Scaling up vaccine production through 'copying exactly'

Waiving intellectual property rights and donating vaccines are not enough to vaccinate the world quickly, write ***Arnab Acharya, Aaron Moment (Columbia), Sanjay Reddy (The New School)*** *and* ***Venkat Venkatasubramanian (Columbia)****. The solution is to scale up production by sharing production methods freely, giving companies a financial incentive where necessary.*

The G7 recently committed to sharing 870 million doses of Covid-19 vaccines with developing countries – in addition to an earlier commitment to donate "over one billion doses". But this is completely insufficient. The G7 itself estimates that "ending the pandemic in 2022 will require vaccinating at least 60 per cent of the global population". With two-shot vaccines the norm, insufficient supplies, and doses that were intended for the rest of the world expected to be diverted to domestic use in India, most people in low- and middle-income countries will not be vaccinated until 2022 at the earliest. This means COVID will continue to circulate and probably develop more new variants. Is it even possible to produce enough vaccines to supply the whole world quickly?

The key to scaling up lies in recent developments in industrial production methods. Production based on modular methods lends itself to replication. Governments can help by ensuring an adequate supply of inputs and technology transfer. By "copying exactly" the existing facilities, as other areas of industry do, current producers can expand production and potential producers can enter. If this approach is applied to at least one vaccine, it will create a low cost and widely available option, both increasing supply and reducing prices. Modular production makes possible what economists call "constant returns to scale", even in the short run.

In practice, there is little distinction between existing producers ramping up production and new ones joining the market. Many COVID vaccine producers are new to producing vaccines of the specific type they are now making, or even new to producing vaccines at all. The transfer of technology between firms has *already* been integral to scaling up production, and has been happening on a large scale – for example, between firms that developed the product and those with production capabilities (such as BioNTech and Pfizer, and Moderna and subcontracting manufacturer Lonza). Others aimed to expand production in firms with existing capabilities (as between Astra-Zeneca and the Serum Institute of India, and Johnson & Johnson and Merck – in the latter case brokered by the US government).

Even where producers have exclusive knowledge, they can still scale up production internally using modular methods. But licensing proprietary knowledge more broadly, or even sharing it freely with others, can make it easier to scale up production *outside* a firm as well as within it. The imperative to do so is clear, which is why governments should provide provide support and incentives. The logic of replication also applies to producers of the specialised inputs required in vaccine production, such as enzymes, lipids or mixing machines.

Date originally posted: 2021-06-25

Permalink: https://blogs.lse.ac.uk/covid19/2021/06/25/scaling-up-vaccine-production-through-copying-exactly/

Blog homepage: https://blogs.lse.ac.uk/covid19/

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Indeed, some pharmaceutical firms have indicated that they have capacity to produce vaccines right away if permitted to use available intellectual property. For others, detailed production know-how may have to be extended. The transfer of Hepatitis B vaccine technology from Merck to China in the late 1980s provides an early example of how this can work.

> MRNA technology allows for faster, more controlled, and distributed geographic production because the molecule is synthetic

Quality and sterility of production, and a reliable supply of inputs, can be achieved through co-ordination between existing producers and new entrants, and by government playing a supervisory role. Regulators should grant rapid approval for new facilities based on replication. Efforts by governments can address potential shortages of reagents, lipids and other inputs.

The modular nature of production makes things easier from a technical point of view because *scaling up* (more at existing sites) and *out* (at more sites) allows production to be broken down into individual elements or "skids" (which contain the relevant equipment and controls), and suites ("rooms") that are all exact duplicates and can be readily copied. The technology used in testing chemicals is similarly standardised, low profile (it fits on a bench-top) and well known. Engineering philosophies such as Portable Miniature Modular Continuous production are regularly used within pharmaceutical firms, including Pfizer, to expand production. Intel, in the arguably more demanding and complicated process of chip-making, pioneered the 'Copy Exactly' manufacturing approach.

MRNA technology allows for faster, more controlled, and distributed geographic production because the molecule is synthetic: it is made in cell-free systems and based on a linearised DNA template that is "made to order". This attractive feature was recognised from the start by the pioneers of mRNA technology, and companies started to work on it *because* of the ease of making it rapidly. This has been borne out in practice, as production of viral-based vaccines has lagged that of mRNA, which firms have found easier to scale up. The formula for both currently approved mRNA vaccines is publicly available on the open source data repository GitHub. This meant that the current mRNA vaccines were developed without ever needing a sample of the virus itself. Although vaccine production does involve a large number of inputs from diverse locations, this is commonplace in modern industrial production. Many countries and companies with a sufficiently sophisticated industrial base could produce mRNA vaccines themselves.

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Places with bioprocessing facilities and trained, specialised workforces in the pharmaceutical sector, such as those in Puerto Rico and Singapore, can be mobilised quickly. Government regulatory bodies such as the National Institute of Standards and Technology and the FDA can ensure that production lots meet the necessary standards. Current IT tools can enhance this process by enabling such approvals to be done at a distance. This can also make the production process less dependent on highly specialised labour, of which there may be limited supply at present (although some workers, such as the analytical chemists needed for quality control, can be redeployed from other industries). Both current producers and new ones with excess capacity can be incorporated into production quickly and reliably by using these approaches. The expansion of production capacity by existing manufacturers by repurposing facilities or building them from scratch shows that it can be done at relatively modest cost.

> A blueprint for co-operation, preferably global, to facilitate "copying exactly" and to identify and address supply bottlenecks must be developed quickly

Many biotechnology production facilities could be producing bulk mRNA for coronavirus vaccines, but are not yet doing so. For instance, the producers of sterile injectables, an important area of existing pharmaceutical production, can pivot to bulk vaccine production with limited retooling. The expansion of production capacity by existing manufacturers by repurposing existing facilities or building them from scratch shows that it can be done at relatively modest cost. Although other products may be temporarily displaced, essential medicines can be prioritised.

Why is the expansion of production through replication of methods not happening more? The answer is that it is not in the leading firms' interest to share their methods with others to the degree necessary. The pandemic-related intellectual property rights waiver currently being proposed in the WTO would not be enough to boost output, since firms need more than a formula or a permission, but rather transfer of every detail of the production process. Backward engineering of production processes is likely to take too long. The most feasible approach to scaling up through copying exactly is to provide public financing and support for at least one existing vaccine producer to actively and willingly share its ways of working with others. Even if governments have to compensate a private producer for lost profits, the benefit of creating an accessible "public option" available to all potential vaccine producers is potentially immense. This approach will ensure a rapid scaling up of supplies, at the lowest possible cost, since the new entrants will also compete with one another.

Ultimately, the transfer of technology to potential producers relies on governments acting as a catalyst. Not only must they encourage existing firms to share their production methods, but they must provide financing, reduce risk and ensure reliable supply chains for inputs. A blueprint for co-operation, preferably global, to facilitate "copying exactly" and to identify and address supply bottlenecks must be developed quickly. Governments and international institutions (such as the WHO or UNICEF) must come together and adopt a systemic perspective to accelerate production. The nature of production today makes this entirely possible. With a combination of a "modular" approach to production by firms and a "systemic" approach by government to addressing bottlenecks, we can quickly scale up vaccine production to supply the whole world.

This post represents the views of the authors and not those of the COVID-19 blog, nor LSE.

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