



**Transcript of virtual press conference with
Gregory Hartl, WHO Spokesperson for Global Alert and Response
and Dr Marie-Paule Kieny, Director of the Initiative for Vaccine Research, World
Health Organization**

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Mr Gregory Hartl: This is WHO Headquarters in Geneva. We welcome you all to this virtual press briefing today. My name is Gregory Hartl and with us today is Dr Marie-Paule Kieny, the Director of the Initiative for Vaccine Research at WHO Headquarters who will make a few opening remarks about the results of the SAGE Committee meeting of last week and their recommendations and then we will open the floor to questions. As always, please, if you have a question to ask please dial 01 to get into the queue to ask the question and state your name and organization. Dr Kieny over to you:

Dr Marie-Paule Kieny: Thank you very much Gregory. It is a pleasure to be with you again to give you this update on the recommendation of the SAGE on H1N1 vaccine and vaccination. The SAGE is the Strategy Advisory Group of Experts, that is the highest level of advisory body in WHO on immunization matters and they met last week on 7 July to be updated about the epidemiological status and the clinical status of H1N1 as well as being provided with an update on expected vaccine availability. They also reviewed the status of production of the current seasonal epidemic vaccine. As you know we are coming to the end of the production campaign for the vaccine which is meant to be used to fight seasonal epidemic of influenza in the northern hemisphere starting this fall and they also met to review various vaccine options that would be available both for seasonal immunization and for H1N1, and to make recommendations to the Director-General. The SAGE, which was helped by a number of experts and also by another committee that we have established in May, which is more specific about the expertise in the area of influenza, so the group together came together with recommendations that were endorsed by the Director-General on Friday. In general these recommendations take into consideration as I said the epidemiology, the severity of the disease, the expected availability of H1N1 vaccine and have come up with a number of recommendations. I will be very happy to detail them following questions but just to give you an idea of how they go. First, the Committee recognized that the H1N1 pandemic is unstoppable and therefore that all countries will need to have access to vaccines. Second, the Committee also recognized, really acknowledged the fact that different countries have different epidemiological and other situations and therefore that the countries themselves will have to take decisions that are best adapted to their own national situation but in terms of giving indicative consideration and guidance to countries, SAGE recommended first that healthcare workers should be immunized in all countries in order to maintain functional health systems as the pandemic evolves. So there are several reasons to protect health workers when they put themselves at risk, when they care for patients; the other one is because they need to remain in good health condition to care for pandemic influenza sick people and the third is because during the time of a pandemic people will continue to be ill with other diseases and these diseases will also need to be taken care of. Second the SAGE considered the gravity of the disease in various groups and considered that countries may have different strategies when they implement

immunization campaigns. So the first one would be to try to stop transmission and if you want to stop transmission as much as you can, and this may still be possible, in certain settings at least to mitigate transmission, you target different population groups, and if you just want to have other objectives: So the first objective is to reduce transmission as much as possible. Another objective might be to reduce morbidity and mortality and the third objective, but there is no priority in order, would be as I said, to protect the health care system. In view of these three objectives countries might have, and depending on their own decision, they may consider immunization of several different groups - one of them being pregnant women e.g. as I am sure you have followed in the news, pregnant women are at elevated risk of severe diseases and death; other groups would be anybody over 6 months of age with chronic health conditions and these induced variety of conditions which are putting more people more at risk from having severe illness. This could be chronic respiratory disease - it could be obesity which has been now shown as being a risk factor. Another group to be considered would be healthy adults of over 15 years of age and less than 49 which have been shown also to be surprisingly, although were healthy, at risk of death. Yet another group would be healthy children and this is mainly to reduce transmission as we discussed because children are amplifiers of infection because they meet in groups. Yet another group would be healthy elderly adults and all country conditions need to be taken into consideration when countries make decisions.

