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THE COVID-19 VACCINE UPSTREAM SUPPLY CHAIN
The Manufacturing Race Is On!

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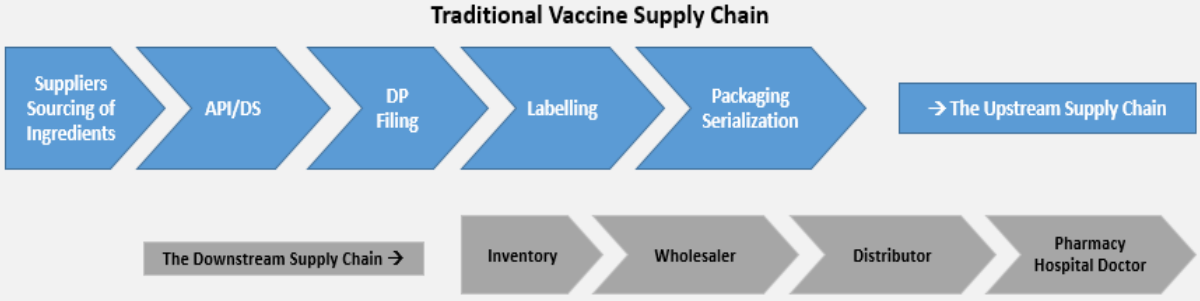
Introduction

The availability of Covid-19 vaccines has become a top priority on the agenda of Health Authorities, governments, politicians and to **all of us 8 Billion people around the world**. Who is battling to get a vaccine to the world? What is at stake? What are the challenges to get these vaccines manufactured and distributed? This and more will be explained in a series of 4 articles. The first article is about the **Upstream Supply Chain Challenges.**

The Upstream Supply Chain

As a reminder, the upstream supply chain consists of a number of manufacturing steps which includes the Active Pharmaceutical Ingredient (API) also sometimes called Drug Substance (DS), the Drug Product (DP) in vials, amps or pre-filled syringes, the Finished Product (FP) and having the final doses tested and released for injection. These production steps are often taken across multiple factories which requires transportation and storage between factory sites typically spread across multiple countries. Logistics plays a critical role in all of this.



As for any pharmaceutical manufacturing chain all the steps are defined in the CMC (Chemistry, Manufacturing, Controls) regulatory file which details all the information required for the submission and the approval of a drug to the regulatory authorities such as the FDA in the USA or the EMA in Europe. Those requirements must be respected during the production, testing and release steps within the different stages of the product manufacturing processes. Timely sequencing of operations is critical to ensure smooth production planning and use of all possible time-opportunities to reduce lead-time and avoid delaying any of the scheduled production batches.

The Battle

There are currently 6 frontrunners in the race to manufacture a COVID-19 vaccine for the world. These are all large pharmaceutical companies. However, as time and scalability are of critical essence here, each of these companies needs to create manufacturing capacity and maximum scalability. This is why these companies are creating manufacturing partnerships across their upstream supply chain to ensure they can ramp up at risk and move quickly.

#	Name of the vaccine	Manufacturer	Country	Estimated launch or Clinical status
1	Sputnik V	Gamaleya Research Institute	Russia	11 August, 2020
2	BNT162b1	BioNTech, Fosun, Pfizer	Germany, China, USA	Phase III
3	mRNA-1273	Moderna, NIAID	USA	Phase III
4	New Crown	Sinopharm	China	Phase III
5	CoronaVac	Sinovac	China	Phase III
6	AZD-12222	Uni Oxford, Astra Zeneca	UK	Phase III

The Battle

The stakes are high. The race is not just to provide the world with a COVID-19 vaccine. At stake is money and potentially big profits. It's potentially about dominating the world with a vaccine which people will need in the years to come. There is also a geo-political angle to all of this. As mentioned by Merck's CEO, Kenneth, we are currently living in a time of ultra-nationalism, where countries are constantly competing against each other for access to the supplies of any potential COVID-19 vaccine. Ultimately, there might be several vaccines which will dominate various markets depending on which countries work together. China will for sure go for a Chinese vaccine. Russia will probably choose its own Sputnik V vaccine. The US will likely go for a US manufactured vaccine. Nonetheless, each of these countries will likely seek to tie in other countries to their vaccine solutions.

