

Dr Michael Etter

Chief Medical Officer, Asia Pacific
Fresenius Medical Care

Speaker

Dr Amgad Gamil

Senior Director, Medical & Scientific
Affairs, Emerging Markets, Vaccines
Pfizer

Speaker

Dr Sanjoy Datta

Vice President Medical & Clinical
Greater China & Intercontinental
GSK Vaccines

Speaker

Professor John Lim

Executive Director
Centre of Regulatory Excellence,
Duke-NUS Medical School

Moderator

Professor Hsu Li Yang

Vice Dean (Global Health)
Programme Leader (Infectious Diseases)
NUS Saw Swee Hock School of Public Health

Panelist

Mr Simon Gordon

Chief Commercial Officer
Accredify

Panelist

COVID-19 VACCINATION FACTS AND FICTION

eBook produced for "Covid-19 Vaccination: Facts and Fiction"
Webinar held on 15 June 2021

SUMMARY

On 15 June 2021, the European Chamber of Commerce (Singapore) invited distinguished speakers from Fresenius Medical Care, Pfizer, GSK, Accredify, NUS SSH School of Public Health, and Duke-NUS Medical School to share their knowledge with the public in a webinar titled "COVID-19 Vaccination – Facts and Fiction". The aim was to discuss the issues related to COVID-19 vaccinations and provide clarity of facts to combat inaccurate information in the public domain.

One of the key takeaways from the event was that the speed of development of the vaccines was not due to any compromise in clinical development standards or regulatory oversight.

The mutation of the virus has been a cause of concern for the public.

As conversations turn towards reopening borders both here in Singapore and elsewhere, there is a need for governments and health authorities to efficiently verify an individual's vaccine information to manage the safe re-opening of the country. Digital vaccine passports were highlighted as a viable solution.

Last but not least, as COVID-19 shifts from a pandemic toward an endemic state, mass vaccinations continues to be a key intervention to protect the population against severe diseases.

INTRODUCTION

There are multiple aspects to consider when looking at the COVID-19 pandemic and the vaccines. Initially, no one knew much about the virus which would later be known as SARS-CoV-2. The speed at which the virus spread, combined with the lack of effective treatment options, put an enormous strain on healthcare systems around the world.

As the epidemic turned into a pandemic – it became clear that vaccination would be one of the best solutions to address COVID-19 going forward. Everyone was enthusiastic about the prospect of vaccines and much of the conversation started revolving around when these would become available.



Mr Anbu Srinivasan,
Chair of EuroCham
Healthcare Committee

THE PURPOSE OF
THIS WEBINAR IS TO
GET THE KEY
ACTORS TOGETHER,
TO ADDRESS SOME
GAPS, TO PROVIDE
NUANCED
INFORMATION.

Several manufacturers promptly announced the development of COVID-19 vaccines. While this process was underway, non-pharmaceutical interventions such as hand-washing, disinfection, safe distancing, and the use of protective equipment such as masks, were key in trying to contain the spread of COVID-19. Protective equipment was of even more importance in the healthcare sector where frontline workers were at high risk. A rigorous implementation of these measures from the beginning, when nothing else was available, have helped control the number of infections until vaccinations became available.

VACCINES ARE NOT A SILVER BULLET AGAINST COVID-19

While global vaccination programmes are being carried out, it is still important to maintain other non-pharmaceutical interventions to protect the population.

Infection prevention and control with non-pharmaceutical interventions includes:

- Hand-washing
- Disinfecting hands and surfaces
- Personal Protection Equipment (PPE) including masks, face shields, gloves etc.
- Social distancing, isolation and cohorting of staff

EDUCATE AND INFORM

It is essential to keep different parts of the population informed and updated - medical workers, caregivers as well as patients.

Communication for each of these target audiences differs and sensitivity to their context can potentially affect how they absorb information.

PRIORITISATION OF VACCINES

As vaccines have become available globally, governments had to make decisions on who should receive the first doses as most countries received a limited supply of vaccines. For many countries, frontline workers were prioritised for vaccines.

However, it was not initially evident that securing vaccinations for patients with chronic diseases was just as vital. It required clear communication and collaboration between the various stakeholders to ensure that the doses of the COVID-19 vaccines reached the right people in the right order according to risk.

MISINFORMATION

Information is key in the battle against the spread of diseases and in this case, COVID-19.

Unfortunately, a lot of misinformation about vaccines spread quickly through social media. Reductionist or sensationalistic news headlines, impeded the acceptance of vaccines, with rejection rates being as high as 50% and above among patients and medical staff in countries where vaccines had become available.

