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Transcript

„Vaccinating the world against COVID-19: evidence on lesser-known vaccines and the effectiveness of established vaccines around the globe“

Experts at the Press Briefing

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Link to video

You can find a recording of the briefing here: https://www.sciencemediacenter.de/alle-angebote/press-briefing/details/news/die-welt-gegen-covid-19-impfen-erkenntnisse-ueber-weniger-bekannte-impfstoffe-und-die-wirksamkeit-etablierter-impfstoffe-auf-der-ganzen-welt/

Transcript

Moderator [00:00:00]
Welcome everybody to the press briefing hosted by the Science Media Center Germany on behalf of the COVID-19 Vaccine Media Hub, a global information project of the Network of International Science Media Centres and their partners. My name is Volker Stollorz from the SMC Germany, and we are proud to have a group of distinguished experts today. And we will have room for questions. And I just want to briefly introduce. So in many affluent countries people are already receiving third COVID-19 booster vaccinations, in many low income countries health care workers and even the most vulnerable people are still waiting to receive the first shot of any of the available COVID-19 vaccines. With the emerging new variants like Omicron – we heard news of today – the world wakes up to the fact that unless we are all protected against severe diseases, no country can feel safe because escape mutants will evolve and transmit more easily between countries. And we will briefly discuss this kind of experts today and your questions. The briefing will be recorded, transcribed and posted on our website as soon as possible. Put your questions you may have in the Q&A tool of zoom, and my colleague will forward them, and I will ask them to the experts. If you have specific questions, Teresa Lambe has to move on in half an hour, so we will try to be quick and start so that she can answer questions you may have. So I will first introduce the panel. We have Associate Professor Theresa Lambe. She's Associate Professor and leading investigator at the Jenner Institute, University of Oxford, UK. Welcome. Then we have Professor Annelies Wilder-Smith, Professor of Emerging Infectious Diseases, London School of Hygiene and Tropical Medicine, and she's also an advisor of the Initiative of Vaccine Research at the World Health Organisation, Geneva, Switzerland. Then we have on the left, Florian Krammer, professor of vaccinology at the Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, USA. And we have Jakob Cramer, physician in Internal Medicine, Tropical Medicine, Infectious Disease, Head of Clinical Development, Coalition for Epidemic Preparedness Innovations, CEPI. I will start with Teresa Lambe. So tomorrow, one year ago, the first patient in the UK was vaccinated. It was a vaccine approved at the time and developed by the Jenner Institute in collaboration with AstraZeneca. And one year on already two billion doses of this vaccine against the spike protein of SARS-CoV-2 and adenovirus vector vaccine has been distributed worldwide. Can you tell us a little bit how the roll-out is going in less developed countries, and what is happening right there at the moment, and what the situation is?

Teresa Lambe [00:02:54]
Certainly. So, I'm an academic, I've worked on making vaccines against emerging outbreak pathogens for a number of years now. And at the University of Oxford, we've been fully committed to ensuring the vaccine that we developed would be provided globally and equitably. And we partnered with AstraZeneca to this. And as you've mentioned worldwide, it's been about two billion doses of the Oxford/AZ vaccine distributed with over 7,6 billion doses of vaccines being given out in the world. And unfortunately, only 6,3 percent of low-, middle- and low-income countries have received vaccines. And we need to do more. Over two thirds of our

vaccine, the Oxford AstraZeneca vaccine, is going to low and lower middle-income countries. But really, I think the emphasis is on us, worldwide, to try and get more vaccines globally. We spend trillions of dollars on defense against each other and we don't spend or have the same investment in protecting each other. That needs to change or will continue to be in this cycle of fighting new and variant viruses continuously.

Moderator [00:04:05]
There were concerns in some developed countries about the very rare side effect of this specific adenoviral vector vaccine. Is there any data or reports from the less developed countries so far in terms of what you get as feedback?

Teresa Lambe [00:04:22]
Yes. So, I think you've hit the nail on the head by calling the very rare side effect. It was not picked up in the thousands and thousands of individuals we tested in the UK, said Africa or Brazil or in the US. There does seem to be a higher incidence of this, but still very rare side effect in northern European countries. We're not seeing the same level of reporting of this TTS (thrombosis with thrombocytopenia symptoms) in other countries.

