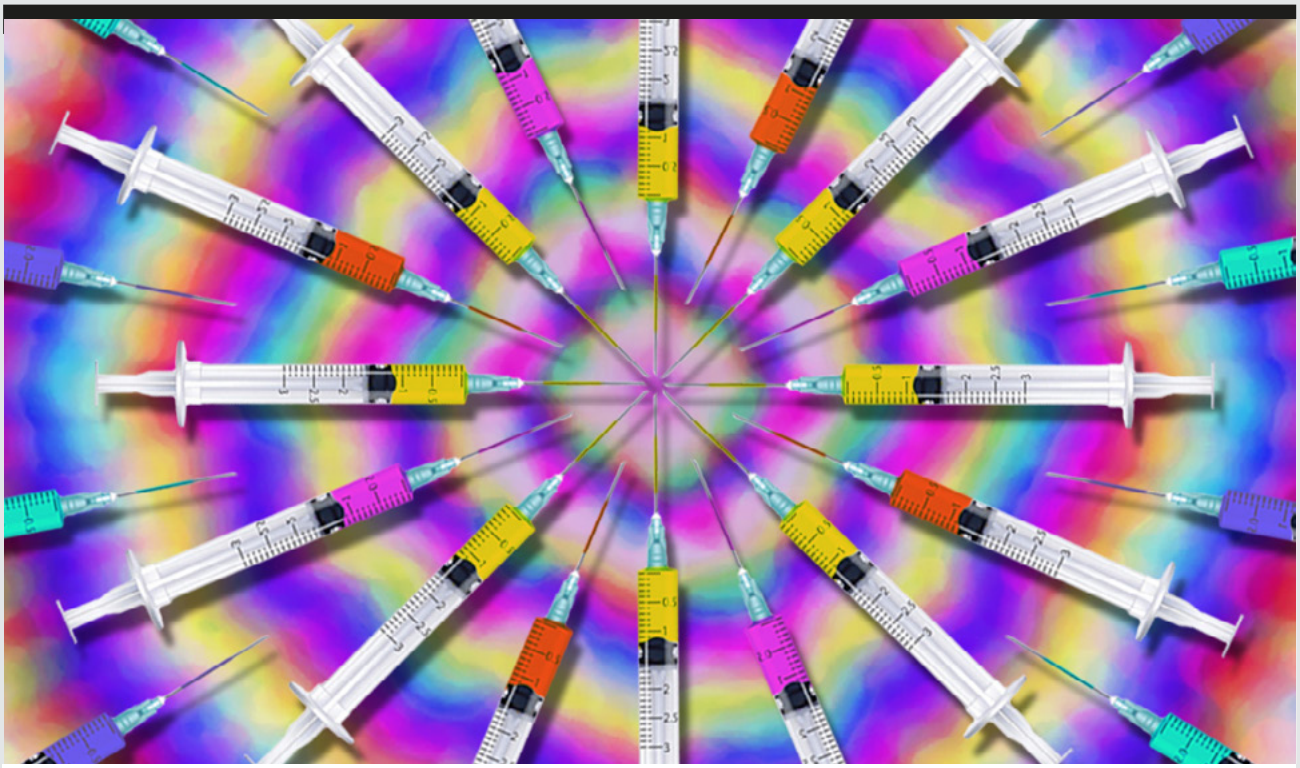
PHARMA BOARDROOM

InFocus

Vaccines



GLOBAL & INCLUSIVE

JANUARY 2021

In collaboration with: Deloitte.

Contents

JANUARY 2021

The special report was produced by PharmaBoardroom.

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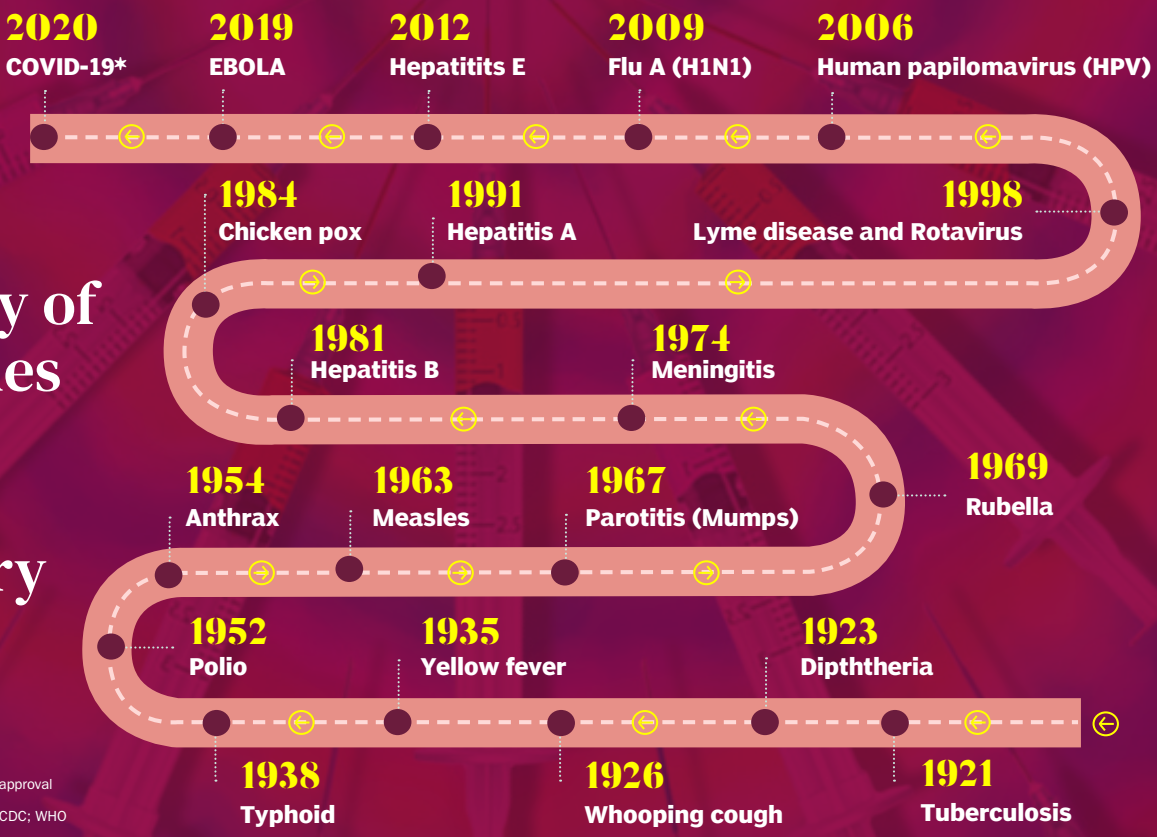
Preface

Long dismissed as the backwaters of healthcare innovation, the tremendous value of vaccines – the single most cost-effective health intervention after clean water – made itself starkly clear in 2020, as the discovery of a novel coronavirus quickly exploded into a full-blown global pandemic that rages on still.

While billions have since been poured into vaccine development for COVID-19 and vaccine candidates have been developed and approved (albeit so far only for emergency use) at unprecedented speed, sector stakeholders are only cautiously optimistic regarding the longevity of this newly awakened global interest and investment in vaccines – and whether the frenetic zeal to discovering and deploying COVID-19 vaccines would translate into sustained and longer-term efforts to support vaccine R&D for a whole host of other infectious diseases that continue to claim tens of millions of lives annually.

This issue of InFocus dedicated to vaccines features a variety of global, regional and local stakeholders across the public and private spheres to provide a snapshot of the four thematics at the heart of the vaccine sector: Research & Development, Manufacturing & Supply Chain, Partnership Models, and Public Health Impact.

The History of Vaccines in the Last Century

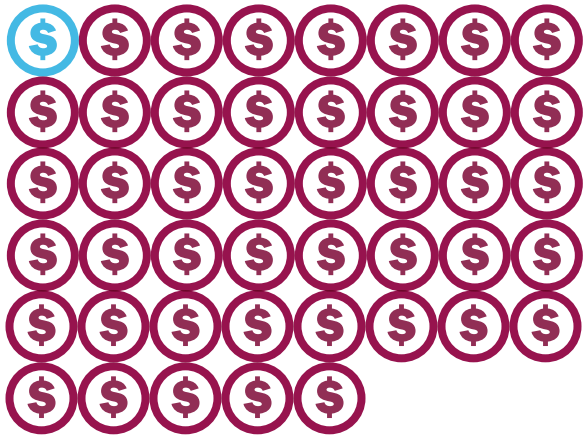


* Leading to conventional approval

Source: Iberdrola; Nature, CDC; WHO

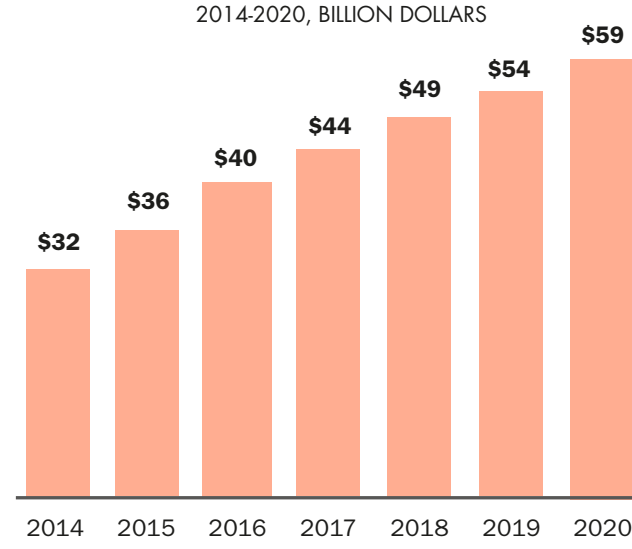
THE VALUE OF VACCINATION

Every **$1** spent on immunization provides a return of up to **$44** in the world's poorest countries.



Source: Return on Investment from Childhood Immunization in Low - And Middle-Income Countries

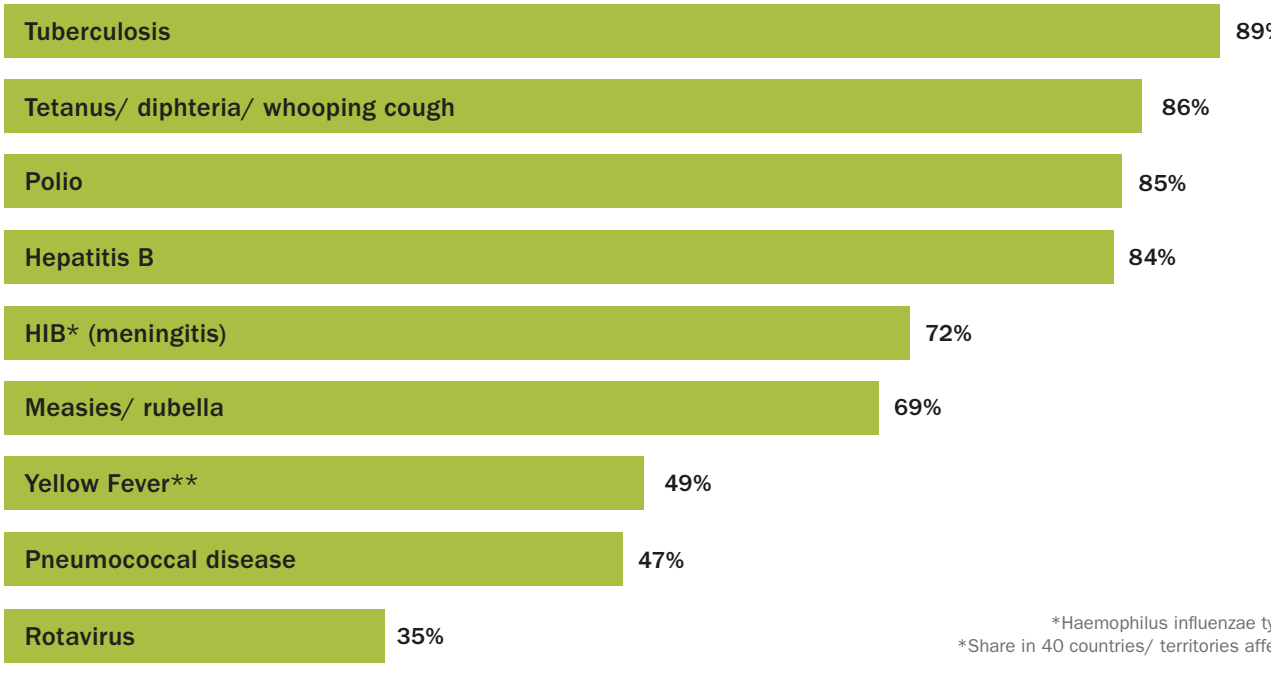
GLOBAL VACCINES MARKET SIZE



Source:

THE MOST WIDESPREAD VACCINES AROUND THE WORLD

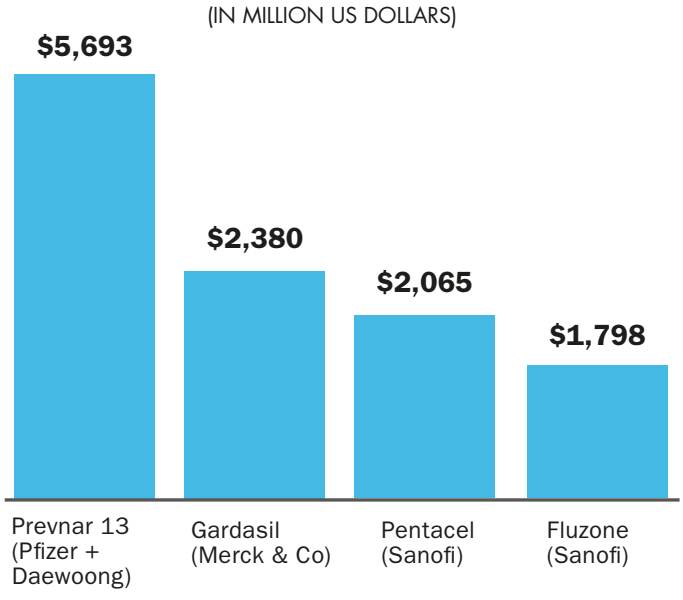
Share of one-year-olds globally who received full set of immunizations for the following diseases in 2018



*Haemophilus influenzae type b
*Share in 40 countries/ territories affected

Sourcce: WHO, Statista

TOP GLOBAL VACCINE PRODUCTS BASED ON REVENUE



Source: Fortune (2017)

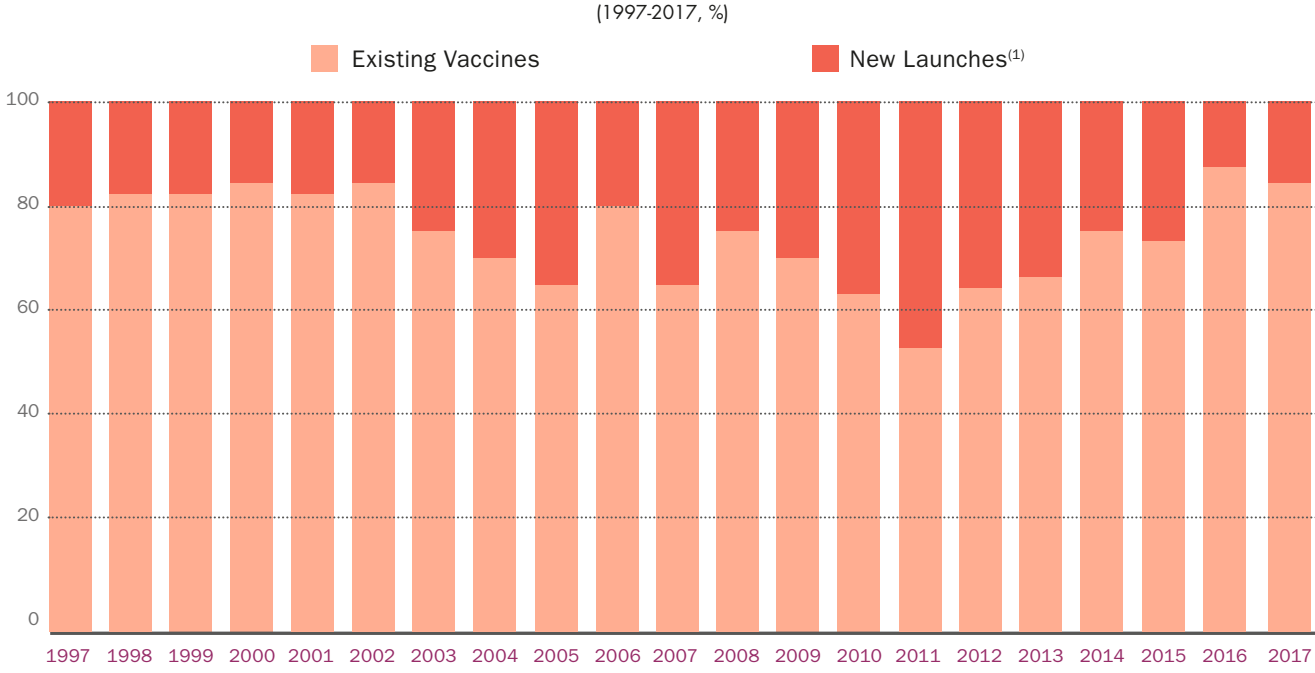
RECOMBINANT VACCINES MARKET

Global Recombinant Vaccines Market Size

North America Recombinant Vaccines Market Size (2018, USD Billions)

Source: Fortune Business Insights

NEW VACCINE LAUNCHES AS % OF TOTAL GLOBAL SALES



(1) Defined as any vaccine that received US Food and Drug Administration approval in preceding 5 years.

