INTERNATIONAL SOS WEEKLY SCIENTIFIC UPDATE
Focussing on immunity and vaccine development

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In this edition:

A. Vaccine Development & Approval

1. UK begins “rolling reviews” of COVID-19 vaccines

Bloomberg reports that the UK Medicines and Healthcare Products Regulatory Agency has begun “rolling reviews” of data related to the Pfizer and AstraZeneca vaccines in order to be able to rapidly approve the first vaccines shown to be effective and safe.

The Agency has also been conducting an expedited review of the AstraZeneca vaccine, which the company is co-developing with the University of Oxford.

The UK joins the EU in conducting this type of “rolling review.”

2. CDC Panel Takes on COVID Vaccine Rollout, Risks, and Side Effects

Medscape (password protected site) reported on a 30 October webcast meeting of the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC).

There were two main decisions that ACIP would have to make when any COVID-19 vaccine is authorized for use:

1. Whether ACIP recommends that the vaccine be given to adults, and
2. The allocation to priority groups to receive the vaccine first.

Note: While the FDA may issue an EUA for a particular vaccine, ACIP then makes the recommendations for the use of the vaccine.

“ACIP members repeatedly expressed discomfort with the prospect of having to weigh in on widespread use of COVID vaccines on the basis of limited evidence.”

“There will be strong pressure to distribute doses as quickly as possible…but questions will persist about the possibility of serious complications from these vaccines, ACIP members noted.”

"’My personal struggle is the ethical side and how to balance these two,’ said ACIP member Robert L. Atmar, MD, of Baylor College of Medicine, Houston, Texas.”

‘"I struggle with following people for two months after their second vaccination as a time point to start making final decisions about safety,’ said ACIP member Sharon E. Frey, MD, a Professor at St. Louis University School of Medicine, St. Louis, Missouri.”

3. CureVac's COVID-19 vaccine triggers immune response in Phase 1 trial

CureVac's experimental COVID-19 vaccine triggered an immune response in humans, the German biotech firm said in a statement on 2 November; mass testing involving about 30,000 volunteers may start later this year.

CureVac uses the mRNA platform, the same as Moderna and Pfizer candidate vaccines, although they started mass testing on humans in late July.

CureVac is backed by German biotech investor Dietmar Hopp, the Gates Foundation and GlaxoSmithKline. The statement said that in earlier trials volunteers developed a level of neutralising antibodies equivalent to people who had recovered from a serious case of COVID-19.

B. Outbreaks and Epidemiology

1. Fourth day of zero cases in Melbourne

We reported on 26 October that Melbourne had begun easing its 111-day lockdown. Today, Melbourne recorded its fourth day of zero COVID cases. Further easing of restrictions, including the ability for Melburnians to visit rural Victoria, is expected on 8 November.

2. United trials rapid COVID tests for New York-London route

Executive Traveler reports that United Airlines will test the utility of rapid coronavirus testing on flights to London from Newark, New Jersey, hoping that a pre-departure testing regime can provide a way to make customers feel more confident about the safety of air travel and to ease quarantine rules. The pilot program will run from 16 November to 11 December.

United will offer the Abbott Laboratories 'ID Now' rapid molecular (PCR) tests free of charge; results will be available within 20 minutes.

Customers flying from the US to the UK, even with a negative test, would still be subject to the UK's 14-day quarantine policy.

Since United introduced testing on its San Francisco to Hawaii flights around two weeks ago, the number to travellers has nearly doubled.

3. Australian study determines true asymptomatic COVID rate

There has also been uncertainty over how many people infected with SARS-CoV-2 are truly asymptomatic, and what that means for efforts to try and limit the spread of the disease.

A new systematic review and meta-analysis has provided the clearest indication yet of how many people who contract coronavirus remain symptomless throughout – as opposed to being pre- or mildly-symptomatic.

According to the paper, only around 17% of cases are thought to be truly asymptomatic, a much lower rate than the US Centers for Disease Control and previous studies have suggested. It also found transmission rates are lower by about 42% for asymptomatic cases when compared with symptomatic cases.

4. Travelers to New York must test negative for COVID before entry

Starting 4 November 2020, out-of-state travellers will be required to test negative for the coronavirus before and after they enter New York, Governor Andrew Cuomo announced on 31 October.

The new testing strategy replaces the state's travel advisory which required people to self-isolate for two weeks when traveling from COVID-19 hotspots.

"There will be no quarantine list. There will be no metrics." Cuomo said. "There will be one rule that applies across the country."

Under the new rule, travellers to New York must test negative within three days before their arrival and have proof of a negative test. While in New York, they are required to quarantine for three days and take another test on the fourth day. If the test is negative, they can end the quarantine. Persons not taking the test must quarantine for 14 days.

For more information on travel restrictions, International SOS Members should login here.

5. Liverpool to trial mass COVID-19 testing

The UK Government has announced that everyone living or working in Liverpool, with or without symptoms, will be **offered** a test for COVID-19. This is the first trial of whole city testing in England.

