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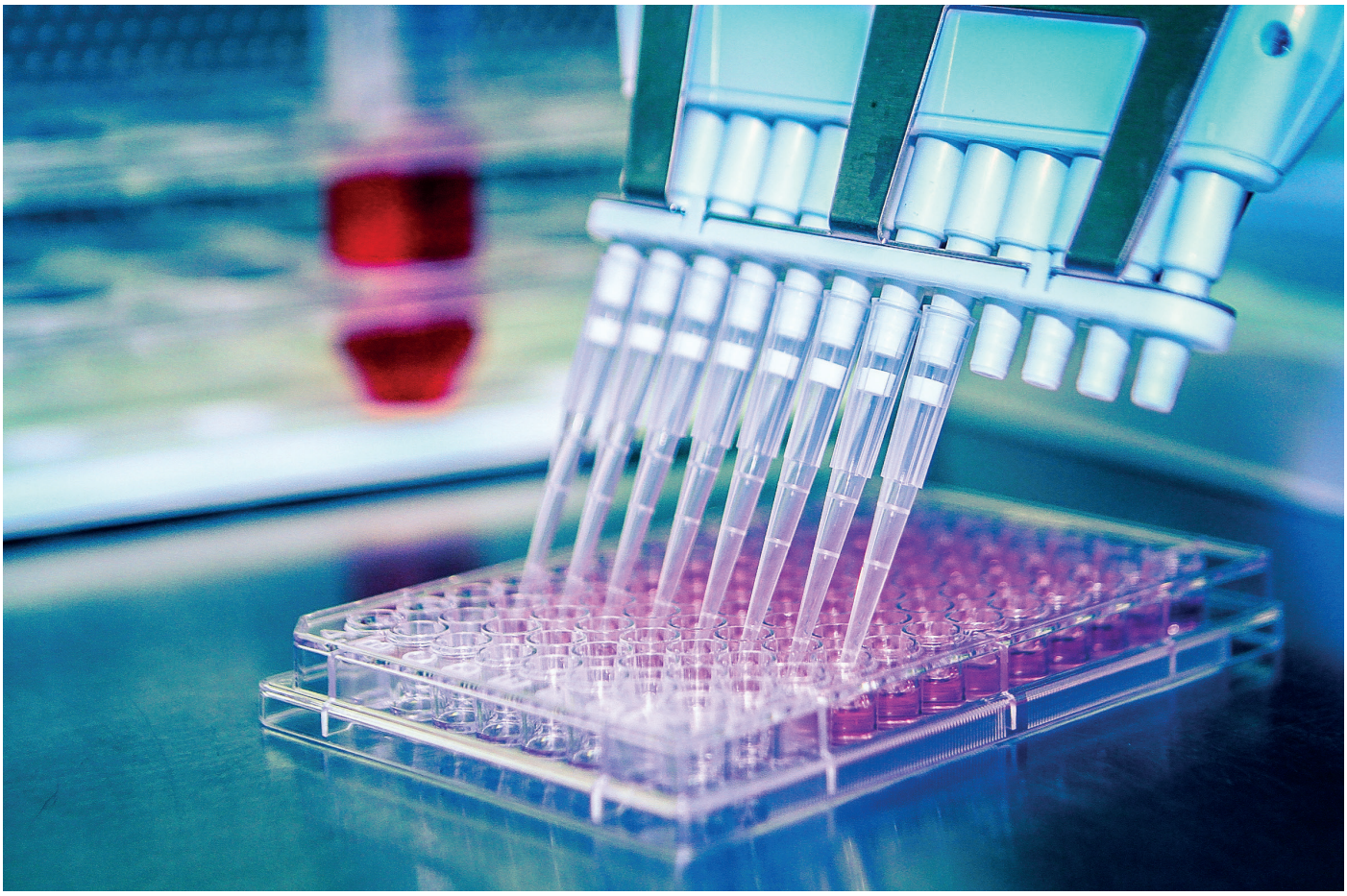
Fluid Technology Group

Watson-Marlow on accelerating vaccine development

How will COVID-19 accelerate vaccine development?



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We find ourselves in a situation that we wouldn't have imagined a few short months ago.

Novel viruses have caused endemic-level damage for many years, rapidly spreading into small populations and yet disappearing just as quickly. Although researchers have developed vaccines against SARS, MERS and Ebola, testing is proving problematic as the viruses simply don't stay in circulation long enough.