The SAGE also then, to further go into decision and in going out with recommendation for target groups, considered the safety of adjuvant vaccines and they noted that there was, so far, no concern of the safety of vaccine adjuvanted with the new oil-in-water adjuvants but that it was urgent to collect safety data in groups for which safety data is not available in numbers for the time being. They also noted that because these vaccines are novel, use for some of them, a very good post marketing surveillance and pharmaco- vigilance has to be implemented when the vaccine is deployed and that international cooperation is requested to have results of any signal that some vaccine might not be safe, which we don't expect but you never know, be shared with the international community as soon as possible. Finally, they considered recommendations on seasonal influenza vaccination. They were informed that the campaign for preparation of seasonal vaccine for the northern hemisphere were close to completion with more than 90% of production being finalized by end of July and therefore considered that there was no need to recommend a switch from seasonal to H1N1 vaccine. They also considered that at the current time there would be no change in recommendation of WHO for the seasonal vaccine for the next season for the northern hemisphere, that preparations should continue for this immunization as if there would not have been a pandemic. So these are the main messages and I will be most happy to answer your questions.

Mr Gregory Hartl: Dr Kieny, thank you very much. Before we go to questions can I remind journalists that the audio file and transcript will be available shortly afterwards as usual on the WHO website. In addition, a web update outlining in summary, the conclusions of the SAGE meeting will be posted shortly. Once again, journalists who want to ask questions please press 01 on their keypad.

Fergus Walsh, BBC: Regarding the southern hemisphere can you tell me were there any decision made to ask companies like CSL and Sanofi Pasteur who will, in the general run of things, make seasonal flu vaccine for the southern hemisphere, they would normally expect in the autumn, to get the strain from you and do that. Whether or not you are planning to allow next winter's southern hemisphere seasonal flu vaccine to go ahead or whether you consider the pandemic is serious enough and that they should just concentrate on the

pandemic vaccine and secondly, when would you expect the first doses of pandemic vaccine from cell culture to arrive?

Dr Marie-Paule Kieny: In terms of southern hemisphere, this was of course discussed and SAGE considered that it was too early to make recommendations on the upcoming production of the southern hemisphere vaccine. Indeed, the southern hemisphere seasonal epidemic has started and now we are in the middle of it. It seems that there is still a significant proportion or number of cases which are caused notably by H3N2, one of the seasonal strains. There really needs to be more data accumulated on what is circulating in terms of the new virus or the traditional H1, H3 and B strains. So we expect that all these data, much more data and evidence will be available in September when traditionally WHO will hold its meeting to determine which strain should be put into the seasonal vaccine and by that time we hope that we will be able to be more explicit in giving recommendations in one direction or another. I still need to note that seasonal influenza is a severe disease in certain population groups, like the elderly or the very young and nobody would want to have an epidemic of severe and preventable seasonal epidemic in nursing homes when winter comes in the southern hemisphere. So this is something which is watched very carefully but it is too early to give any recommendations.

On when the first doses of pandemic vaccine made from cell culture would be available, there are already vaccine doses available. They are produced but they are by no means ready to be licensed yet. So both the doses are available for clinical trials, from both manufacturers who have been making vaccines from cell cultures but also coming very soon or are already there, as you may know, from manufacturers who are making vaccines from egg products. Notably, CSL in the southern hemisphere has really been rushing to prepare for clinical trials. So when we hear that vaccine is available already, certainly, yes, vaccine has been produced but it is still an experimental vaccine awaiting results of both pharmaceutical characterization to be licensed as well as upon request of regulatory authority clinical trials.

Helen Branswell, Canadian Press: If I could ask 2 questions. The first is a clarification. Dr Kieny you talked about a variety of different groups who might be vaccinated - am I correct in thinking that what you are saying is that the SAGE did not say these people should be first, these people should be second, these people should be third, but that it put a strong priority on health-care workers but after that its somehow left in the hands of individual countries? And I would have a follow-up question.

Dr Marie-Paule Kieny: So you are right: the SAGE identified the health-care workers as a main priority group for the three reasons that I already have given. In terms of the other group it really depends on the strategy that each country wants to follow. In certain cases, as I mentioned countries may want to try to mitigate transmission and therefore, children would be an obvious target. In some other cases, they want to rather concentrate on reducing morbidity and mortality and then some other groups may be more the target. But there is identification on various options but no ranking and no priority are given to these options.

Helen Branswell, Canadian Press: The follow-up I wanted to ask in your presentation to that made in last week, you refer to the fact WHO has done a survey of vaccine manufacturers asking them about their plans and if I read the slides correctly, only 12 of the proposed pandemic vaccines are planned to have adjuvants in them. Is WHO getting a sense that a number of manufacturers are not planning of using adjuvants? And do you have a position on whether or not that is appropriate under the circumstances?