Source: EvaluatePharma, Evaluate, September 2018, evaluate.com; McKinsey analysis

FOLLOWING THE SCIENCE

Dr Peter Marks
director, Center for Biologics Evaluation and Research (CBER), US FDA

Dr Peter Marks MD, PhD, director of the Center for Biologics Evaluation and Research (CBER) at the US Food and Drug Administration (FDA), highlights the Center's contributions related to the regulatory science behind vaccine development and his commitment to following the science and remaining steadfast to the truth

Peter, could you start by clarifying the mission of CBER under the US FDA?

PETER MARKS (PM): CBER is one of the smaller FDA centers. Its mission is to facilitate and consolidate the review of complex biological products, including blood and blood products, allergenic products, tissues, cellular and gene therapies, and vaccines.

Due to COVID-19, we have our hands full right now, since we have to deal with many therapeutics like COVID-19 Convalescent Plasma and polyclonal immunoglobulins, as well as COVID-19 vaccines, in addition to work on our existing products such as cell and gene therapies. We have an outsized importance presently, with the products we regulate featured routinely in papers every day, so these are certainly interesting times for us.

How has this public and media scrutiny affected the work of the US FDA CBER?

PM: I have taken a pretty strong stance, as supported by FDA Commissioner Stephen Hahn, to follow the science for these products as they are developed. This is one of the reasons we issued a guidance entitled, Development and Licensure of Vaccines to Prevent COVID-19, and also why we have, in our guidance, addressed the issue of using the Emergency Use Authorization (EUA) process that we have here in the US for COVID-19 vaccines, and also why we have promised to take every COVID-19 vaccine that comes in with an EUA request or a Biologics License Application (BLA) request to a public advisory committee meeting.

Our guidance was intended to place some boundaries on what is acceptable for a COVID-19 vaccine. We wanted to make sure that people had an idea of what we are looking for so that when we receive EUA or BLA submissions they are consistent with our expectations.

> "Refrain from getting lost in all the noise [...] in the current environment"

It is important to note here that it is the FDA Chief Scientist that signs off on EUAs. We make a recommendation based on our evaluation, which goes to the Chief Scientist, who then makes the final decision.

When it comes to the FDA, it is patently clear that we are here to follow science to bring benefit to this country and, when possible, to bring benefit to the entire globe. That is only going to happen if we continue to dedicate ourselves

to objectively working through the evidence, to follow the science, and to come to independent conclusions. This is what we have done and it is what we will continue to do during this time. We have to remain steadfast to the science … and refrain from getting lost in all the noise that is out there in the current environment at this point.

The world needs good vaccines here and that is what we would like to facilitate.

Looking beyond just COVID-19, during your time at CBER, what have been some of your learnings when it comes to regulatory science for vaccines?

PM: First, and particularly as a result of COVID-19, we clearly see the fundamental importance of quality manufacturing for vaccines. There is essentially a new interest in vaccine manufacturing – and more efficient vaccine manufacturing. People have once again realized that if we are having a problem like this today and we lack ways to manufacturing vaccines quickly and in large quantities currently, we are likely to run into the same problem again in the future. Vaccine manufacturing has typically been dominated by batch manufacturing but this pandemic might ultimately advance vaccine manufacturing technologies to include components of continuous and semi-continuous manufacturing in the future.

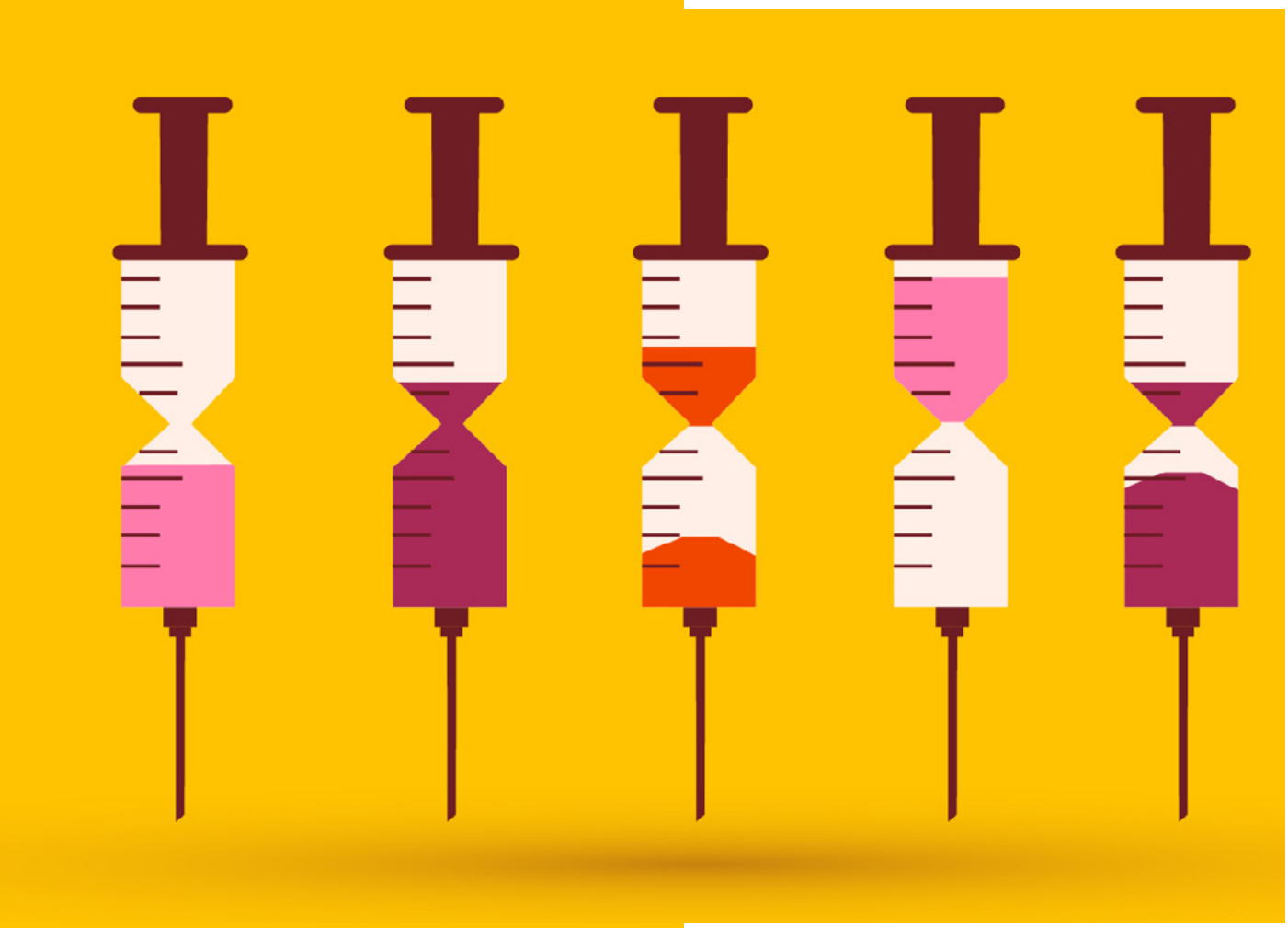
Secondly, we can use immune correlates of protection in areas to speed clinical trials. Once we have immune correlates of protection for COVID-19, that would facilitate new trials. We are using clinical endpoints as a starting point right now since we lack those.

Thirdly, especially with COVID-19, we can see novel vaccine technology, which had previously been used only in smaller trials, coming to the forefront. There are two mRNA vaccines in large Phase III trials, for instance. There are some interesting configurations that could advance the field.

One of the things that is hard for the public to understand is that infectious diseases are each somewhat unique. Our bodies have learnt to generate immune responses to certain pathogens better than others. It so happens that for respiratory viruses like COVID-19, the body does seem to ultimately generate a good immune response, so we are lucky in some ways. It may even be that the immune response is exuberant in elderly people, which is why they become more severely ill, or perhaps the immune response is not quite right.

But in contrast, there are pathogens like HIV that directly harm the cells involved in the immune response, in which case it has proven much harder to find vaccine targets.

Personally, I do have more hope that we will get there much more quickly with a COVID-19 vaccine than with vaccines for other diseases like HIV, which, as you know, has been a target for the vaccine sector for over a decade now.



R&D AT HEART

Two contrasting perspectives from the R&D chiefs of global vaccine leader GSK and aspiring vaccine developer Janssen as they discuss the merits of their approaches to the tricky and at times thankless task of vaccine discovery and development.

In 2014, a major product swap between Novartis and GSK saw a lot of analysts predicting a gloomy future for GSK, with many doubts about GSK's portfolio strategy. However, since then, GSK's vaccines portfolio has outpaced the company's more traditional pharma portfolio in terms of growth. How are you aiming to continue that success story in terms of technology as well as therapeutic fields of focus?

EMMANUEL HANON(EH): Firstly, we work very closely across GSK R&D and collaborate with our colleagues in the pharma organisation as we have complementary expertise that is hugely beneficial for both parts of our organisation. The big differentiator for us versus others has been and it will continue to be innovation: investing in the future, finding new platform technologies that can be applied to more diseases and will allow us to enter into new fields.

The two new fields that we are prioritising are therapeutic vaccines and antimicrobial resistance (AMR).

Most vaccines used today prevent the appearance of a disease in the population: vaccinating people before they are exposed to a pathogen. For example, flu vaccines are administered to patients before flu season. Therapeutic vaccines on the other hand have the ability to treat an ongoing disease or to prevent the cyclic evolution of that disease. GSK has several vaccine candidates in our platform that have this property. Our vaccine preventing shingles is one example and has 90 percent efficacy, across different ages. It is administered to people many years after they have been infected by the virus and is still able to recalibrate the body's immune system against the virus so that it never comes back, or at least does so with very low frequency.

We have another set of vaccines in our pipeline which target RSV – a virus that causes respiratory disease. It can become a very severe disease and we are working on protecting children and older adults with three different vaccine candidates in development.

The other field of huge interest for GSK is AMR – antimicrobial resistance. We realise how dramatic it is to be faced with a pathogen for which there is no treatment. Multi-resistant bacteria such as tuberculosis or gonorrhoea are progressively accumulating resistance to traditional antibiotics. There is a huge complementary intervention that can be made using vaccines. Vaccines can be used to prevent certain infectious diseases and thereby prevent the use of antibiotics, as well of the misuse of antibiotics, for example for flu. This way, the development of antibiotic resistance is slowing down.

It is already well documented that resistance does not develop, or at least develops much slower, against vaccines. That is another really interesting avenue to investigate.

Emmanuel Hanon
Senior VP, Vaccines R&D, GSK

What do you see as some of the most important recent innovations in vaccinology?

EH: Over the last 20 years, we have seen the introduction of new platform technologies. This means working on a certain vaccine approach and, once you have collected the learnings of that approach, you can apply this to different pathogens and create a family of vaccines. This is what we have done in Belgium with the development of our adjuvant technology, where we use a given adjuvant in several different vaccines.

The benefit of a platform technology is that you make the investment once but it benefits a variety of vaccines.

The other up-and-coming technology in vaccines is messenger RNA vaccines. The fundamental change with this technology is that the process of creating these vaccines is extremely fast. In messenger RNA, the antigen – the identity card of the virus or bacteria, a genetic code – is able to be programmed, somewhat akin to 3D printer. The body produces its own vaccine as the body's own cells will produce the antigen that can react against a pathogen, leading to the immune protection.

Another reason why messenger RNA manufacturing is so quick is that the manufacturing process of a molecule for a given vaccine does not change depending on which molecule you produce. In other words, your manufacturing site becomes a multi-antigen manufacturing site, instead of having a manufacturing site for one antigen only (as it is the case for more traditional vaccines). That allows for major economies of scale in the investment needed for vaccine development.

We have the messenger RNA technology in house, but our strategy to develop a COVID-19 vaccine is to use a well-established platform. By doing this, we have potentially higher chances of success but will also be able to produce many doses of a successful vaccine. It does not, however, mean that we are not investing in messenger RNA technology, which we believe represents the future of vaccines.

How far away are we from the widespread emergence of personalised vaccines?

EH: The notion of personalisation is a hot topic in the pharma industry today. Smartphones with health checks drive behaviour, and consumers can easily buy microbiome tests that provide information about the myriad of bacteria and viruses in your gut. There is a possibility that in the future, the population will be fragmented into mini populations with specific criteria defined either by mobile application or by specific diagnostics to be done at home. These might trigger specific behaviours and, among this behaviour, the use of a vaccine may make sense.

GSK is not, today, pursuing personalised vaccines to this extent. Other companies use messenger RNA technology to move quickly between the genetic part of a pathogen and a vaccine candidate. They may be able to use the technology to make vaccines tailored against, for example, cancer in a patient. This is a powerful example that I would call personalised vaccination. There are still a lot of challenges in this field, but it is not impossible.

> “Our strategy is to focus on well-defined areas where we can bring new, unique and transformational vaccines to address high unmet medical need”
>
> Dr Johan Van Hoof
> Janssen

The global vaccines market is largely dominated by four Big Pharma players. Against that backdrop, what role do you see Janssen playing?

JOHAN VAN HOOF (JVH): Our strategy is to focus on well-defined areas where we can bring new, unique and transformational vaccines to address high unmet medical needs, and in doing so, become an important vaccine player globally.