The pilot, due to start on 6 November 2020 will help to collect data on the utility of mass testing for COVID-19 and whether it could / should be used more widely.

"'These tests will help identify the many thousands of people in the city who don't have symptoms but can still infect others without knowing,' said Prime Minister Boris Johnson. 'Dependent on their success in Liverpool, we will aim to distribute millions of these new rapid tests between now and Christmas and empower local communities to use them to drive down transmission in their areas.'

"'It is early days, but this kind of mass testing has the potential to be a powerful new weapon in our fight against COVID-19.'"

6. COVID tests should play bigger role in international travel: WHO Expert

Didier Houssin, Chair of the Independent Panel of Experts advising WHO on the COVID-19 pandemic, said on 30 October in a press conference that COVID tests should be more widely used in international travel than quarantine. Professor Houssin also said that it was important for the UN agency to provide fresh guidance on safe international air travel.

WHO's emergency expert, Mike Ryan, said that travelling was now "relatively safe" and posed a "relatively low" health risk but that "there is no zero risk".

"Therefore it is a trade-off that countries have to make, the risk of a traveller arriving and potentially starting another chain of transmission, against the obvious benefit of allowing travel from a social and an economic point of view," he said.

C. Immune Response

1. T-cell Immunity 'May Last Longer Than Antibodies

A non-peer-reviewed preprint from the UK Coronavirus Immunology Consortium shows robust cellular immunity remains at six months after infection in individuals who experienced either mild/moderate or asymptomatic COVID-19.

The study also found that cellular immunity is stronger at this time point in those people who had symptomatic infection compared with asymptomatic cases.

The study concludes that more research is required to determine whether symptomatic individuals are better protected than asymptomatic individuals against reinfection in the future.

2. Will leading vaccines induce sterilizing immunity?

1. Leaders v's "next batch" of vaccines

The COVID-19 vaccines leading the race to be registered, are also, in general, using newer vaccine technologies. The "next batch" of vaccines are generally using more traditional vaccine technology. This is discussed in a Reuters article published 29 October.

Current leaders (newer technologies)
- mRNA technology: Moderna and Pfizer
- Inactivated cold virus platforms: Oxford/AstraZeneca, Johnson & Johnson and CanSino
- Based on a weakened measles vaccine platform: Merck

Next batch (more traditional technologies)
- Protein-based technology: Sanofi (same technology as "Flublock")
- Purified protein technology: Novavax
- Inactivated virus vaccine: Sinopharm (China)
- Virus-like particle technology: Medicago (Quebec)
- Nasal spray: Xiamen University, Hong Kong University, Beijing Wantai Biological Enterprose)

2. Will the leading vaccines produce sterilizing immunity?

Both Dr Anthony Fauci** and Kate Bingham*** (UK Vaccine Taskforce) have commented recently that the "first batch" of vaccines may only prevent symptoms and severe disease (non-sterilizing immunity) and not stop disease entirely (sterilizing immunity).

Professor Terry Nolan**** discussed the reason for this in the ABC Coronacast on 30 October 2020. Professor Nolan noted that the leading vaccines had produced strong immune responses in humans however none of them had produced sterilizing immunity in animal challenge studies – including monkeys. While severe disease was prevented in the animals, the virus remained in the nose and other fluids and thus the animals were probably still infectious.

Vaccines causing non-sterilizing immunity have implications for:

- The management of vaccinated people who subsequently become infected. Will they need to be isolated as they may still be infectious?

- The concept of herd immunity, as that is only relevant for a vaccine (or infection) that induces sterilizing immunity.

3. Will next generations of vaccines induce sterilizing immunity?

Terry Nolan notes that there is a huge scientific effort with "lots of new ideas" and he expects that some of these vaccines will produce sterilizing immunity.

4. However, leading vaccines MAY produce sterilizing immunity after all

Both Professor Terry Nolan and the Reuters article note that IF one of the leading vaccines safely induces sterilizing immunity, it may make is harder for companies producing "next batch" candidate vaccines to complete their studies and bring their vaccines to market.

We anxiously await the first vaccine trial results…..which could be available in 4-6 weeks.

** **Dr. Anthony Facui:** Director of the National Institute of Allergy and Infectious Diseases, USA
*** **Kate Bingham:** Manager, UK Vaccine Taskforce
**** **Professor Terry Nolan**: Doherty Institute, University of Melbourne, Murdoch Children's Research Institute, Melbourne

D. Operation Warp Speed

In previous editions we have described the COVAX and CEPI initiatives. Today we present information on Operation Warp Speed, a US initiative to provide COVID-19 vaccine to the US domestic market. Operation Warp Speed has also had significant implications for the international development of COVID therapeutics and vaccines.

In this article we will concentrate on only COVID-19 vaccine development.

1. What is Operation Warp Speed (OWS)?

OWS is a US public–private partnership whose major goal is to produce and deliver 300 million doses of safe and effective COVID-19 vaccine to the US market with the initial doses available by January 2021. It is also tasked with delivering COVID-19 therapeutics and diagnostics.