Dr Marie-Paule Kieny: Indeed it is very difficult in a situation like in a pandemic when you want to have a vaccine which can be distributed safely to the population in the shortest possible time, it is very difficult to say that you take the adjuvant of one company and you mix it with antigens of another company when they have never been tested together. So we know for example that clinical trials financed by the US Government have looked at some of these combinations but these are very specific combinations. So it is very difficult to imagine because as you have seen in the slides, manufacturers are actually, although the vast majority of vaccine doses is coming from companies in certain areas of the world, there are actually vaccines manufacturers in other parts of the world, and these are producing less vaccines in terms of output in number of doses, but it would be very difficult to say let us just for the sake of taking an example that you take vaccines from country X in Asia which has never been a mix of any of this new adjuvant and then you just make the mix and you say that this is my vaccine and it will be safe because the safety of adjuvant is not only depending on the adjuvant itself, it is quite often combined fact between the purity of the antigen of a certain characteristics of the antigen and the adjuvant. So this is why a number of manufacturers who currently have never made any other vaccines than non adjuvanted vaccines are still planning to go with non-adjuvanted vaccines. I may also add a comment on that for the time being there is still the question to know whether the immunogenicity of the A(H1N1) vaccine will be more like that we are used to for seasonal vaccine where no problem with 15 micrograms not adjuvanted, just one dose is fine or will it be more like H5N1 where all the trials have shown that you either need to have a very potent adjuvant or you need to increase the dose quite significantly, so in the absence of these responses, yes a number of manufacturers are planning to go ahead with 50 microgram without adjuvant.

Martin Enserink, Science Magazine: Helen Branswell reported this morning or late last night from those presentations that the virus is not growing very well. I wonder if you can comment on that, and whether that will cause any delay? Secondly, has SAGE made any recommendations with regard to international solidarity? Is there any talk of any recommendations to create equity between countries, for instance you mentioned that countries can have different strategies but would it not be recommendable that they use only the vaccine for those high-risk groups and save vaccines for other countries?

Dr Marie-Paule Kieny: First, in terms of yields, maybe there is some confusion between the reality that is in the slides, that is now recognized by the manufacturers and the regulatory authorities and the WHO Network that we have a strain which are currently available to make inactivated vaccine, the manufacturers only get moderately affected yields. This is not to say that the viruses grow poorly, it is that for a reason or another the hemagglutinin they can produce is either not stable or very low. It is not known what is exactly happening but in terms of output that they have of hemagglutinin at the end when they grow a virus, they have poor yields, poor as between 25 and 50 percent of the normal yields that they have with good yielders. What is the reason for this is difficult to know, that it is well known that some strains are good yielders and some are bad yielders, it happens that for the first series of strains which were generated and unfortunately, we did not come up with a good yielder. So that in order to remedy to that the WHO laboratory network is again trying to generate new vaccines viruses from wild type virus isolated from patients, and these will be tested again by the manufacturers and we hope that at least one of them or more than that we hope will be giving higher yields that would be comparable to the ones obtained with seasonal vaccines. So for the time being, these are strains which are available and are still giving of course enough production yields in order to make clinical batches

into test immunogenicity of new vaccines. We understand that the regulatory authorities have said that when better yielders are available there will not be a need to have bridging studies between the results obtained with the strains available now and the new strains because actually there will be difference in yields and not in antigenicity or immunogenicity. So we hope that as soon as possible the situation can be improved upon but for the time being there is no reason to be really anxious about that.

In terms of equity, yes of course, SAGE has also made a note that WHO should try to help with as much equity as is there in the distribution of vaccines. We are all committed to that, we have several strategies, we are discussing with the industry and we have already, this was announced in the press, we have already secured a number of donations from industry, we have also secured access to real time production during the pandemic. WHO at the highest level is discussing with Governments to see how much they can help to either help negotiate some doses with industry but also help finance these vaccines and finally, but very importantly, we are also discussing with new manufacturers who have started to acquire the technology to make influenza vaccines in the past three years with technical and financial support from us, to help them accelerate their preparation and be able to produce some vaccines for their own country. So this is the situation in terms of trying to ensure equity for vaccines.