The areas we are focusing on at the moment are respiratory infections like respiratory syncytial virus (RSV) and a universal flu vaccine; a preventative vaccine for HIV, where many have failed in the past; and vaccines for bacterial diseases, because we think vaccines can be a part of the solution for the problem that is antimicrobial resistance (AMR) today. For example, we are developing a vaccine for Escherichia coli (E. coli), which is a major cause of disease,

Dr Johan Van Hoof
Global Therapeutic Area Head of Vaccines, Janssen

sepsis and death, especially in the elderly.

How has Janssen invested in vaccine development technology platforms? Given the complexity of vaccine R&D, is it an area where it is better to have as many tools in the toolbox as possible?

JVH: We certainly want to have multiple tools in our toolbox but it is not about acquiring or developing a technology just to have it. At the center of our thinking is the disease that we want to tackle – we look at what we might need to design a vaccine, and then we either develop that tool internally or acquire it externally. For instance, adjuvants are something you acquire or produce based on whether it is needed within your development strategy.

For our bacterial vaccines, for instance, for E. coli, we are using bioconjugation, where a bacterial surface polysaccharide from a pathogen is attached to an immunogenic protein.

For other diseases like HIV, RSV and the Zika virus, we are working with non-replicating vectors, specifically the adenoviral vector type 26 (Ad26). We have been developing this for over ten years and we have accumulated a lot of experience. Across these various projects, we have seen consistent results in both antibody production – humoral immunity – and T-cell responses – cellular immunity. This is also the platform used for our investigational COVID-19 vaccine candidate, and while we are still at a very early stage, our Phase 1 data has also shown indications of robust humoral and cellular immune responses. Our Ad26 platform was also used in the development of our Ebola vaccine regimen, which was approved by the European Commission earlier this year. The vaccine regimen contains two doses, our Ad26 vaccine and an MVA vaccine we in-licensed from Bavarian Nordic. Through all these different projects, we have vaccinated over 114,000 people, all within a controlled clinical trial setting, so we have been able to observe and evaluate the safety profile of this platform. There is a level of confidence there and we can be reassured that the backbone of the Ebola vaccine, for instance, has been used many, many times in other people.

Another priority area for Janssen is the development of a HIV vaccine, which has been seen by many as the Holy Grail of the industry. What progress has been made here?

JVH: Having worked in this field for a long time, we have developed various generations of a HIV vaccine, applying the principles of translational medicine. The idea is to work with preclinical and animal models, particularly non-human primates (NHP), until we see promising levels of protection, at which moment we enter Phase 1 human trials to compare NHP and human responses. In that way, going back and forth, we have improved our HIV vaccine formulations, and a few years ago, we reached a point where one particular formulation had as much as over 90 percent protection compared to placebo vaccinated animal models. Even after six challenges, 66 percent of the NHP were still protected, which was when we started doing in-depth analyses of immune markers to see which were correlated with protection.

> “We certainly want to have multiple tools in our toolbox but it is not about acquiring or developing a technology just to have it.”
>
> Dr Johan Van Hoof
> Janssen

Based on that, we could see what type of immune response was needed for animals to fall within that category of being protected after six challenges. These were animals with a certain level of antibodies and a certain level of cell-mediated immunity – and with those thresholds, we saw over 94 percent of animals protected after six challenges. Through our initial Phase 1 and 2 data, we saw that it was possible to also achieve those thresholds in humans, which was very encouraging. We started subject enrolment for a Phase 2b trial in high-risk women in South Africa in 2017, who have now been vaccinated and are being followed up on, and we hope to have a readout of that trial by mid-2021.

HIV vaccine development comes with a lot of risk, and we are still in the middle of the process but we are cautiously optimistic about our vaccine candidate.

TOP GLOBAL VACCINE COMPANIES

Four companies (GSK, Pfizer, Sanofi, and MSD) together occupy over 80 percent of the global market for vaccines. Moreover, vaccines are an important part of these companies' revenue streams, making up between 13 and 21 percent of total revenues in 2019.

	GSK	Pfizer	Sanofi	MSD
2019 overall revenues in USD	46.2 billion	51.8 billion	43.8 billion	46.8 billion
2019 vaccine revenues in USD (% of total)	9.8 billion (21%)	6.5 billion (13%)	6.9 billion (16%)	8.4 billion (18%)
2019 top vaccine product	Shingrix for shingles	Prevnar 13/Prevenar 13 for pneumococcal disease	Polio, Pertussis and Hib vaccines*	Gardasil/Gardasil 9 for certain strains of human papillomavirus (HPV)
2019 top vaccine revenue in USD (& of total vaccine revenues)	2.5 billion (26%)	5.8 billion (89%)	2.3 billion (33%)	3.7 billion (44%)

*Sanofi doesn't publish sales figures for individual vaccines

INSIGHTS ON VACCINES' IMPORTANCE TO GLOBAL REVENUES

"We have more than 10 vaccines and medicines in the late-stage portfolio that could change medical practice and have sales potential in excess of one billion dollars – and several, such as our RSV vaccine in older adults, could have multibillion dollar potential."

Hal Barron - chief scientific officer & president R&D, GSK (January 2021)

"Prevnar 13 is Pfizer's pneumococcal vaccine that protects against infections such as pneumonia and meningitis, as well as other infections caused by pneumococcus including ear and sinus. In 2014, the US Centers for Disease Control and Prevention (CDC) recommended the immunization for adults ages 65 and older in addition to young children, typically those under the age of 2, and adults with certain chronic conditions. And that sent the profits on Prevnar skyrocketing to USD 23.4 billion since just 2015."

Brittany Shoot - Fortune (February 2019)

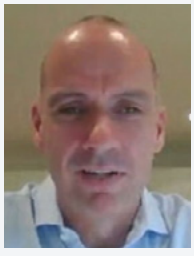
"[Sanofi] enjoys a very, very broad portfolio and it's also a leader in vaccine manufacturing ... the whole move towards vaccination due to COVID has really grown quite a lot and Sanofi is going to benefit from that the next couple of years."

Boris Schlossberg - managing director, BK Asset Management (December 2020)

"We really wanted to have capacity to cover the global birth cohort [with Gardasil]. If you think about the number of births every year, they're somewhere in the order of 125 million globally. If you assume basically an 80 percent vaccine coverage rate, you want around 200 million doses to protect that portion of the population. And that's kind of the ballpark that we've been looking at."

Mike Nally - chief medical officer, MSD (September 2020)

6 Key Points from GSK Vaccines Head Roger Connor



Roger Connor
Global Vaccines president, GSK

During the 2020 FT Global Pharmaceutical and Biotechnology Conference, GSK global vaccines president Roger Connor shared some of his insights regarding the reorganization of GSK's Consumer Health, Pharmaceuticals and Vaccines business units, their pandemic adjuvant system technology, and their – and the industry's overall – commitment to COVID-19 vaccine safety.

On GSK's reorganization and the synergies between pharma and vaccine R&D

"I see the science converging between vaccines and 'traditional' pharma. You will see in our vaccines pipeline [that] we have a breadth of products, we are moving more into older adults, we are moving more into therapeutic vaccination, and we have some joint projects between pharma and vaccines research development … we are making sure that the engines in the new GSK are world-class engines of development … the most exciting bit for me is the scientific synergy between the groups and getting that spark going."

On the growing opportunities in older adult vaccines and GSK's shingles vaccine

"It is the science … [our] scientific understanding of the immune system as we get older is getting better. Only 20 years ago, you say the word vaccine and [people think] that is for kids. Something like Shingrix® , [which is] for people over 50, that is a game-changing vaccine for a horrible condition with an efficacy of over 90 percent. The secret sauce in that vaccine is our adjuvant system, [which] is proven to have an impact on age-related decline in immunity. We are using this in other older adult vaccines like our respiratory syncytial virus (RSV) candidate … if we can switch the world on to older adult vaccination, that will have a very big impact on public health."

On GSK's decision to leverage their adjuvant technology in the COVID-19 vaccine race

"We knew we had to play a very important role … we have this platform technology called an adjuvant[, which] creates an amplified response and reduces the dose you need … in a pandemic where volume is everything, we felt that was absolutely key … we also felt that multiple vaccines were going to be needed, so what we decided to do strategically was to open our adjuvant technology to the world … [the key question was,] who should we best partner with that would have the biggest impact? … We are very comfortable with our choice of strategy."

On the GSK-Sanofi COVID-19 partnership and doing the right thing

"The moment we connected and saw the win-win between us, both companies moved super fast; we suddenly realized there was something special we could do here … The world is waiting for a solution so just being part of this is something special … There are collaborations like the GSK-Sanofi collaborations … that are being done just because they are the right thing to do … We have said that during this pandemic phase, we will discount the price of this adjuvant, and we will [reinvest] any profit that we make … in the R&D associated with either this vaccine, future coronavirus vaccines or pandemic preparedness."

On ramping up manufacturing capabilities for their COVID-19 adjuvant

"The adjuvant technology we have is a backbone technology that already exists. It is not a new formulation; it is something we know how to make. We are ramping that capability up but at least the supply chain exists already. That is why our confidence in that billion is quite high [GSK has committed to manufacturing one billion doses of their pandemic vaccine adjuvant system in 2021 to support the development of multiple adjuvanted COVID-19 vaccine candidates] … to put it in context, GSK typically manufactures 700 million doses across all of our vaccines … we will do a billion doses of adjuvant alone next year."

MRNA TECHNOLOGY

Dr. Thomas D. Madden, CEO and founder of Acuitas Therapeutics, outlines the company's revolutionary lipid nanoparticle (LNP) technology, their involvement in Pfizer and BioNTech's COVID-19 vaccine, and what mRNA vaccines might mean for the future of the biopharmaceutical industry.

Acuitas Therapeutics' revolutionary lipid nanoparticle (LNP) technology

"We have developed an LNP delivery technology to enable our partners to be able to move new classes of drugs – drugs that are essentially based on biological molecules or systems – into the clinic and the marketplace. These are nucleic acid drugs, including RNA interference (RNAi) or soluble RNA (sRNA) drugs intended to inhibit the production of particular proteins.

More recently, we have focused on working with partners developing mRNA therapeutics. Our delivery system is critical here for two reasons. Firstly, the mRNA itself is very rapidly broken down within the body, so it needs to be protected within a carrier system. Secondly, the mRNA also needs to enter cells within the body in order to be active but it is too big to enter on its own. Our LNP technology protects the drug after it has been administered and also delivers it into the cell cytoplasm so that it can start expressing proteins.

Over the years, we have built a number of different partnerships, including with BioNTech – one that has culminated in our technology being used in the development of COVID-19 vaccines.

The COVID-19 Pfizer, BioNTech and Acuitas partnership

"When the pandemic hit, BioNTech recognized that our technology could be used to help them develop a vaccine. We began discussions with them in January, and then we flew to Germany in early February to meet the German regulatory authorities, as well as BioNTech, to map out the clinical program necessary to support a COVID-19 vaccine candidate.

Throughout the process, we have been working extremely closely with BioNTech and Pfizer to support selection of the vaccine candidate, since a number of different mRNA constructs expressing different proteins were being looked at.

We have also supported the work necessary for the manufacturing scale-up so that our partners are able to provide as many doses as possible. Pfizer and BioNTech are projecting to manufacture 1.3 billion doses in 2021, which requires a huge commitment. The Acuitas model is that we transfer our process technology through specialized cGMP organizations, as we do not do manufacturing, and so we have also worked closely with these organizations to improve the manufacturing scale. We helped them see how they could produce much larger batches – and much more quickly – which required some development work to be undertaken internally and subsequently transferred.

mRNA – the future of the industry?

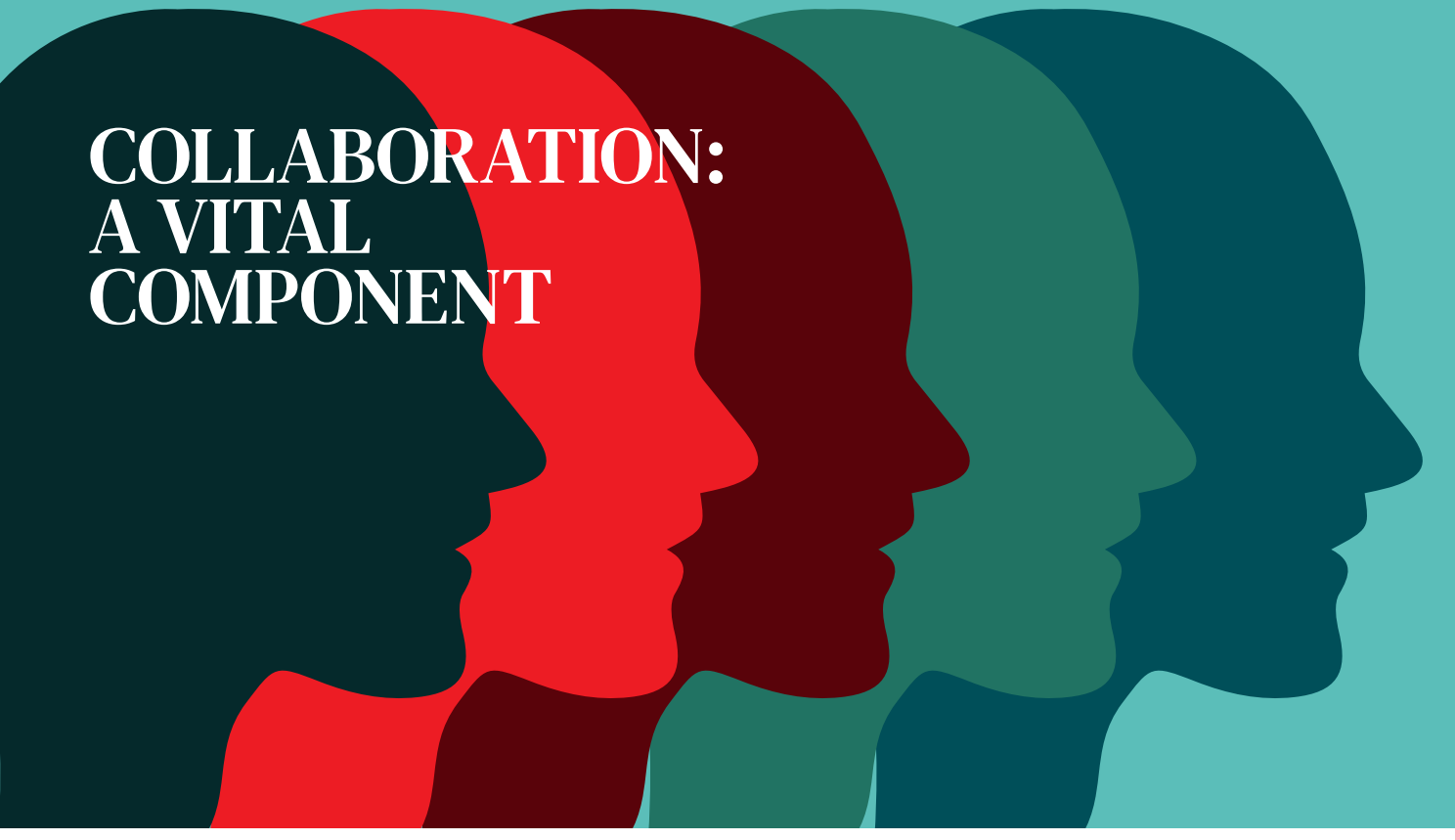
"When COVID-19 emerged, we quickly recognized that the mRNA vaccine approach was potentially ideally suited for the rapid development of a vaccine to address COVID-19. Compared to conventional approaches taken, where killed or attenuated viruses – or adenoviral vectors – are used, mRNA vaccines are inherently a much more precise and elegant approach. Rather than using an entire virus, we are simply providing the instructions to allow the body to construct a single component found in the virus that would trigger an immune response. I think there are potential safety and potency advantages with this approach.

