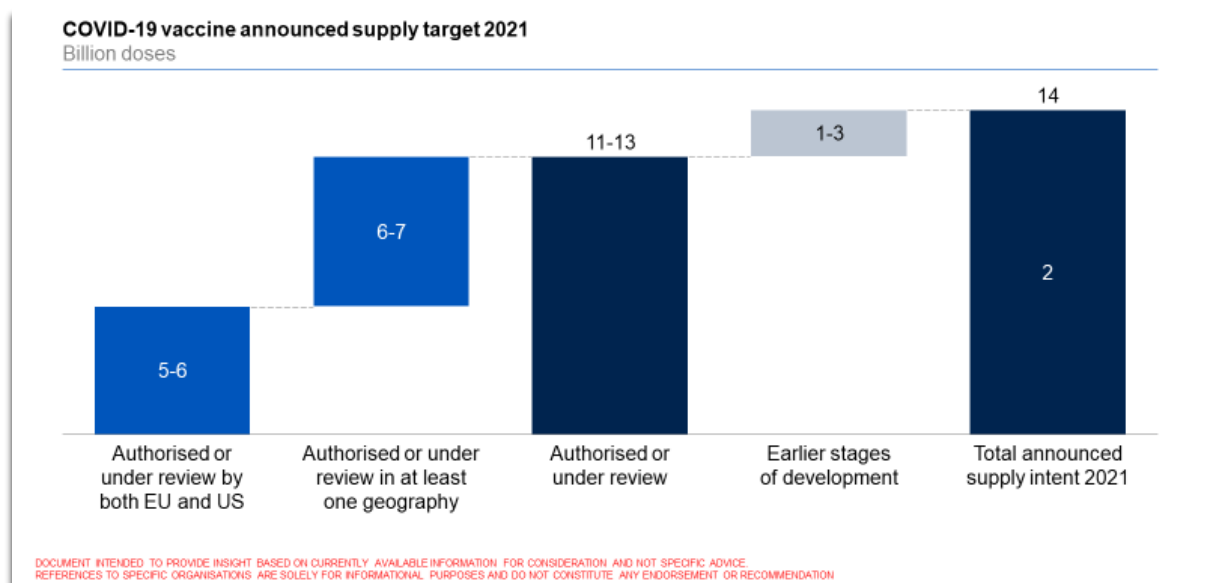
1. How much additional volumes will be procured for 2021 and beyond?
2. What is the need and frequency for boosters? How does this affect 2021 demand?
3. How will inefficient supply chains affect demand (e.g. expiration of products, hoarding behaviours due to erratic market developments)?
4. How will donations and exchanges (e.g. via COVAX) influence order patterns and volumes?
5. What will demand in 2022 and beyond look like and what are the supply implications?

2.2 COVID-19 Vaccine Supply Overview

The global response to the COVID-19 pandemic has triggered an unprecedented effort in vaccine development that has so far translated into around 250 candidates,¹¹ some based on technology platforms that have not before been used widely or even not used at all for human prophylactic vaccines. Moreover, the COVID-19 vaccine manufacturing capacity challenge has resulted in expansive collaborations among companies to scale-up and scale out production. More than 150 partnerships¹² with contract development and manufacturing organisations (CDMOs) have been formed and multinational biopharmaceutical companies support production for other companies.

The announced target supply of all manufacturers combined has the potential to reach up to 14 billion doses by the end of 2021 as outlined in Exhibit 4 and detailed in Annex 3.¹³ Some 85% of this (11-13 billion doses) are of vaccines that are already authorised or under review in at least one geography. This planned supply is prone to changes as new manufacturing partnerships are continuously announced (e.g. just recently some manufacturers have announced significant additional volumes¹⁴). In 2022, no further capacity has yet been announced, but supply could further increase assuming the implementation of further process improvements and introduction of additional capacity. This planned expansion would represent a quadrupling of the world's historically supplied annual vaccine output of 3.5-5.5 billion doses and is unprecedented in history.¹⁵

Exhibit 4 – COVID-19 Vaccine Announced Supply Target 2021



The realised supply in 2021 will depend on four major parameters:

- **Success of five late-stage vaccine candidates:** 1-3 billion doses of the announced target supply is accounted for by late-stage vaccine candidates that have not yet received authorisation or are under final review. The success rate of these candidates will have an impact on the potential 2021 total supply. It is also important to note that some of the announced supply target accounted for in the present discussion document is accounted for by vaccines that have so far received emergency use authorisation only in certain geographies.
- **Actual output of planned ramp-up during 2021 and success of expanding capacity of manufacturers:** industry analysts estimate that ~400 million doses have

been manufactured up to 3rd March 2021.¹⁶ This represents ~3% of the committed supply for 2021, so an exponential increase of effective production capacity is required. Even for highly experienced vaccine manufacturers, successful technology transfer between sites and with partnering manufacturers and production start-up will require months to accomplish, not weeks. Further, the quick ramp-up implies that manufacturing processes might not yet be optimised, and yields might be lower or input needs higher than they could be.

- **Success of mitigating upstream supply challenges:** the scale-up is likely to pose both known and currently-unknown challenges in the supply of critical raw materials, testing reagents for batch release, single-use systems, and equipment required for vaccine manufacturing, and third-party sterilisation and gamma irradiators. The degree to which these can be mitigated could have major knock-on impact for other vaccines and medicines that use these inputs and on the realised 2021 supply. These will be detailed in Chapter 3.
- **Success of pivoting to new vaccines, if required:** when new variants/mutations emerge, there is a risk that some platforms and/or vaccines could show reduced effectiveness. This will affect supply capacity in two ways: first, there is de facto less supply. If more variants of concern emerge (for which vaccines would need to be adapted), the existing vaccine manufacturing capacity might need to be split towards each relevant strain. Second, it takes time to adjust vaccines for new variants. While production of prior versions of the vaccine can likely continue during the majority of the adjustment process, it will take months or years (depending on the tech platform) until capacity for vaccines efficacious for the new variant is ramped-up. For example more than 50% of supplies are likely to need 6-12 months or more to adjust for new variants. Further details can be found in Annex 4.