While conspiracy theories abound, it was and is imperative for the healthcare industry to address the different concerns of different stakeholder groups such as patients, caregivers, and health professionals. Targeted approaches are needed for each group to give accurate information about vaccines, allowing them to make informed decisions.

THE MEASURES
WE HAVE IN
PLACE SHOULD
CONTINUE UNTIL
THE POPULATION
HAS ACHIEVED
IMMUNITY.



Dr Michael Etter
Chief Medical Officer, Asia Pacific
Fresenius Medical Care

Dr Etter shared his views on the importance of continuing non-pharmaceutical interventions while the population is receiving vaccination.

CONTINUED VIGILANCE AND DISCIPLINE

Until vaccines are able to offer protection to a greater proportion of the population, it is important that everyone continues diligently the habits that ensure infection prevention, such as the wearing of masks and hand-washing.

STAGES OF COVID-19 CLINICAL TRIALS

Phase I:

Small study with 50 participants after the pre-clinical stage; the aim is to look for proof of principle and the safety of the vaccine.

Phase II:

Involves between 50 to 100 individuals; proof of concept is established at this stage, and again, the safety of the vaccine as well as the immunogenicity of the vaccine. This is also the stage of the trials to determine the optimum dose and to examine the different schedules used.

Phase III:

Also known as the Pivotal Licensure Studies, this is a bigger study that can reach up to 10,000 participants where the main focus is on vaccine efficacy and vaccine immunogenicity, and once again, the safety of the vaccine.

Phase IV:

Referred to as the Post Marketing Studies, this is where the vaccine is introduced to the population. Safety of the vaccine remains a top priority as well as its effectiveness.

The difference between the vaccine efficacy in Phase III and effectiveness in Phase IV is that efficacy is measured in a trial setting with a small inclusion/exclusion criterion and a well-defined design of the study, whereas effectiveness refers to the vaccine's performance in real-world setting.

AN ACCELERATED COVID-19 VACCINE DEVELOPMENT PATHWAY

During the pandemic, many clinical trials were carried out simultaneously. Results from these trials were collected, published and analysed, and necessary amendments were reviewed and made with regulatory authorities without the usual wait.

Most companies were also studying multiple platforms at the same time.

For example, Pfizer-BioNTech was studying four different mRNA platforms until they arrived at the one that was finally selected.

Recruitment of patients and individuals for the clinical trials was also much easier and faster due to the on-going pandemic. Pfizer-BioNTech was able to test its mRNA-based COVID-19 vaccine candidate on 44,000 individuals in five different countries and the same is true for the other pharmaceutical companies producing COVID-19 vaccines.

700 MILLION
DOSES HAVE
BEEN
DISTRIBUTED
ACROSS 100
COUNTRIES.



Dr Amgad Gamil
Senior Director
Regional Medical Lead
Emerging Markets, Vaccines
Pfizer

Dr Gamil shared his views on the scale of Pfizer-BioNTech mRNA vaccines distributed and how real-world evidence of efficacy and safety continues to be observed from different countries.

Regulators such as USFDA and EMA also showed great agility during the pandemic by expediting their reviews and using emergency use and conditional authorisation.

By prioritising and channelling resources, and using expedited pathways, National Regulatory Authorities were able to accelerate access to vaccines without compromising on safety or efficacy.

EVALUATING COVID-19 VACCINE CANDIDATES

VACCINE EFFICACY

The US FDA required the vaccine to have a minimum of 50% vaccine efficacy for authorisation. The majority of the authorised vaccines have at least 50% vaccine efficacy or above. The Pfizer-BioNTech and Moderna mRNA vaccines had a high efficacy of 90% and above in their Phase III trials.

NEUTRALISING ANTIBODIES

Another important criterion is the level of neutralising antibodies produced by those vaccinated.

Because there was no correlate of protection, the levels of neutralising antibodies (of those who were vaccinated) were compared with the antibody levels of convalescent serum (ie, from those who had recovered from COVID-19).

IMPACT ON CELLULAR RESPONSE

The impact of the cellular response was likewise important for the regulatory authorities as it was evident from the beginning of the pandemic that CD4 and CD8 played a key part in the transmission of COVID-19. Some vaccines showed an effect on these cells in a way that they helped to decrease the transmission and by providing a longer duration of protection.

DURABILITY

Regulatory authorities also look at the durability and the duration of protection of the vaccine. Although the majority of the pharmaceutical companies producing vaccines published their studies after three or six months, they are still tracking the population health trends and gathering additional data.

