



**Transcript of virtual press conference with
Gregory Hartl, Spokesperson for H1N1,
and Dr Marie-Paule Kieny, WHO Director of the Initiative for Vaccine
Research, World Health Organization**

24 September 2009

Gregory Hartl: Welcome to the WHO's virtual press briefings, today Thursday 24 September 17:00 o'clock Geneva time. My name is Gregory Hartl. The speaker today is Dr Marie-Paule Kieny, who is the Director of the Initiative for Vaccine Research, at WHO Headquarters, and she will in just a second or two she update you about what is happening with H1N1 Pandemic vaccine. One or two house-keeping matters before we go to Dr Kieny, to let you know that tomorrow, Friday, on the WHO website, you can expect to see the weekly update on the epidemiology of the pandemic and secondly, there will be an update tomorrow on antiviral and antiviral resistance. Today is for pandemic vaccine and the transcript will be up tonight on the WHO website. Welcome. I will turn over now to Dr Kieny.

Dr Marie-Paule Kieny: Thank you Gregory. Good morning and good afternoon. It is a pleasure to have this opportunity, to give you the briefing on pandemic vaccines. I will try to address 3 points successively, and will try to discuss when the vaccine will be available, the second point is how much of it will it be, and the last point is for whom.

So in terms of when, vaccine development is on track. In May, we announced that it will take about five months from the time of the identification of the pandemic virus to the time the first vaccine will become available for use, and not for experimental trials. So here we are and the first vaccines have indeed been licensed and plenty of results have come out of clinical trials, in China, in the USA, as well as some other places in the world. These trials have actually given very good news, and have demonstrated to immunize a protective level of immunity with a single dose of vaccine, at least in the general population. Special populations, eventually children, people with immuno-deficiencies may need to have more than one dose, but in the vast majority of people, one dose will be sufficient.

The big impact of this is that with the same dose of vaccine, we will be able to immunize as many as twice the population. The second good news is that, a formulation which has been shown to work with the normal seasonal vaccination, seemed to work very well with this pandemic virus. So is this surprising? Yes, and no. Some people predicted that may be it will be possible, but many people thought of as an example of the effort they had to develop H5N1 potentially pandemic vaccines, and for H5N1, it had been very difficult to make vaccines, in the senses that either you need to have very high doses or to add adjuvant in order to reduce the dose, or/and of course, to use two doses. So this is very good news, and it shows that all manufacturers who are producing usually seasonal vaccines, will be also to make pandemic vaccines and that there will be no problem of access or intellectual property rights associated with/to adjuvant, of which most of them are proprietary.

So vaccines have been licensed in a few countries. The first country to license is China, and China has also been the first country to have reported the first clinical results. This has been followed by other countries. The US FDA has licensed vaccines as well as Hungary and many countries will come now and follow suite.

Why is then that not all countries have licensed vaccines? Well not all vaccines are equal. Vaccines which have been licensed right now are vaccines which are similar to traditional seasonal vaccines, and in these, they are not new vaccines, and are registered by the USFDA, for example, a strain variation variation of seasonal vaccines. For some newer vaccines in a number of countries, they will need to have a bit more time to look at the dossier with more scrutiny, I may say, because this will be considered as new and therefore certain vaccines may take a little bit longer to be licensed and this due to the consideration. The overarching consideration that national regulatory authorities are given to safety.

Now these vaccines are here, today. They will not be all. All the doses will not be available on the first day. This is quite obvious. They had started now to be deployed. The first country to deploy was China, and the Chinese have reported that 34,000 people have been immunized in the area of Beijing. Other countries are following suit. Hungary has indicated their intentions to start a roll-out vaccination campaign, on the 29th of September, so this is next week, and other countries will follow suit.

Safety? Well, there has been a report of 14 of these adverse events in China. Out of 44,000 vaccinated all these adverse events have been reported were mild. Many of them may not even be associated with the vaccine. And this is about the range that you will expect for any seasonal vaccine or any vaccine as a matter of fact. There is dizziness, headache, something which is quite common, when we administer vaccines.

So is there a chance that there will be more adverse events, yes of course. There could be and these volunteers will need to be followed a lit bit longer than what we know from the outcome of the vaccination right now. And it may be when millions of population are vaccinated, there would be some incidents of severe adverse events. So these adverse events will either be investigated, all of them, and then the investigators will find that either yes, they are associated with the vaccines, and immediately, this will prompt more research into seeing if other people receiving the same type of vaccines also have had adverse events. But the vast majority will be unrelated. Because when you vaccinate thousands and millions of people, of course, some of them were going to have heart attacks, some women were going to have miscarriages, and these may - because they have just been vaccinated – be associated in the mind of people with vaccinations. So there will need to be some careful analysis, to try to see which adverse event, which is really a worry, is associated with vaccination, and which are only co-incidental.