The geographical distribution is concentrated in certain regions:

Looking at the distribution of supply capacity across the world, concentration of capacity in certain regions (notably East Asia, Europe, and North America) can be observed. In terms of capacity ramp-up as of 3rd March 2021, Asia is fastest in absolute terms (~196 million doses produced), followed by North America (~103 million doses produced), and Europe (~99 million doses); the rest of the world combined has produced fewer than 0.5 million doses thus far.

Overall, at least three questions remain regarding the COVID-19 vaccine supply:

1. How much of the up to 14 billion planned supply is likely to materialise in 2021, given the risks set out above?
2. What can be done to strengthen the likelihood of delivery on time and in full?
3. How likely is the occurrence of variants and what impact will they have?

2.3 COVID-19 Vaccine Supply and Demand Synthesis

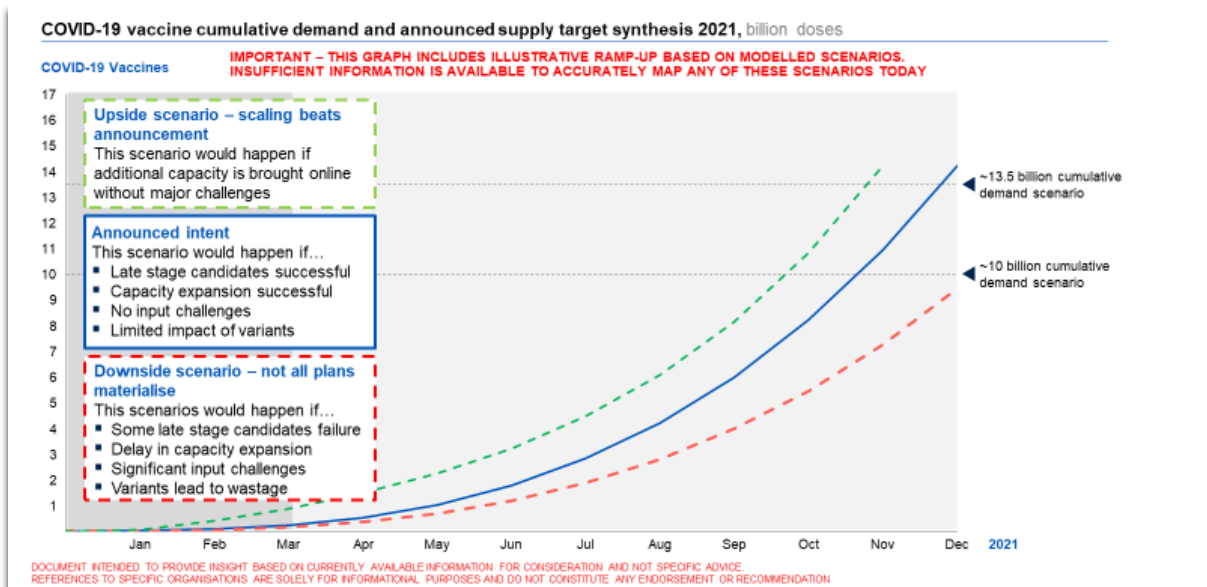
The first observation from analysing COVID-19 vaccine supply and demand is that at least three scenarios need to be considered (see Exhibit 5). Please approach this Exhibit with care: the announced supply capacity is likely to be directionally correct, but insufficient information is available for drawing fully-accurate scenarios. The downside and upside scenarios are largely illustrative, although the downside scenario is informed by the current trajectory.)

Announced intent scenario: COVID-19 vaccine supply could meet demand if the announced target of 14 billion aggregated doses in 2021 materialises. This would require all pipeline candidates to be authorised, manufacturing processes to be stable and expansion successful, no input supply challenges to occur, and the impact of variants to be limited. In this scenario, the demand/supply gap will remain for most of the year (10 months or more) as every economy aspires to scale vaccination campaigns as fast as possible. But over the course of 2021, most demand can be fulfilled, even if significant booster volumes are required.

Downside scenario: COVID-19 vaccine supply could fall below the announced total capacity if late-stage pipeline candidates are not approved, manufacturing processes turn out to be less stable than hoped and capacity expansion runs into challenges, input supply challenges cause production interruption, and/or the impact of variants is significant. The degree to which the 2021 demand can be filled depends on the scale of impact of each of these challenges.

Upside scenario: finally, there is a theoretical upside scenario that could be achieved through a combination of additional capacity being brought online successfully beyond the current plans and/or in a further-accelerated fashion, and additional successful candidates to emerge. However, this scenario is quite unlikely in the 2021 timeframe and is possible only if input supply is able to cope with even higher vaccine manufacturing scale.

Exhibit 5 – COVID-19 Vaccine Cumulative Supply and Demand Synthesis 2021



Overall, at least four questions remain regarding COVID-19 vaccine supply and demand:

1. What implications will course-regimens (e.g., one vs. two-course regimens) have on demand?
2. Which of the three scenarios is most likely?
3. What interventions can help decrease the likelihood of the downside scenarios?
4. What implications will course-regimens (e.g., one vs. two-course regimens) have on demand?

3 Input Supply Challenges

Key insights

- There is not yet have a complete and aligned view on the current and to-be-expected input supply challenges (raw materials, consumables, equipment).
- Signs of input supply challenges are being observed across all vaccine manufacturing steps, e.g. bioreactor bags, single-use systems, cell culture media (upstream), filters, gamma sterilization (upstream and downstream), vials (fill-and-finish). These individual challenges are amplified as the absence of any single input can disturb the entire manufacturing process (compounded risk).
- The capacity limitations are further aggravated by a tendency towards higher stock-keeping to counter uncertainties and trade barriers.
- New challenges beyond the ones identified are likely to arise. Moreover, knock-on effects of input challenges for non-COVID-19 health products are already emerging.