We have also shown that this technology is capable of developing a vaccine more rapidly. Therefore, I think this will generate a lot of interest in other vaccine opportunities, as well as in the investment of an infrastructure that would allow us to respond much more rapidly, should a new viral threat come along. No one who has lived through COVID-19 wants to live through a COVID-20 or a COVID-21.

Personally, I think Big Pharma can sometimes feel trapped by the scale of investments they have made. If a company has invested USD 5 billion in manufacturing plants based on a particular technology, it would potentially be political suicide to suggest that they move away from that technology. That is a challenge Big Pharma faces, so it is a difficult sell to suggest that they think about adopting a new technology.

But I think we should always be open to evaluating new ideas and to accepting that better approaches may exist out there, as opposed to saying that, well, we have always done it this way, so we will continue to do it this way.

The good news is that companies do seem open to collaboration. There are three major mRNA companies today: CureVac, BioNTech and Moderna. Obviously, BioNTech has partnered with Pfizer, and CureVac recently announced a major collaboration with GSK, so there are opportunities to work together to gain expertise and technology from major players in this new field.



COLLABORATION: A VITAL COMPONENT

Vaccine research, development, manufacturing, supply, administration does not occur in a bubble, but rather requires the efforts of a variety of stakeholders to realise. Here, representatives of the Innovative Medicines Initiative (IMI), World Bank, and Swiss Tropical and Public Health Institute (Swiss TPH) outline the importance of collaboration – both between public and private sector actors, as well as between high, middle- and low-income countries – to the vaccine industry as a whole.

Dr Pierre Meulien looks at how the vaccine industry has benefited from public-private collaboration.

Dr. Pierre Meulien
Executive Director, Innovative Medicines Initiative (IMI)

The reason vaccines have been a prime subject for public-private partnerships (PPPs) is because of the complexity of vaccine R&D. The entry ticket for aspiring vaccine developers is extremely expensive, and the high price is motivated by safety concerns. This is a good thing, in reality, because vaccinations are preventative measures. Every time you vaccinate someone, you are injecting a novel substance into someone who is perfectly healthy. To add to that, that someone is typically a two- or three-month-old baby. The safety bar has traditionally been extremely high, for very good reasons. Therefore, in normal circumstances, it typically takes ten to 15 years to develop and obtain marketing authorization for the widespread use of a vaccine. In the case of Ebola, it took five years, which is already an impressive record.

From the public perspective, vaccines are of huge public health interest because of the valuable contributions they make to disease prevention that, honestly, we take for granted every day. Therefore, the public, academia, researchers and the private sector all have to come together to tackle these challenges.

Muhammad Ali Pate
Executive Director, Innovative Medicines Initiative (IMI)

Muhammad Ali Pate on how the COVID-19 crisis reinforces the need for pooled resources and communication across borders on global health challenges.

Key priorities include addressing health workforce shortages and ensuring equitable access to new diagnostics, medicines and vaccines. We believe that fair and equitable access to safe and efficacious vaccines and therapies, when developed, is essential for all countries, including the poorest, to rebuild livelihoods and set a course toward recovery. We are working closely with partners across the public and private sectors to ensure global and fair access to COVID-19 vaccines, therapeutics and diagnostics that are being developed.

To support the most vulnerable countries, we need to pool resources and coordinate to prevent disruption of commodities such as medicines. This includes resources from governments, donors, multilateral organizations, non-governmental organizations, and the private sector. The pandemic requires that governments prioritize health investments now: the costs are small compared with the economic costs of not acting.

Prof Dr Jürg Utzinger
director, Swiss TPH

Prof Dr Jürg Utzinger highlights how Switzerland collaborates with low- and middle-income countries (LMICs), and why this is especially important in vaccine R&D.

It is important that low- and middle-income countries (LMICs) participate actively in the COVID-19 vaccine R&D efforts because that way, they can ensure that the vaccines developed ultimately meet their population profiles. If we are looking at a vast country like the Democratic Republic of the Congo where there is not even a very advanced road network, we need a vaccine that can reach marginalized populations in the most remote areas. Vaccines that need to be stored at ultra-cold temperatures will pose considerable logistical challenges to reach the most neglected people. The fact of the matter is that COVID-19 anywhere is COVID-19 everywhere, and hence we need to find ways of fair, equitable and rapid access to essential commodities, such as personal protective equipment, novel treatment and ultimately a vaccine.

THE GAVI ACCESS MODEL

To untie the knot of unaligned or misaligned incentives, public-private partnerships have been established to offer novel models for the discovery, development and deployment of vaccines to developing markets. The Global Alliance for Vaccines and Immunizations (GAVI), the Coalition for Epidemic Preparedness Innovations (CEPI), the Innovative Medicines Initiative (IMI), and the European Vaccine Initiative (EVI) are all examples of global efforts to bridge demand and supply.

GAVI was established to reshape the global vaccine market through a number of core elements.

It aggregates demand from the world's poorest countries to define a clear and viable market for vaccines (GAVI-supported countries today represent more than half the world's birth cohort), which also gives them the market power to negotiate lower prices from manufacturers

- It combines long-term donor support (79 percent from governments and 21 percent from private sources) with gradually increasing co-financing payments from participating countries to guarantee predictable funding so that
  - o Countries have the financial security to implement vaccine programs while maintaining a level of fiscal responsibility with GAVI
  - o Manufacturers feel confident enough to make new investments in production capacity, which help to decrease manufacturing costs

As an indication of success, for instance, the Advance Market Commitment program GAVI initiated in 2009 for pneumococcal vaccines is credited to have facilitated the immunization of over 184 million children between 2009 and 2018. Two countries – Mongolia and Bhutan – have been able to 'graduate' and fully self-finance routine immunization programs.

"Since 2011, I have been proudly serving Gavi as its CEO. During this time my focus has been to use my experience, as an epidemiologist and expert in vaccine development, to lead Gavi in its mission to improve access to new and underused vaccines and improve coverage and equity in poor countries. Under my leadership, in 2015 Gavi successfully raised US$ 7.5 billion in commitments during its last replenishment and has helped to reduce vaccine prices and assure a healthy vaccine market. This supported Gavi's largest expansion, immunising an additional 300 million of the world's poorest children and preventing 5-6 million deaths."

Dr Seth Berkley
CEO, GAVI

CEPI: NEW VACCINES FOR A SAFER WORLD

The Coalition for Epidemic Preparedness Innovations (CEPI) is a global partnership launched in 2017 to develop vaccines to stop future epidemics. CEPI was founded in Davos by the governments of Norway and India, the Bill & Melinda Gates Foundation, the Wellcome Trust, and the World Economic Forum.

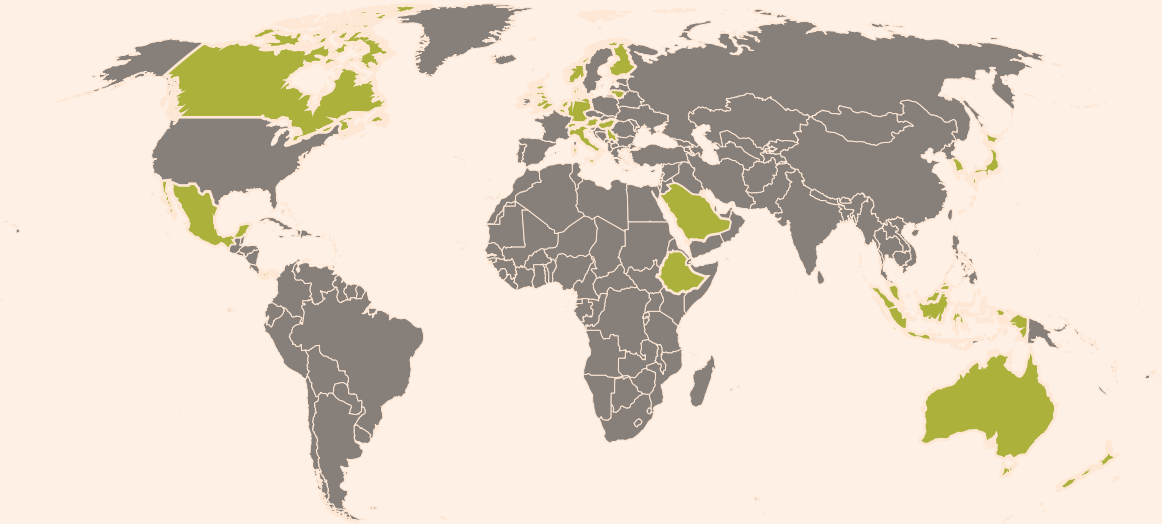
Since its launch, CEPI has mobilized more than US$750 million to support its mission.

To date, CEPI has secured financial support from:

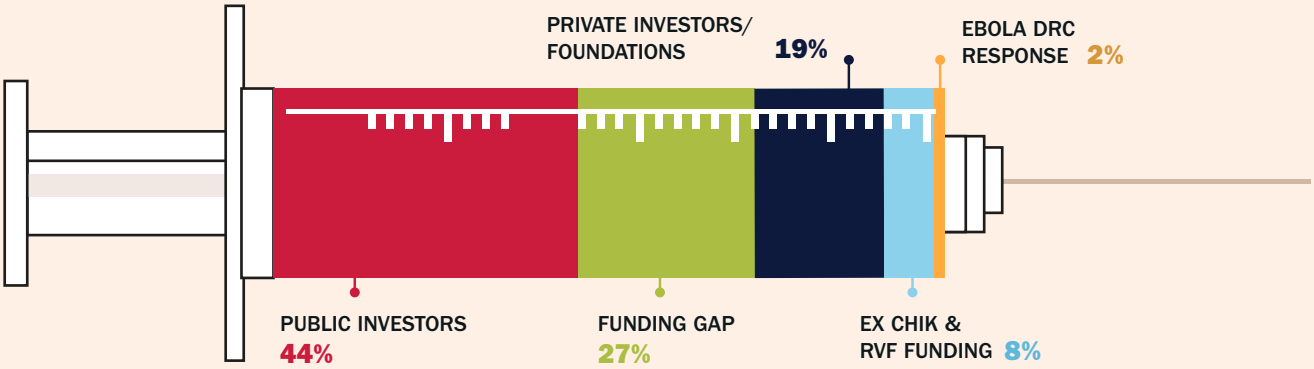
CEPI FINANCIAL SUPPORT

THE BILL & MELINDA GATES FOUNDATION · THE EUROPEAN COMMISSION · USAID · THE WELLCOME TRUST

AUSTRALIA
AUSTRIA
BELGIUM
CANADA
DENMARK
FINLAND
GERMANY
HUNGARY
ITALY
JAPAN
KUWAIT
LITHUANIA
LUXEMBOURG
MALAYSIA
MEXICO
NETHERLANDS
NEW ZEALAND
NORWAY
PANAMA
SAUDI ARABIA
SERBIA
SINGAPORE
SWITZERLAND
UNITED KINGDOM
ETHIOPIA
THE REPUBLIC OF KOREA
INDONESIA



TOTAL CONTRIBUTION PER INVESTOR CATEGORY, PERCENTAGE SPLIT 2017-2023



$570bn

The estimate annual global cost of moderately severe to severe pandemics

Eleven

The number of diseases WHO identified as public health risks due to epidemic potential and lack of biomedical countermeasures

$2.8bn

The minimum average cost for progressing one vaccine against each of WHO's 11 priority epidemic infectious diseases

THE 11 PRIORITY EPIDEMIC INFECTIOUS DISEASES:

- CRIMEAN-CONGO HAEMORRHAGIC FEVER
- EBOLA VIRUS DISEASE
- MARBURG VIRUS DISEASE
- LASSA FEVER
- MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS (MERS-COV)
- SEVERE ACUTE RESPIRATORY SYNDROME (SARS)
- NIPAH DISEASE
- HENIPAVIRAL DISEASE
- RIFT VALLEY FEVER
- ZIKA
- DISEASE X (A PATHOGEN CURRENTLY UNKNOWN TO CAUSE HUMAN DISEASE THAT COULD CAUSE A SERIOUS INTERNATIONAL EPIDEMIC)

CEPI INVESTMENTS IN PLATFORM TECHNOLOGIES

	ATTENUATED VIRUS	INACTIVATED	VIRAL VECTOR	PROTEIN SUBUNIT	DNA	RNA
Lassa			· Emergent rVSVNC4AG · Themis Measles vector · IAVI rVSVAG · U. Oxford/ Janssen ChAdOxl		Inovio DNA	
MERS-CoV			·Themis Meales vector · IDT MVA		inovio DNA	
Nipah			· U. Oxford/ Janssen ChAdOxl · PHV rVSVAG · U. Tokyo Measles vector	Profectus Subunit		
Rift Valley Fever	· Colorado State U. r RVF 3rd gen · Wageningen U. r RVF 2nd gen					
Chikungunya	Valneva Live attenuated	Under negotiation Inactivated	Themis Measles vector			

Source: CEPI Progress Report 2019

THE WORLD'S BESTSELLING VACCINE – FOR HOW LONG?

With sales of nearly USD 6 billion a year – just over 10 percent of overall revenues – Pfizer's Prevenar 13 (a Pneumococcal 13-valent Conjugate Vaccine) has emerged pretty quickly as the undisputed champion since its approval in the European Union in December 2019. Today, it is the most widely used pneumococcal conjugate vaccine in the world, and is included in the pediatric National Immunization Programs in 102 countries. In addition, it is the only pneumococcal vaccine approved for use for essentially all age groups.

Prevenar 13 is a vaccine for the prevention of serious and potentially fatal pneumococcal infections caused by 13 Streptococcus pneumoniae (S. pneumoniae) serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). Serious pneumococcal infections can result in pneumonia, blood poisoning, meningitis, permanent brain damage, and even death. Pneumonia is currently the single largest infectious cause of death among children under the age of five globally.

Prevenar 13 is slated to lose patent protection only in 2026, offering more breathing room to the world's largest pharma company, but the company already has a next-generation vaccine in development – a 20-valent pneumococcal conjugate vaccine, which covers seven additional bacterial strains as well as the 13 already addressed by Prevenar 13.

However, Pfizer's reign within the pneumococcal vaccine space is coming under threat as MSD (Merck & Co. in the US and Canada) is also developing a next-gen pneumococcal vaccine, though it would only cover 15 bacterial strains. (MSD does have an existing polysaccharide vaccine, Pneumovax 23, targeting 23 strains, but it is only approved for children two years or older). Both vaccine candidates have received Breakthrough Therapy designations from the US FDA. US biotech Affinivax also has a Phase 3 pneumococcal vaccine candidate that targets 24 pneumococcal serotypes and is being developed in partnership with Astellas. Affinivax's candidate uses the company's Multiple Antigen Presenting System (MAPS) in lieu of the traditional conjugate vaccine platform.