Now, we have tried to address the when, so how much? At the beginning of the pandemic in May, WHO had conducted a survey, with all manufacturers that we thought will be able to make potential pandemic vaccine and we asked 36 manufacturers to give us what will be the prospect for capacity to make H1N1 vaccines. We had a 100% response and 26 manufacturers indicated their willingness to make pandemic vaccines. We asked them also to indicate how much they would be able to produce, which gave us a total of a little bit less than a 100 million doses at the best, in the best case scenario per week, which, saying that a year had 52 weeks, by just calculating and extrapolation of the weeks per production capacity to a year, gave us a total production capacity of a little bit less than 5 billion per 12 months, 4.9 to be more precise, but of course, this was a theoretical number.

Where are we now? And are the assumptions that were underlying figures still thought as being realistic?

Not all of them.

The first assumption was that, the yields for the quantity of vaccines that the manufacturers could produce would be similar to what they routinely have seasonal vaccines. You have seen that we have discussed numerous times that the yields were not good. We are talking recently about a third to a half of what they would expect. Now there has been good news and we know that the yields that are obtained with the latest strain which have been given to the manufacturers, are closer to what they obtained usually with seasonal vaccines, but not completely quite there yet. So the yields are a little bit lower.

The second assumption is that they will be able to produce, the formulation which could give the most dose-sparing effect that they had and this is still the type of assumption that we think is correct right now. And the third assumption was that they will be producing only pandemic vaccines in their facility where they can make flu vaccines. So this we knew was unrealistic because as you know there is need to have seasonal influenza vaccines for the southern and northern hemisphere, and because of downtime that the manufacturers will have to implement in their production plan, we know that this figure of 5 billion doses, per 12 months, will not be reached. How do we think that the figure will be, right now? So our latest assumption is 3 billion doses per 12 months, into the pandemic, and we will launch another survey with the manufacturers in October, to try to refine this prediction, and to base the new figures that we will be able to give on actual data and responses directly from the manufacturers.

Third point, for whom. Who will get the vaccine? Well, of course the first countries to receive the vaccines will be two categories of countries. First are the rich countries, with a high income. These are the ones which have already in the beginning even before the pandemic started, purchase agreements with manufacturers. They will be served first, because they have binding contracts with the manufacturers and some of them have already received vaccines in their countries and are ready to start vaccination campaigns. The other type of countries to be served very early with the vaccines is the countries that they do not have to be rich, but who have domestic production. Among those is China, as being demonstrated by the fact that China has already started to vaccinate. Another country, maybe another producing country although we do not have the precise data, may be Russia, or others. So other countries will follow suite and we will see in which order they start to vaccinate.

Which population should be the first ones to be vaccinated? The WHO SAGE, which is the Strategic Advisory Group of Experts, the highest level of advisors to the Director-General on immunization matters, has recommended that all countries should vaccinate their health workers. These would represent about 2 percent of the world's population, and WHO is working currently with donors, with manufacturers, through donations, and when we have, or when we do not have enough donations, we have a purchase agreement with the manufacturers to obtain vaccines at reduced prices for the developing countries. We are trying, the Director-General has announced that she will try to obtain enough vaccines to be able to provide to countries in need, which are the countries that will not have access without WHO, to cover up to 10% of their population. So this will cover - about 2% of the population that will be health workers, and other populations to be decided among the priority groups by the national governments. Indeed the choice of a population to be vaccinated is a national prerogative and each country will have to take this decision in view of their own epidemiological and national characteristics.

So we hope that the vaccines will be made available to most people in need, in all countries as quickly as possible. WHO expects to receive the first doses of vaccines to be distributed to the poor countries somewhere by end of October; we may be able to start the first delivery during November, or this is still exactly to be defined. We need to discuss with the governments of the receiving countries to see when they will be ready to receive the vaccines.

Now there have been many questions about the health workers. Does it mean that the fact that WHO has recommended that health workers should be vaccinated. Does it mean that there will be an obligation for all health workers to be vaccinated? Well, WHO does not recommend that vaccinating is mandatory. It is up to a person to decide. It is a voluntary choice to be vaccinated. Nevertheless, there are plenty of reasons for health workers to be willing to be vaccinated. One is to protect themselves because they may be more exposed than other people because they will be caring for sick patients, with the H1N1 pandemic flu. The second is also to help maintain a functional health system, because if health workers are sick and have to stay at home, then there is nobody to take care of the patients from influenza or other patients. And the third reason, which calls really upon the social responsibility of the health workers, is that health workers who would be sick with pandemic flu, are or will be putting their patients at risk of getting infected themselves. So for all these reasons, we think that they are good reasons for the health workers to seek vaccinations against pandemic flu.