Vaccine manufacturing requires a large bill of material of often highly manufacturer-specific inputs in the form of raw materials, consumables, and equipment that are used along the upstream, downstream, and fill-and-finish manufacturing process. Many of those are provided by a limited supplier base and face significant peak demand compared to before COVID-19. Given that the absence of even one single input can challenge the outcome of the production process, challenges in the upstream supply chain pose significant compounded risk to vaccine manufacturing and uninterrupted supply.

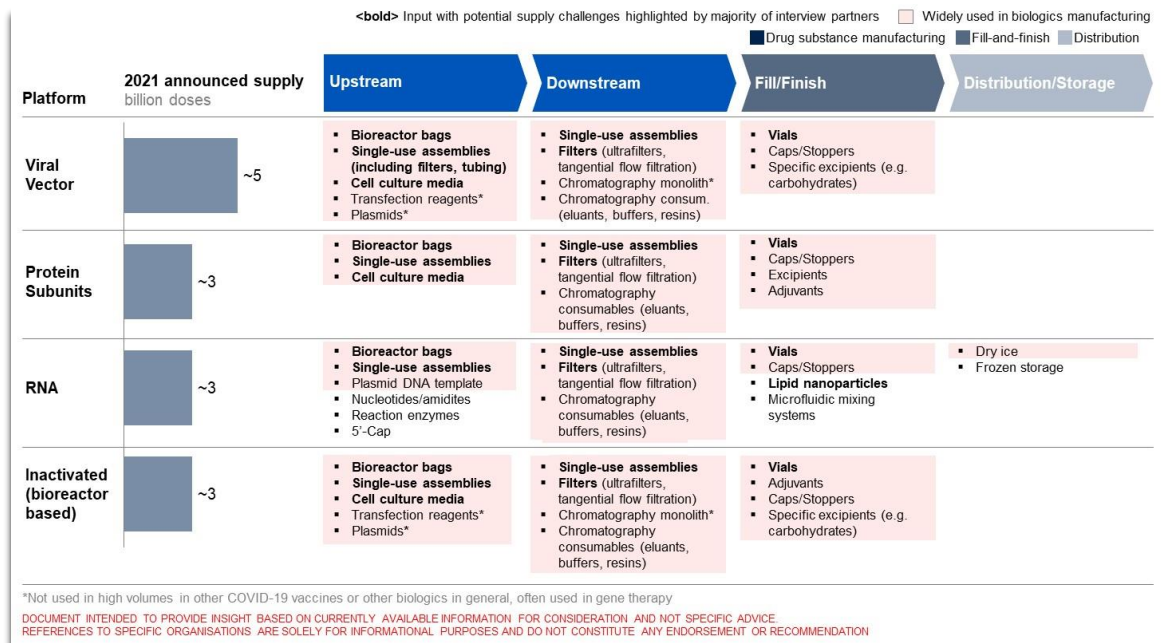
Experts highlight three emerging challenges that make it hard for market participants to get access to materials even if the total capacity and available volume are sufficient:

- **Limited data to forecast supply and manufacturing needs:** an ongoing challenge is the ability for purchasers and manufacturers to accurately forecast projected needs, particularly as new variants are identified. Collaboration between the public and private sectors to improve forecasting of potential needs and communicating those needs becomes to be a key priority. Many upstream suppliers highlight significant challenges associated with short lead times of orders across the supply chain. There remains limited visibility regarding parameters such as long- and short-term demand as well as prioritisation and allocation of supplies as far as this is compliant with applicable regulations. Higher visibility and quality information at an aggregate level would facilitate planning and help anticipate potential capacity constraints.
- **Increased safety stocks:** given this lack of visibility, the uncertainty of demand and supply scenarios, and potential absolute volume challenges in supply chains, there are indications of increased safety stocking (e.g. glass vials). The challenge of this uncertainty-induced increased stocking is that it can lead to negative consequences beyond direct input availability for COVID-19 vaccines, including write-offs and impact on production of other health products requiring the same inputs.
- **Increased trade and regulatory barriers:** there are increasing concerns over the expansion of trade and regulatory barriers (e.g. required package of stability and validation data for supplement/variation) as these have been observed for other essential COVID-19 supplies (e.g. PPE), and will potentially disrupt supply chains.

Today, there is no exhaustive and aligned view on what raw materials, consumables, and equipment are potential challenges for at-time manufacturing of COVID-19 vaccines. Exhibit 6 is an overview of inputs that are showing signals of potential supply challenges and

highlights in bold items that have been flagged by the majority of the 15 input suppliers, vaccine manufacturers, and CDMOs that have been interviewed for this discussion paper. Exhibit 7 details the potential drivers for the highlighted supply challenges and defines interdependencies to other medical products.

Exhibit 6 – Potential Supply Chain Challenges Along Vaccine Manufacturing Value Chain



- Bioreactor bags/single-use assemblies:** single-use bioreactor bags are used for e.g. cell culture and fermentation, while single-use assemblies consist of plastic components that are used in diverse bioprocessing steps (e.g. tubing). These single-use inputs show signals of potential supply challenges, which is relevant for all four technology platforms, and are likely influenced by four drivers. First, the COVID-19 demand represents a massive capacity surge for suppliers and sub-suppliers, which comes on top of pre-COVID-19 capacity challenges with single-use bioreactor bags back orders amounting to four months, according to Summit participants. Accordingly, several suppliers have expanded their capacity by 50% in 2020 and are planning to expand capacities by another 50% in 2021.¹⁷ More data would be needed to holistically assess if these expansions are sufficient. Second, given a lack of supply visibility and signs of shortage, safety stocks are increased, driving further imbalances, as described above. Third, as major manufacturing sites are located in regions with export restrictions, global availability is reduced. Fourth, the high degree of specificity and the lack of standardisation of these items represent a hurdle to short-term supplier switches and thus flexibility. The flexibility of switching supplies is further impeded by complex regulatory process requirements. In general, bioreactor bags can be substituted by stainless steel; this, however, takes 6-12 months taking into consideration order lead times and validation.
- Cell culture media:** cell culture media are essential to produce inactivated-virus-, viral-vector-, and protein-subunit-based COVID-19 vaccines. The supply of cell culture media might potentially become constrained as the required foetal bovine serum and amino acids face potential supply constraints. Additionally, cell culture media production depends on a small set of recombinant proteins and hormones suppliers that are located in a small number of geographies. Given that cell culture media are

essential for three out of four technology platforms, geographic constraints could significantly impact the manufacturing capacity of COVID-19 vaccines.

