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Why tech transfer may be critical to beating COVID-19

How quickly COVID-19 vaccine production ramps up will depend on technology transfer—the capabilities and processes that can speed vaccines from development to manufacturing. Are we ready?

by Cormac O'Sullivan, Paul Rutten, and Caspar Schatz

July 2020

Vaccines are considered to be our best chance for beating COVID-19, and many governments are counting on them to enable economic recovery. But to innoculate people worldwide as soon as vaccines are proven will require the pharmaceutical industry to ramp up quickly to unprecedented volumes of supply. The available global production capacity will be critical to that capability. And technology transfer—moving the knowledge about and the ability to produce a vaccine from development to manufacturing—will determine how fast it happens.

But tech transfer is as much a craft as a science. And it hasn't usually been on the critical path to production, so it comprises an underappreciated set of capabilities. To ensure adequate and timely supplies of COVID-19 vaccines and treatments, global institutions and pharma companies must collaborate to make tech transfer an industrialized, at-scale process—before we need it.

Vaccine production at scale will depend on tech transfers

Today, more than 200 COVID-19 vaccine candidates are in development. Most countries are hoping broadscale vaccination will put an end to the pandemic. Consequently, any successful vaccine will face a problem: it will immediately be out of stock, since the whole world will want access to it right away. The picture may be similar for an effective therapeutic, especially for prophylactic use or for treatment of mild to moderate disease, where demand volumes also will be high, whether for a repurposed existing treatment or a new compound.

As successful compounds emerge from development, ample manufacturing capacity and a rapid scale-up of production will be essential. The capacity exists, and presumably governments could intervene to prioritize COVID-19 vaccines. However, rapid scale-up of production will rely on technology transfer from development to production, which has not had the same level of attention.

There will likely be several vaccines, since more than one may be successful. The billions of doses we estimate will be needed will require multiple manufacturing plants. Moreover, workstreams that are typically sequential in a nonpandemic situation are being pursued in parallel. Companies are building manufacturing capacity, transferring technology, and even starting large-scale production of candidate vaccines before they have conclusive clinical data, because the economic cost of delays is so high. And because some of these vaccines will fail, manufacturers will need to ramp up even more capacity than might eventually be used, making a tremendous challenge even harder. Developers are already transferring to multiple production sites in parallel. AstraZeneca, for example, has announced it will transfer production to contract manufacturing organizations (CMOs), while Pfizer has announced it will shift legacy products at scale to CMOs to free up internal capacity for COVID-19 vaccines.

Not only will industrial-scale tech-transfer capabilities be crucial for global vaccine supply, but also tech transfer is complex and requires a large number of specialized skills. Industry and governments need to invest in these capabilities now to help the world meet the challenges in 12 to 18 months.

Why tech transfers are difficult

The safety, quality, and efficacy requirements of life-saving but potentially toxic pharmaceuticals put high demands on production. Producing complex pharmaceuticals is not just a matter of building the required production line or hardware. It also involves a complex (and often finicky) manufacturing process, a large team of experts, a lot of time, many detailed steps, and the right regulatory registrations—and all of this against the highest quality standards.

The production process for vaccines, as for any biopharmaceutical, can be hard to control for

many reasons (Exhibit 1). The products are grown in live microorganisms or are parts of live microorganisms. The variability of biological processes needs careful calibration, validation, and constant tuning to ensure consistency.[1]

This, in turn, requires a complicated dance of multiple experts in manufacturing, quality, regulation, engineering, and logistics—also, trainers, lab technicians, smart builders, maintenance crews, scientists, and capable leaders. An average transfer requires six to nine full-time equivalent hours (FTEs) from a dozen disciplines. If we have ten to 20 vaccine candidates with four to eight sites per candidate, we will need 300 to 1,200 specialist FTEs. Owing to the discipline split, this might amount to as many as 2,000 to 6,000 professionals.