SAFETY

Safety is such a priority for regulatory authorities and pharmacovigilance departments in industry. Pharmaceutical companies often have independent data monitoring committees who also evaluate safety alongside the pharmacovigilance departments of manufacturers.

STORAGE AND DISTRIBUTION

The last evaluation criteria revolve around storage and distribution of these vaccines.

FOR VACCINE PLATFORMS LIKE THE MRNA, WE DID NOT SEE ANY CONCERN THAT PROTECTION HAS BEEN REDUCED (AGAINST THE DIFFERENT VARIANTS).

SCHEMATIC OF A VIRUS

In order to understand the impact of mutations and variations in a virus, it is important to understand the basic components of a virus particle.

Viruses are either DNA- or RNA-based. A virus is a very simple form of life and its main goal is to reproduce itself but it is unable to do this on its own. The virus can only reproduce itself by having its genetic material enter another cell.

When a virus infects a cell, it takes over the functions of that specific cell to reproduce itself, but by doing so it can manifest disease in the host.

Viruses often have surface proteins which enable the genetic material to enter the cells, and hence, understanding the surface protein is often important to stopping the virus from entering the cell.

IMPACT OF MUTATIONS ON DISEASE AND VACCINES

Mutations are common in viruses, and especially so for RNA viruses.

DNA viruses tend to be more stable, meaning that when the parental virus reproduces itself the progeny viruses are usually quite well preserved.

RNA viruses are not as stable, and often have random mutations when reproducing themselves, which is why the genetic material such as surface protein is very important. An example would be the influenza virus which has a different predominant circulating strain almost every year due to mutations, which requires an adapted vaccine to be developed accordingly.

However, sometimes a shift can also potentially occur through reassortment of the genetic material, which creates an almost immunologically unrecognisable virus compared to the original. This is the case with the SARS CoV-2 virus.

THERE ARE LIMITS TO HOW MUCH THE SPIKE PROTEIN CAN EVOLVE - BECAUSE IF IT MUTATES TOO MUCH, IT CANNOT INFECT AS WELL AS IT WOULD OTHERWISE.



Dr Sanjoy Datta
Vice President
Medical & Clinical
Greater China &
Intercontinental
GSK Vaccines

Dr Datta explained why it is good news that present vaccines have selected the spike protein as an antigen.

Many types of coronaviruses are constantly circulating but a large shift in a virus is what can make it particularly dangerous to humans and starts a pandemic.

While the surface protein enables the virus to enter the cell, the surface protein is also easily recognised by the immune system which makes it an excellent vaccine antigen candidate.

However, as the virus mutates the surface protein may change, thus impacting the efficacy of the vaccine.

If the change in the surface protein is not too significant and similarities remain, the vaccine may yet still be protective. In some cases, it could also be an option to add an adjuvant to the vaccine (which almost behaves like a “turbo booster” for the immune system in terms of its response) which may enable broader protection to mitigate against mutations.

VACCINE PASSPORTS

Following cases of fraudulent COVID-19 test results being reported around the world, there is a need for governments and health authorities to efficiently verify an individual's vaccine information to manage the risk of community infection once domestic and international movement is permitted.

Such verification processes place considerable strain on governmental resources, and a more efficient and secure method is needed.

A unique solution of digital vaccine passports, typically in the form of a mobile application, storing verifiable COVID-19 vaccination records can resolve this issue.

The technology to verify the authenticity of COVID-19 vaccination documents provides governments, immigration officials and airlines with a reliable method to ensure that an individual has been vaccinated. The vaccination schema could include which vaccine and when the vaccine was administered.

In addition, due to the nature of blockchain technology, which verifiable COVID-19 vaccination records leverage on, any changes made to the contents of an individual's vaccination record will be displayed once the document has been scanned for verification. A verifiable vaccination record's proof-of-tamper would hence provide relevant parties with the necessary information for their COVID-19 compliance policies which may be implemented once the world opens up for travel.

Digitally verified documents also provide the opportunity for automation which would be in line with automated processes many airports have already implemented for regular passports.

Currently, verifiable COVID-19 test results which are being issued in some countries allow authorities to easily verify a traveller's COVID-19

health status with a QR code scan within an individual's digital vaccine passport.

This solution can be integrated into international immigration gantries at airports or even domestically in offices and shopping malls to facilitate the safe reopening of international travel and re-entry into the workforce.

**WE NEED A
BETTER WAY
FOR VERIFYING
PARTIES TO
AUTHENTICATE
(VACCINATION)
INFORMATION.**



Mr Simon Gordon
Chief Commercial Officer
Accredify

Mr Gordon demonstrated why it may be necessary to look into verifiable document solutions to overcome security risks related to the leak of healthcare information.

