INSEAD Humanitarian Research Group

Sharing is (S)caring: Partnerships for Pandemic Response[i]

Hopes for returning to a more sustainable post COVID-19 "new normal" rest largely on the development of effective vaccines and/or treatment options. News headlines from around the world are closely tracking the arrival of a long-awaited vaccine or antiviral drugs for COVID-19. While we hope science can work faster than ever before, we have questions on how to make sure there will be sufficient supply for everyone in the world. The day safe and efficacious vaccines or treatments are ready, they will need to be produced in volumes that are unheard of and distributed to all corners of the world – large *and* small. No business can snap its fingers and magically produce billions of something out of thin air overnight. With huge demand before these vaccines even exist, how do we cope? – better yet: how do we prepare? One thing is certain: hope alone won't get us anywhere. We must carefully prepare in advance.

To do so, we need to work together. In scaling up the production, we can look at past successes and learn from failures gone by. Often, it has been tough to collaborate on sharing goods and information in supply chains with the goal of preparedness. After all, collaboration generates questions around accountability, allocation, distribution, margins, fairness, governance, i.e. around trust in general. Hard as it may be, supply chain collaboration can and will greatly help us overcome issues of shortages and delays. This pandemic might just teach us how to work together and towards global partnerships (UNSDG 17). It has certainly taught us about urgency, since we have become acutely aware of the time it takes to develop a vaccine. But what can be done?

Vaccine development takes time, yet smart planning can significantly accelerate the timeline

The development of vaccines involves many steps and typically takes many years.[1] Roughly, the development of a vaccine consists of 3 stages: research, testing and manufacturing (see Figure 1 one for an overview). Vaccine research is a time-consuming funnel trying a multitude of vaccine designs – some faster than others. Each design has its own pros and cons, but no single approach is guaranteed to work, and all require time-consuming and hugely expensive research. As of August 10th 2020, twenty-eight such candidate vaccines are in clinical evaluation, another 139 are in pre-clinical evaluation.[2] A candidate that is safe and demonstrates immunogenicity (the ability to provoke an immune response) can move into the clinical testing phase, which can be further divided into three phases. The first phase

[i] This piece, published in AUGUST 2020, was written by Gina Fialka, Luk Van Wassenhove, and Prashant Yadav (INSEAD Humanitarian Research Group).

of testing is aimed at establishing the vaccine's safety and neutralizing properties. If so, it moves onto the second phase in which the right dosage and delivery schedule is determined. In the last phase, typically involving thousands to tens of thousands of people, the safety across the targeted population is further tested and possible side-effects are discovered. Because the testing phase is focused on long term safety, it is difficult to shorten this process without taking health risks. Strict safety criteria need always be met, and a vaccine that passes through all stages needs approval by national and international agencies before it can go into production.[3] Despite being a complex and precise process, some of the steps can be performed in parallel, making the total lead time shorter. Developing vaccines quickly won't be enough: we need to simultaneously work on preparing for production and distribution. It is critical that there will be sufficient supply of the most suitable COVID-19 vaccines as soon as possible and supply needs to be accessible globally.[4]