Typically, the tech-transfer process is invisible to patients and even to many professionals in the

Exhibit 1

The production process for vaccines, as for any biopharmaceutical, can be hard to control for many reasons.

Factors causing variability of biological processes and their implication

Cause of variability	Description	Implication
Molecule or virus complexity	2,500–25,000 atoms in protein-based vaccines; even greater complexity in virus-based vaccines	High-value product
Molecule or virus stability	Great sensitivity to heat, pH, and organic solvents	Relatively short shelf life (18–36 months)
Production principle	• Recombinant technology, typically with >15 steps • Sterile design for drug substance and drug product	Complicated and expensive production requirements
Scalability	Difficult, up to approximately 20,000 liters	Limited output per production line
Cell banking	• Sterile handling • Master cell banks maintained at, eg, –120°C	Complicated process
Raw materials	Typically >50 raw materials with many critical specs (eg, residual heavy metals)	Heavy test load on raw materials; difficult quality control
Purification	Multistep chromatography	Expensive step with high-cost consumables
Lead time to drug substance	Weeks to months	Long lead time
Storage	Cold room (2–8°C) and frozen	Tight supply chain control required
Transport	Cold chain transport in frozen state for drug substance and at 2–8°C for drug product	Tight transport control required

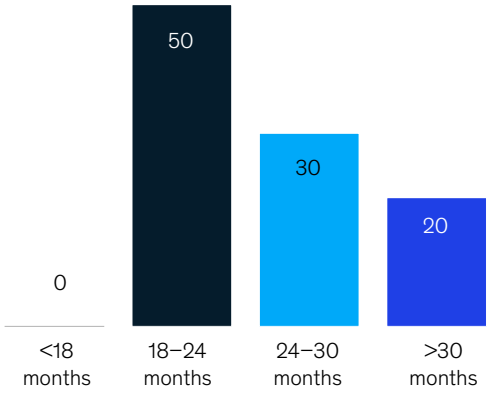
[1] Ralf Otto, Alberto Santagostino, and Ulf Schrader, *From Science to Operations: Questions, Choices and Strategies for Success in Biopharma*, 2014, McKinsey & Company.

Quality standards for vaccines are strict, since vaccines are administered to healthy people.

Exhibit 2

Sterile tech transfers typically take more than 18 months.

Distribution of lead times for tech transfers,
% of respondents



Source: McKinsey tech-transfer survey, October 2019

industry. Clinical trials in pharma can take between five and eight years. Tech-transfer times for sterile dosage forms, such as injectable vaccines, range from 18 to more than 30 months (Exhibit 2). Because this timeline is shorter than the average clinical-trial length, pharmaceutical engineers can work carefully and diligently on the transfer process, knowing it is not on the critical path.

That will not be true for a COVID-19 vaccine or therapeutic. Society will demand the shortest possible timeline. Once a successful vaccine is confirmed, manufacturers will be under extreme pressure, and tech transfer will need to happen as soon as possible, within a few months.

The duration of a tech transfer is driven by eight main steps with eight functions at two sites, often also involving equipment and material suppliers. Each of the steps contains around 20 to 30 separate activities, so individual actions number in the hundreds. The wide variety of functions involved is spread across the donor site, the receiving site, and sometimes also a headquarters site (Exhibit 3).

In normal times, tech transfers can suffer from a lack of attention during routine production. They can receive little priority at donor sites and often are not top of mind at receiving sites. In the current situation, manufacturers are focused on delivering other essential vaccines or coping with the exceptional swings in production caused by lockdowns. Also, many smaller vaccine producers will be doing a tech transfer for the first time, which creates risk.