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	Manufacturer	Country	Manufacturing Partners	Anticipated Price
Sputnik V	Gamaleya Research Institute	Russia	Parana Technology Institute - Brazil, India	*Not announced yet*
BNT162b1	BioNTech, Fosun, Pfizer	Germany, China, USA	None	$19.50
mRNA-1273	Moderna, NIAID	USA	Lonza and ROVI – Europe, Catalent – Indiana	$32 - $37
New Crown	Sinopharm	China	None	$145 (for two shots)
CoronaVac	Sinovac	China	None	*Not announced yet*
AZD-12222	Uni Oxford, Astra Zeneca	UK	Emergent BioSolutions - US, Serum Institute - India	$4

The Challenges

There are many challenges which will influence the upstream supply chain and we would like to list a few of them to highlight the risks and the opportunities which will impact the overall throughput and ultimately the number of patients that can get the vaccines. Margaret (Peggy) Hamburg, foreign secretary of the National Academy of Medicine, in a recent discussion stated that with Covid-19, the world is moving at a record speed, in terms of the history of vaccine development. However, safety and efficacy are two things that we cannot compromise on.

Components and Raw Material Sourcing

The sourcing of the materials required to manufacture the upstream API's will be the first challenge to overcome. Will there be enough starting materials (e.g. embryonated eggs) to initiate and maintain production and will there be enough production suites to be dedicated to these activities? Can the procurement activity already start at risk while we don't even know what will be the exact bills of materials for each production steps?

Prioritization of production will be challenging, and decision processes will be tougher and more complex than ever. Material availability may be conflicting with other vaccine production cycles such as the twice a year influenza vaccine production campaigns.

Moreover, different companies are targeting to build the vaccine through different formulations therefore, it is crucial to make sure that raw material sourcing is enough not only for clinical trial stages but also for the commercial production requirements.

Virus vaccines: At least seven teams are developing vaccines using the virus itself, in a weakened or inactivated form. Many existing vaccines are made in this manner. For example, those against measles and polio. However, these type of vaccines require extensive safety testing. Notably, Sinovac Biotech in Beijing has started to test an inactivated version of SARS-CoV-2 in humans.

Viral-vector vaccines: A virus such as adenovirus is genetically engineered so that it can produce coronavirus proteins in the body. These viruses themselves are weakened so they cannot cause disease.

Nucleic-acid vaccines: Aiming to use genetic instructions (in the form of DNA or RNA) for a coronavirus protein that induces an immune response. The nucleic acid is inserted into human cells, which then churn out copies of the virus protein – typically these vaccines encode the virus' spike protein.

Protein-based vaccines: Many researchers want to inject coronavirus proteins directly into the body. Fragments of proteins or protein shells that mimic the coronavirus' outer coat can also be used.

Manufacturing Capacity

The world has a population of 8 Billion people. There is already talk that some of these vaccines will require an initial 2 shot dosage. Like other flue type vaccines there might be a need for a yearly vaccine shot. Therefore, there will also be a major challenge on the longer-term manufacturing capacity for vaccines. Capacity usually cannot be scaled up quickly. Therefore, building additional capacity potentially across multiple sites is a large undertaking which will take time.

Most of the manufacturer frontrunners have already decided to invest in up-scaling their capacity at risk and countries such as the US and the EU have started providing funding to a number of companies for the scaling of manufacture, in return for guaranteed access to a specific number of doses. Production bottlenecks within the upstream supply chain are bound to take place.

The challenge for the manufacturer will be to sequence the production activities when not knowing what will have to be produced when and how. Agility and reactivity in scheduling operations will benefit to the most efficient producers.

