

By DINA MURAD
sunday@thestar.com.my

ADDITIONAL booster shots may be necessary not only if the protective effects of Covid-19 vaccines wane but also if new coronavirus variants become increasingly resistant to present vaccines, says Dr Leow Chiuann Yee, a senior lecturer specialising in vaccinology and immunology at Universiti Sains Malaysia's School of Pharmaceutical Sciences.

At this moment, the Malaysian National Pharmaceutical Regulatory Agency (NPRA) has only approved the same brand of vaccine to be used for primer (first and second) jabs, says Dr Leow. However, he believes it is possible to mix vaccines in the future if clinical studies show encouraging results.

"Given that more countries are carrying out clinical trials for mix and match vaccine combination programmes, the clinical data will be a useful reference for Malaysian healthcare authorities, including the NPRA, for the identification of safety, quality and efficacy of the mix and match vaccination approach," he says.

On Thursday, National Covid-19 Immunisation Programme coordinating minister Khairy Jamaluddin told Parliament that the Special Committee on Covid-19 Vaccine Supply will discuss the need for a third booster shot for those already vaccinated and the possibility of mixing vaccines to enhance immunity next week, when it is briefed by its technical working group.

According to the Science, Technology and Innovation minister, they are still waiting for recommendations by a group of health experts led by Institute for Clinical Research director Dr Kalaiarasu Peariasamy.

"We will receive recommendations from the panel of experts based on real-world and clinical

Indonesia and Russia are also considering offering extra doses in a bid to beef up protection. The United Kingdom is expected to start its booster programme in September.

Dr Anthony Fauci, the White House chief medical adviser and the United States' leading infectious disease expert, last Sunday walked back his earlier statement and said there may be a need for booster shots for those with suppressed immune systems such as cancer or transplant patients.

Addressing the growing issue of

mixing vaccines as policy.

It is also reported that the practice was quietly authorised in England in January by the Public Health of England agency when vaccine supplies were limited.

On July 12, Thailand announced it would give the AstraZeneca shot to those who had already received their first dose of China's Sinovac vaccine, in an attempt to increase protection.

Sinovac, like most of the Covid-19 vaccines produced by China, uses the older but tried-and-tested inactivated-virus technology while

A boost for vaccination?

Can booster shots and mixing vaccines bolster our fight against Covid-19?



Sunday STAR
20110812021) MIS
14/8/21

In the mix

Countries that are considering, or have decided to adopt, the mixed-vaccine solution for their second doses or booster shots:

BHUTAN

Bhutan's Prime Minister Lotay Tshering said on June 24 he was comfortable about mixing and matching Covid-19 vaccine doses to immunise the country's population of about 760,000 people.

it is mulling booster shots for the rest of the population.

ITALY

Italy's medicines agency, Aifa, said on June 14 that people under the age of 60 who were inoculated with a first dose of the AstraZeneca shot can receive a different second shot.

RUSSIA

On July 26, Russia approved clinical trials combining an AstraZeneca shot with its Sputnik V vaccine, according to the country's state drug register.

based on real-world and clinical data to see if heterologous vaccinations – the mixing of vaccines – are safe and whether those who are fully vaccinated can receive a third booster shot with a different vaccine,” Khairy had said.

Global shift

Malaysia is not alone in considering these approaches to bolster vaccine efficacy amid the surge of Covid-19 cases due to the Delta variant, which is said to be more transmissible and infectious.

Israel will become the first country to offer a booster shot to its citizens today – those over 60 who got their second jab at least five months ago are eligible for a third Pfizer-BioNTech jab from Aug 1.

Addressing the growing issue of “breakthrough infections” – when a person contracts Covid-19 despite being fully vaccinated – Dr Fauci said the issue of a third shot was discussed on July 22 by the country’s Advisory Committee on Immunisation Practices, “which will continue to review the data that might push us in that direction.”

According to Reuters, a growing number of countries have switched or are looking at switching to different Covid-19 vaccines for second doses or booster shots amid supply delays, safety concerns and the recent Delta variant surge. The news agency said that several countries, including Bahrain, Bhutan, Canada, Italy, South Korea and the United Arab Emirates have begun

the older but tried-and-tested inactivated-virus technology while AstraZeneca is a viral vector-based vaccine which uses a genetically modified common cold virus – the adenovirus derived from chimpanzees – to trigger an immune response against Covid-19.