In other key markets such as China and India, local vaccine manufacturers are also eyeing a piece of the global pneumococcal pie. The Chinese regulator approved a 13-valent pneumococcal conjugate vaccine from Chinese drugmaker Walvax Biotechnology in January 2020 and the company expects to produce at least 30 million doses a year. In 2018, Pfizer supplied 3.85 million doses of Prevenar 13 to mainland China – whereas over 15 million babies were born that year. At the end of 2020, India announced its first indigenous pneumonia vaccine as well, which had been developed by the Serum Institute of India (SII) in collaboration with international partners like the Bill and Melinda Gates Foundation. SII touts itself as the world's largest manufacturer of vaccines by number of doses produced, with every third child in the world immunized by a vaccine from SII.

LESSONS FROM MSD'S EBOLA VACCINE DEVELOPMENT: BALANCING AMBITION WITH REALITY

While outbreaks of the devastating Ebola virus have – thankfully – generally been highly localized to West Africa, the highly infectious and lethal disease has generated global trepidation due to its characteristic haemorrhagic fever, a 50 percent chance of death on average, and the absence of any approved treatment. The most serious outbreak, occurring in early-2014 and ending two long years later, affected nearly 30,000 people and cause over 11,000 deaths, predominantly in Guinea, Liberia and Sierra Leone, igniting global efforts to develop a vaccine that could prevent future Ebola epidemics.

In 2019, MSD (Merck & Co. in the US and Canada) won that race when its vaccine, ERVEBO®, was approved by the European Medicines Agency (EMA) and the US FDA. All in all, it took just over five years for ERVEBO® to move from Phase

1 trials to regulatory approval, a significant advancement from the typical ten to 15 years it typically takes for vaccines to complete that journey.

However, ERVEBO® is not just MSD's triumph. The Ebola vaccine was initially discovered as a biodefense vaccine at the Public Health Agency of Canada (PHAC). Once efficacy was established in animal studies, a multitude of actors, both private and public, were assembled to take the Ebola vaccine candidate through clinical development. National governments from Canada, the US and Africa; agencies like the US National Institutes of Health (NIHs) and the US Biomedical Advanced Research and Development Authority (BARDA); global institutions like the World Health Organization (WHO), the Wellcome Trust, Gavi and Medecins San Frontieres (MSF) – all came on board.

Part of this extensive collaboration was necessary because, in spite of MSD being one of the Big Four vaccine players globally, the pharma company nevertheless lacked any prior experience with Ebola virus or clinical development expertise in the specific West African countries.

In addition, as Jayanthi Wolf [executive director, Global Regulatory Affairs, at MSD] et al. identified in an article ("Applying lessons from the Ebola vaccine experience for SARS-CoV-2 and other epidemic pathogens") regarding lessons learnt from MSD's Ebola vaccine development experience, each entity played a specific contributory role across the broad global partnership, spanning aspects including preclinical studies, Good Manufacturing Practices (GMP) materials, clinical studies, public health responses and so on.

> "Over 300,000 people were vaccinated through various emergency access programs"

Particularly relevant to the current COVID-19 pandemic, the authors also flagged the challenges with the necessary manufacturing scale-up. For instance, they noted that "technology transfer and the establishment of a new manufacturing facility has many steps and requires significant time to execute (3-4 years is typical for a new vaccine). There is limited understanding outside of vaccine manufacturers and regulators on the rigorous requirements leading to approval of a vaccine manufacturing facility." Furthermore, "manufacturing site selection for vaccines is a complex decision … [with] multiple factors, such as existing space, technical capability, infrastructure, and capacity."

For that reason, the authors exhorted, "all parties involved must work to balance the desire to be ambitious (e.g., rapid development timelines) with execution realities and stakeholder expectations. Aggressive timelines are enticing for public health partners, but also require "right-first-time" execution to qualify the facility and manufacturing process, for which the probability of success for a new vaccine is likely medium to low."

Another important lesson is the central role that the WHO has to play in rapid global approvals. The authors highlighted, "in order to accelerate vaccine access to African countries, the World Health Organization's Prequalification Team (WHO-PQT) in collaboration with the EMA and AVAREF [the African Vaccines Regulatory Forum] developed an innovative facilitated process (roadmap) for decision making on the acceptability of the vaccine for registration. This allowed the company to make simultaneous submissions to EMA, WHO-PQT, and regulatory authorities in 14 African countries, with EMA acting as the reference agency." Once ERVEBO® was conditionally approved in the EU in November, the WHO granted prequalification within 36 hours, and a month later, African countries began to approve the vaccine, resulting in near-simultaneous approval of the much needed vaccine in the areas where it was most desperately needed. For the MSD team, the takeaway when it comes to COVID-19 vaccines is that "regulatory agencies should prepare for the simultaneous approval of candidates in multiple countries. WHO's leadership will be needed to facilitate innovative review processes and collaborative mechanisms to expedite approvals."

Prior to regulatory approval, during the 2018-2020 Ebola outbreak in the Democratic Republic of the Congo, over 300,000 people were vaccinated through various emergency access programs. MSD has announced that licensed doses of ERVEBO® should be commercially available in Q3 2020. While prices have still not been officially set, the company has committed to pricing the single-dose injection at the lowest possible access price for poor and middle-income countries.

LOOKING LONG-TERM

Ole Olesen, executive director of the European Vaccine Initiative (EVI), outlines the mission of EVI to support the development of non-commercially viable vaccines as well as to create a global vaccine infrastructure.

Ole, you joined the European Vaccine Initiative (EVI) in January 2020 as executive director. Could you share the important work that EVI is doing within the global vaccine space as well as your motivations for joining the organization?

OLE OLESEN (OO): EVI is a non-profit organization focusing on vaccine development, and we have two fundamental missions. The first one is to support the development of new or improved vaccines that can have a major impact on global health but are not commercially viable and the pharma industry therefore is reluctant to invest in. We try to bridge that gap.

The second one is to work with other vaccine development organizations, academia, biotech and industry to create a network, and vaccine infrastructure, of stakeholders and partners for cross-cutting vaccinology related to aspects like pre-clinical development, standardization of assays for vaccine development, capacity building and advocacy.

Ole Olesen
Executive Director, European Vaccine Initiative (EVI)

With COVID-19 vaccine development updates making headlines almost every day, how has the pandemic affected the state of the overall vaccine industry?

OO: Looking at the big picture, the COVID-19 situation has generated a lot of global interest in vaccines, whether from public funders and private investors or amongst the general public. Whereas previously vaccines were a little out of fashion, and the sector was rather dusty and forgotten, now, people can see the importance of vaccine R&D quite clearly. The pandemic has reignited global interest in vaccine development, which is fantastic.

Of course, there has been similar events in the past such as the SARS outbreaks, the Ebola virus in West Africa and the flu pandemic but in those cases, the sudden interest ended up being relatively short-lived. This time, however, COVID-19 has had such a major impact globally that I believe it will be different. The other outbreaks were also much more geographically limited and in general never really hit the developed countries in Europe or North America, where, the reality is, most of the funding and also industrial activity are based.

As a vaccine community, we can continue to refer to this for many years to come – and we should in order to remind the world that with relatively small amounts of money consistently invested in vaccine development and public health programs, we can avoid outbreaks with such major economic impact in the future.

While more people seem to know about vaccines, it is unclear that many truly understand the mechanics of the vaccine industry. What should organizations like EVI do to address this?

OO: As a community, we have to seize this opportunity to stress that vaccine development needs a long-term perspective. With the support of the European Commission, EVI has been working for some years to establish a sustainable vaccine research infrastructure in Europe that can connect individual research teams and boost the development of new vaccines. This is an important step, but the vaccine sector will need sustained and substantial investments in infrastructure, vaccinology, immunology and related sciences over a long period. That is one of the messages that we should

make sure to communicate at both political and the societal levels.

Another message is that COVID-19 is unlike many other infectious diseases. Even if the COVID-19 vaccine process proves to be successful within a couple of years, it does not mean that other infectious diseases like malaria can see the same success. We do not want investors or the public or other stakeholders to start questioning why vaccine development for other diseases takes such a long time in comparison. The COVID-19 virus may turn out to be relatively simple to develop a vaccine for but diseases like malaria, tuberculosis and HIV are extremely complicated.

We also have to remember that there are many other diseases that are far more fatal than COVID-19. While COVID-19 fatalities are unfortunately increasing, a disease like tuberculosis, for instance, causes 1.3 million deaths every year, and yet tuberculosis remains a very forgotten disease that sees very little investment. in vaccine development. This indicates the mismatch between political priorities and the actual disease burdens that exist globally.

What has been quite interesting and a little unexpected is the level of cooperation and collaboration between public and private players during the COVID-19 crisis. What are your expectations for how this could carry over to other areas of vaccine development?

OO: A very positive takeaway has been the unprecedented levels of sharing and collaboration in science and research, for both publicly-funded and privately-funded projects. All players have been very open with their results and data. Many agencies have been pushing for open science and better data-sharing globally, and with the COVID-19 experience, we can see that it really does work in practice, and in fact, is probably a large part of the reason things have advanced so quickly.

One of our flagship projects is TRANSVAC2, which in collaboration with 25 vaccine research institutes across Europe, establishes a vaccine research and development service platform offered to vaccine developers. As individual research groups may not have the capacity to undertake a full vaccine development project on their own, the network helps connect researchers developing vaccine candidates to services and know-how that will contribute to the advancement of their vaccine candidate and their competences, for instance, in clinical development, animal models, adjuvants and so on. TRANSVAC2 creates the critical mass needed for vaccine development, and allows researchers with promising vaccine candidates to approach us to have their candidates and ideas tested and further developed.

We have been working on this concept since 2009 and we are now looking to develop a strategy to make this infrastructure permanent and sustainable. This could involve working with industry through means of sponsorship or potential licensing agreements, or with other entities.

Taking a longer-term perspective for the vaccine sector, what is needed to maintain the momentum generated by the COVID-19 pandemic?

OO: All available data, analyses and figures point in one direction: vaccines are some of the most effective and cost-efficient health interventions that could be made. Unfortunately, global investment has dropped steadily over the last couple of decades – if we do not consider the current COVID-19 period – to a large extent because many pharma companies have pulled out of vaccine development. That has reduced the total investment and overall interest because industry interest tends to attract academic research and public funding.

> “We do not want investors or the public or other stakeholders to start questioning why vaccine development for other diseases takes such a long time in comparison.”

From the industry perspective, the economic analysis is that the potential profit in vaccines tends to be smaller for vaccines compared to other therapeutic areas. Therefore, we do need to look for ways to improve that equation in order to incentivize vaccine development. This is another message I think is important to communicate to stakeholders, especially public investors, in a positive manner: vaccines are so important that we need to find a way to better reward people that work in this area.

A DISTRIBUTABILITY INDEX

Joe Lewis, managing director of Deloitte's Life Sciences Supply Chain Practice highlights some of the major issues surrounding vaccine allocation and deployment.

Joe Lewis
managing director, Life Sciences Supply Chain Practice, Deloitte, USA

Many industry leaders have highlighted the unprecedented scale of collaboration between companies and other institutions for the R&D and manufacturing of therapeutics and vaccines. How challenging has it been to integrate all the relevant manufacturing and supply chain systems and processes?

JOE LEWIS (JL): For COVID-related production, what we are seeing today is that governments and other public entities have commissioned a vertically integrated R&D, manufacturing and distribution network, and the major pharma manufacturers are effectively acting as contract manufacturers for these national and international entities. Within the US, that is Operational Warp Speed, who has procured large volumes of material, and globally, there is the COVAX facility, and of course, others.

These do present unique challenges. The main question that we have been grappling with surrounds clear decision rights and governance, i.e. who should be making what decisions. While many companies have the capacity and certainly deep experience in making all these decisions for themselves, they now need to collaborate with others to ensure the consistent delivery of product into the market.

When that product is a COVID vaccine, companies also need to account for the many differences that exist, for instance, in the regimens and the distribution requirements of different vaccine candidates. Against the backdrop of those differences, an important consideration is how to minimize the degree of variability that frontline healthcare workers have to deal with so that the vaccination process can be more efficient. Given the importance and scale at which COVID vaccines would be deployed, it is essential to minimize the opportunity for human error, which can occur if an individual is confronted with multiple decisions to make.

Having worked on vaccine allocation mechanisms for the flu vaccine, could you outline some of the considerations that would or should be going into these decisions?

JL: In the US, a lot of these decisions are being made based on the Advisory Committee on Immunization Practices (ACIP) guidance that has been delivered at the Federal level. Within that, the States are the ones with the task of identifying the relevant patient populations and then ultimately determining the final allocation methodology. From a theoretical perspective, state-level allocation depends on a number of fairly tangible factors such as population distribution, size and characteristics of at-risk groups, and so on. These are the quantifiable bases on which state-level allocation decisions are made.

Where it gets interesting is allocation below the state level, i.e. which hospital system the product should be sent to? That can, in theory, also be determined through factors like the vaccination capacity of each hospital systems, which, in turn, depends on the distribution requirements of the product. For instance, a product that has to be maintained and distributed at -70 degrees C is much more challenging to work with. A single-dose vaccine regimen likely requires less complicated planning than a double-dose vaccine regimen.

Another really interesting consideration comes in when a governmental agency may start calculating optimal distribution based on forecasted infection rates, with the idea that they could actually redirect vaccines into a specific area in advance of a predicted spike in infections. That is much more complicated because it is based on modeling and forecasting instead of quantifiable and observable elements, which means there could be different degrees of precision based on the tools used and the extent to which we are looking ahead into the future.

The challenge with such an approach is that it becomes much harder to explain why a decision was made. A much higher degree of trust within the population is required, particularly in the institutions and stakeholders undertaking such decisions.

Considering the global scale of the COVID-19 pandemic, how would the need to, say, store a vaccine at negative 70 degrees Celsius affect its manufacturing and supply chain planning process?

JL: The important question that we have encouraged companies to ask is not how a COVID vaccine would be similar to what exists in the marketplace but rather, how it would be different. I think about this in terms of a 'distributability index': the more distributable a product is, the more people that product can reach. A product that has to be maintained at negative 70 degrees Celsius and requires 22 kilograms of dry ice to keep the freezer cold could be really hard to administer outside of large population centers. That being said, these are engineering challenges that have solutions and there are robust precedents for products with similar requirements being successfully deployed.

The real issue is not actually delivering the product into the market, it is ensuring that individuals are successfully vaccinated. For COVID, we are talking about huge numbers of people that would ultimately need to go through the vaccination process. Beyond the delivery of the actual vaccine to be used, what processes and pathways are involved in the vaccination of an individual? We need to have healthcare personnel ready to administer the vaccine, we need to get the individual to the vaccination center, and so on. It is much easier to get the individual to the center once than to have him return in a few weeks for a second dose. This is the kind of concern that stakeholders need to look at.

Just looking within the US alone, we have a wide variety of population groups with different characteristics that need to be vaccinated. People in rural versus urban areas, people within at-risk populations, homeless populations, and so on – all have different access levels and behavioral factors that affect the likelihood of their being vaccinated successfully. In general, a product with a higher distributability index would be able to access a large portion of the overall population, whether we are talking about individual countries or the world as a whole.

As a hypothetical scenario, assuming that we have a number of approved vaccines with similar efficacy, I think it is reasonable that products with a lower distributability index could still be deployed within populations that are easier to reach, such as frontline healthcare workers. It is all about looking at the available vaccine options and then assessing the optimal portfolio and distribution of products based on the needs and characteristics of the population groups that need to be vaccinated that would ultimately improve community health outcomes.