Richard Knox, National Public Radio: Dr Kieny, you said earlier that you do not expect safety issues to arise with the pandemic vaccine and tests but do you think that there is less risk of Guillain-Barre syndrome with this new swine flu vaccine than there was in 1976 and why? And secondly, I wonder with the accelerated safety tests that will be necessary, how many subjects will you expect to have tested and how can experts draw conclusions about safety from these tests when the vaccine has put into a hundreds of millions of people.

Dr Marie-Paule Kieny: It is not completely known why the vaccine which was distributed against the swine flu in 1976 induced higher risk of Guillain-Barre syndrome. There are a number of hypotheses and one of the hypotheses is that the vaccine was contaminated by a component coming from a bacterial infection that was inducing antibodies that cross reacted with self protein and therefore, caused Guillain-Barre syndrome. The vaccines which are produced now are much better purified than the way they were in 1976, so we really do not think that it is likely that we will have these side effects again, but to be absolutely honest, of course it is only when you have a large scale distribution of vaccines that you know with certainty the safety profile of the vaccine. Modern vaccines such as those which are used to immunize children and adults currently in all countries of the world are very safe products. Nevertheless, in a very small numbers of people they do induce adverse reactions and this can be the case as well for adjuvanted vaccines and non adjuvanted vaccines. So what needs to be put in place and everyone is working towards this direction is a very good surveillance system and monitoring adverse effects so that as soon as a signal pops up it can immediately be followed-up, investigated and adequate public health measures be taken to respond to that. Now, in terms of these new vaccines, new adjuvants there is one manufacturer who has had an oil-in-water adjuvanted influenza vaccine in use for many years for seasonal vaccination and the safety database for this particular antigen is very large although mainly in elderly people and there does not seem to be any signal for any unexpected severe event like Guillain-Barre. But as I said, all must be put in place to detect any signal as early as possible.

Journalist, Sky Television: Your referred previously that the obese people should probably be among those that the national government should consider to vaccinate. On

what scientific basis are made these recommendations and if you could elaborate more on the body mass index? And the second question is, if we have the vaccine later than October in the Northern Hemisphere, don't you think it would be too late to protect the people from the second pandemic wave?

Dr Marie-Paule Kieny: In terms of obesity, obesity has been observed as being one of the risk factors for more severe diseases other than H1N1 influenza. This is an observation. We still don't know exactly if it is obesity itself which is a risk factor, or if it is other health conditions which arise because of obesity. For the time being it is an observation and a lot of investigations are conducted to try and understand this better.

It has been observed in several countries that people with a body mass index over 30, and even more, over 40, have a higher chance of having a severe disease than non obese people. This is why one of the groups that was mentioned, that was listed by SAGE, and that was worth considering for pandemic influenza vaccination contains all populations over 6 months of age with risk factors, and one of the risk factor listed is obesity. Its not the only one of course, you have asthma, chronic lung disease. All these are considered as being risk factors based on observation so far. About availability of vaccines, all the manufacturers and the regulatory authorities are working to have vaccine available as soon as possible. Vaccines will be available starting from September or October. If the situation remains as it is, of course the regulatory authorities will certainly want to have a better handle at the safety in clinical trials and dosing in clinical trials and these clinical trials will take some time, and therefore, to have a full license of this new vaccine may take until the end of the year. This being said, many countries have provision in their law, so if there is an emergency they can invoke an emergency situation to use vaccine for which you would have already good characterization in terms of pharmaceutical data but not yet, all the data on clinical trials. We certainly look towards seeing how the epidemic evolves and when it unfolds, to see what is the situation in countries and we will take our own decisions on whether or not to use vaccine under an emergency provision as compared to waiting for full registration of these vaccines.

Maggie Fox, Reuters: If WHO wants to reassess its best case scenario for how many vaccine doses might be available – I think the last number for the best case scenario was 4.9 billion. And I am also wondering about this issue with the virus strain not producing good results. Was this also the same for the live vaccine or only for the killed vaccine?