- **Filters:** single-use filters, such as tangential flow filters (TFF), are used in the downstream process of all four COVID-19 platforms. With a historic market growth of around 10%, filters were already in high demand before COVID-19.¹⁸ The COVID-19 surge as well as export restrictions have stretched or imbalanced the supply situation further. Vaccine manufacturing process improvements (like batch size increases) can reduce the number of single-use filters needed and could reduce the demand slightly, but are unlikely to solve the situation. In general, tangential flow filtration can be substituted by depth filtration and centrifugation and vice versa. This would require process reconfiguration and revalidation of 3-6 months.
- **Gamma Sterilisation:** the above described single-use systems need to be sterilised before being used, leveraging technologies like gamma sterilisation. Gamma radiation is generated by the decay of the radioisotope Cobalt 60. Gamma rays pass readily through plastics and kill bacteria by breaking the covalent bonds of bacterial DNA. Given the overall COVID-19 vaccine capacity surge, and the predominant use of single-use systems, external sterilisation services show initial signs of supply challenges. These supply challenges extend to sub-supplier level, with Cobalt supply being unable to fully meet the market demand.¹⁹
- **Vials:** vials are essential for the distribution of all COVID-19 vaccines. Today, mixed signals exist regarding potential supply challenges of glass vials with increased lead times and risk of tubing furnace (tanks) failures to be counted among the vulnerabilities. Based on industry estimates, the global vial market is 16-18 billion vials strong.²⁰ With an estimated yearly vial need of <2.8 billion, the COVID-19 vaccine would utilize ~15% of the global vial market and thus a significant share. Accordingly, investments in capacity expansions have already been conducted, e.g., \$204 million BARDA investment in Corning's Valor® Glass tubing and vial facilities in New York, New Jersey, and North Carolina.²¹ To holistically assess whether this and similar expansions underway by glass manufacturers are sufficient, more data would be needed. Besides the vial manufacturer capacity, vial supply is also dependent on sufficient supply of the tubing capacity which relies on special tanks to heat raw materials need to be closely watched (Annex 7). Finally, vials can also have an impact on overall COVID-19 vaccine output as glass breakage in cold storage or lower throughput in fill/finish lines due to vial failures or higher coefficient of friction will cause delay in vaccines supply. This requires a close collaboration between suppliers and vaccine manufacturers.
- **Lipid nanoparticles (LNPs):** LNPs are critical for the manufacturing of mRNA vaccines and are used to encapsulate the drug substance for its delivery. LNPs rely on specific raw materials, out of which some show signals of potential constraints. Non-animal-based cholesterol, for instance, could be subject to capacity challenges and geographic constraints. The supply of cationic and PEGylated lipids could also be considered a challenge, as few suppliers for GMP lipids at scale currently exist. Moreover, some LNP suppliers rely on specific types of equipment such as microfluid and nanofluid mixers, which bear potential constraints as their supply relies solely on two suppliers. In general, the LNP supply similarly to the overall mRNA production needs to adjust to the rapid shift from the clinical to the commercial stage.

Exhibit 7 – Summary of Major Supply Challenges and Potential Drivers

	Input	Impacted Platforms	Initial perspective on potential drivers (not exhaustive)	Impact on other medical products
Upstream	Bioreactor bags/single-use systems		<ul style="list-style-type: none"> Demand surge translates into capacity increase at supplier/sub-supplier level (e.g. 50% capacity increase) No standardisation and thus no flexibility between vendors Export restrictions and no transparency on supply prioritisation criteria Increase of safety stocks due to early shortage signs leading to bullwhip effect 	✓
	Cell culture Media		<ul style="list-style-type: none"> Possible shortage of raw materials (e.g. fetal bovine serum, amino acids) Possible geographic constraints (e.g. export restrictions) due to reliance on a small set of recombinant protein and hormone suppliers in limited geographies 	✓
Down-stream	Filters		<ul style="list-style-type: none"> Unexpected capacity surge at supplier and sub-supplier level Export restrictions and no transparency on supply prioritisation criteria 	✓
Fill-and-Finish	LNP		<ul style="list-style-type: none"> Limited availability of raw material inputs (e.g. potential capacity challenge and potential geographic constraints of non animal based cholesterol) Possible supply bottleneck due to limited suppliers of upstream key components (e.g. PEGylated lipids) Possible equipment related constraints as some LNP suppliers rely on microfluid/nanofluid mixers, which are only produced by two suppliers 	
	Vials		<ul style="list-style-type: none"> Bottlenecks in tubing (e.g. due to disruption of glass melting tanks) and borate supply, which is sourced to ~40% from a single mine Lack of vial standardisation reduces flexibility to respond to shortages Cold-storage (e.g. for mRNA vaccines) requires reduced filling volume to minimise risk of breaking, increasing the total number of needed vials 	✓

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On top of all of these detailed input supply challenges, long-term demand uncertainties represent an additional challenge that complicates investment decisions and could potentially lead to decelerated capacity expansions.

Solving the supply challenges described above is essential not only for COVID-19 vaccine supply, but also for the other 3.5-5.5 billion doses of vaccines such as polio (1.5 billion), diphtheria and tetanus (0.7 billion), meningococcal meningitis (0.7 billion), seasonal influenza (0.5 billion), and other life-saving biopharmaceutical products, that rely overwhelmingly on the same input supplies as the COVID-19 vaccine. Exhibit 6 highlights this interdependency by following grey boxes. Accordingly, key stakeholders of the other impacted health products should be included in the solution discussion.

Overall, at least four questions remain regarding the COVID-19 input supply challenges:

1. Are all items covered that might show near- to mid-term supply challenges?
2. How can newly arising supply challenges be quickly identified and mitigated?
3. Are there other market efficiency challenges that need to be considered?
4. What are the implications of the described supply challenges from a country, manufacturer, and supplier perspective?