Of course, the calculus becomes much more complex if different vaccines have different levels of efficacy, and especially if it is up to the frontline worker delivering the vaccination to select the right vaccine for the person in front of them. Here again, we return to the question of trust: the public would need to trust that the decisions being made are optimal for them and their communities. One critical aspect to remember here is that we are talking about complex manufacturing processes, which could come with challenges and missteps, so it is even more important for companies to build and then maintain public trust as they navigate these processes.

THE LARGEST VACCINE BUYER IN THE WORLD

UNICEF Supply Division director Eva Kadilli makes a call for further solidarity between stakeholders across the public sector, private industry, and civil society.

Eva, could you recap the important work that UNICEF is doing?

ETLEVA KADILLI (EK): UNICEF, or the United Nations Children's Fund, is the UN agency responsible for providing humanitarian and development aid to children worldwide. Our mission here in UNICEF's Supply Division is to deliver sustainable access to lifesaving supplies where they are most needed, accelerating results for the most vulnerable children.

UNICEF Supply Division is based in Copenhagen, Denmark, where we manage around USD 3.8 billion for the procurement of goods and services every year. Our supply operations support the overall program implementation of UNICEF, and our global warehouse in Copenhagen is the largest humanitarian warehouse in the world. We currently have a team of over 420 staff based here in Copenhagen and additionally nearly 1,200 supply chain staff working across 190 countries, where UNICEF delivers a multitude of programs across sectors such as health education, child protection, and sanitation.

We are the world's largest single buyer of vaccines, purchasing around 2.4 billion doses every year. Due to the particular needs of the storage and distribution of vaccines, we work with industry to ensure that the vaccines we procure move directly from the manufacturers to the governments and end users in nearly 100 countries.

Historically, how critical has the role of vaccines been in UNICEF's work with children globally?

EK: In the past two decades, we have provided life-saving vaccines to over 760 million children worldwide, preventing over 13 million deaths. We are also a founding partner of Gavi, the Vaccine Alliance. There is a well-established body of literature demonstrating the highly beneficial and cost-effective impact of vaccines as a public health intervention. Through vaccines, we have been able to address diseases like cholera, measles, and polio.

In addition to the provision of vaccines, we have also had a major role in market shaping for vaccines, in coordination with our partners, including Gavi and the Bill & Melinda Gates Foundation. Market shaping means ensuring that we are able to obtain affordable, quality-assured vaccines to ultimately reach every child.

Presently, there are still around 14 million children in the world that unreached by our efforts each year; we call them the 'zero dose children'. Major efforts will be needed to reach these children, particularly in the light of COVID-19, because the pandemic has had a major negative impact on immunisation programs globally. Countries have postponed over 100 immunisation campaigns this year. This means that many children are not receiving their vaccinations, putting them at risk for preventable diseases, and increasing the risks of outbreaks globally.

What are the typical challenges of access when it comes to these 'zero dose children'?

EK: It varies from vaccine to vaccine, but first and foremost, the issue could be awareness. This is why UNICEF works with local communities and community leaders, including religious leaders, as well as families directly, to communicate the life-saving impact of vaccines. We also work with and train local health workers to administer the vaccines and deliver these public health messages.

Etleva (Eva) Kadilli
Director (Supply Division), UNICEF

The second issue is distribution and access to hard-to-reach areas, particularly in remote or conflict-affected parts of the world. For most of these 'zero dose children', there are significant inequities and inequalities within the society that hinder access to vaccines, for instance, if we look at migrant or refugee populations. This is why we also have to work with governments across all levels.

The third aspect is affordability, which is why UNICEF invests in market-shaping efforts. Some vaccines are quite expensive. While lower income countries can benefit from negotiated pricing and development aid, we have seen that pricing may be prohibitive for middle- and upper-middle income countries, limiting access to these life-saving vaccines for children in these countries. Therefore, we also work with industry to try to promote a healthy market with appropriate pricing for equitable access to these life-saving tools.

The global COVID-19 pandemic is not the first public health emergency UNICEF has had to manage, though certainly the most global. What lessons has UNICEF learnt from previous crises like the Ebola outbreak that have proven useful this time around?

EK: The biggest challenge for us is that while responding to the immediate crisis caused by the global pandemic, we still needed to continue and coordinate our responses to other emergencies, such as the provision of vaccines and other health supplies to children in countries facing crisis, such as Yemen, South Sudan, Venezuela, even as COVID-19 has dramatically disrupted global supply chains to an extent we have not seen before.

About Eva Kadilli

Eva has been with UNICEF for nearly 25 years, including assignments at different country offices in the field in Africa as well as Central and Eastern Europe. In her current role, she oversee UNICEF's global supply chain functions, as well as manage UNICEF's supply response to humanitarian crises.

In addition, she is currently leading the Organisation's strategic procurement and logistics emergency response to the COVID-19 pandemic. She also represent UNICEF on the UN COVID Supply Chain Task Force.

DEMAND INCREASE

Source: UNICEF
Note: The demand surges represent estimates of UNICEF's procurement as a response to COVID-19 companing approximate quantities procured in 2019 to 2020. These numbers do not represent global demand surges since numerous actors procured medical supplies during the pandemic.

Another challenge we faced was the presence of counterfeit products, which is especially dangerous when it comes to medicines and personal protective equipment (PPE). It is reassuring that we have seen that our existing due diligence processes have proven strong enough to address situations like this in order to prevent sub-quality products from entering our supply chains at this critical time.

One of the learnings from our Ebola experience is the experience of implementing a Health Emergency Strategy. Back in 2014 and 2015, we worked out how to requisition PPE and other essential health supplies quickly so when COVID-19 occurred, we already had the contract processes, equipment specifications and so we needed to move fast on establishing an emergency global supply chain.

Through our experience and expertise in emergency responses, we have also been able to anticipate and prepare for potential challenges and situations that could arise as a result of COVID-19. For instance, we foresaw that access to therapeutic food (RUTF) for children with severe acute malnutrition could become compromised, so we worked quickly to diversify our global prepositioning of supply.

Ultimately, the most important aspect of our response has been the fact that we have extensive experience working in emergencies and we have boots on the ground, staff who know the local context extremely well and are able to undertake risk management. This helps our teams upstream understand the actions and initiatives they need to work on with partners such as industry manufacturers and global institutions, to support the right downstream response.

PLAYING ON REGIONAL STRENGTHS

Charles Chen of Taiwanese firm Medigen Vaccines Biologics Corp (MVC) reveals his company's commercial and growth strategy in a global vaccine market dominated by Big Pharma players.

Charles Chen
Vice Chairman & CEO, Medigen Vaccine Biologics Corp. (MVC)

Charles, could you start by introducing Medigen Vaccines Biologics Corp (MVC) and yourself to our international audience?

CHARLES CHEN (CC): I am the CEO and co-founder of MVC, and concurrently I am also a Distinguished Adjunct Professor of Bioinnovation at Temple University in Philadelphia, USA, and Chair Professor of Industry-Academia Collaboration at National Yang-Ming University in Taiwan. I have been in the vaccine business for nearly 40 years, working with both animal and human vaccines.

MVC is the first cell-based vaccine manufacturer in Taiwan with solid R&D capabilities to develop and manufacture vaccines and biosimilars. MVC is involved in several human vaccine developments, including H7N9 pandemic vaccine, H1N1/H5N1 pandemic flu vaccine, and vaccine against the EV71 virus that causes hand-foot-and-mouth disease (HFMD) for children under the age of six. We have also obtained a license for a dengue vaccine and an S-2P protein subunit adjuvanted COVID-19 vaccine from the National Institutes of Health (NIH) in the USA.

We were listed on the Taiwan OTC stock exchange in 2018. That same year, we received PIC/S GMP certification for our vaccine manufacturing plant.

What is MVC's commercial strategy for the vaccines you are developing?

CC: We have a local, regional, and global approach. Our COVID-19 vaccine will first be manufactured to meet the local needs. Taiwan has 23 million people so it has a significant market, and the government would very likely be our initial and most important customer. Already, the Taiwan government has demonstrated its willingness to financially support the development and production of COVID-19 vaccines.

Beyond Taiwan, we see our neighboring countries in Asia as important secondary markets. Countries like Vietnam, Thailand and Indonesia do not have cell culture production facilities, so these countries are potential markets. Japan and South Korea only have a couple of vaccine companies that use cell culture production. These countries are potential collaborators for us. We have already pursued a partnership with GC Pharma of South Korea for the import of their QIV.

From a global perspective, other markets also exist for us in Latin America and Africa. Of course, we also hope to address vaccine needs in developed countries since we have a PICS/GMP manufacturing facility that meets EU EMA and US FDA requirements.

The vaccine market is dominated by a couple of Big Pharma companies. What do you see as MVC's competitive advantage in this sector?

CC: Taiwan is not part of the WHO, so for us, it is important to establish bilateral, regional and international collaborations with other entities. We have to be nimble and work with both local and foreign partners.

I think we have a very strong pipeline and R&D activity, especially since many of our technologies and vaccines have been licensed from top institutions like the U.S. NIH. Some of the diseases we are targeting like the seasonal flu and dengue fever are global challenges; others are more regional. In some areas like HFMD, we are working in markets where Big Pharma is not involved.

Any final message you would like to send to the global vaccine community?

CC: Vaccine companies need to collaborate, not just compete. Preventative vaccines are essential to public health and I would like to see more regional, as well as global collaboration. After all, even if you solve a problem in your own country, if your neighbors are struggling with the same disease, you are still at risk.

MVC's goals are to serve local public health needs, build regional trust and alliances, and actively participate in meeting global needs.

Deloitte.

SECURING TRUST IN THE GLOBAL COVID-19 SUPPLY CHAIN

From development and delivery to acceptance and administration

Scientists have come together in an unparalleled worldwide collaboration to advance a COVID-19 vaccine.[1] As rollouts become reality, multiple vaccines will be necessary to meet the need for worldwide vaccination.[2] Each vaccine has its own specialized requirements, and each country has varying resources to accommodate them—making an already complex supply chain, even more complex and uncertain.

Trust will be a cornerstone for the successful launch, distribution, and acceptance of vaccines. Life science leaders will need to focus on the areas they can control, such as product integrity, behaving ethically, and communicating transparently.[3] To secure public trust, organizations will need to:

- Advance industry collaboration across the value chain
- Embrace and promote global standards for supply chain security
- Anticipate challenges for safe and efficacious delivery of vaccines
- Use clear and transparent communications for vaccine confidence

Being proactive is key.[4] Those who achieve a strong degree of public trust will have successfully conveyed their humanity and transparency, while meeting uncertainty head-on in the global COVID-19 supply chain.[5]

Advancing industry collaboration

According organizations like ClinicalTrials.gov and FasterCures, there are approximately 4,000 studies underway globally for vaccines and therapies related to COVID-19.[6] More than 200 trials are specific to vaccine development and vary by technology, conditions for storage, location, and size of clinical trial.[7] The World Health Organization (WHO) tracks progress on the development of vaccine candidates around the world.[8]

Key trials open to public scrutiny

Rapid development of COVID-19 vaccines was driven by unusually open and transparent information sharing among all stakeholders. Vaccines moved from concept to Phase 3 trials to Emergency Use Authorization (EUA) in a record-breaking 11 months.

A few companies with leading COVID-19 vaccines (e.g., Oxford/AstraZeneca, Johnson & Johnson's Janssen Pharmaceuticals, Moderna, and Pfizer/BioNTech) shared protocols for a "real time" exchange on the scientific, deliberative, and inclusive trial process. Industry cooperation, that includes universities and other unaffiliated organizations, is a great win for public trust.[9]

According to Johnson & Johnson's Chairman and CEO Alex Gorsky, pharmaceutical companies are not competing against each other on the development of a vaccines but collaborating with the world's top scientists to save lives.[10]

> **The best possible position we could be in is where we have four or five or six of these vaccines available in the year 2021.** Alex Gorsky, Chairman and CEO, Johnson & Johnson[11]

Leading candidates are already demonstrating exceptional efficacy rates from clinical trials, and vaccines will continue to be robustly tested and monitored for safety as they are administered in real world conditions.[12]

The difference between efficacy and effectiveness

With such high degrees of efficacy being achieved for early vaccine candidates, it is important to communicate that efficacy is not the same as effectiveness. According to Gavi, the Vaccine Alliance, efficacy is the degree to which a vaccine prevents disease, and possibly also transmission, under ideal and controlled circumstances, i.e., comparing a vaccinated group with a placebo group in a clinical trial. Effectiveness refers to how well the vaccine performs in the real world. It will require several months after a vaccine is administered to a population to demonstrate its effectiveness.[13]

Worldwide demand for billions of vaccine doses

As production ramps up, countries and groups have secured their supply with contracts from multiple vaccine manufacturers (Figure 1). For most COVID-19 vaccine products, two doses of vaccine, separated by 21 or 28 days, will be needed from the same manufacturer. Not only does a vaccine need to be available for a patient at a specific time interval, it will need to be the same vaccine.

The UK has begun vaccinating those over 80,[14] and priority access will likely go to health workers in the EU. In the US, initial doses will be designated for frontline health care workers followed by nursing home residents and staff.[15]

From laboratory to patient, extraordinary collaboration will be required between governments, NGOs, private companies, not-for-profit organizations, and health care providers to ensure that no single dose is wasted and to enable pharmacovigilance.[16]

	VACCINE MANUFACTURERS & DOSES CONTRACTED								
Country/ Group	Pfizer/ BioNTech	Moderna	JNJ	AstraZeneca	Sanofi/ GSK	Novavax/ Takeda	CureVac	Valneva	Sinovac
USA	100M (initial purchase w/ opp to buy add'l 500M)	100M (initial purchase w/ opp to buy add'l 400M)	100M	300M	100M	100M	n/a	n/a	n/a
EU	200M (initial purchase w/ opp to buy add'l 100M)	160M	200M (initial purchase w/ opp to buy add'l 200M)	400M	300M	n/a	225M (initial purchase w/ opp to buy add'l 180M)	n/a	n/a
Japan	120M	50M	n/a	120M	n/a	250M	n/a	n/a	n/a
United Kingdom	40M	5M	30M	100M	60M	60M	n/a	60M (initial purchase w/ opp to buy add'l 130M)	n/a
Latin America (excluding Brazil)	n/a	n/a	n/a	250M	n/a	n/a	n/a	n/a	n/a
Brazil	n/a	n/a	n/a	100M	n/a	n/a	n/a	n/a	120M
Canada	20M	56M	38M	n/a	72M	76M	n/a	n/a	n/a
Australia	10M	n/a	n/a	33.8M	n/a	40M	n/a	n/a	n/a
Indonesia	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	40M

* Data as of November 25, 2020 Source: Deloitte Analysis

Supply chain will rely on public-private partnerships and institutional trust

In response to the pandemic, the Access to COVID-19 Tools (ACT) Accelerator was launched to provide innovative and equitable access to COVID-19 diagnostics, treatments and vaccines.[17] COVAX is the third pillar of the ACT Accelerator focused on vaccines, and the initiative is being coordinated by Gavi–the Vaccine Alliance, the WHO, and the Coalition for Epidemic Preparedness Innovations (CEPI).[18] COVAX is working with manufacturers towards an initial aim of 2 billion COVID-19 vaccine doses by the end of 2021, and more than 180 countries have joined the initiative.[19]