Moderator [00:04:50]
Okay. Thanks for now. So now we'll move on to Professor Annelies Wilder-Smith. And as Teresa Lambe just said virtually no low-income countries is on track to vaccinate 40 percent of the population this year, the goal set by the WHO (World Health Organization). And many will miss the 20 per cent mark COVAX set as a minimum by the end of 2021. And can you comment a little bit on where we stand with vaccinating the world? We just heard how important that is, and the new Omicron variant, of course, makes that obvious. Can you just comment on where we stand and why we stand where we stand and what that means for the near future and these new variants coming?

Annelies Wilder-Smith [00:05:31]
So let's start with the good news first. The good news is that more than eight billion doses have been administered and that now 54 per cent of the world's population has received a first dose and about 42 per cent have received two doses. That is good news, and it is really a public health victory and also a political victory in many senses. But there's also the bad news. The bad news is that the vaccine distribution remains not fairly distributed, inequitable, with many of the low to middle income countries with very low vaccine coverage rates for various reasons. With some other countries hoarding vaccines and now eight times more booster doses being given over a first dose. And some countries have not even started vaccinating yet. So, the current goal is really, you know, we need to accelerate, we need to accelerate further

production vaccine supply. But we also need to accelerate vaccine delivery. It's not only now about vaccine supply, it is also about vaccine demand and vaccine delivery.

Moderator [00:06:51]
So what are the major bottlenecks in the delivery, which you see? I heard from some countries who kind of refuse supply exceeds to just import because they are not able or capable or feel not capable to do the logistics of the distribution to basically get the vaccines into the arms of the people. Because that's basically what we aim at not just producing vaccines but giving that to the people in need first. So, what are the bottlenecks?

Annelies Wilder-Smith [00:07:19]
There are many bottlenecks. First of all, we have to acknowledge it's a very challenging task to quickly roll out vaccines to a population that we normally do not vaccinate. And that's the older adults. I know, all countries are used to and have systems in place for their childhood vaccination programs, but really do not have systems in place how do you really get access to older populations? Older populations, you know, in villages may not come forward. Older populations may not be as literate or computer literate to really know that they have to come forward. This vaccine is also not easy just to deliver from house to house, like we did for the oral polio vaccine. So, it needs much more logistics. It needs creative new approaches, how now to reach those most vulnerable, and that's the older people. All these programmatic delivery issues need to be in place at a time – and very rapidly. And furthermore, another complicating factor is that many countries actually cannot totally predict when the vaccine supply arrives or they have no on and off vaccine supply. They expected the vaccine supply. It didn't come to be prepared. It didn't come or suddenly it comes and they're not prepared. There are multiple factors that make delivery so difficult in some of those low to middle income countries. So indeed, it's not only vaccine supply now, that was [the issue] maybe a year ago. Now it is about: How can we help them also with vaccine delivery?

Moderator [00:09:05]
We come back to that in the Q&A session, I move over to Professor Florian Krammer. You have a good overview on the different vaccines which are already delivered worldwide. And from your vaccinology view of the emerging variants of SARS-CoV-2 like the Omicron, where we have seen first data just today coming out about neutralizing antibody capabilities. How good will these different types stand up against the ongoing evolution of this virus? Your statement?

Florian Krammer [00:09:40]
That is a good question, which is, you know, any answer to that is basically pure speculation. But we do see performance differences, right. There is a very nice study in Brazil, for example, where AstraZeneca was compared to CoronaVac, and you could see that the AstraZeneca

vaccine was doing better. The CoronaVac vaccine was working too, but the vaccine effectiveness was lower, right. We also know, if you look at neutralizing antibody titers, some vaccines induce lower titers than others. Some vaccines have more ability to induce T-cell responses than others. And so the vaccines that I'm more worried about right now are vaccines that are one shot vaccines and vaccines that are basically inactivated vaccines that, by their nature, don't necessarily give you a good T-cell response and might induce low neutralizing antibody titers. I think that's where I would assume that the effectiveness goes down to most. For vaccines that give good T-cell responses or that induce very high neutralizing antibody titers, I am a little bit less worried. But again, this is speculation, we need to wait for the data. And right now, we don't even have effectiveness data with vaccines like BioNTech/Pfizer or Moderna.

Moderator [00:11:03]
And that is a very important point you raised about this inactivated whole virus vaccines because – like the kind from China for example – we have these vaccines given to lots of people also in Africa and South America. And your point is that, compared to these newer mRNA vaccines, you expect them to be less protective if I understand it correctly?