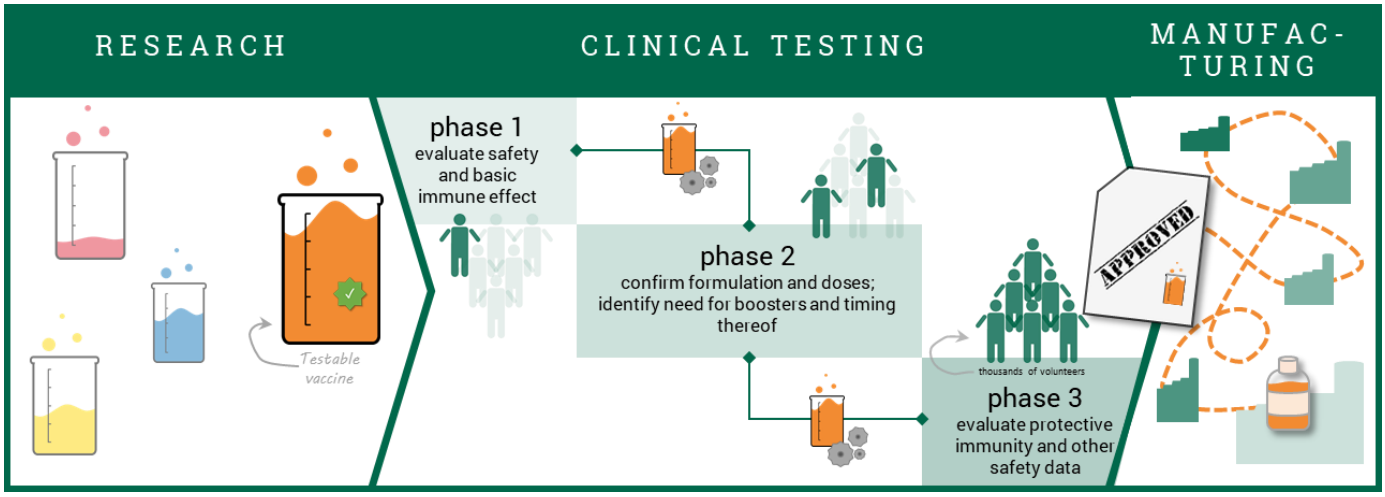

FIGURE 1. SCHEMATIC, SIMPLIFIED VIEW OF THE PROCESS OF THE MAKINGS OF VACCINES

Scaling up manufacturing of a vaccine

When a promising vaccine has been developed and approved by the regulatory agencies, it needs to get to people as fast as possible. If manufacturers wait till regulatory approval and Phase 3 results, manufacturing capacity will be insufficient and a bottleneck will be created, leading to long waiting times to obtain sufficient quantities of the vaccine. Hence, the vaccine production supply chain for COVID-19 needs to prepare before a vaccine has been approved. Although global manufacturing facilities are equipped to produce billions of vaccine doses for routine childhood immunization and seasonal influenza, the required scale has never been seen before.[5] Manufacturing vaccines is a complex process, one that typically takes 1 to 2 years.[6] Adding to this is the fact that we're talking about something that hasn't been developed and approved yet and is therefore not entirely defined in terms of production ingredients and steps. There are substantial investment risks in the preparation of production scale-up for a new vaccine given that one is not sure that it will be

effective. However, investing in manufacturing and distribution before a vaccine is approved will save precious time.

The case of Roche's Tamiflu scale-up[ii]

Although the scale and implications of COVID-19 are unprecedented, rapid scale-up for vaccine or pharmaceutical production is not such an unusual endeavour for the pharmaceutical industry. One example is when Roche, a Swiss pharmaceutical company, faced a unique challenge which required rapid and tremendous scaling up of production for one of its products for global public health. That scale-up effort provides important learnings for COVID-19 and other products where supply is of public interest. In the early 2000s, Roche was working on getting governments around the world interested in preparing for a flu pandemic by stockpiling their influenza antiviral drug Tamiflu (oseltamivir). The threat of a pandemic was perceived by most country governments as a theoretical and very low probability risk. Most countries around the world had very limited interest in stockpiling Tamiflu. Then in 2005, the US government requested production of 200 million courses of treatment for Tamiflu on US soil. Being four times their annual capacity, Roche decided to shift gears and meet that challenge: they set a production capacity goal of 400 million by 2006. Operation 'Scale-Up-Tamiflu' involved several components. Firstly, they found 18 partners with production capabilities fitting for any of the five parts/tiers of the upstream supply chain. They asked these suppliers to reserve capacity in case Roche would need to quickly ramp up production. For this network of partners, Roche covered all costs associated with the capacity reservation for the scale up. Secondly, to ensure that the goal would be met, they built in a safety net by engaging an extra supplier in each of their 5 parts of the chain. Third, to increase availability across the globe, Roche granted sub-licenses to three companies in China and India to ensure manufacturing capacity coverage for the developing world. In addition, the drug was not patent protected in the least developed countries, allowing them to make Tamiflu themselves. Yet Roche did something else, too: they publicly shared information about their price and capacity – something highly unusual for the industry at the time (and even today). By being transparent about these aspects, they addressed public anxiety, were able to manage expectations, and to inform the world about the complexity of the process. Through these methods, in collaboration with the World Health Organization (WHO), Roche was ready and able to provide sufficient Tamiflu during the 2007 Avian flu outbreak.