Protecting supply chain integrity is an important aspect of ACT's broader multi-agency effort,[21] and all coordinating members of COVAX have extensive experience in resolving logistics challenges. Collectively, these organizations also represent a high degree of institutional trust.[22]

Institutional trust is a critical factor in influencing preventive behavior during an outbreak.[23]

> "Our belief in a fast-moving pandemic is you're not safe unless everyone is safe. What the COVAX Facility (figure 2) is trying to do is to get a vaccine out to all countries, rich and poor, at the same time." [20]
>
> Dr. Seth Berkley, Chief Executive Officer, Gavi

Embracing global standards

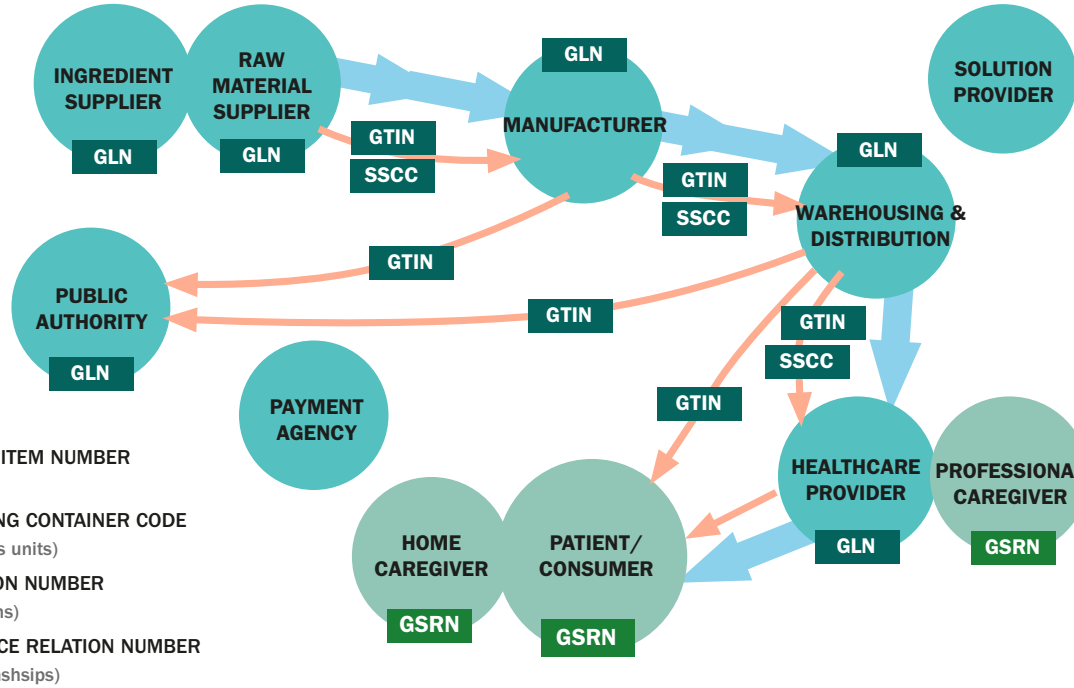
Minimizing supply chain hiccups, advancing interoperability

COVID-19 vaccines and therapeutics, plus associated medical devices and consumables, present an urgent need for a system of traceability built around globally identified products. The not-for-profit global standards organization GS1 (Figure 2)[24] has developed the most widely utilized supply chain standards.[25]

Use of global GS1 standards means that every product, at every level of packaging, is uniquely identified. This identification information is captured in a standardized barcode that is able to be read by all supply chain partners.[26] In addition to vaccines, standards provide a level of trust for:

FIGURE 2: GS1 GLOBAL DIGITAL THREAD IN SUPPLY CHAIN

Source: GS1



GTIN - GLOBAL TRADE ITEM NUMBER
(product identification)

SSCC - SERIAL SHIPPING CONTAINER CODE
(identification of logistics units)

GLN - GLOBAL LOCATION NUMBER
(identification of locations)

GSRN - GLOBAL SERVICE RELATION NUMBER
(identification of relationshsips)

- The medical supplies needed to administer vaccines
- The medicines and medical devices required to treat COVID patients
- The personal protective equipment needed to protect clinical caregivers and the population

Vaccine identification information (like product identifier, lot number, and expiration date) is essential for health care providers to administer vaccines with confidence. Embracing GS1 standards harmonizes implementation of regulatory requirements and adds an element of trust at all levels of the supply chain—a trust that ultimately extends to the patients themselves.[27]

Marking vaccines with GS1's DataMatrix

More than 70 countries have health care regulations or trading partner requirements for which industry uses GS1 standards. Today, these countries, as well as Gavi and UNICEF, rely on GS1's DataMatrix two-dimensional (2D) barcodes that can encode vaccine information to reduce errors and improve efficiency and safety.[28]

Following the WHO's recommendations, a DataMatrix should be applied on the secondary packaging (carton boxes), and if possible, also on the primary packaging (vial or prefilled syringe). While every country has its own specific requirements, the DataMatrix is able to encode:

- The vaccine identification code
- Date of expiration
- Lot number
- Serialization (depending of the packaging level)

The global alignment on the use of global standards for identification and barcoding of the vaccines will enable traceability across borders to reduce falsification, enable precise product identification in patient health records, and facilitate recalls or adverse event reports. The European Medicines Agency (EMA) and EU Member States agree that COVID-19 vaccines will have to meet the requirements for the EU Falsified Medicine Directive for identification and labelling.

Scaling up product identification and traceability

In the first wave of the pandemic, hoarding was, and may continue to be, an issue. Traceability gives health care providers and authorities better visibility and control of medicinal inventory and allows manufacturers and health authorities to accurately plan. Traceability is the ability to track forward the movement of product through specified stages and trace backward its history, application, or location. Today, more than 70 countries today have track and trace systems, while the EU has established an end-to-end verification system.

Serialization is a form of product identification whereby a specific drug pack has a globally unique number. This number is used to confirm its authenticity along the supply chain prior to sale, dispensing, return, or recall. Although not every country with traceability requirements has serialization requirements, many countries and regions have established traceability systems or are developing them.[29] Building a traceability system now, not only addresses immediate challenges, but is an investment for the future.

Anticipating challenges for safe and efficacious delivery of vaccines

Product integrity and safety monitoring

Globally unique identification and barcoding of the vaccines will not only be critical for clinical trials and distribution, but for administration sites. It is important to identify and label the vaccines, capturing precisely which patient, received which vaccine, and when. Visibility enabled by aggregating global data will engender a higher degree of trust.

While controlled randomized trials may reveal some side effects, adverse reactions that are uncommon, or that occur in subpopulations, may not emerge until the vaccine is widely distributed.[30] A robust patient contact protocol is essential for contacting affected patients quickly and efficiently.

Optimizing delivery and last mile cold chain challenges

Administration sites will need to have capabilities for storing, handling, and administering vaccine products, and the cold chain requirements for these vaccines are an unprecedented logistical challenge.[31] Health care workers may not be equipped to deal with these special requirements, and

vaccine administration will need to be organized in such a way that vaccines are tracked and not wasted. Multi-dose vials, once opened, may expire within hours.[32]

What is a "cold chain"?

Delivering vaccines around the world takes a chain of precisely coordinated events in temperature-controlled environments. Vaccines need to be continuously stored and transported in a specific temperature range, that varies by vaccine—from the time they are manufactured until the moment of vaccination. To keep vaccines at specific cold temperatures requires special equipment like cold rooms, refrigerators, freezers, cold boxes, and vaccine carriers. For example, Pfizer's mRNA vaccine needs to be stored at "ultra-cold" temperatures. [33]

The Pfizer/BioNTech vaccine requires "ultra-cold" storage at minus 70° Celsius ±10°C (-94° F) and can be kept up to 15 days. Once thawed, the vaccine vial can be stored for up to 5 days at refrigerated (2 - 8oC, 36°- 46°F) conditions.[34] Moderna's vaccine requires standard refrigerator temperatures and can be kept up to 30 days. [35] CureVac says its mRNA vaccine, currently in Phase 1 trials, could be stored for up to three months under normal refrigeration.[36]

According to German logistics company DHL, only 25 countries have the necessary ultra-cold storage infrastructure, and remote areas throughout the world are not likely to receive some of these vaccines. The already limited refrigeration in most of Africa, central and southeast Asia, India, and smaller countries in Latin America, cannot accommodate minus 70° Celsius.[37]

Vaccines being developed via traditional methods and with less stringent refrigeration requirements, like the Oxford/AstraZeneca and Johnson & Johnson vaccines, will be critical for low- to middle-income countries with limited cold chain capabilities, extreme weather conditions, or very remote populations.[38] However, even in the developed world, rural areas will be disadvantaged.[39]

Technologies, such as barcodes and Vaccine Vial Monitors (VVM), will be critical to ensure that product integrity is preserved, and the cold chain has not been broken. Trust at the last mile will also mean that patient safety protocols are followed, and patients can be assured that vaccines are safe and not counterfeit.

> "Nothing would undermine delivery of successful COVID-19 vaccines and therapeutic treatments faster than the emergence of fake vaccines."
>
> Tom Woods, Chairman of the Global Steering Committee for Quality Assurance of Health Products for the World Bank [40]

Track and trace and global standards play a critical role in monitoring product integrity. During the first few months of the pandemic, an 18 percent increase in counterfeit products was observed, and the first fake COVID-19 vaccines already came onto the market in South America.

Anticipating alternative administration sites for marginalized populations

Vulnerable, remote, and minority populations need to be engaged earlier to earn and build trust. Vaccine manufacturers are already trying to educate the public and are creating vaccine content especially targeted to minority communities most impacted by the virus.[41]

Individuals may be fearful or wary of seeking vaccination at sites that have historically caused mistrust or are otherwise unsafe. Alternative sites to traditional medical settings should be considered that may also provide urgently needed services, like food aid, employment aid, or other preventive health services.[42] These off-site locations will require additional precautions —like social distancing and masks—to protect caregivers and patients and ensure trust.[43]

Achieving herd immunity and vaccine uptake

Some experts are optimistic that multiple vaccines could represent an end to the pandemic,[44] while others are concerned that people will be reluctant to take the vaccines, especially in rural or remote areas.[45]

Herd immunity cannot be achie-ved without sufficient uptake of COVID-19 vaccines that some experts believe will need to be higher than 70 percent.[46] Vaccine uptake may be threatened in any country, region, or community where there is waning confidence in the government, doctors, or public health officials.[47]

> **Vaccines don't save lives. Vaccinations save lives. Persons for whom vaccines are recommended need to receive them if there is to be a benefit to the individual as well as society.**
>
> Walter Orenstein, MD, Professor and Associate Director, Emory Vaccine Center [48]

Using clear and transparent communication to build vaccine confidence

Vaccine uptake will need to be facilitated by clear, evidence-based, and tested communications. Culturally appropriate, translated materials for education should be available to clinicians tasked with vaccinations, and public health workers will also need to be culturally competent.[49]

People trust those in their networks, and act when they trust the messenger. Trusted voices and immunization of community leaders and celebrities could play a role in compelling members of the public to vaccinate. Vaccine expert Dr. Walter Orenstein suggests collaborating with trusted leaders of culturally diverse groups to disseminate information and to reassure people. These communications need to be transparent and include:

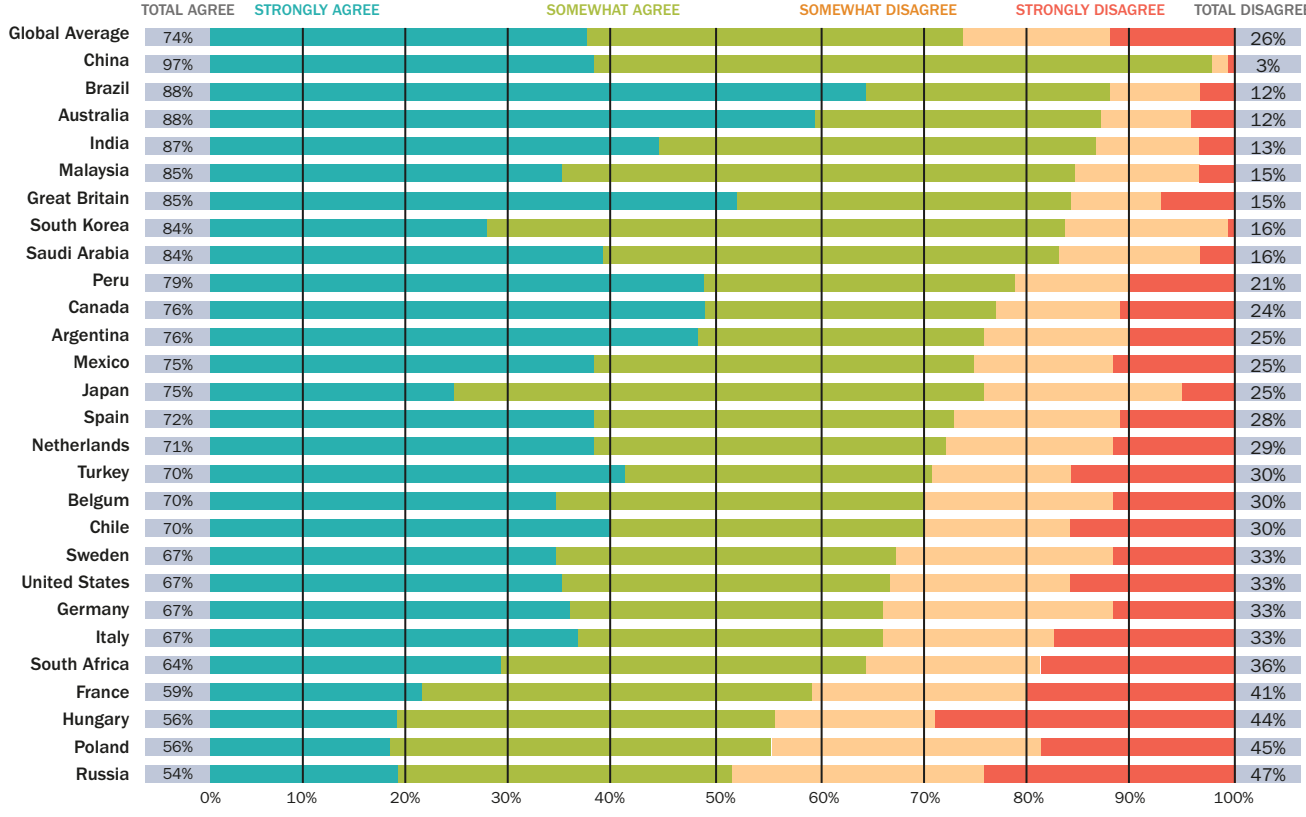
- Information on vaccine development, including criteria for approval
- Strength of the data for each vaccine's safety and effectiveness
- Information on how side effects and adverse events will be monitored[50]

Tracking vaccine confidence

Confidence in the safety of vaccines fluctuates around the world.[51] In September 2020, the World Economic Forum and Ipsos conducted a global survey of nearly 20,000 adults across 27 countries (Figure 3). Those willing to get a COVID-19 vaccine accounted for 74 percent of people surveyed. But the 26 percent shortfall in

FIGURE 3: INTEREST IN GETTING A COVID-19 VACCINE*

* Data as of September 1, 2020 Source:World Economic Forum



those not willing is significant enough to compromise the effectiveness of rolling out a COVID-19 vaccine.[52]

Trends in public sentiment around the globe are being tracked by the Vaccine Confidence Project at the London School of Hygiene and Tropical Medicine (LSHTM). This project seeks to monitor public confidence by listening for early signals of public distrust through population surveys and social media analysis.[53]

According to the project's founder and director, Dr. Heidi Larson, public engagement strategies for COVID-19 vaccines[54] will require building trust, not take down misinformation. "It will just move," she says, as an advisor to health ministries, pharmaceutical companies, NGOs, and social media companies.[55]

Overcoming vaccine hesitancy

The WHO defines vaccine hesitancy as 'the delay in acceptance or refusal of vaccines despite the availability of vaccination services'[56] Wider skepticism of COVID-19 vaccines is being led by anti-vaccination groups and concerns about the speed of the vaccine development process.[57]

Doubts may be further increased by:

- Any falsified or substandard product
- Unplanned side effects and serious adverse events
- Unavailability of vaccines or associated products when needed

Establishing an interoperable traceability system that ensures product integrity is key for both worldwide perception of trust and the actual trustworthiness of vaccines, as well as other medicinal products.