QUESTIONS

Vaccination versus antibodies:

How different will the results of an antigen test turn out, between a vaccinated person and that of someone who has recently recovered from COVID-19?

EXPERT ANSWERS

An antigen test attempts to diagnose an active COVID-19 infection. If a vaccinated person does get infected, and the antigen test is administered early enough, that antigen test will become positive. If a recently recovered COVID-19 patient gets infected (which is unusual), that antigen test will also become positive. So because they test for antigen and not antibodies, there really is no difference between a vaccinated and a recently recovered person or a vaccine-naive person.

Why are these two populations (vaccinated and unvaccinated) not treated equally for quarantine?

For people who have antibodies, and who have recovered, they are assumed to be free of the infection. As they have passed the period where they are infectious, they can be released relatively earlier. Whereas for a vaccinated person, currently, we still err on the side of caution because we understand that vaccinated persons can still be infected, so they are quarantined still for the full period when they are in Singapore.

Mixing Vaccines:

Many people have received the first dose of the Vaccine A, but there's a shortage and they will not be able to receive the second dose of Vaccine A. However, they have a large supply of Vaccine B. Should they receive a second dose of another vaccine?

At this stage, there is no clear scientific or regulatory basis for the mixing of different vaccines in terms immunogenicity and the safety of one vaccine. However, the governments in some countries, have started also to use different vaccines for individuals due to supply shortages and the desire to protect populations. Ideally, the scientific basis for this should be available, whereas it currently is not.

IDEALLY, THERE SHOULD BE PROPERLY DESIGNED CLINICAL TRIALS TO HAVE THE DATA FOR REGULATORS TO MAKE THAT DECISION, AND THEN FOR THE MINISTRIES OF HEALTH TO IMPLEMENT THEM.



Professor John Lim
Executive Director
Centre of Regulatory Excellence
Duke-NUS Medical School

Prof Lim shared his views on vaccine mixing.

Misinformation:

Could you comment on the misinformation that is circulating and causing concern, and causing people to think twice about taking vaccinations?

It is good to acknowledge that these concerns are real and not all of these concerns are malicious. Vaccines are safe. In fact, virtually all vaccines have no long term side effects, or no side effects that come on long term after more than a few months. It is true that we don't know enough about mRNA vaccines, so we are collecting that data systematically as we go along. We should take an approach where we acknowledging what we do not know, while also strongly advancing what we do know about the safety of these vaccines when addressing such concerns.

**IT IS GOOD TO
ACKNOWLEDGE
THAT SOME OF
THESE
CONCERNS ARE
REAL. AND NOT
ALL OF THESE
CONCERNS ARE
MALICIOUS.**



Professor Hsu Li Yang
Vice Dean (Global Health)
Programme Leader (Infectious Diseases)
NUS Saw Swee Hock
School of Public Health

Prof Yang discussed addressing vaccination fears and misinformation about vaccines.

Is there a common clearing house for vaccine safety information?

At the global level, the regulators communicate. For example, there is the International Coalition of Medicines Regulatory Authorities (ICMRA) which played an instrumental role last year when evaluations were ongoing for new COVID-19 diagnostics and vaccines. And they continue to facilitate sharing of information, including on adverse events. There is also the Uppsala Monitoring Center under the World Health Organisation. So, there are mechanisms for sharing such information globally.

Can one safely assume that an infected person has recovered fully from the virus will no longer be infectious? And if that is indeed true, how have medical trials and treatment proven that the pathogen has been eradicated?

What different countries have done, (China, US, Germany, much of Europe and even Singapore) was to systematically test patients with COVID-19, at the start of the pandemic, and then cultured out the virus from the samples. We know that, for the most part, we are not able to obtain viable virus after about 11 days. This is borne out by the real-world experience of the US CDC. The US was releasing patients from isolation after one week, and in other jurisdictions after about two weeks. We have found that these people generally did not cause secondary infections. There are exceptions, for example those who are severely immunocompromised and who can still shed viable virus for several weeks. They, presumably, could still be infectious but those are just a very small part of the population.

Dr Michael Etter
Speaker

Dr Amgad Gamil
Speaker

Dr Sanjoy Datta
Speaker

Professor John Lim
Moderator

Professor Hsu Li Yang
Panelist

Mr Simon Gordon
Panelist

COVID-19 VACCINATION FACTS AND FICTION

View the webinar on:
[https://eurocham.org.sg/event/
webinar-covid-19-vaccination-facts-and-fiction-2/](https://eurocham.org.sg/event/webinar-covid-19-vaccination-facts-and-fiction-2/)