SARS-CoV-2 had all the marks of a similar endemic-level virus – until it didn't.

Now, the whole world is watching as biopharmaceutical companies work to accelerate vaccine development and production to an unprecedented scale.

Jim Sanford, Dr Sade Mokuolu and Peter Birch from Watson-Marlow Fluid Technology Group (WMFTG) discuss how the biopharmaceutical community is coming together to solve this global challenge. Do we have the technology, skills and resources to respond to COVID-19? And what will this mean for vaccine development in the future?

THE RACE TO MAKE A BILLION DOSES

Developing vaccines is crucial to combating existing and novel diseases. A World Health Organization (WHO) report based on 2013 data found that immunisation averts two to three million deaths every year in all age ranges, across the world.

Vaccines must be produced in large batches, at a low cost per dose to offer broad and effective protection. From drug discovery to biomanufacturing, technology innovation continues to thrive with advancements in process intensification, cost reduction and risk mitigation initiatives.

Vaccine production is big business. The WHO reported that from 2000 to 2013 the market grew from $4 billion to $24 billion and pre-COVID-19 predictions estimated that the market would be worth $100 billion by 2025.

Gavi, the Global Vaccine Alliance, estimates that the costs for producing hundreds of millions of doses of a COVID-19 vaccine would run into $50 million for those companies that already have facilities and $700 million for those who are opening new facilities. The alliance has already re-allocated $200 million in funds as an immediate response to this crisis.

As COVID-19 continues to affect communities throughout the world, there is collective hope that a vaccine can be developed, and subsequently manufactured.

With over 100 COVID-19 vaccine candidates in research stages and others in promising clinical trials, it seems likely that a vaccine will be developed.
But is the biggest problem still to come? Once a vaccine is proved safe and effective, how will the industry mass produce these vaccines to such a demanding schedule on a global scale?

ACCELERATION STARTS IN RESEARCH

We've already seen research and development (R&D) on an unprecedented scale. Processes that would usually take years have been accelerated to just months as researchers use existing platform technology to expedite development, with some level of assurance of efficacy and safety extrapolated from other trials. Now it's time to take this approach into the manufacturing space.

R&D teams focus on using their skills and understanding to create a therapy, the link between researchers and the manufacturing process has never been so important. In recent years, vaccine production has moved to a continuous bioprocessing model and we've seen process intensification on a scale-out, rather than a scale-up basis. Put simply, the bioprocessing equipment used in research stages can now be carried through to mass production. When time is short, process design engineers and researchers need to work together to ensure that the vaccine can be replicated reliably at scale for clinical trials and then again at an even greater scale for mass production.

Production won't take place in just one location; multiple vaccine manufacturers will need to support product demand and for these vaccines to be available at scale they will need to be produced in numerous locations all over the world. Processes and equipment need to be standardised and this activity needs to start at the R&D stage. Each biocontainer, clamp and tube assembly needs to have an equivalent for use at scale.

Never has research been so focused on a singular, tangible goal. Although there is a fascinating exploration into novel vaccine technologies, the current requirement is for tried and tested techniques, performed and understood by skilled teams.

Manufacturers, such as WMFTG, have a role to play in this process. Our teams help form a link between R&D and process engineer groups and we assist in ensuring our equipment is used appropriately in the different stages of vaccine development. Scalable versions are manufactured using the same materials and processes, reducing additional validation steps and accelerating the progression from bench to production.

REPRODUCIBILITY OPENS THE BLACK BOX

Single-use bioprocessing systems enable regional production on a global scale. Biopharmaceuticals and their contract manufacturing organisations (CMOs) are already creating vaccine production hubs on an extraordinary scale using single-use technology that delivers drug product consistency.

Once manufacturing systems and fluid pathways are tried and tested, and can demonstrate a safe and efficacious vaccine, this system has the opportunity to be replicated anywhere in the world. The process becomes the most important proof of safety and efficacy. Vaccines produced in the millions can't all be tested and bioprocessing by in its very nature is subject to the behaviour of individual cells and the black box of molecular interactions. But the process can be controlled and replicated assuredly.

Suppliers of biological manufacturers continue to design innovative bioprocessing systems that deliver reproducibility, in addition to process flexibility, cost control, risk mitigation, security of supply and sustainability.