[ii] If you'd like to know more about Roche and Tamiflu, please refer to the case studies written by the authors: *Fighting the Flu: Tamiflu Stockpiling - A Pandemic Preparedness Policy* here, and *When Supply Is of Public Interest: Roche & Tamiflu* here.

Sharing and the greater good in times of COVID-19

The Roche case demonstrates how working together with partners to scale up production can be a success. But this comes at a cost and someone needs to pay. In this case, paying the price of production scale-up was worth it:

"We took informed risks early on and fast. The risk of building capacity or inventory was balanced against a responsibility which was to respond to a medical need. The fact that we could be sitting on what could be a number 1 antiviral drug in case of a pandemic carried a weight with it. If you do not take the appropriate measures, you will have failed society. No company can sustain that sort of failure." – David Reddy, Roche [7]

However, in the 2020 COVID-19 pandemic, there is no vaccine or treatment yet, and pharma companies have relied on covering their business through grants and advance purchase agreements by national governments or international agencies. Roche's collaboration was a *vertical one*: it involved working together with suppliers in their own global chain. What COVID-19 vaccine efforts require first and foremost is *horizontal collaboration*, where competitors collaborate at the same stage of development or tier of the supply chain. This is substantially more complicated for commercial and compliance reasons, among others. What then can realistically be done in terms of collaborating and setting up manufacturing so that a vaccine can be produced as quickly as possible?

Building 'capacity at risk' with risk sharing between companies and (inter)national agencies

Pharma companies and international agencies can/should collaborate to build sufficient manufacturing capacity, specifically 'capacity at risk'. This entails companies manufacturing vaccines which are still being tested for effectiveness. As such, a few million doses of vaccines are being made – they are needed for the clinical trials – and they keep making more. The challenge is that the companies that are investing in setting up manufacturing capacity or those that are making significant quantities of doses still don't know whether their vaccine will be successful. In fact, research suggests that historically vaccines that haven't entered human trials yet have a 7% probability of succeeding, which rises to 17% once they are in clinical trials.[8] And so we should be cautious about early vaccine results and going after the first vaccine to be approved. In typical vaccine trials, first generation vaccines are usually replaced by much improved second-generation versions.[9] It might well be that the tortoise wins the race. Yet a mechanism is needed to incentivise manufacturers to expand production capacity while they are still developing vaccines. To coordinate global actors and to address the challenge of equitable access, the WHO launched the Access to COVID-19 Tools (ACT) Accelerator. Direct financial support to expand manufacturing capacity is not provided by ACT Accelerator but through its collaborating partners.[iii] Part of

[iii] Coalition for Epidemic Preparedness Innovations (CEPI) and the Bill and Melinda Gates Foundation (BMGF), amongst others.

its vaccine pillar, the COVID-19 Vaccine Global Access (COVAX) facility has been created to enable collaboration across country governments, vaccine manufacturers, and international agencies. Part of this facility is the GAVI COVAX Advance Market Commitment (AMC), an innovative finance instrument. Using two types of pull mechanisms, the COVAX will incentivize manufacturers to increase capacity and develop products. Manufacturer-specific contingent volume guarantees are in place to decrease the risk of increasing capacity. Additionally, a market-wide demand guarantee further incentivizes manufacturers to expand production. By creating security of demand, COVAX provides its participants with insurance against the risk of vaccine candidates not being successful.