Florian Krammer [00:11:27]
Again, [this is] speculation, but that's what I would expect. There are differences between the inactivated vaccines, too. There seems to be data that, for example, the Sinopharm vaccine is doing a little bit better than the CoronaVac vaccine. So, there are differences also between the inactivated vaccines, but that would be what I would expect. Inactivated vaccines are typically not good vaccines to induce T-cell responses. Looking at the data sets from Alex Sigals and Sandra Cieseks lab you see that Omicron is a very strong escape variant when it comes to in vitro neutralization. And so, we might need to rely on our immune system we might need to rely on safety nets like T-cell responses, like not neutralizing antibody responses like anamnestic responses from the B-cell compartment. But the lower your baseline status is, the less antibody you have, the less of a T-cell response you have, the easier it will be for a strong escape mutant like Omicron to cause disease. So, I think that's what we have to keep in mind. And we have to be honest, it's not that all vaccines are equal. We do see differences.

Moderator [00:12:50]
Okay. Then we move on to Jakob Cramer from CEPI. So CEPI is kind of looking into the future of what novel vaccine types we are going to need in the future, not just today where we're trying to roll out as fast as possible the existing vaccines. Can you tell us a little bit about what type of vaccines you are actually testing right now in phase one, phase two, and how that could impact on these newly emerging viruses, which come up at the moment or may come up in the future?

Jakob Cramer [00:13:25]
Well, thank you for this question. I would also like to start with good news. Vaccines work, vaccines work against severe disease for the variants so far. Omicron we'll see further data emerging over the next days and weeks. But I would like to start with saying that it is important that we understand what we expect from those vaccines. And we still have a good vaccine efficacy against severe disease, whether or not we maintain efficacy against any severity or maybe even transmission or at the very best and against infection, even, that is to be seen. But as long as we keep our hospitals away from compensation with good vaccines against severe disease, we have already an important step forward. Now we need to see moving forward if this is maintained. So, in light of the different objectives in relation to vaccine efficacy that, which I just mentioned, the two most important characteristics I think that we need to look into moving forward is to maintain vaccine efficacy against severe disease and to have a broad coverage against new variants that may emerge. So, these are probably the two most important characteristics that we need to look into moving forward with the second version future or adapted vaccines. There is a few additional characteristics mentioned already that we need to understand the immune system or protective immune response better. Right now, regulatory pathways are primarily based on neutralizing antibody titers, and if we see an escape variant, you may have really very high antibody titers, but they are gone if they no longer work against the new variant. But we maintain other functions within the immune system, T-cell mediated immune responses, other immune responses that may maintain a certain protection against a severe disease. So, this is something, that we need to look into more broadly moving forward. But obviously, there's a few additional characteristics in terms of improving the longevity of the protective immunity, single dose regimen, maybe even intranasal formulations that have a better protection against transmission or even infection. And then also to speak about other characteristics like shelf life, storage conditions and so on, that reflect the situations in normal income countries or tropical areas, is something that we look at. But again, I'd like to mention the broad coverage against newly emerging variants, so-called broadly protective betacoronavirus vaccines, is something that CEPI has a focus on.

Moderator [00:16:04]
Okay, then I would start giving you the questions. I think, I will start with Teresa Lambe. And the very simple question is, is the team of the AstraZeneca vaccine already working on vaccine adaptations related to a potential Omicron variant vaccine, whether that's needed or not? What are your considerations at the moment?

Teresa Lambe [00:16:31]
So, I would echo what Florian and Jakob have already said. We don't know if we need a new vaccine yet. It is very, very likely that we will see a fall in neutralizing antibodies, and we have yet to come across a variant where we've seen an impact on protection against hospitalization and death. And unfortunately, we need to be a little patient to see the results from those types of product data to come out. And we, like other vaccine manufacturers, can go fast. We've

already made a different variant vaccine, AZD2816 against Beta, so we've got the processes and the willpower to go fast, if we need to. We don't know yet.

Moderator [00:17:17]
Can you comment for the journalists out there, also Florian, maybe: How long will it take before we can make an informed decision, whether or not we really have to move and switch to another variant type booster vaccine? I mean, when will these data emerge, two weeks or one month or …?

Teresa Lambe [00:17:42]
Certainly the data that is coming at the moment from South Africa is largely encouraging because the data that is being reported is that it's a generally mild disease. The caveats are that we're looking at a population that is much younger. They've had an exposure to different types of variants, and I'm not sure that we've given enough time for us to be able to accumulate the data on hospitalization. So, I think we need to wait a little bit longer before we can be fully confident of what the data is telling us. Florian?