OWS also supports the mass production of multiple vaccines based on preliminary scientific evidence allowing for faster distribution if clinical trials confirm one of the vaccines is safe and effective.

OWS has three focus areas: vaccine development, vaccine manufacture, and vaccine distribution.

2. Finances of OWS

US Congress allocated approximately $10 billion for Operation Warp Speed.

3. Who is involved in Operation Warp Speed?

The main "players" in OWS are:

- Private companies
- US Department of Health and Human Services (HHS)
    - Centers for Disease Control and Prevention (CDC)
    - National Institutes of Health (NIH)
    - Biomedical Advanced Research and Development Authority (BARDA)**
- US Department of Defense (DoD)

** BARDA: The Biomedical Advanced Research and Development Authority (BARDA) is a US Department of Health and Human Services (HHS) office responsible for the procurement and development of medical countermeasures, principally against bioterrorism, including chemical, biological, radiological and nuclear (CBRN) threats, as well as pandemic influenza and emerging diseases.

4. OWS Vaccine Development

OWS has a goal to build a diverse project portfolio including two vaccine candidates based on each of the four platform technologies. Throughout 2020, OWS has selected the most promising vaccine candidates and has been providing coordinated support. This allows vaccine trials to proceed more quickly.

The selected vaccine candidates are:

- Johnson & Johnson (Janssen Pharmaceutical)
- AstraZeneca-University of Oxford
- Pfizer-BioNTech
- Moderna
- Merck and IAVI
- Novavax
- Sanofi and GlaxoSmithKline

To speed development, rather than eliminating steps from traditional development timelines, OWS has allowed steps to proceed simultaneously, such as starting manufacturing of the vaccine before the demonstration of vaccine efficacy and safety as happens normally. This is called "at risk" manufacture.

Major OWS vaccine development milestones:

- March: $456 million in funds for Johnson & Johnson's (Janssen) candidate vaccine
- April: $483 million in support available for Moderna's candidate vaccine
- May: $1.2 billion in support for AstraZeneca's candidate vaccine
- July: $1.6 billion in funds to support the large-scale manufacturing of Novavax's vaccine candidate
- July: $1.95 billion to Pfizer for the large-scale manufacturing and nationwide distribution of 100 million doses of their vaccine candidate
- July: $2 billion to support the advanced development, including clinical trials and large-scale manufacturing, of Sanofi and GlaxoSmithKline's (GSK) investigational adjuvanted vaccine

- August: $1 billion to support the large-scale manufacturing and delivery of Johnson & Johnson's (Janssen) investigational vaccine candidate
- August: $1.5 billion to support the large-scale manufacturing and delivery of Moderna's vaccine candidate

Note: OWS funding of diagnostics and therapeutics are not included in this list.

5. OWS Vaccine manufacture

OWS is investing, at its own risk, in vaccine manufacture allowing firms to develop capability and capacity.

Major OWS vaccine manufacture milestones:

- March, April, May: agreements with AstraZeneca, Moderna, and Johnson & Johnson regarding their manufacturing capabilities
- June: $628 million task order with Emergent BioSolutions for domestic manufacturing capabilities and capacity for a potential COVID-19 vaccine as well as therapeutics,
- July: $625 million task order with Texas A&M University and FUJIFILM to advance domestic manufacturing capabilities and capacity for a potential COVID-19 vaccine
- August: $160 million contract with Grand River Aseptic Manufacturing Inc., (GRAM) Grand Rapids, Michigan for domestic aseptic “fill and finish” manufacturing capacity
- October 13: $31 million agreement with Cytiva to expand the company's manufacturing capacity for products that are essential in producing COVID-19 vaccines, such as liquid and dry powder cell culture media, cell culture buffers, mixer bags, and XDR bioreactors

6. OWS Vaccine distribution

Experts from DoD and the CDC are developing a US vaccine distribution plan.

Major OWS vaccine distribution milestones:

- May: $138 million contract with ApiJect for more than 100 million prefilled syringes as well as the development of manufacturing capacity for over 500 million prefilled syringes in 2021
- June: HHS and DoD announced a joint effort to increase domestic manufacturing capacity for vials that may be needed for vaccines and treatments
- June: $204 million to Corning to expand the domestic manufacturing capacity to produce approximately 164 million Valor Glass vials per year if needed
- June: $143 million to SiO2 Materials Science to ramp up capacity to produce the company's glass-coated plastic container, which can be used for drugs and vaccines
- August: Announcement that McKesson Corporation will be a central distributor of future COVID-19 vaccines and related supplies needed to administer the pandemic vaccinations
- September: HHS and DoD released a detailed strategy to deliver safe and effective COVID-19 vaccine doses to the American people

7. Summary

COVID-19 vaccine candidates have been developed throughout 2020 with remarkable speed. We await the initial efficacy results of the first Phase 3 trials, which should be available later this year, to guide us as to whether these vaccine development efforts have produced successful COVID-19 vaccines.

OWS has been significantly involved in these developments.

References:

HHS fact sheet:

New England Journal of Medicine

Wikipedia