Equipment versatility also plays a role here. Quantum 600 from WMFTG delivers low-shear and low-pressure pumping specifically for downstream process steps, and the complete portfolio of scalable peristaltic pumps help to increase yields. Using multiples of the same model reduces risk, cuts the list of inventories needed for each manufacturing location and minimises the number of consumable parts. Fewer processes also mean quicker upskilling for operators.

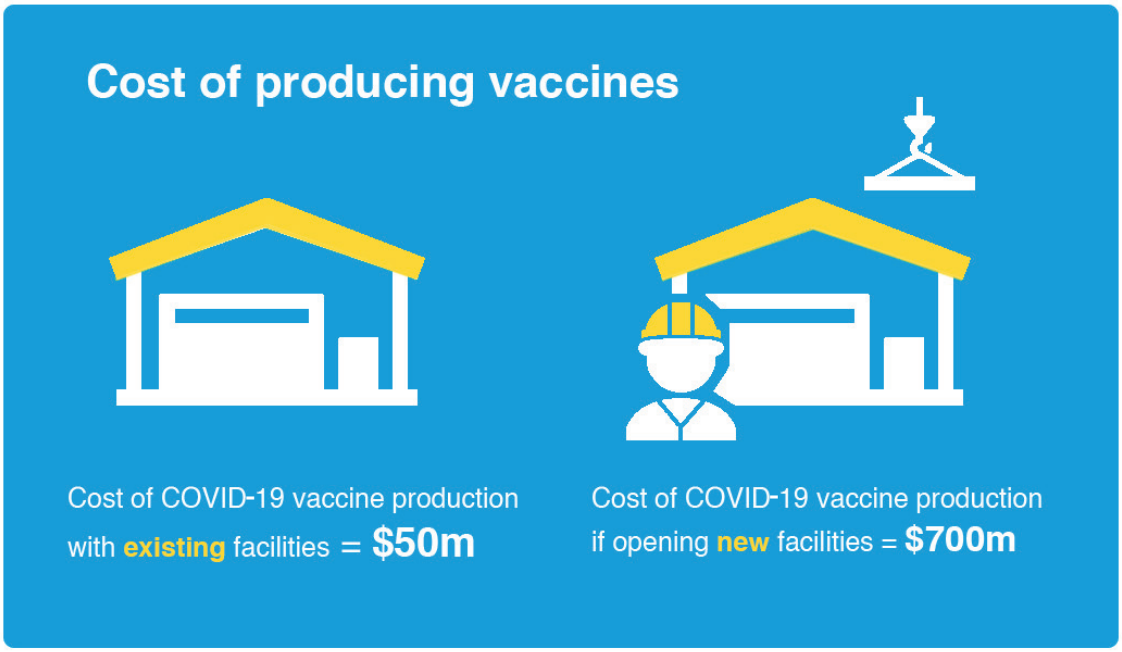
OUTSOURCING QUALITY FOR REGULATORY APPROVAL

By using tried and tested bioprocessing technology, biopharmaceutical companies can increase production by outsourcing to CMOs. But outsourcing doesn't stop with production, it can extend to quality too.

Equipment validation is crucial in an effective bioprocessing pathway. To ensure the highest quality, the process must demonstrate reproducibility and safety. To do this, each piece of equipment needs to be qualified and validated. WMFTG works with its customers to provide robust validation documentation for every piece of equipment. Tubing such as PureWeld® XL is stress tested to failure, demonstrating a clear and safe operating range, with low spallation and supported with extractables. Single-use components that demonstrate exceptional life and accurate flow rates with excellent chemical resistance providing confidence during drug manufacturing.

Qualification of components such as PureWeld XL is crucial when validating manufacturing processes for regulatory approval.Critical process parameters can be established and, as long as the vaccine is produced within these parameters, biopharmaceuticals and regulatory bodies can be assured of safety and consistent reproducibility.

When the process is verified and validated, quality is built-in by design.