Florian Krammer [00:18:16]
I agree, I mean, we need to wait and look, but while we wait and look, I think the vaccine manufacturers need to move and make a vaccine that can be used if it's needed because we have to keep the timelines in mind. Moderna is moving now. They said that they might be able to deliver something in March that depends on the regulatory path issues that may come mid-next year. And then, if Omicron continues to spread, Omicron waves might be over in most countries. So, I think for the vaccine producers right now, the most important thing is to get going and to dock the regulatory agencies and find out how to get this to the market fast if needed. If you don't need it in the end, that's great. I would love to be over with it. And if vaccine effectiveness against severe disease or even moderate disease holds up, I would be super happy. I think that's kind of all we need, but we don't know that. And to wait and see, for us, I think, that's important. But for the vaccine manufacturers, if they wait and see, that means that there will be long delays. And I don't think we can risk those long delays, honestly.

Moderator [00:19:28]
Before I come back to Omicron, I just wanted to put the question maybe to Annelies Wilder-Smith. Developed countries like Germany and other countries also are rolling out booster programs and we are speeding it up. Should this be stopped now in light of the goal of worldwide vaccinations? And how does WHO sees it because Omicron may call for an update? So, is it more important to keep on pressing worldwide vaccinations? And is that not a new dilemma between boostering the rich countries and giving access to low-income countries with the vaccines they need to protect the vulnerable people? How do you see it?

Annelies Wilder-Smith **[00:20:14]**
The clear message is: We need more first dose coverage, higher first dose coverage, more people need to be vaccinated. You get a much bigger public health impact in terms of averting death and hospitalizations; the more people have received the first and second dose. That said, Europe and many other countries are now in the winter season and are seeing a major resurgence. And we have seen the positive impact of a third dose on restoring vaccine effectiveness, and all governments have a duty to protect their own citizens. So, we are here in a tension. And so indeed, we need to go in parallel. Whilst we roll out more boosters, especially for the vulnerable and the higher risk of dying, we must make sure that we have also a broader and higher coverage with first and second doses in the rest of the world.

Moderator [00:21:21]
I have a question, probably for Jakob Cramer, and that is concerning these plans of a 'one euro vaccine', so putting down the price to get more vaccines out, more fast, to vaccinate the whole world because it seems with all these ever increasing new variants, we would need a big effort to basically reach most of the world population and not just in specific countries. Is it feasible or realistic or what needs to be done to bring this number of vaccines to the people?

Jakob Cramer [00:22:00]
Yes, of course, this is important. But we should not address too many aspects in parallel. First of all, we need good vaccines, and we need to have enough vaccine and we need distribution capacities and so on. CEPI calls for new vaccines, second generation vaccines, broadly protective betacoronavirus vaccines investigates the so-called cost of goods. This is certainly one of the aspects that we keep in mind if we do fund additional programs. But first of all, we need good vaccines that tackle new variants, maintain protective efficacy for those in need while at the same time maintaining that discussion. CEPI has created a marketplace where we connect developers with glass vial producers and fill-finish capacities and so on to connect, but also to ...You know, the market, as you can imagine, is a little bit stretched at the moment, everyone needing glass vials and so on. So, we try to keep this open and transparent and to help to this end, but obviously the first priority will be enough of good vaccines while at the same time looking at prices.

Moderator [00:23:17]
And maybe to both of you, Annelies and Jakob, how CEPI and WHO can ensure faster reach of vaccine coverage. What is being done right now to reach more people? Maybe you can both comment on that question to be a little bit more specific. And then I move on to Florian and the Omicron.

Annelies Wilder-Smith [00:23:41]
We need to spend much more time into building up delivery capacity, that means more trained personnel, trained logistics, you know, all the background that is needed from fridges to syringes. It's not only about the vaccines to enable countries to roll out the vaccines, but also more than that. We also need, you know, national deployment plans that are feasible and context specific. It may differ between Nigeria and Mongolia, for example, but also trying to focus. And that's very important. I think, countries need to continue to focus on high priority groups. We hear from countries, including developing countries, that have started to vaccinate children whilst that is not the priority. The priority is to vaccinate older people, vaccinate people that are at higher risk of severe disease outcomes. So, it's a multi-armed approach that we now need to do, and it's not far beyond vaccine supply. And the other issue is really vaccine demand. You know, the social media is also strong, and conspiracy theories are mushrooming, also in low to middle income countries and also in Africa. And one of the reasons why the take up is not as high as we wish is also the demand issue. People do not want to give their arm. It's much easier to give a third dose to people who are already willing to have the first and second, then to give a first dose to many. And we in Europe have failed miserably as well, or we in the US have failed miserably as well. We are also not as high. If you compare, Brazil has already overtaken most of Europe now. There were late, but there are no better. Chile is very high, Mongolia. Thailand has achieved, and China has achieved very high vaccination coverage rates. And also that said for New Zealand, I'm very impressed, 90 percent. So, I think the whole world needs to learn. It's not about high-income countries are doing it better than low-income countries. There are problems everywhere. The problems are different. But we need to tackle them in the context specifically.