Besides potential inputs challenges discussed above, additional aspects need to be considered for effective programmatic roll-out of COVID-19 vaccines (e.g. syringes/needles for vaccine injection, healthcare worker capacity).

4 Manufacturing Capacity and Interdependencies Beyond COVID-19 Vaccines

Key insights

- Availability and needs for drug substance capacity depend on the technology platform:
 - mRNA vaccines are a novel technology, requiring new capacity. According to industry proponents, the built capacity is likely to be sufficient, at least to meet announced supply targets for 2021.
 - Protein subunit and viral vector vaccines can draw on significant installed base, potentially requiring the repurposing of 1-5% of existing capacity to meet 2021 announced supply targets.
 - Data for capacity and repurposing potential of inactivated virus based vaccines is limited.
- Visibility on the availability and need for fill-and-finish capacity is limited. COVID-19 vaccines are likely to need less than 2.8 billion vials capacity, juxtaposed to an estimated existing capacity of more than 10 billion vials, according to industry observers. To what extent such capacity is available and what repercussions repurposing would entail on other health products, is unclear.
- To facilitate rapid and effective repurposing and building of new capacity (where needed and sensible), better data, effective tech transfer, adequate quality of capacity, and sufficiently deep partnerships are needed.
- Overall, implications of capacity expansion for COVID-19 vaccines on other health products need to be carefully considered especially for fill-and-finish.

Manufacturing capacity for COVID-19 vaccines depends on drug substance and fill-and-finish capacity. Exhibit 8 summarises manufacturing capacity considerations for drug substance and fill-and-finish across vaccine platforms.

Exhibit 8 – Overview of Manufacturing Capacity by Platform

Value step	Tech platform	Specificity of production capacity	Needs to meet 2021 announced supply targets	Considerations for potential expansion
Drug substance	mRNA	<ul style="list-style-type: none"> ▪ Novel technology ▪ (Almost) exclusively for COVID-19 Vx production 	<ul style="list-style-type: none"> ▪ Rapid scale-up since beginning of pandemic; most produced tech platform thus far ▪ According to industry interviewees sufficient capacity online to meet 2021 announced supply targets 	<ul style="list-style-type: none"> ▪ Requires building of new capacity or potentially process/OEE improvements ▪ No potential for repurposing
	Protein subunit/ viral vector	<ul style="list-style-type: none"> ▪ Uses bioreactors that are needed for, e.g. biologics or other vaccines 	<ul style="list-style-type: none"> ▪ Can draw on significant installed base ▪ Meeting 2021 announced supply targets would require <1-5% of existing capacity 	<ul style="list-style-type: none"> ▪ Further repurposing likely possible ▪ Risk for supply chains of other health products likely limited, given existing installed base and expected excess capacity available
	Inactivated virus	<ul style="list-style-type: none"> ▪ Uses different technologies, e.g. bioreactors, chicken embryo expression ▪ Similar production to many common Vx, e.g. influenza 	<ul style="list-style-type: none"> ▪ High fungibility with other bioreactor-based inactivated vaccines ▪ Low fungibility with other types of capacity due to viral containment needs 	<ul style="list-style-type: none"> ▪ Repurposing of additional capacity difficult due to viral containment requirements to handle live virus
Fill-and-finish	All	<ul style="list-style-type: none"> ▪ Same production capacity as for other vaccines (that come in vials) and, e.g. biologics 	<ul style="list-style-type: none"> ▪ Expected global announced supply targets of >10 billion vials according to industry observers ▪ Likely need of <2.8 billion vials capacity for COVID-19 Vx (2021) 	<ul style="list-style-type: none"> ▪ Repurposing/expansion potential lacking sufficient data ▪ Potential risk of competition of capacity with other health products (e.g. vaccines, biologics)

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To the extent that repurposing and/or bringing online new capacity is in fact needed, five key requirements need to be considered:

- **Visibility** into existing capacity and interdependencies with the production of other health products. Current knowledge gaps e.g. on the available fill-and-finish capacity need to be closed.
- **Industry collaboration/technology transfer** to ensure rapid and effective build-up/repurposing of capacity. Given the usual timelines of several years to build/repurpose capacity, individual manufacturers need to build on each other's expertise to ensure rapid expansion of capacity. A critical enabler for such tech transfer between partnering manufacturers is the availability of skilled human capacity, which has been described as a key challenge.
- **Quality** of installed base/new production to ensure viability of outputs. There are significant unknowns around this factor which might facilitate/or alternatively complicate capacity expansion.
- **Standardisation** of printed materials (e.g. label, cartons, leaflet). The more standardised the printed materials are, the fewer changeovers are needed. Changeovers are a significant cause of sub-optimal use of capacity in fill-and-finish.
- **Depth of partnerships** between stakeholders to ensure effective collaboration and ensure targeted interventions to build out capacity and enable early identification of gaps, and to strengthen efficiency.

For all the aforementioned key requirements, regulatory aspects (e.g. inspection and validation of manufacturing sites based on Chemistry, Manufacturing and Controls data, requirements for regulatory application review and current Good Manufacturing Practice) are expected to play an important role and need to be considered.

In addition, the scale-up of COVID-19 supply chains, distribution, and administration could potentially bring significant programmatic and operational challenges to the supply chain and distribution of other vaccines and health products. It is critical that the quick ramp-up of capacity does not disrupt the production and supply of other medicines and vaccines. This topic is not discussed further in this discussion document but needs to be considered.

