Influenza Vaccine Update

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Coordinator: Welcome and thank you for standing by. All participants will be able to listen only until the question and answer session of the call. At that time, to ask a question, please press star 1 on your touchtone phone.

Today's conference is being recorded. If you have any objections you may disconnect at this time. Now I will turn over the meeting to Loretta (Jackson) Brown.

Loretta (Jackson) Brown: Good afternoon, my name is Loretta (Jackson) Brown, and I am representing the Clinician Outreach and Communication Activity -- COCA -- with the Emergency Communication System at the Centers for Disease Control and Prevention. Welcome to today's COCA conference call; Influenza Vaccine Update. We are very excited to have Dr. Anthony Fiore and Dr. Karen Broder, both from the Centers for Disease Control and Prevention.

We are using a PowerPoint presentation for this call. The PowerPoint is available from our Web site. If you have not already downloaded the PowerPoint presentation please go to emergency.cdc.gov/coca. Click on Conference Call Information Summaries and Slide Sets. The PowerPoint can be found under the Call-In Number and Passcode.

The objectives for today's call are that participants will be able to; describe recent changes in Advisory Committee on Immunization Practices recommendations for use of influenza vaccines; describe recent epidemiologic findings in vaccine coverage for groups at higher risk for influenza-related complications; discuss the U.S. safety monitoring in place for 2009 influenza A H1N1 monovalent vaccines; describe preliminary findings from the U.S. Vaccine Adverse Event Reporting System regarding the safety of H1N1 vaccines.

In compliance with continuing education requirements, all presenters must disclose any financial or other relationships with the manufacturers of commercial products, suppliers of commercial services or commercial supporters, as well as any use of an unlabeled product or products under investigational use. This presentation will not include any discussion of the unlabeled use of a product or products under investigational use. There is no commercial support for this presentation.

The first presenter is Dr. Anthony Fiore. Dr. Fiore has worked at the CDC since 1995 and is a Captain in the Commissioned Corps of the Public Health Service. He has co-authored recent Advisory Committee on Immunization Practices recommendations for hepatitis A vaccines, hepatitis B vaccines, and both seasonal and 2009 H1N1 influenza vaccines.

His current duties include acting as CDC Liaison to the Advisory Committee on Immunization Practices Influenza Vaccine Working Group, and developing influenza vaccine policy. He is Board Certified in internal medicine, infectious disease and preventive medicine.

The second presenter is Dr. Karen Broder. Dr. Broder is the acting Team Lead for the CDC's Surveillance in Public Health Response team. She is a member of the leadership team in CDC's Immunization Safety Office, which along with the Food and Drug Administration, has primary responsibilities for vigilant vaccine safety monitoring to assess vaccine safety and ensure detection of potential vaccine safety problems.

An internationally recognized expert in vaccine and vaccine safety, Dr. Broder has led national vaccine safety emergency responses and developed evidence based vaccine recommendations. Dr. Broder has authored scientific articles and abstracts on vaccines or vaccine preventable diseases, including two landmark studies published in the New England Journal of Medicine.

She currently leads CDC safety monitoring of the 2009 influenza A H1N1 monovalent vaccines through the Vaccine's Adverse Event Reporting System. Dr. Broder is Board Certified in pediatrics and practices in a community clinic in Atlanta.

Please welcome our first presenter, Dr. Fiore. Dr. Fiore?

Dr. Anthony Fiore: Hello and thank you for inviting me on this call. I hope in the next 20 minutes to provide you with a quick update on both the epidemiology of influenza -- both seasonal and H1N1 -- and also some updates on vaccine coverage, and finally wrap it up with some information about the new recommendations that will be available for the seasonal vaccine in this upcoming influenza season.

We'll start off with the epidemiology update. So you should be looking at -- at least on my slide set -- Slide 7 and its titled Epidemiology Update.

Let's move on to the next slide then, which describes the different kinds of influenza surveillance that CDC conducts together with their state and local partners. And that includes surveillance for outpatient illness, geographic spread, hospitalizations, virus monitoring, antiviral resistance and mortality from influenza.