So where are we now with WHO in terms of working on access for pandemic influenza vaccine? As we have said before numerous times, we have been offered 150 million doses from two manufacturers. This is still the same. We are discussing with more manufacturers who have expressed interest to give us vaccines. There has been also announced very recently in the press and we are discussing with governments that some nine governments right now have made an official offer to WHO to give up to 10% of the supplies that they have bought for themselves. And we really look forward to discussing with those and other governments and other stakeholders, to help to get more equity in the distribution of this very important vaccine. Indeed as you know again, vaccines are the most important tool to combat infections and pandemic influenza vaccine, and pandemic influenza in particular. So we count on the generosity of the governments of the manufacturers to help WHO and the international stakeholders to make more equity in this world. Thanks for your attention.

Gregory Hartl: Dr Kieny, thank you very much. Now before we open it up for questions, just a couple of reminders, that the transcripts and the audio file for this briefing will be available on the WHO website, shortly after the briefing is over, and to all journalists listening if you would like to ask a question, dial 01 on your keypad to enter the question cue. So the first question is from:

Frank Jordan, Associated Press: Hi Dr Kieny. It seems obvious now that not all of the world's population will be getting the vaccine in the first year. In fact, you said there will only be 3 billion doses available. So the question is how are you going to prioritize and what percentage of the population definitely needs the vaccine? I will appreciate if you could talk a little bit about that, and also mention which populations you think will need two doses.

Dr Marie-Paule Kieny: In terms of the countries, we think that, as already said, all countries will need access to vaccines so we are working with the Regional Offices to identify those countries which are the most in need. Our estimate is that we will have to cover countries accounting for about three billion of the population so a little bit less than half of the world and as I said we intend to provide these countries up to 10% of the population-worth of vaccines and will use the 150 million doses/donations that we have from manufacturers as well as donations from governments and we will also purchase vaccines if needed. So who would be in this population? As we said, the health workers would be the first priority and then it would be up to the decision of the national governments, they would consider, of course, people with underlying health conditions such as people with asthma, with a cardiac condition, people with immunodeficiency, people with other health problems of all ages, pregnant women and other minorities for some countries - so it will really be each country's government to make a detailed analysis of which population at the national level will most benefit from pandemic immunization.

So of course we are lucky that the pandemic is moderate in severity that most people experience a mild illness and recover spontaneously, therefore although one would want to protect everybody. Of course one always wants to give the maximum protection to everybody, it is also clear that most people will do well without vaccines. In terms of the number of doses it is clear that in clinical studies so far (we are not at the end of it) - we don't know yet for example what the duration of protection induced by a single dose of vaccine - the earliest data that we have indicates that at least in adults and in adolescents, one dose is sufficient, so in young children in special groups it is probable that two doses would be needed. Not all vaccines have been tested but generally it is likely to be one dose.

Gregory Hartl: Thank you very much so the next question will be from Elizabeth Sukkar. Go ahead please.

Sukkar: Hello. It is to do with the regulatory process to approve the vaccines, the US versus the EU, do they use similar application processes and secondly recently in Australia the CSL vaccines were approved there for an age group of ten years and over strangely the US FDA approved the same vaccines for eighteen years and upwards, so I was just wondering if you can comment on those two new questions?

Kieny: So now all countries have slightly different regulatory pathways as you know. So the vaccines which have been licensed so far by the US FDA have been licensed on the basis of a strain change, which is that they were considered as seasonal vaccines with a different strain which is a pandemic one. Therefore in the US the vaccines have obtained the licensing indications so for the population for which these vaccines are licensed for seasonal flu in the US. So the vaccines where the corresponding vaccine is licensed six months to no limit of age, this is the indication that the pandemic vaccine will get into the US, because it is a strain change. In Europe where there is not this procedure of strain change, there are two procedures in place, one is the mock-up dossier which is to register vaccines which are similar and which are made out of a model which was the H5N1 vaccine prototype, and other vaccines will take a little bit longer because they will have to undergo a full regulatory approval. In Australia they have their own way of licensing vaccines; the producer could come with clinical trial results in the population covering the indication that was given. So yes it is the case that all the products are different and also that all the pathways or most pathways where the regulators are different and therefore this is why the vaccines get different indications.

Hartl: Thank you the next question is from Mr Gold of Deutsche Presseagentur in Geneva, go ahead please.