4.1 Deep Dive on Drug Substance

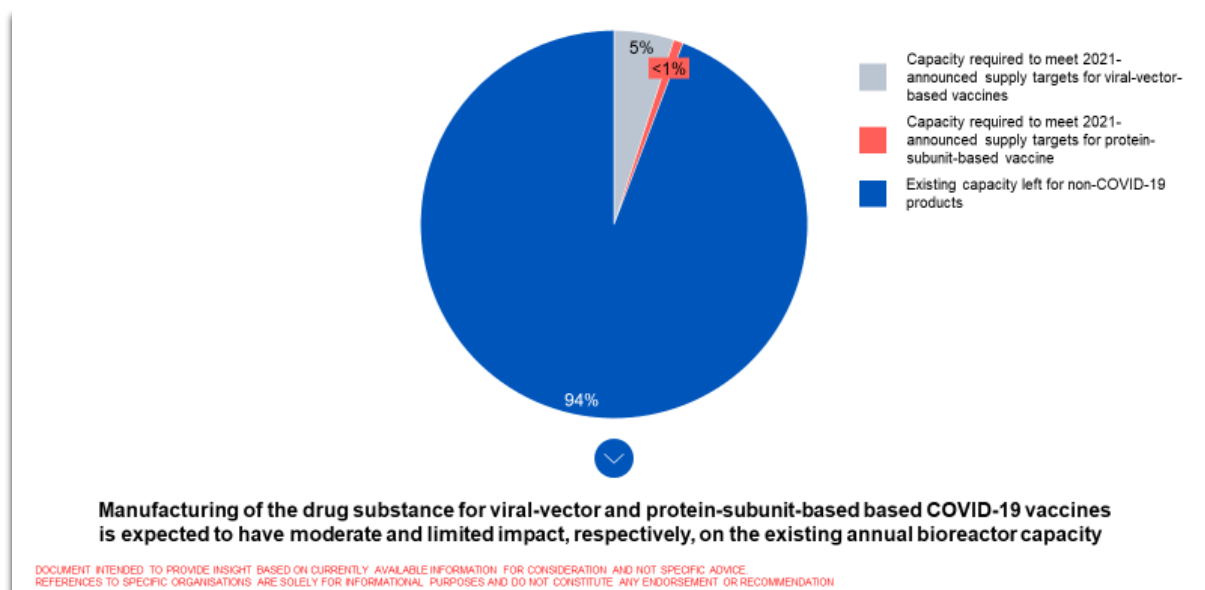
Most technology platforms rely on specific manufacturing processes to produce the relevant drug substance (upstream and downstream). Hence, manufacturing capacity needs to be assessed from a technology platform perspective.

- **mRNA-based vaccines** are based on a novel technology. Production of mRNA-based vaccines rely on drug substance manufacturing processes that are specific to this emerging technology platform. Hence today, the manufacturing of the drug substance for mRNA-based vaccine relies on recently-installed commercial-grade mRNA and LNP GMP manufacturing capacity by manufacturers themselves or in close partnerships with CDMOs. While according to industry stakeholders it usually takes three-to-four years to build new capacity, greatly accelerated timelines have been observed. Indeed, mRNA vaccines are so far the most-produced platform, accounting for around 45% of production to date. According to industry stakeholders, currently

built new capacity is likely to prove sufficient, at least to meet 2021 announced supply targets. The rapid scale-up has however entailed productivity challenges affecting the output of new production lines that will need to be addressed. Further, new capacity may be needed, including if demand increases in the future.

- **Viral-vector- and protein-subunit-based vaccines** employ different approaches and technologies, but both rely on cell growth in, typically, fixed 1000L+ bioreactors. Global bioreactor capacity is also required for the production of other biologics (e.g. other vaccines, monoclonal antibody therapies). Given the broad installed base, global existing bioreactor capacity is significant. The production of the drug substance required to meet 2021 announced supply targets would thus require only ~1-5% of the annual existing bioreactor capacity. This would probably have limited to moderate impact on the capacity needed for the production of other health products requiring bioreactors, given expected global excess capacity. That said, access to capacity (especially for smaller players) and requirements/timelines for repurposing could potentially be a barrier to the scale-up of capacity ready for COVID-19 vaccines production.
- **Inactivated-virus-based vaccines** are based on the infectious virus itself, which is produced in bulk, then chemically inactivated via treatment with formaldehyde, formalin, or other substances. Inactivated virus capacity is diverse: many different cell lines are used to make bioreactor-based inactivated viruses, and others are made in genetically modified chicken embryo expression systems. Many common vaccines are inactivated virus vaccines, most notably the various influenza vaccines. Global capacity is significant, but data on exact capacity and repurposing potential are lacking. Given the involvement of infective pathogens, capacity is dedicated and requires high biosafety levels. Building of new capacity usually requires more than two years and repurposing is likely to prove challenging (e.g. because of containment requirements).

Exhibit 9 – Share of Existing Bioreactor Annual Capacity Required for Viral Vector and Protein-Subunit-Based Vaccines



4.2 Deep-Dive on Fill-and-Finish

Fill-and-finish capacity is needed for all COVID-19 vaccines, and beyond that for many other vaccines (i.e. all that come in vials) and health products, such as biologics. While there are no accurate estimates of worldwide fill-and-finish capacity, it could be well over 10 billion vials, according to industry observers. This includes pre-existing capacity for the production of vaccines (likely to have been 3.5-5.5 billion doses annually pre-COVID-19), biologics, and other health products, new capacity brought online since the outset of the pandemic, and potential excess capacity in the system.

The available capacity to meet the 2.8 billion or less required vial-capacity* for COVID-19 vaccines and potential repercussion for the production of other health products is currently largely unknown. Assuming five doses per vial (although there are vaccines with over 20 doses per vial), around 2.8 billion vials fill-and-finish capacity would be needed to meet the 2021 announced supply target of up to 14 billion doses, potentially even less†. The available capacity for these 2.8 billion vials, and repercussions on other health products requiring fill-and-finish, depends, among other considerations, on the assumption of doses per vial and according to implications on productivity (e.g. due to slower filling times), newly built capacity, and repurposing. The latter repurposing potential depends predominantly on potential needs for requalification, retooling, and reengineering needs for production lines, implications of productivity (e.g. because of longer filling times), and the potential to leverage fill-and-finish capacity beyond other vaccines e.g. from animal health products. Moreover, biosafety requirements (e.g. BSL-2 for viral vector or BSL-3 for inactivated virus) of the filling lines need to be put into consideration.