Greater horizontal collaboration on manufacturing capacity across companies

The case of Roche's Tamiflu illustrated the effectiveness of vertical collaboration. The present situation requires greater horizontal collaboration, so that parts of manufacturing capacity which are fungible across vaccine candidates can be shared if one candidate fails and another succeeds. That way, more capacity can be transferred to the one that succeeds. Yet this kind of collaboration may not occur by itself and requires coordination and information exchange. Much like the Tamiflu case, most vaccine development companies are bringing together contract manufacturers (manufacturing partners). If a company's candidate vaccine fails, how can we quickly transfer the contract manufacturing capacity from that company to another company? What coordination and information needs does it create? What contractual agility does it require?

Equally important is what happens to supplies such as vials, stabilizers, and syringes. We may need over 9 billion doses to vaccinate a significant portion of the global population and minimize the disruptions caused by COVID-19. If each company tries to source supplies for itself, we will fail. The manufacturing of these supplies should continue to be scaled up to make sure there will be enough, but no product should be claimed. This creates an additional need for coordination and collective action which no one company can solve individually. To be able to reach any kind of goal, these supply chains rely heavily on resource sharing, information sharing, and coordinated decision making. On these fronts, there is room for improvement. Companies could be given incentives, subsidies or purchase assurances so that they can jointly secure surge capacity or stockpiles of key ingredients to allow faster production of the final product and avoid supply bottlenecks. No company can do this alone. Information on who has stockpiles of certain material means exchanges and allocation to urgent needs may be facilitated. Information on production capacity would enable swift collaboration in manufacturing processes. Roche kept the WHO informed of its manufacturing capacity and its order book i.e. which governments had purchased how much. Enabling such information exchange and coordination for COVID-19 vaccines and therapeutics requires a strong global agency to act as an information intermediary. Would the WHO-ACT-Accelerator and COVAX play that role?

COVID ergo collaborate?

Collaboration across actors in the pharmaceutical supply chain to prepare for vaccine production, whether it be through sharing material (capacity or stockpiles) or information, would help speed up the process to have effective vaccines available for the entire global population. However, all this requires good governance, trust (sharing information), and vertical collaboration between competing firms. COVID-19 vaccine development and manufacturing efforts also remind us that the system supporting this needs to be designed up-front to be prepared, instead of ad hoc when a pandemic hits. People need to be trained in well-agreed upon procedures and processes. Companies understand their reputation depends on their goodwill and are ready to help, but they also cannot be the ones who pay. Who will make sure there is good governance to enable collaboration and instill much needed trust?[10] And even when collaboration has been achieved in terms of overall manufacturing capacity, what will happen when there is a vaccine to distribute? If some countries are producing large quantities and others (the less developed, perhaps) aren't, who will make sure there is a fair distribution, leaving no one behind? Will the low-income countries of the world need to wait until all wealthy populations have been vaccinated? Collaboration, hard and scary as it may seem to companies and government leaders, will go a long way if we give it a chance.

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[1] Plotkin, S., Robinson, J. M., Cunningham, G., Iqbal, R., & Larsen, S. (2017). The complexity and cost of vaccine manufacturing—an overview. *Vaccine*, *35*(33), 4064-4071.
[2] https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines
[3] Plotkin, S., Robinson, J. M., Cunningham, G., Iqbal, R., & Larsen, S. (2017). The complexity and cost of vaccine manufacturing—an overview. *Vaccine*, *35*(33), 4064-4071.
[4] COVID-19 Vaccine Global Access (COVAX) Facility: Preliminary technical design (2020).
[5] https://www.weforum.org/agenda/2020/05/coronavirus-vaccine-search-how-we-re-preparing-to-make-enough-for-the-whole-world/
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[7] Samii R., & Van Wassenhove L. (2008). Fighting the Flu: Tamiflu Stockpiling - A Pandemic Preparedness Policy. *INSEAD Case Study, case number 5501*, page 7.
[8] COVID-19 Vaccine Global Access (COVAX) Facility: Preliminary technical design (2020).
[9] https://www.cgdev.org/blog/vaccine-preliminary-results-here-why-we-need-exercise-caution
[10] https://hbr.org/2020/05/the-danger-of-vaccine-nationalism