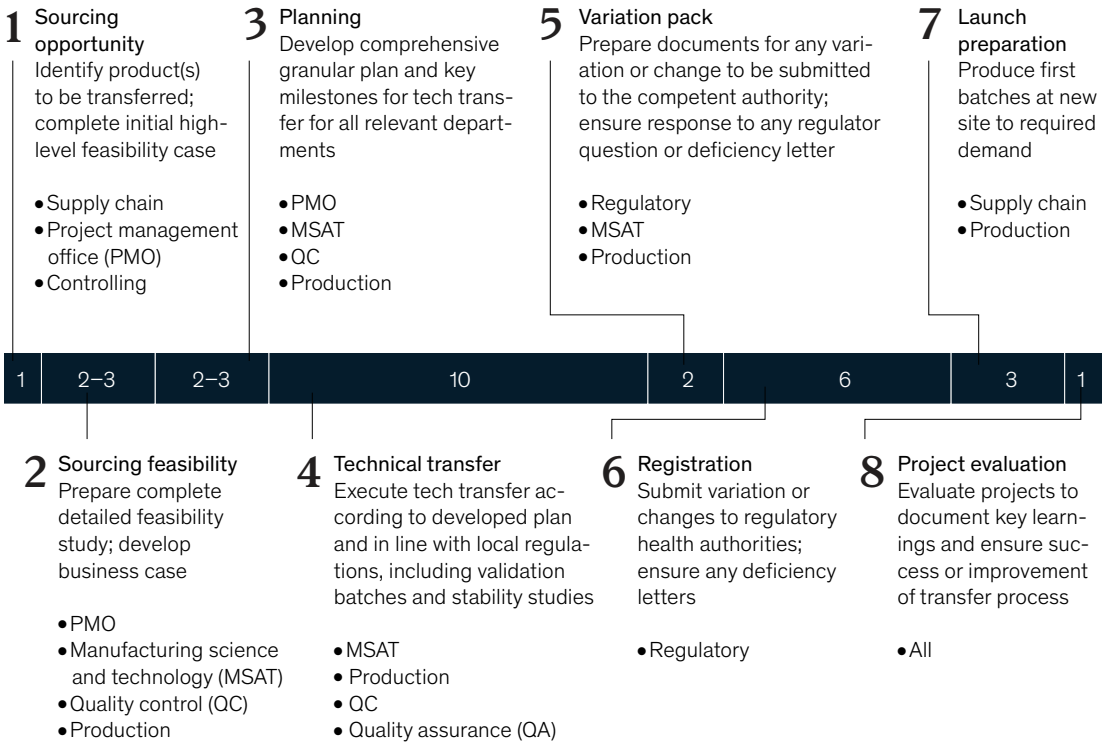
The transfer for new COVID-19 vaccines will likely involve a scale-up step, where equipment is used for the first time, placing high demand on process development and experts in manufacturing science and technology. And commercial transfers between sites often require equipment modifications and process adaptations, which add complexity.

Also, quality standards for vaccines are strict, since vaccines are administered to healthy people.

Exhibit 3

Transfer steps typically take 27 to 29 months and involve many key stakeholders.

Step activity typical lead time timeline, months



Therefore, regulators require quality controls logged in a set of documents and submissions—chemistry, manufacturing, and controls (CMC)—which allow the regulators to manage whether manufacturers and developers are taking proper precautions. Creating the filing, registration, and underlying data is a labor-intensive process.

Finally, doing this between companies is even more complicated than doing it inside a single one. Transfers to an external party take on average 5.8 months longer (Exhibit 4).

Tech transfer today is a non-industrialized process requiring a lot of tradecraft, but we can still reduce its timeline.