* 14 billion doses divided by 5 doses per vial

† Depending on e.g. the number of doses per vial, filling times, retooling, and new technologies

5 Overview of Potential Solutions for Discussion

Key insights

- A broad range of potential solutions could be considered to mitigate acute supply challenges and enhance longer-term supply sustainability:
 - Three levers could be considered to directly scale input supply and manufacturing: (i) increasing efficiency of existing capacity; (ii) repurposing of existing capacity; (iii) adding new capacity.
 - Five enablers could be considered to support the scale up and enhance efficiency: (i) free flow of goods; (ii) regulatory; (iii) collaboration; (iv) financing; (v) visibility.
- The solutions outlined under the scale-up levers and enablers aim to show the breadth of potential interventions and do not constitute recommendations. Potentially, a combination of solutions may need to be employed that carefully considers trade-offs and externalities.

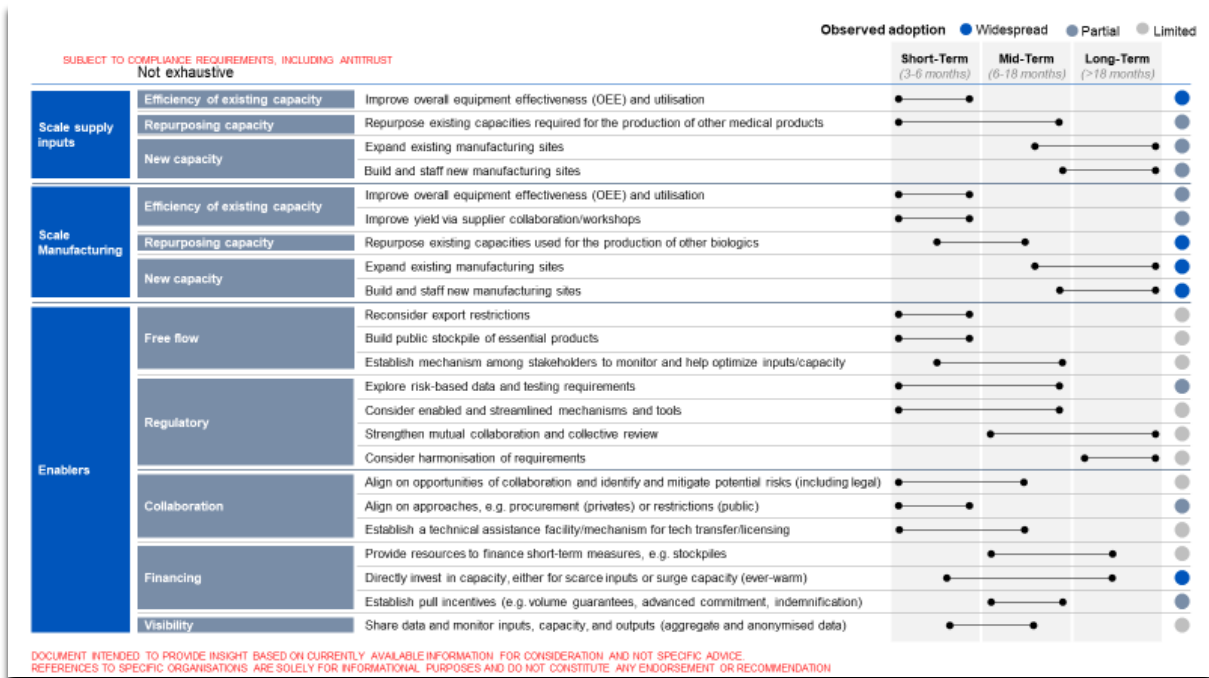
Exhibit 10 below lays out a broad range of potential solutions that could be considered to address the challenges identified. These solutions are not normative recommendations but aim to broadly and descriptively map out the potential “solution space” within which stakeholders could consider addressing supply challenges. The solution space covers both shorter- (weeks/months) and longer-term (6-18 months) interventions.

The Manufacturing Summit will offer an opportunity to discuss solutions and their respective merits in more detail and among key stakeholders. Five key dimensions could be considered when discussing potential solutions:

- **Focus:** different solutions may be better suited to address some of the challenges laid out. Some solutions could help tackle a broad range of challenges (e.g. data to forecast supply and manufacturing needs), while others are more specific (e.g. funding to expand manufacturing of selected supply inputs).
- **Time horizon:** as indicated in Exhibit 10, the time horizon in which solutions can be implemented and be effective differs greatly. It will be important to align time horizons with the objective pursued, i.e. addressing acute challenges vs. strengthening long-term market sustainability.
- **Contributions:** whilst this discussion document does not fully analyse the contributions of each actor, it is clear that governments, international mechanisms, and manufacturers are all essential to the successful launch, set-up, and implementation of these solutions.
- **Trade-offs:** some solutions appear to be net positive while others constitute direct trade-offs. Collaboration for instance could be net-positive and expand the overall capacity. Other solutions might involve direct trade-offs amongst themselves (e.g. allocation of financial resources) or with other solutions (e.g. some more interventionist solutions might contravene collaboration targets). Such trade-offs should be identified early.
- **Externalities:** for all solutions, the respective opportunities/challenges and implications/risk for both the COVID-19 ecosystem and broader health, society, and economy need to be assessed and carefully considered.

In addition, any specific initiative that would involve sharing of information or collaboration between industry players would require careful antitrust review before potentially being implemented. That analysis would be specific to the situation and would need to be considered on a case-by-case basis that is outside the scope of the present discussion document.

Exhibit 10 – Overview of Potential Solutions Along Time Horizons



- **Scaling supply inputs and scaling manufacturing:** in areas where capacity is or could be the major challenge, three levers can be envisioned to increase capacity:
 - Increasing the efficiency of existing capacity (e.g. improving overall equipment effectiveness; enhancing biological yield).
 - Repurposing some other existing installed base (e.g. other vaccine production to COVID-19), including (temporarily) unused capacity.
 - Adding new capacity (e.g. adding new production lines in existing sites; building new sites).