Source: gavi.org/covid19

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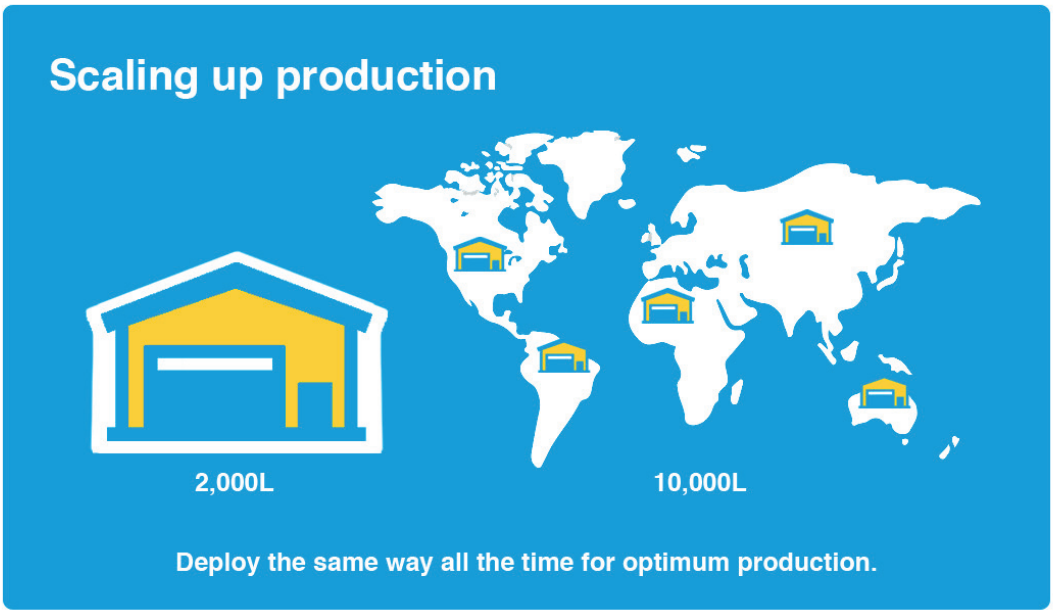
SINGLE-USE TECHNOLOGY HOLDS THE KEY TO REGIONAL PRODUCTION

Single-use technology has increased the regionalisation of drug manufacturing. Drug products like vaccines are more likely to be manufactured in the regions where they are required, providing more cost effective products without the reduction of efficacy caused by potential logistics issues impacting product quality.

In these new regional facilities, flexibility of production spaces is key. As such the 'ballroom' concept and other manufacturing techniques can be employed to give highly functional multiple product facilities. The 'ballroom concept' of manufacturing can use non-classified spaces because of the integrity of sterile, single-use bioprocessing equipment. With this approach, developing nations can access the same manufacturing techniques as those in developed countries such as in the USA, Western Europe and China. Process validation can be largely location-independent, assuming that the conditions of the manufacturing protocols are met. A 'shopping list' of single-use equipment and consumable parts can be sourced locally through manufacturer distribution and supply networks. Skilled staff can be employed locally and trained to ensure safe and compliant production.



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SCALING OUT AND SPREADING THE DEMAND

Before the COVID-19 crisis, biopharmaceuticals were already focused on capacity. The BioPlan Associates 16th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production asked the following question in 2019: "If this industry is to avoid significant capacity constraints, the most important areas to be addressed are…"

There were marked differences between the US and Western European responses with 42.2% of Western European responses focused on developing better downstream purification technology, versus 28% of US responses. 45% of US respondents would develop better continuous processing technology versus 33.3% of Western Europeans and both groups saw new single-use facilities as important with 40% Western European and 35.5% US respondents highlighting this choice.

COVID-19 has amplified this need, Capacity is now under strain and the scale of this production effort must not be underestimated. In order to produce the billions of vaccines needed to fight this pandemic, there will be a huge demand for materials. Producing enough drug product doesn't matter if the delivery devices aren't there. To meet the requirement for all aspects of vaccine production, we will likely see innovative resource reallocation and pioneers from other industries lending a hand, just as we did with Dyson ventilators and the pop-up 3D printing firms making face shields for frontline health workers.

The many and diverse vaccines entering the COVID-19 race can only be a good thing. No one biopharmaceutical or research institution can manage worldwide production of a single vaccine. There are likely to be multiple winners in this race and through collaboration with different CMOs and suppliers, the production and demand for raw materials can be dissipated. Although the WHO planned for a coordinated effort, success will be seen in the smaller collaborations formed between industry leaders in their areas of expertise.

COULD COLLABORATION LEAD TO THE UK'S FIRST COVID-19 VACCINE?

We're already seeing organisations use their collective brainpower and experience to tackle the COVID-19 problem. Collaborations include academic instutions, big pharma and smaller biotechs and CROs such as GSK and Sanofi, AstraZeneca and Oxford University, and Merck and IAVI, and are already seeing promising early stage results as vaccines reach clinical trials.