Vaccine risk communications and community engagement

According to the Framework for Equitable Allocation of COVID-19 Vaccine, those responsible for vaccination risk communication and community engagement programs need to have:

- Agility, to respond rapidly to changing circumstances and feedback
- Competence, to apply relevant risk communication research
- Diversity, to involve needed perspectives
- Independence, to secure trust and provide candid feedback[58]

People's choices are affected by how they see the world, and supplying a narrative provides value.[59] The motivation to be vaccinated results in actual vaccination only if practicalities of availability, accessibility, cost, convenience, service quality, and incentives are all addressed.[60] For vaccine developers, health care stakeholders, and society at large, the level of transparency and public trust will determine COVID-19 vaccine acceptance and confidence.[61]

Conclusion

In an unprecedented way, the world has come together quickly for the fair and equitable distribution of vaccines to conquer the largest disease threat of our time, COVID-19. How we continue to respond and collaborate will define the world we continue to inhabit. Health care providers have been tasked with the biggest burden. Government leaders, regulators, and public health authorities need to continue to be sensitive to their safety and the resources they need. Leaders need to behave ethically and reassure the communities they represent.

The life science industry's innovation is on a world stage, and the pandemic has accelerated adoption of new technologies. We need to not step back, but collectively move the world forward. Global standards, like GS1, ensure supply chain security, increase patient safety, and provide trust in the vaccines, medicines, and medical products distributed.[62]

Health care workers will need to be trained and equipped to handle the massive undertaking of vaccine administration. Public-private partnerships should be maximized, and community leaders and influencers engaged. Raising immunization levels will depend on product integrity and transparent, culturally appropriate communications. Public health authorities will need to reduce vaccine hesitancy and build vaccine confidence. Public trust is paramount.

Everyone deserves to be safe. Meeting this challenge depends on all of us.

> "As the world gears up for the largest deployment of vaccines in history, it is more important than ever that supply chains are up to the task of maintaining trust and ensuring effective, timely delivery. We need to be able to trace every vaccine dose—from shipping to delivery and finally administration—using technologies such as 2D DataMatrix barcodes, and we need better adoption of common standards across to optimize cost and product visibility."

Dr. Seth Berkley, Chief Executive Officer, Gavi

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COMBATING VACCINE HESITANCY

MSD SVP and President of Mid-Europe Region (Nordics, Mid-Europe, CEE & Balkans) Cyril Schiever outlines why vaccine hesitancy is such a threat to global health, the misinformation around vaccines being spread online, and how multi-stakeholder collaboration can help counter this emerging problem.

The World Health Organization (WHO) recently identified vaccine hesitancy as one of the top 10 global health threats for 2019, alongside major health challenges such as climate change, non-communicable diseases, antimicrobial resistance, and Ebola. The problem is magnified by the spread of fake news and online misinformation.

Europe's measles epidemic isn't likely to end without major changes in the approach to vaccination

We are witnessing a global trend of decreased vaccine confidence. According to a recent survey in 67 countries, the least confident seem to be the population of France (41%), Bosnia (36%), Russia (28%), Mongolia (27%), and Greece/Japan/Ukraine (25%).[1] This compares to the global average of 12%, and points to a problem that goes beyond each country's borders.

One only has to turn on the TV these days to see and hear about measles outbreaks causing deaths or disabilities, long after we have discovered a very effective vaccine to prevent the disease. Measles is a serious cross-border health threat in the EU. The cost of these outbreaks, socially and economically, will be substantial not only in the short term, but also in the long term, and it will take a long time for Europe to recover. Europe's measles epidemic isn't likely to end without major changes in the approach to vaccination.

But the problem is not confined to Europe. Many countries are in the midst of sizeable measles outbreaks. Current outbreaks include the Democratic Republic of the Congo, Ethiopia, Georgia, Kazakhstan, Kyrgyzstan, Madagascar, Myanmar, Philippines, Sudan, Thailand, and Ukraine, causing many deaths – mostly among young children.

This is why, recently, the World Health Organization (WHO) identified vaccine hesitancy among the top 10 global

Cyril Schiever

Cyril Schiever is Senior Vice President and President of Mid-Europe Region for MSD (Nordics, Mid-Europe, CEE & Balkans), leading a $2.7 billion business in a region of 25 countries and over 2000 employees. Prior to this role, Cyril was SVP and Managing director of MSD in France, successfully leading a business of $1.5 billion. Cyril was a Board member of the LEEM (industry association) and was elected President of the LEEM legal commission in December 2014. He was also Secretary of Agipharm (French association of US pharmaceutical companies). Prior to that, Cyril led MSD's subsidiary in Canada. Cyril's entire career has been international, first with Sanofi, then Schering-Plough and MSD. He held several executive roles in different geographies.

health threats for 2019, alongside major health challenges such as climate change, non-communicable diseases, antimicrobial resistance, and Ebola. [2]

A lot has been written globally on the causes of vaccine hesitancy: what can be done to mitigate it and improve immunisation coverage rates? But I want to touch on one of them, namely, misinformation.

There has been a rise in online misinformation on vaccine safety

There has been a rise in online misinformation on vaccine safety. False information, which is created, liked, and shared by vaccine sceptics, is circulating on social media, damaging the public's confidence in vaccines. Consequently, there is an increasingly poor understanding of the value of vaccines, which then has a knock-on effect on immunization rates across the world.

Community members are fueling each other's concerns behind closed doors. To complicate matters, people are able to create (closed) virtual communities of like-minded individuals, who seek out information sources they feel comfortable with. Thus, people get more information they already agree with and few (if any) alternative views in online "echo chambers". This results in anti- and pro-vaccine messages being shared and replicated in isolated groups, which polarizes conflicting views even further.

Additionally, search engines filter content based on an individual's online behaviour and perceived preferences. This means social media users effectively surround themselves with content which aligns with their pre-existing values and beliefs and fail to see the other side of the argument. This leads those who hold 'extreme' or controversial opinions to have a distorted perception of the prevalence/popularity of their views.

Studies have shown that fake news spreads six times faster than regular news.[3] The lack of accountability, freedom of speech, leveraging emotions, and the lack of effort required to share something online, are only a few of the reasons why false messages spread fast. Anti-vaccination influencers know very well how to use these tactics. On the other hand, the public health and scientific community is struggling to engage with the public and communicate the right messages. Evidence-based statements, and the reports and the voices of trusted, credible scientific and public health leaders, don't reach this social media space. To be effective communicators, we need to bridge this gap.

Just as vaccine hesitancy is complex and multifaceted, so, too, is the solution to building confidence and preserving trust. There is no "one-size-fits-all" approach. Vaccination programs exist in the context of a broad and diverse ecosystem, comprised of multiple stakeholders ranging from individuals and communities to health systems, as well as governments and public health leaders.

Coordination among these groups can create resilient systems, which are critical for generating and preserving high levels of vaccine confidence and driving vaccination uptake. In addition, we now see social media platforms taking action, by, for example, demonetizing and reducing recommendations and rankings of anti-vaccination content or groups – some of them even decided to block or remove anti-vaccination materials.

We are also learning from the collective experiences of a variety of vaccines across the life course – from polio to measles, and from influenza to HPV. We are now starting to identify and document the characteristics that comprise a resilient immunization system, and that can protect and build vaccine confidence across the life course.

As a pharmaceutical company, we have a role and responsibility to work alongside public health authorities, healthcare providers and communities around the world to communicate the benefits of vaccination and improve access to potentially life-saving vaccines. We recognize that collaboration across all sectors of the immunization ecosystem is critical to improving public health through vaccination.

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DELIVERING HEALTH GLOBALLY

Larry St Onge
president, Life Sciences and Healthcare, DHL

Sitting atop the DHL life sciences and healthcare supply chain infrastructure, Larry St Onge shares his experience and insights dealing with an unprecedented global pandemic.

When the COVID-19 pandemic began, how did DHL begin to respond to the emergent and urgent needs of the pandemic while at the same time maintaining normal supply chain operations for your regular customers?

ROGER CONNOR (RC): The first challenge was the breaking down of the global supply chain in relation to personal protective equipment (PPE). This was a struggle faced by institutions across all sectors, and especially the public sector, and while we worked to restore and protect the integrity of that supply chain, we also took the opportunity to step back and take a more macro perspective instead of being granularly focused on it at the ground level.

Therefore, at that point, we took a step back and thought, okay, we have built this enterprise infrastructure, the 'Life Sciences and Healthcare System', comprising more than 9,000 associates across more than 130 locations around the world, that is designed to support our Life Sciences and Healthcare customers. We are able to leverage our extensive knowledge of the global supply chain landscapes, and serve the urgent needs of our customers by mapping their global supply chains to identify the new potential risks that would arise as a result of the COVID-19 pandemic – and thereafter, to support the supply chains and build more resilience into them.

In addition to the risk and resilience challenges, we needed to understand the quality requirements of different institutions and geographies, and how we can manage the routine audits of respirators and other equipment to guarantee that they met these standards? These were all questions we were able to formulate and answer quickly due to our deep experience and track record within this sector.

We also identified the need for a public-private interchange or a form of network or system that could better track global movements of medicines and medical supplies. If logistics companies like ours would have been given the visibility at the worldwide level of the medicines, therapies and equipment being used to treat COVID-19 during the initial outbreak, perhaps we could have helped the world reposition some of that inventory and, as a result, reduce casualties, to some degree.

All of the above have been key factors for us as we have pushed forward through the crisis to ensure that we can leverage our capabilities and knowledge in the best possible way. Ultimately, I think supply chains will never be the same as they were, pre-pandemic. This is now the "new-normal". If companies are still managing their supply chains in the same way as they had pre-coronavirus, they are probably going to get it wrong. We do not want to get it wrong. We want to be part of the solution and to support our customers' ability to deliver the best services and care to patients globally.

The COVID-19 pandemic has also compelled many governments and other institutions to reevaluate their approaches to pandemic preparedness efforts, which had previously been underfunded. How can DHL support these types of strategic planning initiatives at the governmental and institutional levels?

RC: We have published a White Paper on 'Delivering Pandemic resilience' in September, where we highlighted some key points and opportunities for the world to prepare for a better healthcare supply chain in the event of another pandemic and also regarding how public and private sectors can partner for success in the delivery of COVID-19 vaccines.

What is absolutely imperative for all of us is the need to build a collaborative public-private framework that can drive a focus on the creation of a more resilient supply chain globally. We need more data tools to be able to map, manage and retain visibility of the flows of products. This might come in the form of a blockchain-enabled platform, for instance. Ultimately, the goal is to connect the supply chain all the way from labs to patients, so as to speak.

LOGISTICAL IMPLICATIONS OF COLD CHAIN REQUIREMENTS - EQUIPMENT EXAMPLE FOR A POTENTIAL SUPPLY CHAIN SETUP

Source: DHL, McKinsey

We also see an important opportunity for the private sector to be of value to the public sector here. Governments have found themselves quite challenged and stretched at various moments during the pandemic, and this is a result of them lacking the 'intellectual sweat equity', as I would call it, when it comes to understanding and dealing with the stringent requirements and standards of the life sciences and healthcare industries. We are talking about critical aspects like Good Distribution Practice, Good Manufacturing Practice, compliance, and so on, that are incredibly complex.

But DHL has invested heavily in solutions for all types of medical supplies and products, including high-value drugs, cold chain capabilities, and so on, so we can provide that expertise and that knowhow to public institutions and government entities. Right now, the focus is on deploying the COVID-19 vaccines and hopefully the world will return to some semblance of normalcy by the second half of next year, but beyond that, we need to keep pushing and rebuild a stronger global supply chain infrastructure for the world.

Fingers crossed that we do not see another global pandemic but if you had to gift a few words of wisdom to your successor, what would you like to say?

RC: If I were passing the baton to someone else right now, I would say, continually be pushing to think about what could happen. Think about all the 'what if's, even as some seem absolutely beyond the realm of reality. I think that is critical. 12 months ago, no one predicted this COVID-19 situation – not a single forecaster or AI machine.

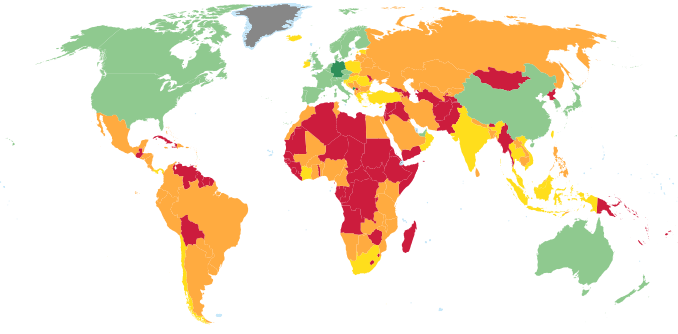
Healthcare is one of the focus sectors for DHL as an enterprise, and the company is committed to this sector from the very top down. Healthcare is absolutely the most important thing we help to provide, and the underlying imperative that I strongly believe everyone – from a DHL company perspective to manufacturers to healthcare providers to patients – needs to understand is the fact that, healthcare works best when the logistics do too.

FEASIBILITY OF IN-COUNTRY LOGISTICS AT DESTINATION

Feasibility LOW HIGH

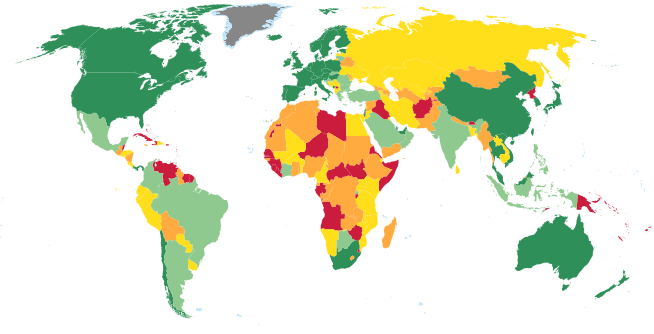
SCENARIO 1: STRINGENT TEMPERATURE REQUIREMENTS

High feasibility at scale[1] in ~25 countries with total population of ~2.5bnof ~5.0bn



SCENARIO 2: CONVENTIONAL TEMPERATURE REQUIREMENTS

High feasibility at scale[1] in ~60 countries with total population of ~5.0bn



1 "Feasibility" considered as high and relatively high feasibility to distribute COVID-19 within destination countries (marked with dark green and green color code)

Source: World Bank, DHL, McKinsey

We speak directly with healthcare leaders and pharmaceutical executives globally.

PHARMA BOARDROOM