Interestingly, it has emerged that even China is planning to administer booster shots using a different vaccine technology from its current primer doses.

On July 15, Chinese media outlet *Caixin* reported that the country is now considering using an mRNA vaccine, jointly developed by China’s Fosun Pharma and German company BioNTech, as a booster shot for those who have been fully inoculated with its inactivated-virus vaccines.

However, it is still not clear if third booster shots and heterologous vaccinations are the most effective way to tackle Covid-19 as new variants spread.

Data vital

World Health Organisation chief scientist Dr Soumya Swaminathan has advised individuals against mixing Covid-19 vaccines from different manufacturers by themselves, saying such decisions should be left to public health authorities.

“Data from mix and match studies of different vaccines are awaited – immunogenicity and safety both need to be evaluated,” Dr Swaminathan tweeted.

WHO has also said that there isn’t enough data to determine if booster shots are necessary at this moment. An internal WHO report nonetheless estimated that those most vulnerable to Covid-19, such as the elderly, may need to get annual vaccine boosters to be protected against variants, and boosters every two years for the general

population. The country’s population of about 760,000 people.

CANADA

The National Advisory Committee on Immunisation said on June 17 that the provinces should offer recipients of a first dose of the AstraZeneca vaccine a different shot – the Pfizer-BioNTech or Moderna mRNA vaccines – for their second dose.

CHINA

Researchers are running a trial using one dose of CanSinoBio’s viral vector-based shot as a booster for those who have received one or two doses of an inactivated vaccine, clinical trial registration records in June show.

INDONESIA

Indonesia started giving a Moderna booster shot to its healthcare workers immunised with the Sinovac vaccine, as thousands of them tested positive for Covid-19 in July. On July 27, the Indonesian government said

population.

A recent Oxford University study found that a third shot of the Oxford-AstraZeneca vaccine has proven effective in keeping up immunity against Covid-19.

Another Oxford study also suggests that two doses of AstraZeneca followed by a third dose of a different vaccine could lead to a stronger immune response.

Malaysian health experts have called for more local data on the long-term efficacy of the different vaccines to know whether booster jabs are necessary. Studies have shown that even after being fully vaccinated with two doses of vaccine, or single dose for one-shot vaccines like the Johnson & Johnson variety, people may still be

SOUTH KOREA

A study from South Korea found in July that a mixed vaccination of an AstraZeneca shot first and then a Pfizer-BioNTech one boosted neutralising antibody levels six times more than two AstraZeneca doses.

THAILAND

Thailand said on July 12 it would use an AstraZeneca shot as a second dose for people first inoculated with Sinovac in an attempt to increase protection.


UNITED ARAB EMIRATES

The UAE, which initially used the Sinopharm shot, started making the Pfizer-BioNTech vaccine available as a booster in July.


VIETNAM

Vietnam said on July 13 it would offer the Pfizer-BioNTech mRNA vaccine as second dose option for those who received the AstraZeneca vaccine as their first dose.

Leading by example Several world leaders have also mixed vaccines in recent months:




German Chancellor Angela Merkel, 66, received a second dose of the Moderna vaccine after receiving a first dose of AstraZeneca.



Italian Prime Minister Mario Draghi, 73, switched to Pfizer for his second dose after having received an AstraZeneca shot.

Source: Reuters



Canadian Prime Minister Justin Trudeau, 50, also switched vaccines, receiving a Moderna shot after an AstraZeneca one.



Growing global real-world and clinical data

WHILE Pfizer, BioNTech and Johnson & Johnson have raised the strong probability for the need of an extra dose of vaccine to provide enough immunity against Covid-19 variants, AstraZeneca says it is not yet sure whether a booster dose of its vaccine will be necessary for continued protection against the coronavirus.

As AstraZeneca CEO Pascal Soriot explained on news channel CNBC recently, "There are two dimensions to this immunity – antibodies [which] decline over time, but the second, very important dimension of vaccination is the so-called T-cells. They tend to protect people against severe disease, but they also provide durability.

"With the technology we use, we have very high production of T-cells. We're hoping we have a durable vaccine that protects for a long period of time. So whether we will need a third booster or not is not clear yet, only time will tell," Soriot was quoted as saying.