Moderator [00:25:58]
Jakob, you want to add the CEPI perspective on this. How to move on fast?

Jakob Cramer [00:26:03]
I think Annelies has covered it well. Just to underline, there is vaccine skepticism, not just in high-income countries, but also in low- and middle-income countries, which is something that needs to be addressed. Just to add one point: The COVAX facility has, as we speak, delivered 623 million doses to low- and middle-income countries so far, which is a big achievement, but which is not enough, certainly. So, what we need is supply, direct supply of vaccines into the COVAX facility, not just maybe donations of vaccines, which have a limited shelf life not used in high income countries, which then comes with delivery issues as well in normal income countries and kind of some urgency to get them distributed. So, we need cooperation support from governments, from developers, we are prepared to deliver these vaccines.

Moderator [00:26:57]
Okay, Florian, now to you and the Omicron questions, of course, lots of people are kind of

worried and have some questions, and I start with the first. What would it mean for the global vaccination campaign if the apparently more contagious Omicron variant displaces the dominant Delta variant worldwide? And then the question is, and I think maybe it's misplaced, would that be a good thing? Because Omicron potentially leads to milder disease causes, as far as I know, this is not yet certain. What do you think?

Florian Krammer [00:27:30]
I mean, I think we can only speculate about this. The notion that Omicron might be milder is based on some data from South Africa. And there's all kinds of data from South Africa in terms of disease severity right now. And this is already said, we have to be very careful here. We're talking about the young population that has a very high baseline immunity from previous infection. And that's why we may be seeing a little bit of a milder disease phenotype, maybe. If that hits non-vaccinated older populations somewhere else, I don't think that ... We have to be careful that might not hold true. So, I think what we need to do as a base assumption right now is to assume that Omicron is going to be very similar to other variants in terms of disease severity. I can't really judge what that all would mean for global vaccination campaigns. Honestly, I'm not an expert in that, and I don't know what the best strategies would be if it really replaces Delta. I think the bigger issue would be – or not the bigger issue, but an additional issue would be if there is strong co-circulation of Delta and Omicron, because for people who have not been vaccinated right now, it would then have to make a choice of what vaccine to use if really different vaccines are needed. Or, you know, you might have to develop bivalent vaccines. And so, I see that as an additional complication.

Moderator [00:28:58]
And here's another question concerning this. On the one hand, this booster dilemma we were just talking about. And if you could delve in a little bit more about the reasoning: If Omicron is taking over rapidly, should people even refrain from a booster dose shot? No, I guess you would say, no, please don't. What is your opinion about this?

Florian Krammer [00:29:20]
There are many layers here, right. From a pure immunological point of view and from a I-want-to-protect-myself point of view I think a booster dose is a very good idea. From an ethical point of view, that was just discussed, that's a very different story. But I think we have to face reality. There are increasing numbers of Omicron cases in several countries, we know that there might be community transmission in several countries. But what we're facing right now, specifically in Europe and in North America, it's a very strong delta wave. And I think the most important thing would be to get those people vaccinated who haven't received the vaccine yet. The first shot, the second shot. Those are the important ones right now. Yes, I think a booster is doing great in helping to control infections even in the delta wave, because the protection against

infection goes up rapidly after the booster. But I'm more worried about the people who were not vaccinated yet. Those are really the ones who need to get vaccinated.

Moderator [00:30:22]
Okay, then there is one more technical question and then I move on again to the other issues. Could Omicron have evolved in a highly vaccinated population? Or at least, would it have been less likely to have involved in a highly vaccinated population, that comes again? So, where does this virus come from? And has it had specific ways of how it could evolve? What is your opinion? I know, you are not an expert on origins of new variants, but do you have a vaccinology view on this question?