Dr Marie-Paule Kieny: In terms of updating the figures that we have published for likely vaccine supply over the next 12 months, we will update these figures but we want to wait to have some further information to update these with some meaningful changes. First as we have to have a definite idea of what yield manufacturers are getting with inactivated vaccines: is it the same as seasonal, which was the assumption that we took when we made the first calculation, or is it 50%, and these of course as you may imagine will change the total output. The other information which is still lacking as what is a dose of inactivated H1N1 vaccine. Is it, without adjuvant, is it 50micrograms, is it 30 micrograms, we don't know. And we will know as soon as the result of the first clinical trial will come out, although the result will certainly be very adapted or relevant only to the vaccine which will be tested, it will still give a flavour of what kind of results we will have with the other inactivated vaccines. You asked a question about the live-attenuated vaccine, the response and the way this vaccine induces an immune response is very different because these are replicative organisms, so they induce antibodies and also anti-cell response. So for the time being, the results that we have from the manufacturers who make live-attenuated vaccines,

is that in terms of yields, and this is yields in terms of growth this time – how these vaccine strains grow – there does not seem to be any surprise and they grow with the same titres as the seasonal vaccine that they have obtained in normal production for a seasonal vaccine. Still there need to be clinical trials to know what titres of these live-attenuated vaccines will have to be used in a dose to make an effective dose. So the quick response is that we don't know, but in terms of growth they seem to be behaving normally.

Journalist, Scrip Pharmaceutical News: When the new pandemic vaccine becomes available later this year, will WHO or Member States have any new pharmaco-vigilance initiative to pick up ADRs to this new vaccine. For example, in some countries, they allow patients to report ADRs as other do not. Is WHO thinking about this or are you quite happy with existing pharmaco-vigilance systems?

Dr Marie-Paule Kieny: Although in some countries the pharmaco-vigilance system is working very well and we will pick up signals very easily, in other countries there need to be an increased attention to the pharmaco-vigilance system, notably in the developing countries and WHO is already working with countries to try and use systems in place, like the system that the Polio Initiative uses to detect cases of acute flaccid paralysis to try and help detect any signs of Guillain-Barre for example. We are both strengthening the network as well as working on new guidelines that will be more adapted to the detection of adverse events following vaccination with pandemic influenza vaccine.

Helen Branswell, Canadian Press: I would like to get some information about adjuvants and children. Obviously young people are among the people hardest hit by this strain so far but I don't think that there is much evidence at all about safety of adjuvants in that group. I was looking at a document yesterday that shows that with MS59 for instance, it has been given to 6 or 700 children which is not a long safety record. Are there any other vaccines – not influenza vaccines – but marketed vaccines with these kind of adjuvants that children receive now and that might give us a sense of whether or not they are safe to use in children?

Dr Marie-Paule Kieny: You are absolutely right that safety data, at least in terms of numbers are lacking in certain population groups. You mentioned the children, certainly there are no data in children more than 6 months old and less than 3 years, there are no data in pregnant women, there are no data in asthmatics, so there are quite a number of populations for which there are no data. SAGE has also made the point that as quickly as possible data should be obtained on these populations groups if they are to be vaccinated with these new vaccines. In terms of use of this new novel adjuvant in children, there is no vaccine for very young children that is using the formulation. The closest being the vaccine which is currently developed as the malaria vaccine, which has been tested in a few thousand children and is being tested now in Africa with this indication for malaria in a few thousand children, but apart from that, these data are still lacking.

Journalist, German Television: If I understand correctly, talking about the doses for the next winter, do we have to go for a mid-seasonal vaccine and then also to go for two other doses for the new pandemic vaccination, will there be enough vaccine for all the countries then?

Dr Marie-Paule Kieny: The vaccine against seasonal influenza for the Northern Hemisphere is finishing production. We expect to have more than 90% of doses which were planned to be produced, so this is very close to the number of doses that were produced in 2008. We don't envisage changes in the recommendation for seasonal vaccination, so vaccination will still target the same persons and as in the previous national recommendations mainly in most countries these people will be the elderly, over 60 or 65 years of age, also in some countries children as well, so yes, certain of these groups may receive during the upcoming fall three shots which could be one of seasonal vaccine and two for the pandemic vaccine.

Mr Gregory Hartl: Dr Kieny, thank you very much. That closes our virtual press conference for today, 13 July, from WHO headquarters in Geneva. And just before we say goodbye, one last reminder that there will be 3 things posted on the WHO website shortly: the normal audio file and transcript and in addition, a web update which outlines recommendations from the SAGE meeting will also be shortly available. Goodbye.