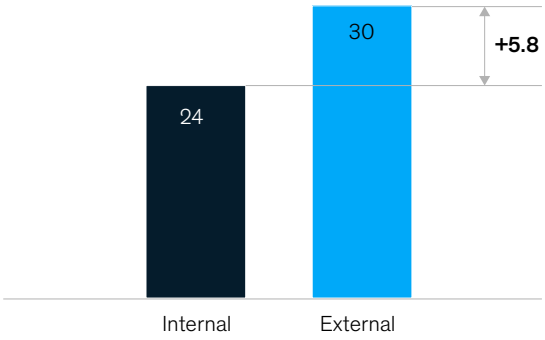
How to streamline transfers and shorten timelines

Critical to shortening tech-transfer timelines will be a proven set of best-in-class transfer practices (Exhibit 5), which we have collated from benchmarks and comparisons across the pharmaceutical industry. They start with a detailed best-practice process map. Fast tech transfer requires an unambiguous sequence of events, using best-practice tools. Also, we see companies that do it fastest use a control-tower approach, where all activities are visible and a clear meeting cascade ensures fast communication and escalation of issues for leadership attention. Finally, the team involved will be challenged to deliver in a fashion they have never done before—with an

Exhibit 4

Transferring externally increases lead time relative to internal transfers.

Average lead time, internal and external transfers, months



Source: McKinsey tech-transfer survey, October 2019

industrial mindset for tech transfer, as well as the right capabilities:

— Agile ways of working, embedded in a structure rigorously focused on performance

— Nonhierarchical and fast decision making, prioritizing effective and efficient solutions

— Early, risk-tolerant investment and fast capacity ramp-up with the flexibility to adapt to negative vaccine candidate outcomes

— A high level of expertise open to challenge from interdisciplinary team members

— Ability to be simultaneously science and technology driven as well as patient focused

— Treatment of quality requirements as enablers rather than barriers

In some ways, the pandemic situation is similar to wartime. Regular team structures may not be fast and effective enough. Companies might consider setting up nerve centers with access to senior company leadership, such as divisional CEOs, to resolve bottlenecks and make quick decisions.

The collective knowledge of the pharmaceutical industry should be enough to resolve any issue. However, communications between functions within a company and especially between companies have historically not been smooth. A common process and vocabulary will likely be needed if we are to improve them sufficiently to respond quickly to the pandemic.

In normal times, the fastest transfers have taken as little as six months under exceptional circumstances, such as having to restart sterile production lines after microbial contamination or remediation after a regulator closed down a site. Also, generics companies have performed transfers at scale during site divestitures or large portfolio acquisitions—as many as 50 products in 24 months. And contract manufacturers are champions at insourcing products, since that is a key enabler of their business model.