Florian Krammer [00:30:56]
I mean, there's a broader global population view, and that basically says: If you have more people vaccinated, you have fewer infections. And even when people have breakthrough infections, there might be fewer replication cycles of the virus and all that decreases the risk of getting new variants, right. But there's another issue here, and we have seen that, that's very well documented. There might be people who are immuno-suppressed who are more persistently infected, and a lot of the mutations that we see in variants come up in these persistent infections. This has been well documented, and that is another way of, in a way, how these variants could emerge. But again, the more people you vaccinate, the more you restrict the circulation of the virus in the global population, the lower is the chance of getting a variant. Every replication cycle gives the virus a chance to probe another degree, another mutation and add another mutation. Every time it replicates is bad, and the more you vaccinate, the less global replication you get.

Annelies Wilder-Smith [00:32:11]
May I add to this. There is indeed a misconception. I mean, must clear that misconception. New variants emerge where you have a lot of virus circulation. The more virus you have, the higher the probability that you will have an emergence of a variant of concern. And older variants so far have always emerged in areas where there was an incredible resurgence. So Alpha was in the UK during the time of a peak. Beta in South Africa, when they had an unvaccinated outbreak, Delta doing it in India when it had a major outbreak. New Zealand has no cases, hardly has a 90 per cent coverage rate. No emergence of any variant comes from New Zealand, and I think that's a message, that needs to come across to people because that's wrong messaging. That's part of the conspiracy theory that vaccination drives new escape mechanisms. No, the message is: They are driven because there's a lot of virus circulating. And just to give you a figure, and Florian may correct me, but I was told that an infected person who is viremic may have up to one billion viruses. So, you have a lot of people with one billion viruses. Yes, one of them will mutate. We need to keep that down with broad coverage of vaccination.

Moderator [00:33:29]
I understand that. But Florian, as I understood, in South Africa the incidence was down, quite low. So nevertheless, Omicron emerged in that population. At least, they didn't see it or it wasn't there, I don't know.

Florian Krammer [00:33:46]
As you said earlier, I'm not an expert on the emergence of variants, but we have to be very careful to say this emerged in South Africa. I don't think we can actually prove that, right. If you really look at who detected it, where it was detected, there were experts from all kinds, all different types of countries from Africa. And it's not clear where the virus actually came from, it was detected in diplomats in Botswana. We don't know where they came from. There are probably even earlier cases in other places. I think we have to be careful, to kind of jump to conclusions here.

Moderator [00:34:26]
Jakob, you wanted to add something.

Jakob Cramer [00:34:29]
So again underlying that high vaccine coverage is key, of course, but new variants will always emerge in future. In immunocompromised, for example, stopping international flight is probably not going to prevent these variants from travelling around the globe. If you detect them somewhere, they're probably out of the country already. So, I just wanted to underline again what I said initially: It is important to at least look at maintenance of vaccine efficacy against severe disease and also to look into the development of not just broad coverage of vaccinations, but also broad coverage of new variants with new vaccines.

Moderator [00:35:08]
And here's a question I don't know, Mrs. Wilder-Smith, whether you can answer it: If vaccine producers would start now, if we need it, to produce a vaccine that is adapted against the Omicron strain, will this influence the ongoing production of the vaccines we are trying to distribute already? Or would there be a gap in production? And would that decrease even vaccine output for maybe even countries who need the vaccines for a delta wave? Can you comment on that question?

Annelies Wilder-Smith [00:35:47]
Well, the first question we need to address is, you know, if you have a variant adapted or a

Omicron adapted vaccine, would you just use it as a booster? And those with the primary series with the previous vaccine. And what would you do with people who have not had a vaccine? Would you start with an Omicron vaccine or would you start with the usual primary series? And my gut feeling is and, Florian, I see him nodding, is that you still have to give to the coverage against the ancestral strains, which still is working against Delta. And remember, Delta is still our current problem, not Omicron. But indeed, maybe also, Jakob, you could discuss when it would have a knock-on effect on production because we definitely would need to increase production. Jacob, what is your take?

Jakob Cramer [00:36:45]
Yes. I mean, that's of course a valid point. I mean, we are still struggling with production capacity for the four vaccines against the canonical original strain and then, you know, we are already adapting to Omicron strains, which is probably thought to be rolled out as a booster primarily in high income countries. There are a lot of initiatives to expand vaccine manufacturing and fill-finish capacities also, for example, in the African countries. CEPI and the African Union are engaged in this. Other developers have announced to expand into this, but production capacity takes time to be built. This is an important issue. I also want to mention – we launch this again on Monday in the WHO consultation – that natural infection rates are also very high in low-income countries or in those countries that have not yet seen a lot of vaccinations. So, 70 percent or even higher proportions of the populations had been naturally infected without vaccines. To understand what a variant adapted vaccine, a single dose moving forward or a combination of different platforms or different variants does in … populations primed by natural infection is also something that we need to look at.