Tony Hitchcock, Technical Director, Cobra Biologics explains how collaboration is driving this development.

"Cobra Biologics' background is traditionally in gene therapy, taking pre-clinical trials through to GMP-approved clinical manufacturing. Our experience in working with viral vectors lends a particular strength to vaccine manufacturing. Although vaccines have been universal in responding to endemic diseases, COVID-19 is a completely new scenario for us all. Thankfully, we can draw on related understanding to mount a strong and collective assault on this virus.

"What's powerful about several of these vaccine approaches is the use of well-established technology and processes to expedite the development. The vaccine development timeline has already been reduced from five years to four months by utilising existing platform technologies such as the chimpanzee adenovirus platform that was established more than 15 years ago and was used to develop SARS and MERS vaccines. Although these vaccines couldn't enter clinical trials as the levels of infection dropped, we already have important dosage and efficacy data as the technology was tried, tested and approved for use in vaccine development.

"This is true for much of the manufacturing process too. By utillising single-use technology at the pre-clinical stage that can be pulled through to the scale-up stages, existing validation documentation can be used to prove the effectiveness of the manufacturing process.

"The strength in this approach lies in its simplicity. Through tried and tested bioprocessing techniques, we can produce a stable and effective vaccine. Once the vaccine is proven to work in clinical trials, we can quickly scale up this process to produce millions of vaccines.

“When responding to a pandemic, the tried and tested techniques work. Although there are more innovative techniques being developed, such as plant, RNA and virus-like particle (VLP) vaccines, we simply haven’t yet established techniques for scaling these processes.

“Clinical trial volumes for vaccine candidates will need to be manufactured at multiple sites simultaneously in order to provide the required volumes across several locations. This model of scaling out production can be replicated anywhere in the world using the agreed processes and specified single-use technology. The technology must be the same in every manufacturing site, that’s how we’ll achieve process validation and meet the regulatory standards. Mapping a critical path to ensure a safe and secure supply of consumables and protect long-term production of these vaccines is also essential, so the relationship between developers and bioprocessing partners is crucial.

“Although vaccine production is traditionally isolated from that of other biologics, such as monoclonal antibodies and cell and gene therapy, the process uses much of the same equipment and requires a similar skill base. As an industry, we have access to both, making large-scale production a reality.

“Collaboration across multiple organisations is clearly important, with each partner bringing unique expertise to the project. Hopefully, these collaborations will create something truly ground-breaking, based on the very real and solid foundation of tried and test technology.”

WHAT WILL WE LEARN FROM THIS PANDEMIC AND HOW WILL IT CHANGE THE COURSE OF VACCINE PRODUCTION?

Some of the world's brightest minds have been working on the COVID-19 crisis and the dedication and hard work of scientists, engineers and manufacturing teams will surely bear fruit. Science is an evolution. Just as we've used learnings from SARS and MERS vaccines to fight this pandemic, so too will we learn from COVID-19 vaccine development.