T-cells are a type of white blood cell that stimulate antibody production and help combat virus-infected cells. Antibodies prevent viruses from invading cells but don't last as long as T-cells.

Soriot explained further that the only way to be sure whether booster shots would really be needed was to watch whether the vaccine's efficacy declined over time.

In a new study funded by Pfizer and BioNTech, findings showed that the effectiveness of their



About 57% of Israel's 9.3 million population have been fully vaccinated.

It added that the Pfizer-BioNTech vaccine was just 39% effective in keeping people from getting infected by the contagious Delta variant in the country in recent weeks, but provided a strong shield against hospitalisation and more severe forms of the virus.

Hence, Israel announced that from today, it will start offering Pfizer-BioNTech booster shots to those over 60 who got their second jab at least five months ago.

To boost or not to boost

patients who recovered from the disease.

The study published on July 16 in *The Lancet Microbe* journal said there could be a need for "alternative strategies" for those given Sinovac.

"The difference in concentrations of neutralising antibodies identified in our study could translate into substantial differences in vaccine effectiveness," the researchers were quoted as saying in the *South China Morning Post*.

A study conducted in Chile, published recently in the *New England Journal of Medicine*, showed that Sinovac has an efficacy rate of 65.9% against Covid-19, is 87.5% effective at preventing hospitalisa-

"This programme is important for us to determine the levels of antibodies and neutralising antibodies among vaccine recipients in Malaysia and this can be found out through several means.

"One is determining the level of seroconversion antibodies that increases and neutralises the SARS-CoV-2 virus at eight different points of time across two years after the first dose.

"The second is determining the level of reaction from the T-cell receptors and salivary antibodies towards SARS-CoV-2 at three different points in time across three months among the general public who have received all types of vaccines, and to project the Covid-19 infection rate after vaccination," he told Parliament on Thursday.

To mix or not to mix

Around the world, several ongoing studies are also investigating the effects of mixing coronavirus shots.

News channel Al Jazeera reported that Oxford University's Com-COV trial showed that mixed schedules involving the Pfizer-BioNTech and AstraZeneca vaccines generated a strong immune response against the virus. The study, which involved more than 800 volunteers, investigated the efficacy of either two doses of AstraZeneca and Pfizer-BioNTech, or one of them followed by the other.

According to Al Jazeera, the results of the study suggest that the

Researchers said it was unclear how the decrease in antibodies would affect the shot's effectiveness, since scientists have yet to figure out precisely the threshold of antibody levels for a vaccine to be able to prevent Covid-19.

Apart from durable antibodies, other components in humans' immune systems such as T-cells and B-cell memory elicited by the vaccine may also contribute to protection, researchers involved in the study said, although the study did not provide data on those factors.

"In the short to medium term, ensuring more people complete the current two-dose schedule of Sinovac vaccine should be the priority," the paper said.

Covid-19 vaccine steadily declines over time, dropping to about 84% for vaccinated people about four to six months after getting their second dose.

It was reported that the study, which has yet to be peer reviewed, found the Pfizer-BioNTech vaccine's effectiveness was strongest, at 96.2%, between one week and two months after receiving the second dose. It declined an average of 6% every two months, according to the study, which signed up more than 44,000 people across the United States and other countries. Planning to submit the data to US and European health regulators soon, Pfizer and BioNTech said they hope to get the authorisation for a booster dose of their Covid-19 vaccine there in the near future.

Data from Israel meanwhile shows that there is a waning of immunity for those who have been fully vaccinated with the Pfizer-BioNTech shots in the country. According to Israel's Health Ministry, what used to be 100% effective against hospitalisation is now, after a six-month period, becoming low 90s and mid-to-high 80s.

could be after a year or more and might not protect against other variants of concern or variants of interests that emerge and mutate," she says.

While there isn't enough data to show a necessity for booster doses now, it's likely that a booster shot to enhance the immune system may be proposed after six months to one year after the completion of the primer doses, says Dr Sharifa.

Dr Sharifa explains that the type of vaccine used as a booster dose can be a continuation of the original vaccine type, may be a modified version, and can also be from a different vaccine altogether – the last being a mix-concept dosage.

"The vaccine recommended for boosters is still being studied,

other countries are also conducting efficacy studies of the Covid-19 vaccines administered in their country.