Moderator [00:38:02]
There's an additional question for you, and that is: If in the end, that's what you said, we need much more doses for the global south and boosters even for the vulnerable, there's always this question, lots of discussion also in Germany about this patent pool and technology transfer, CTAB and the TRIPS waiver. What is the situation on there? Would you think that there needs to be done more on this front? Or is that the way to go?

Jakob Cramer [00:38:33]
Well, it's difficult for me to comment on tech transfer or, you know, to lift the barriers on intellectual properties, for example. What I would like to comment on is that vaccine production is a very complex procedure. It's probably one of the drugs that is most difficult to produce and at high standards and high quantities. So simply to lift kind of restrictions on intellectual properties itself is certainly not a solution. One has to secure that the vaccine production is maintained at a quality level everywhere because if you start substandard vaccine production on a certain platform somewhere, it will challenge the entire platform, no matter where it is or at which standard it is being produced. And the second point I'd like to make is

that there are alternative options as well, rather than completely lifting intellectual properties, and that is tech transfer. So, in cooperation with vaccine manufacturers to start production elsewhere and there is a lot of tech transfers underway also from the AstraZeneca vaccine, for example, produced by the Serum Institute of India, Fiocruz and other partners around the globe. There are technologies, but in the end, what is the best to achieve high vaccination production is to be debated still.

Moderator [00:40:01]
Florian, I have a technical question for you and that is: What role could play the as yet unapproved protein-based vaccines in the international vaccination campaigns because they are maybe easier to distribute. What do you think?

Florian Krammer [00:40:18]
I mean, one of them is approved in Indonesia and is used in Indonesia right now. That's the vaccine from Novavax. That's in the second phase of approval in the European Union or at EMA (European Medicines Agency) right now. There are other candidates that have good clinical results globally, the protein-based vaccine from Clover pharmaceuticals for example. So, these vaccines could be used. The question is what's the production capacity? Can they deliver in the end? Novavax had some back and forth and some issues with its production. So, I think they can make a big impact and I think there are also places that can produce them under contract in all kinds of countries, and that would be important. I think they can make a big impact, but unfortunately a lot of or at least one of the protein vaccines was, you know, I wouldn't say leading the field, but was in the back of the quickest developers in the beginning. And so far, this has slowed down quite a bit. So, I think the recombinant protein vaccines can contribute a lot. But we still have to see their full potential not in terms of their immunogenicity – they are great, and we know the clinical data – but in terms of getting them actually delivered and getting the doses shipped and getting the vaccines approved.

Moderator [00:41:40]
One question to all of you is: What do you think why for certain vaccines who are given to hundreds and millions of people that we still do not have very good clinical data from huge phase three trials, I mean, why is that or do you think there is something missing? Or would you say that we have enough data about how the different types of vaccines are working, given to many people? Annelies, maybe you start.

Annelies Wilder-Smith [00:42:13]
I'm not so sure what you mean, because any vaccine that goes for regulatory approval will need, you know, the full clinical development assessment phase one, two and three and therefore also, you know, a big sample sizes for phase three. There's no vaccine, that's

important to say, no vaccine that will go to EMA or two WHO or to FDA without good data. The problem for some vaccines was that they actually did have very good clinical data, but that they were still lacking high quality data for the good manufacturing process or for CMC *(chemistry, manufacturing and controls; Anm. d. Red.)* data, and that slowed down the process. So there are various factors – every vaccine is different. And Sputnik, for example, it was delayed because of GMP issues, good manufacturing issues. When they did a site visit, they found some problems. It was not delayed because they were lacking clinical vaccine trial data.

Moderator [00:43:15]
Now, Florian, do you wish any data which you have not seen on a certain vaccine which is distributed, or would you say, well, the evidence base is quite good we have?