While efficiency improvements and, to some extent, expanding existing installed base are less capital expenditure (CAPEX) intensive and faster, they may also be more constrained in the capacity they can add compared to bringing new capacity online. Repurposing can be fast and effective, but potentially entails negative externalities on other health products.

Exemplary use cases: OEE improvements (e.g. cell culture media); expanding installed base (e.g. fill-and-finish); adding new capacity (e.g. glass vials, mRNA drug substance production); repurposing (e.g. protein subunit/viral vector drug substance production).

- **Enablers:** to address capacity challenges and strengthen longer-term supply capacity, there are five key sets of enablers:
 - **Free flow:** given the length, complexity, uncertainty, and sensitivity of supply chains, many industry stakeholders highlight the importance of free flow of products to enable flexibility and efficiency of manufacturing. This includes the free flow of goods (e.g. inputs, drug substance, finished products), technical capacity (e.g. human resources), and production capacity (e.g. the ability to scale-up/-down utilised capacity across sites, as needed).
 - **Regulatory:** agility, alignment, and consistency of regulation can improve the fungibility of supplies and the capacity and the reactivity of supply chains. Regulatory bottlenecks would need to be further explored further and were not in the core scope of this discussion document. Potential needs that have been raised by industry stakeholders include risk-based data/testing requirements and regulatory agility (e.g. testing of batches, approval of substitutive products such as salts, post-approval challenges); enabled and streamlined regulatory mechanisms and tools (e.g. virtual site visits, adjusted pathways); strengthened mutual recognition and collaborative review; harmonisation of requirements.
 - **Collaboration:** further collaboration across public (incl. regulators) and private stakeholders could help enhance input supply availability, reduce write-offs and product expirations, and strengthen adequate distribution of scarce inputs/capacity by e.g. increasing visibility across the supply chain, adopting standardised approaches, establishing mechanisms for licensing and technology transfer, or even assigning production of goods to specific manufacturers. Some forms of collaboration may require careful design to ensure consistency with competition and other laws. The European Commission has discussed in the context of COVID-19 various options and the extent to which antitrust regulation can help accommodate or facilitate such efforts.²² Antitrust agencies in the United States have similarly highlighted options for lawful private sector collaboration, and made a public commitment to providing businesses responding to the COVID-19 pandemic with “expeditious guidance” on how to do this in compliance with antitrust laws.²³ The potential advantages of enhanced collaboration could be manifold and include streamlining the supply chain, fully leveraging economies of scale, and ensuring continuity of manufacturing.

Exemplary use cases: “pre-production collaboration” as identified in the EU communications,²⁴ mechanism to share information to help identify and avoid bottlenecks, surge-contracting, regulatory reliance mechanisms, mechanisms for tech transfer and licensing (including for e.g. specific enzymes), consultancy models for expert knowledge (e.g. biological yield improvements)

- **Financing:** implementing solutions requires resources, whether directly to expand capacity or to enhance the ecosystem, which then indirectly leads to capacity expansion. Options include direct “push” investments in new capacity (e.g. public-private partnerships or commissioned manufacturing), “pull incentives” for capacity expansion (e.g. subsidies, tax credits, advanced market commitments, volume guarantees, or other financial incentives that strengthen the economic attractiveness of the intended activity) or investments in joint mechanisms (e.g. setting up a supply cockpit or other ‘neutral’ entities for stakeholder collaboration). These options are similarly applicable for the vaccine manufacturing side as well as input supply side to increase ability to surge and fulfil manufacturers demand. Financing can be a critical enabler for solutions, and a solution in itself by directly “solving” challenges. However,

deep collaboration, aligned targets, sufficient guardrails, and buy-in are needed for larger-scale investments, especially across a broad base of stakeholders.

Exemplary use cases: ever-warm capacity for surge capacity needed e.g. fill-and-finish; financing of collaboration mechanisms (e.g. sharing of anonymised aggregate data); incentivisation of partnerships (e.g. between biopharmaceuticals).

- **Visibility:** visibility along the supply chain is in some instances very limited and a lack of high-quality data and evidence can hamper the various market participants and stakeholders to make timely and effective decisions and can lead to inefficient product allocation (and thus disruptions or, conversely, write-offs/wastage). An effort to enhance visibility could potentially, whilst not being a sufficient solution in itself, be a critical enabler for other solutions. It could include creating an overview of capacity and resources across the supply chain (by site, location, geography, etc.) subject to appropriate antitrust compliance measures (such as ensuring aggregated and anonymised data are handled through a third party to avoid sensitive exchanges between competitors). Individual manufacturers have already started implementing efforts²⁵ of this sort within their own supply chains. The advantage of enhanced visibility would be the generation of key insights to help prevent and address challenges and respond to acute situations. However, the investments required and risks need to be considered, including antitrust compliance as discussed above, and the effectiveness would depend on the quality of data generated and the breadth of buy-in and contribution. Further, it would probably require collaboration across many ongoing initiatives and many players given international supply chains, which might need time and resources to install. Last, effectiveness would depend on adequate solutions or mechanisms to translate insights into action.

Exemplary use cases: this lever could be applied along the entire value chain to enable monitoring and exchange of commodity-like required equipment and single-use systems across various players. Moreover, such an effort (potentially spanning stakeholders from various sectors) could be helpful to unlock in good time situations where highly technology-platform-specific items are subject to constraints (e.g. LNPs and their key components, enzymes, plasmids).

Overall, at least three questions remain regarding the solution space:

1. Are these the right levers overall? Any major omissions?
2. Which lever would be most effective for which challenge?
3. What is the appropriate contribution of governments, international mechanisms, and manufacturers to each?

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6 Abbreviations

Abbreviation	Definition
AMC	COVAX advance market commitment
CAPEX	Capital expenditure
CDMO	Contract development and manufacturing organisation
COVID-19	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
GMP	Good manufacturing practices
HIC	High-income country
IP	Intellectual property
LNP	Lipid nanoparticle
mRNA	Messenger RNA
OEE	Optimised/overall equipment effectiveness
PEG	Polyethylene glycol
PPE	Personal protective equipment
UMIC	Upper-middle income country

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