In Thailand, a joint study between Thammasat University's Faculty of Medicine and the National Centre for Genetic Engineering and Biotechnology showed that antibody levels in people fully vaccinated with the Sinovac vaccine decline by half every 40 days.

As reported by the *Bangkok Post*, the study that looked at 500 fully vaccinated people found that vaccine efficacy within 60 days of the second Sinovac shot ranged between 60% and 70% against the original coronavirus strain, declining to about 50% in people who received their second dose after 60 days.

In Hong Kong, a University of Hong Kong study of 1,442 health-care workers showed those who received the Pfizer-BioNTech vaccine had 10 times more antibodies than those vaccinated with Sinovac. It found those who received Sinovac reportedly had "similar or lower" levels of antibodies to those seen in Covid-19

whether it might be possible to mix and match doses from different types of vaccines," she explains.

It might also be necessary to make alterations to the original vaccine to ensure that it continues to respond well to strains circulating at that point in time, she adds.

It is reported that the government is in talks with vaccine manufacturers – especially Pfizer-BioNTech – about the possibility of buying booster shots for 2022. As Khairy told Parliament, "We have a special focus on Pfizer's new products, which are specifically for booster shots and for children".

He, however, clarified that even while discussions are ongoing, they are still waiting for recommendations from the panel of health

experts on whether booster shots are needed.

On Wednesday, Reuters reported that a lab study in China showed antibodies triggered by the Sinovac vaccine declined below a key threshold from around six months after a second dose for most recipients, but a third shot had a strong booster effect. According to the news agency, Chinese researchers reported the findings from a study of blood samples from healthy adults aged between 18 and 59 in a paper published on July 25, which has not been peer reviewed.

Among participants who received two doses, two or four weeks apart, only 16.9% and 35.2% respectively still had neutralising antibodies above what researchers regard as a detectable threshold level six months after the second shot, the paper said.

Those readings were based on data from two cohorts involving more than 50 participants each, while the study gave third doses of the vaccine or placebo to 540 participants.

Khairy gave an assurance that if required, the booster shots will be subsidised by the government and he is confident that the third jabs will be given to the people for free.

Like flu vaccination, if additional boosters are needed in the future, it will likely be done annually, Dr Leow predicts. Vulnerable communities like the elderly or the immunocompromised may also be prioritised.

"Given the current data is still at an early stage of being gathered, global vaccination data compiled from now onwards will provide public health specialists a better and more insightful picture about what decision to make," he says.

Participants in some cohorts who received a third dose of the Sinovac shot about six months after the second showed around a three- to five-fold increase in antibody levels after a further 28 days, compared with the levels seen four weeks after the second shot.

On July 15, Chinese media outlet *Caixin* reported that the country is now considering using an mRNA vaccine (similar to Pfizer-BioNTech's) – jointly developed by China's Fosun Pharma and German company BioNTech – as a booster shot for those who have been fully inoculated with its inactivated-virus vaccines.

In Malaysia, the National Institutes of Health is conducting an antibody immune surveillance programme to establish the efficacy of administered vaccines and the level of reaction among the general public.

According to Science, Technology and Innovation Minister Khairy Jamaluddin, RM15mil has been allocated for the study by the Health Ministry's medical research body, which, he said, "has a monitoring period of up to two years".

order of the vaccines makes a difference, with AstraZeneca followed by Pfizer-BioNTech "inducing higher antibodies and T-cell responses than Pfizer-BioNTech followed by AstraZeneca".

The research also showed that two doses of Pfizer-BioNTech produced the highest level of antibodies. Both of the mixes generated better results than the still very effective two-dose AstraZeneca vaccines, it said.

Another study in Spain in May involving more than 600 volunteers also found that an AstraZeneca dose followed by a Pfizer-BioNTech one was more effective than two AstraZeneca doses. In Germany, a third study also revealed that the immune response of mixing coronavirus doses was better than two AstraZeneca shots and as good as or better than receiving two doses of the Pfizer-BioNTech vaccine.

No results from the studies have suggested that mixing leads to severe side effects. However, experts say there is a lack of sufficient clinical data to fully determine whether mixing is effective. – Agencies



Alternative strategies: Malaysia is not alone in considering different approaches to bolster vaccine efficacy. Canada's prime minister Justin Trudeau is a proponent of mixing vaccines. — AFP