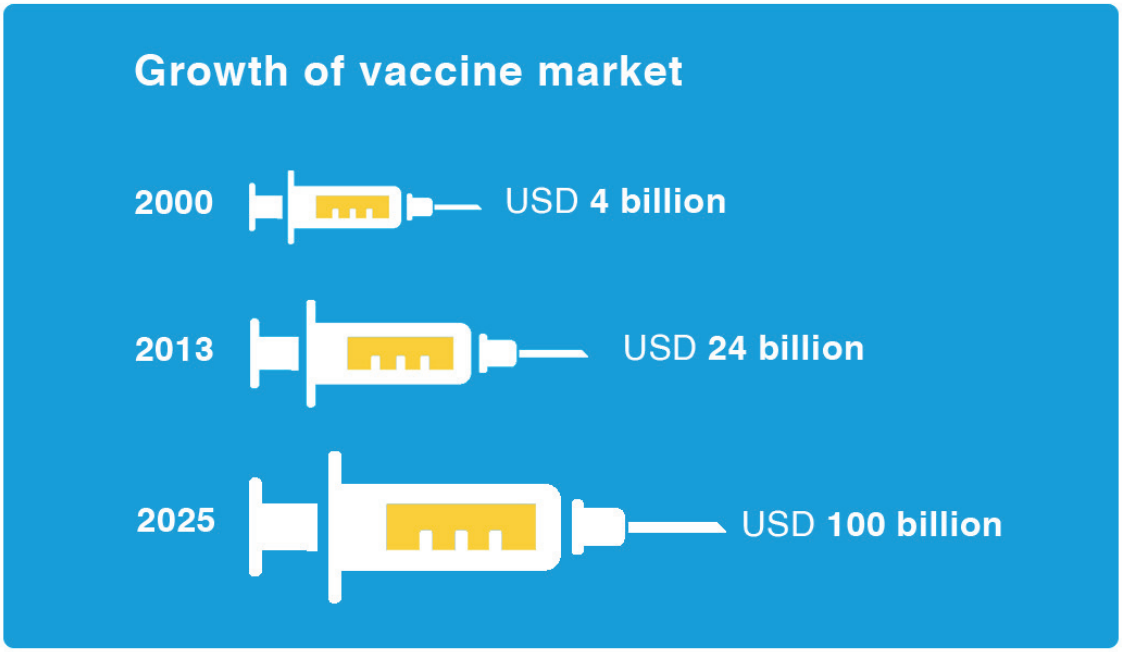
The advancements to accelerate vaccine production, intensify processes and scale-out production will set the scene for even greater development in these areas. But most of all, collaboration will be the lasting reminder from this crisis. Biopharmaceuticals, CMOs and suppliers—including competitors—have come together with a common purpose. We will have cost-effective vaccines against COVID-19 and we will have them soon.

As we move towards a challenging future, an ageing population requiring a diverse range of medication, a push towards personalised medicine and the more likely emergence of other novel viruses and future pandemics, we stand firm in the knowledge that we can meet these challenges with a blend of innovation and established solutions.

Sade Mokuolu is Global Regulatory and Validation Services Manager at WMFTG. She is a co-author on Biophorum's Single-Use user requirement (SUUR) guide and has published a number of articles on validation and qualification of single-use systems. She has presented at international conferences on behalf of the Bio-Process Systems Alliance (BPSA), as well as delivering single-use validation training to the Australian regulatory agency (TGA), and European GMP inspectors.

Peter Birch is Global Business Development Manager for Biopharmaceutical Equipment at WMFTG. Peter has extensive experience developing strategic relationships and collaborating with customers to build effective alliances, having worked for Thermofisher Scientific, Hans Buch+Co, Sartorious Stedim Biotech and Copenhagen University Hospital.

Tony Hitchcock is the Technical Director at Cobra Biologics, specialising in the development of cell and gene therapy. As a founding staff member of Cobra, Tony has been responsible for the development of much of Cobra's manufacturing technologies in the field of DNA and virus production and was involved in one of the first licenced gene therapy projects. Additionally, Tony is currently a member of the BIA Science and Innovation Advisory Committee (SIAC) and of industrial advisory boards for Aston and Loughborough Universities.



REFERENCES

https://www.who.int/immunization/monitoring_surveillance/global_immunization_data.pdf
https://www.who.int/influenza_vaccines_plan/resources/session_10_kaddar.pdf?ua=1
https://www.ft.com/content/87d1170a-78bc-11ea-bd25-7fd923850377
https://www.gavi.org/covid19
https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines (accessed 16th June 2020)
https://www.wmftg.com/Documents/knowledge-hub/White%20papers/wp-pureweld-xl-continuous-bioprocessing-en.pdf?utm_source=website&utm_medium=whitepapers&utm_campaign=pureweld-xl-cont-bioprocess A study of the peristaltic life and pumping performance of three TPE tubing products to assess their suitability for continuous bioprocessing, Dr Chris Brown and Rebecca Govier, Watson Marlow Tubing. 16th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production, BioPlan Associates, April 2019
https://www.who.int/news-room/detail/13-04-2020-public-statement-for-collaboration-on-covid-19-vaccine-development
https://www.sanofi.com/en/media-room/press-releases/2020/2020-04-14-13-00-00
https://www.astrazeneca.com/media-centre/press-releases/2020/astrazeneca-and-oxford-university-announce-landmark-agreement-for-covid-19-vaccine.html
https://www.mrknewsroom.com/newsroom/news-releases/news-details/2020/IAVI-and-Merck-Collaborate-to-Develop-Vaccine-Against-SARS-CoV-2/default.aspx