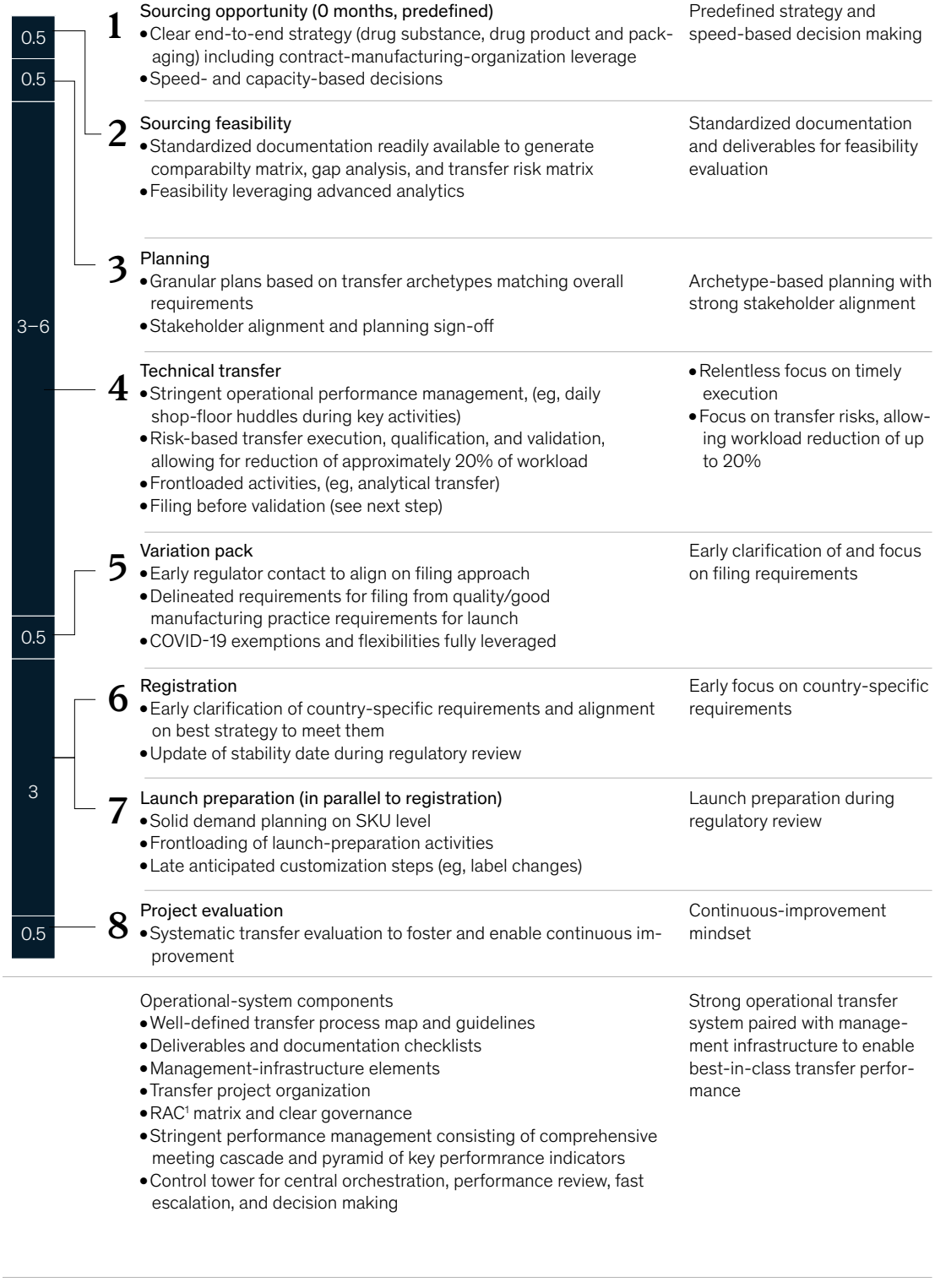
The industry has therefore proven that it can act at amazing speed, and we believe it can achieve best-in-class transfer times of eight to 11 months, 60 to 70 percent more quickly than usual, at scale. With regulatory flexibility that has already been announced, it may be possible in six. Every month taken off the timeline will save countless lives and likely at least tens of billions of dollars for the global economy. But to do it for the global economy, rather than piecemeal, we need common mechanisms that will enable us to learn from each other and work together.

The way ahead

No single player has all the answers. A professional institution, such as the International Society of Pharmaceutical Engineering (ISPE), or a philanthropic organization, like the Global Alliance for Vaccines and Immunizations (GAVI) or the Coalition for Epidemic Preparedness Innovations

Exhibit 5

Proven best-in-class transfer practices can shorten tech-transfer timelines.



[1]A RACI matrix describes typical key roles: responsible, accountable, consulted, and informed.

(CEPI), may be best positioned to orchestrate the collaboration needed. These organizations can play an important role in developing and sharing best-practice playbooks. And they can organize professional knowledge networks able to act at the speed of COVID-19.

One solution may be to create a team of ten to 20 professionals and organize a hackathon based on existing process maps to determine best practice for tech transfer, to create the knowledge-management infrastructure, and to apply digital and advanced analytics tools to transfers. In this way, we can respond quickly to any technical challenge and, in doing so, speed up transfers, enable faster supply of critical medicines, and help save lives and livelihoods.

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The authors wish to thank Tim Curran, Mackenzie Donnelly, Parag Patel, Mikhail Razhev, and Boyd Spencer for their contributions to this article.

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