Gold: I just wanted to ask about this issue of donations to the developing world and if you could be a bit more specific about what exactly, what amounts you will be expecting the developing world to receive and secondly you said that it would be up to the governments to decide how to distribute that, do you have any concerns that certain governments might not distribute the vaccines to the most vulnerable populations and might do it on a favouritism basis?

Kieny: Well we hope not! The governments are usually very responsible for that, one of the strict recommendations that we have is that it is used for health workers so that is really an important recommendation that we give to these governments. One other important factor before we deliver the vaccine: we need to have an assessment of the readiness of a country to distribute the vaccine and the readiness will include, of course, having a plan and having identified the target groups and we will review all this with the government before we send the vaccines, because nobody wants the vaccines to be sent and to stay in a warehouse for months or go wasted, even worse! So therefore one of the important factors that will help us define at what time point a particular country receives vaccines is the readiness and as I said we need to identify the priority groups because if we need to target health workers or pregnant women or children these are completely different strategies that

we need to put in place to be sure that we reach the maximum number of this type of category of people. So we are really confident that the vaccine will be put to good use.

I didn't respond to the beginning of your question, sorry. The number of doses, as I said we have currently access to 150 million doses through the manufacturers. With the calculation of what we know of what the countries who are willing to give us 10% of their own supply have purchased on their own, we know that from this we are likely to receive 50 more million doses, so that this would get us to 200 million doses. We hear and we are in contact with other governments who are willing to do something also to support this effort so this quantity is very likely to increase and we will try our best with funds raised by sister UN Organizations to be able to purchase what will be missing to allow us to deliver up to 10% in each of the countries.

Hartl: Thank you very much, so just a reminder to those listening if you would like to ask a question dial 01 on your key pad to enter the queue. The next question is from Helen Branswell of Canadian Press, go ahead please.

Branswell: You said that at this point you think that the estimate is more likely to be three billion doses over twelve months. Does that number hold if manufactures resume making seasonal flu vaccines for the Southern and Northern Hemisphere?

Kieny: Well this is what we factored in in decreasing from five billion to three billion. We don't know for the time being exactly how many vaccines will need to be produced for the seasonal immunization and there haven't been any WHO recommendations on the formulation of the seasonal vaccine. So you may have seen that the Melbourne expert meeting this week has made a recommendation of the composition, not on the formulation, of seasonal vaccination of the Southern Hemisphere and that the pandemic strain is among the strain identified. So this and whether the pandemic strain is introduced in the seasonal vaccine or is kept as a stand-alone will have an impact on the number of doses so we will - this is an estimate for the time being and we will try our best in October to refine it as I said based on real data.

Hartl: Thank you very much, the next question is from Mr Mackmillen, go ahead please.

Mackmillen: I comment that it would be ideal to vaccinate the entire population at the same time but that would not be possible, what could possibly be the drawback in vaccinating half the world and let's say the other half not being vaccinated? I am referring to the chances of the virus becoming resistant sooner than we expected because there will be this divide between those who have the vaccination and those who do not have it.

Kieny: Well we hope that the whole world will have some access to vaccinations, this is certainly the commitment of the Director-General and the Secretary General of the UN, not to let a country to be without a vaccine so of course, you are right, in some countries it will be possible to vaccinate the whole population, in some other countries it will be only 10%. So will this have a role to play in the apparition of variants of drift variants, this is not sure. You know the influenza virus is unstable by nature so we know it will evolve. For the time being it hasn't changed and the viruses circulating are still like the ones which have been isolated at the beginning. So what will happen if a virus drifts, changes, well if it doesn't change too much the vaccine that we have now will still be efficient. If a virus drifts a lot then a new formulation of vaccine will have to be developed and produced. So we hope that the best use will be made of about three billion doses that the world will be able to produce.

Hartl: Thank you very much, the next question from Ms Favaro, CTV. Go ahead please.

Favaro: Two questions. Number one, would it have been better for the world to go with just one vaccine so that one didn't have this difference between countries and its readiness and its testing and number two I am wondering if you are aware of this unpublished study

from Canada that is linking prior seasonal flu vaccinations to an increased risk of H1N1 infection and if you have seen it and what the implications might be.