Looking at the next slide, what you're seeing here, this graph, is depicting the percentage of visits for influenza like illness that occur through our surveillance network called ILINet, and this looks at the proportion of persons that walk into a provider's office and say that they have respiratory illness that's influenza like -- in other words, it could be influenza. We don't test these persons for influenza; it's just a general gauge of respiratory illness in the U.S. that fairly closely tracks a typical influenza season.

You see three seasons worth of data here. First you - the first bump there you see is the 2006-07 influenza season; a fairly mild season dominated by seasonal H1N1 viruses. The next bump up you see there is this - the higher peak is the H3N2 season of 2007 and '08 where we saw a more severe illness, especially in older persons, as we typically do in H3N2 seasons.

Next you see the 2008-09 season which was a pretty slow season. Mostly H1N1 up until April, when of course the pandemic showed up. That's where you see that most unusual second bump up there, that's aligned over the 2009 20 marker on the X axis.

You see a decline after that, which was the influenza like illness over the summer. Never got down to our usual summer trough. And then a great big

peak again, of course, when children returned to school. And going on into November and December and finally trailing off in the past few weeks.

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At the present time, we have relatively low influenza activity across the country. We do have some activity right here in the Southeast where we sit. There's regional activity in a few states, including Georgia, and some local activity in other states. But many other states are reporting no, or just sporadic, activity at the moment. This is fairly unusual for this time of year, but not unprecedented.

Next slide please.

This slide is showing you three different influenza seasons to give you a sense of how different this pandemic was, in terms of the people it affected compared to a usual season. The yellow bars are showing H3N2 - a typical H3N2 season -- that was the 2007-08 season -- where most of the hospitalizations occurred in persons who were over the age of 65 or younger than 4 years old. And relatively few hospitalizations occurred in - persons in the middle age groups.

The green bar shows a typical seasonal H1N1 season, 2008-09, where you saw even lower proportions of hospitalizations all across the age groups there, with still 0 to 4 year-olds being pretty hard hit, but really most of the other groups not having much in the way of hospitalizations at all. And I should mention this data is from our Emerging Infections Program that actually tracks laboratory confirmed influenza from hospitalizations in multiple states.

Finally, you see the pandemic. And in the pandemic you'll note in the red bars that the rate of hospitalizations was much higher in the middle age groups than it is in a typical influenza season -- either H3N2 or an H1N1 season, a seasonal H1N1 season. And you also will not that the rate of hospitalizations in older persons was really much less than it is typically in an H3N2 season. And so this is a very different pattern from what we usually see for seasonal influenza, the pattern that we saw for the pandemic, and this slide, I think, best captures that difference.

In the next slide I'm showing you, and this - you should be on what I have as Slide 12, showing you the frequency of underlying conditions among adults who were hospitalized. And this is - the important point here is that most adults who were hospitalized ended up having at least one underlying condition that predisposed them to more severe infection.

The orange bars depict the percentage of patients who were hospitalized for 2009 H1N1, who had that condition, and the green bar shows the prevalence of that condition in the general population. So you can see asthma, diabetes, cardiovascular disease, COPD, and on down the line, are overrepresented amongst persons hospitalized. And perhaps most strikingly, 9% of hospitalizations were in pregnant women, whereas at any given time only about 1% of the population is pregnant.

The next slide please, which is Slide 13 and shows the same sort of data for children. Again, asthma is the predominant condition, but neurologic and developmental disorders was the second most common condition. And of course, that's a pretty rare condition in the general population, but among persons hospitalized with 2009 H1N1, it was about 11%.

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This shows the influenza positive tests that we get through our viral surveillance system. And the important point here is that virtually all of the viruses, over 99% of them that we've seen since last summer, have been 2009 H1N1.

The other influenza viruses that typically we see during the season are just barely there. We've seen a few cases, but they have not really shown up yet. We're not fully certain that they won't show up again till next season at this point. We still have some time to go during the usual timeframe when we see influenza viruses, but it's been pretty slow-going for the H3N2s and the influenza Bs and so on, that we usually would be seeing this time of year.