The other components of capacity will be the timely availability of human resources to manage the API/DS/DP/FP production sites while the pandemic continues to spread, and the second wave may re-confine part of the population at any time. This is another huge uncertainty which will directly impact manufacturing capacity.

Production planning of the upstream supply chain will be an enormous task to manage due to materials availability, production constraints and limits, late approval of the bills of materials, constant reprioritization of production cycle due to unplanned hick-ups and overall conflicting capacity levels impacted by the availability of production workers on-site.

Mastering the IBP (Integrated Business Planning) or S&OP (Sales & Operations Planning) processes will be a critical advantage to orchestrate the upstream manufacturing activities. The most flexible and agile consortiums will win the supply game and be first on the market.

Quality and Release

Within the biopharma environment quality plays a strategic role where no compromises are typically allowed. Large regulators such as the FDA and the EMA will be closely monitoring this aspect. However, overseeing the upstream manufacturing processes and making sure that all the processes within this evolving environment are managed correctly to ensure product integrity and safety is not compromised will be a big challenge due to the time pressure to get a vaccine to market.

Time pressure to release intermediate materials to the next production step is guaranteed. Manufacturing of substances not yet released and still under quarantine will have to become the standard which the industry is not familiar nor acquainted with. In some cases, such as mRNA-based COVID-19 vaccines from Moderna and Pfizer, vaccines under development needs to be held in storage at -80° Celsius. Such cases will bring a major challenge to the supply chain and severely reduce the ability to easily transport these vaccines and constrain clinics' ability to administer them to the public.

Sophisticated risk management programs are there to support addressing those quality production hurdles which will need to be applied to gain time along the upstream production cycles.

Just-in-Time Inventory Management

Another challenge will be the just-in-time inventory management processes that will have to be operationalized. While the industry has traditionally always worked with months of released inventory on-hand, this time it will probably ship what is available at any given moment in time. Already vaccines are being produced at risk and being shipped to governments around the world without knowing whether they will really work. This production at risk represents a large financial risk to governments who wish to have early access.

Time and Anticipation

The race for the vaccines supply chain has already started prior to finalizing the vaccine product development and the required regulatory approval. While clinical trials are still on-going and having taken already short passes at least 5.7 billion of doses have been pre-ordered by Governments around the planet.

In a recent interview, Paul Stoffels, Vice Chairman of the Executive Committee at Johnson & Johnson said that, "The collaboration is unprecedented. If I look at how we work today with the regulators in the world, where normally we have paper processes which take weeks and months to get feedback, today we talk about getting feedback from regulators within the day."

Conclusion

The upstream manufacturing supply chain will be constrained by time and resources as never before. The best connected and most agile manufacturers will ultimately win the game and bring large quantities of vaccines to populations around the globe.

A hybrid manufacturing strategy solution to bring everything together through a manufacturing consortium seems to be the best current strategy; merging the best of manufacturing, design and innovation, supply chain networking and infrastructure. Doing so will speed up the process of manufacturing and shipping vaccines around the world. Expanding manufacturing capacities and building production consortiums to ensure global demand is met makes sense as long as product safety and integrity are not compromised as a result. Global politics will for sure play a role in the formation of such consortiums.

Date: 2nd September 2020

What is the best current strategy to speed up the process of manufacturing and shipping vaccines around the world, keeping in mind safety and efficacy?

MANUFACTURING CONSORTIUMS

Pharma companies around the globe are signing agreements to expand manufacturing support of COVID-19 Vaccine and countries around the globe are providing billions of funding to a number of companies in return for guaranteed access to a specific number of doses.

Europhia Consulting is an international management consulting company specialized in the logistics and supply chain industry in the life sciences sector. We operate global assignments for our clients. The opinions are based on the author's own experience and understanding of the dynamics within the sector.

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Supply Chain Operations SA, based in Switzerland, is a specialized healthcare supply chain consultancy firm created in 2011 to serve the bio-pharmaceutical and medtech industry. We bring more than 120 years of end-to-end supply chain expertise to our valued customers.

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