Florian Krammer [00:43:25]
There are a number of vaccine candidates out there, where it would be nice to see more effectiveness data. We have effectiveness data for some vaccines, there's a lot of studies. For other vaccines there is little data. What I found really good, for example, is the study that was conducted in Brazil, where they basically looked at the whole population and compared AstraZeneca, CoronaVac. I think we need a lot more studies like that. And there is data missing on some of these vaccines in terms of effectiveness. We have to be careful. Efficacy, which is measured in the clinical trial in the phase three, is actually required for approval rate. Nobody will approve without that. But what is also important is the effectiveness. How well does the vaccine work in the population? So, we have to make a distinction between effectiveness and efficacy. And effectiveness data for a lot of these vaccines is not very solid yet, and we need we need more data to be able to cross compare. But again, that's different from efficacy and from what was measured in the clinical trials.

Moderator [00:44:34]
Maybe the last question, before we have the final question, is for both of you, Annelies and Jakob: From your perspective, what more could the vaccine manufacturers do to improve vaccine equity in the world?

Annelies Wilder-Smith [00:44:52]
Hmm, Jakob, you want to take the first step.

Jakob Cramer [00:44:58]
Produce more vaccine. Help us deliver the vaccine equally around the globe. Focus. Help us focus on those populations that are really in need of vaccinations first, so populations at risk.

Older adults, chronic diseases, immunocompromised, and then certainly partner with us, sit around the table. Maybe advanced developers help less experienced developers, sit around the table, speak with WHO, with the regulatory agencies and in workshops to explore ways forward for rapid reaction to emerging challenges, including new variants.

Moderator [00:45:46]
Annelies …

Annelies Wilder-Smith [00:45:48]
Totally agree with Jakob and almost nothing to add. I think a commitment to COVAX to deliver on time and not when another country offers a bigger price then to not to divert asupplies to those that offer more money. [Countries should] keep commitments to COVAX, to deliver it to COVAX in time and to come down with the prices to COVAX.

Moderator [00:46:19]
OK, then we move on to the final question just for each of you maybe a short answer. And that will be: Jeremy Farrar just said that he thinks that we are closer to the beginning than to the end of this pandemic. And I would ask each of you, what is your perspective on that? Some people felt that we are now through it, but it seems to be not. What is your view? How is going to proceed from here with Omicron in mind? Florian.

Florian Krammer [00:46:55]
I think I'm a little bit more optimistic, but I think what he says indirectly is we need to take this seriously. And I think we need to take the current Delta wave serious, and we need to take Omicron serious. And I think that's the message. [It would] be nice if this will be over soon, but Omicron might prolong the problem.

Moderator [00:47:16]
Annelies, what is your perspective?

Annelies Wilder-Smith [00:47:19]
I agree with Jeremy in many ways, in the sense that it will be very difficult to eradicate this virus. What we need to do is to do everything to protect healthcare systems and to avert deaths. And we're doing that with our current vaccines. But the problem is we need to keep the society together and to keep them confident in the science and for them to understand that we do need booster doses or may need to have variant adapted boosters. But the good thing is we

now know how to prevent severe deaths. We will be able to relax some of our restrictions. But I think this will be with us for many, many years to come.

Moderator [00:48:17]
Jakob …

Jakob Cramer [00:48:19]
It is certainly not on me to disagree with Jeremy Farrar, and I see his point, you know, from a timeline perspective. The pandemic started pretty much two years ago, and we are still not at all in a position to control this pandemic. We have no idea how Omicron will emerge. But, like Florian and Annelies, I'm much more optimistic. I'm in general also optimistic, which I'm sure Jeremy is as well, in that we have new technologies. We have a very well-functioning mRNA-vaccines for the very first time licensed. With this technology, we can react very quickly to new variants. We have other platform technologies. We have learnt a lot more about viral vector technology. We have learnt a lot about combining different platform technologies and to learn about advantages. We have invested in manufacturing capacity. We have invested in early warning systems. I do think we have learnt a lot, not just about this pandemic, but also about future pandemics, which CEPI will certainly look into. Lessons learnt to develop future pandemic preparedness strategies as well. So, all in all, I think, yes, we're not there yet, but there is also a lot of room and reason for optimism.

Moderator [00:49:37]
Okay, after a close 50 minutes, we come to an end. I first thank you experts for taking your time and answering all these questions. Thanks for the many questions from the journalists. We couldn't answer all of them. But anyhow, we hope that we could clarify the most important issues. There will be a transcript and the video available at the Science Media Center and also at the International Vaccine Hub. And with that, I leave you and we all hope that the next weeks will be not as bad as some of us fear. Thank you again and bye. Have a nice day.

All [00:50:15]
Thank you. Thank you very much.

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