Kieny: So in terms of having one vaccine, of course it would make logistics easier, but there are individual manufacturers and they all make their own vaccines. There are historical reasons for this - there are all intellectual property rights reasons from time to time and regulatory reasons why they might be different. So it is like as if you have different cooks in different countries all making a choucroute, this may be different or roast beef or something and it may taste a little bit different - this is why these vaccines are also different. In terms of the Canadian study which is still unpublished of course, we have heard about it and we are of course linking with the investigators. This data for those of you who are not aware of it yet seems to indicate that having received a seasonal vaccine puts you more at risk of contracting H1N1 pandemic influenza or be infected. So we are trying to discuss with other experts and the Canadians themselves are trying to put a panel of experts together who will allow them to review their data. These investigators are well known, they are very capable but all studies can have biases - we are in contact also with investigators in other countries knowing these findings, [they] have tried they have looked in their own data in their own country whether they could find a similar observation and none of the other countries have been able to find anything like this. So the reason why this may be different in Canada and in this particular study as in other places in the world is not yet identified. It may be that it may be a study bias, it may be that something is real but certainly the WHO as well as the regulators in all these countries are looking forward to be able to see the data, to study the data and to come with a better understanding of whether this has any chance of putting people at risk, the fact that they have received the seasonal vaccination. I must say also that years and years of seasonal vaccination has not indicated that a previous vaccination has an adverse impact but again more data, much more investigation of data already collected and investigation of new data will be needed to see if this is really real.

Hartl: Thank you very much, next questions from Jennifer Tryon, go ahead please.

Tryon: You have indicated nine countries are willing to donate up to 10% of their countries supply, is Canada one of those countries and can you list the other countries.

Kieny: I will have a hard time to name the countries, they have been put in a press release so I don't want to miss any one of them but I will try. The US started the movement, there is the UK, France, Norway, Brazil, Italy, New Zealand???, Switzerland and not Canada yet. We are discussing with Canada and we will see. Canada and other countries may be coming forward, maybe not on the initial list but we hope that as many as possible will come forward and will help with providing another vaccine.

Hartl: Thank you very much, next question is from Ms Udi from Japan.

Udi: I have two questions, one is concerning the early data of the clinical trial, you said for healthy adults one dose is enough, I would like to know why only one dose is enough, does that mean that some adults have some immunity for the pandemic influenza or not, and the second question is concerning the safety of the vaccine with a new type of adjuvant and produced by cell culture.

Kieny: Why one dose, it is true that it is a little bit striking because if everybody is naive which we would expect with a new virus and a new pandemic virus you would expect that one would need two doses - it may well be that there is enough similarity between this H1N1 virus and other H1N1 viruses which have been circulated before to make it that people are already primed, they are not immune but they have already seen something which resembles this virus and therefore they respond immediately after the first dose. It is interesting in the sense that numerous experiments have shown that immunization against the seasonal flu of last year for example did not induce any immune response that was

neutralizing the pandemic virus so it seems to function in one direction and maybe not in the other one.

In terms of safety, the safety of seasonal vaccine without adjuvants has been demonstrated in millions and millions of people in all types of populations from 6 months to old people, pregnant women. In fact it is recommended for pregnant women. So this is one thing, the other vaccines which use adjuvants are newer there is no doubt that the safety data base is not as large, nevertheless the safety data base with one of the adjuvant vaccines, the one from Novartis includes 40 million individuals, usually elderly people but still it is quite a large safety data base. The safety data base with the other adjuvanted vaccines - the one from GSK - also includes tens of thousands of people - is not that high, it hasn't been tested or evaluated in special groups of the population.

We have currently no reason to think that they will not be safe. We had an expert consultation on this topic in June, and the experts' opinion was that, in all likelihood, these vaccines will be very safe.

David Brown, *The Washington Post*: Can you give an estimate of how many countries are going to be dependent on WHO for their supply of vaccines and what 10% of that total population, the summed population of those countries is?

Dr Marie-Paule Kieny: We estimate that the population that will be dependent on WHO is about 3 billion people, and this is a little bit more than 90 countries. Therefore, 10% of these 3 billion would be 300 million doses and this is our target in terms of getting access to vaccines right now.

Melda Albano: I would like to get your spot on the fact that developing countries like the Philippines cannot totally complete their vaccination in the purchase of the H1N1 vaccines. ...Prices are expected to go up because of the big demand.

Dr Marie-Paule Kieny: We are aware of the fact that many of the developing countries have two hurdles to get access to vaccines. The first one at the very beginning was the price of the vaccines. Of course, vaccine is expensive and some countries don't have the financial means to buy pandemic vaccine. The other one is also supply because of the limited number of doses of pandemic vaccine which can be produced in a year – this is what we discussed a bit earlier –, and therefore because a lot of countries have already placed their orders, there is no offer any more, or very little. This is exactly for this reason that WHO is looking forward with the help of the other stakeholders to provide direct access through donations to these countries of pandemic vaccine.