We haven't seen antigenic drift; meaning that the viruses have not mutated much at this point – the 2009 H1N1 viruses. We see virtually all of them being susceptible to the antiviral drugs that we recommend at the current time, whereas virtually all of them are resistant to the adamantine drugs; drugs that have fallen out of favor in recent years because of widespread resistance among the seasonal flu viruses.

Next slide please.

This slide shows the number of pediatric deaths over the past three influenza seasons. And I think it's a good slide to use when you're thinking about whether this really was a mild pandemic, as some people have described it.

As far as children go, as far as children deaths goes, we've seen a lot more deaths in children during this pandemic than we typically do during a seasonal

influenza outbreak. So for 2006-07, we had 77 reported deaths. For 2007-08, 88 deaths; but 2008-09 -- now remember that goes right through April -- we had 133 deaths.

But the purple - the purple - purple box is depicted persons, or rather children who died of 2009 H1N1. So you can see, towards the end of that season most of those deaths were in 2009 H1N1.

And then going on across the graph farther you can see a very large peak in deaths that occurred over this past season, virtually all of them due to 2009 H1N1; 267 total. And even those deaths that you see depicted in green during that timeframe were probably due to 2009 H1N1, we just don't have the viral information to know for sure.

Next slide please.

Now of course we know that influenza infections are underreported. And that means that we have to use models to try to estimate how many people have actually been infected or been hospitalized, or who have died.

And so our models are indicating that at this point, between April and February -- April 2009 to February 2010 -- we estimate we had 59 million cases total, about 265,000 hospitalizations and about 12,000 deaths. And you can see the methodology that went into those models by looking on the Web site that I've listed below.

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And then just a couple more slides to really give you a sense of why this pandemic was different from a usual, typical influenza season. This breaks out the proportion of deaths due to 2009 H1N1 into three age groups, and you can see that those over 65, that blue wedge of the pie, is a pretty small piece of the pie. Whereas the large proportion of the pie is made up of 18 to 64 year-olds.

Next slide please.

The next slide shows what we typically see in a usual season, and that's 90% of deaths in those over 65 and only 10% those less than 65. And so you can see this - the way these graphs look is really quite different for the pandemic compared to a usual season.

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And finally, I just want to summarize the epidemiology with this slide, more or less saying the same sorts of things that you've seen in the previous slides. We had the highest incidence of lab confirmed infections in school-aged children. We had a distribution of hospitalizations and deaths that was quite different from seasonal influenza.

We had our highest hospitalizations rates in 0 through 4 year-olds. We saw hospitalization rates -- even in the timeframe April to October 2009 which is when we don't usually see much influenza -- that exceeded the usual rates for a season among school-aged children and among younger adults. And relatively few, although some, but relatively few severe cases among adults that were older than 65. Certainly less than you might have expected for a H3N2 typical season.

Most of the deaths occurred - deaths and hospitalizations, occurred among persons with risk factors for complications. It's pretty clear pregnancy was a high risk condition during this pandemic.

But we also might have some newly recognized conditions that put you at risk for influenza complications including; morbid obesity; being a member of an indigenous population like American Indians or Alaskan Natives, who seem to have higher rates of death and hospitalizations than the White population; and then neuromuscular diseases, which we've always known as a risk but it really did stand out during the pandemic.

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So just to give you a preview of what's going to be in the vaccine in this upcoming year, you probably already know this. The health authorities -- both the WHO and FDA -- decided that the pandemic H1N1 2009 viruses still pose a significant public health risk this upcoming season - that the currently circulating pandemic viruses are really quite similar to the recommended vaccine virus that's in the monovalent viruses.

And therefore, for the Northern hemisphere, for this upcoming 2010-11 season, the recommendation was that we; use the same virus that was in the monovalent vaccine -- that's called California/7; that we change out the H3N2 virus to A/Perth, this is a pretty routine sort of thing that we do according to Viral Surveillance; and that the B strain, influenza B strain, remains the same as it was in the previous year.

Now a few words about vaccination coverage; this - these slides are really, pretty much, lifted straight from Dr. Jim Singleton's presentation at the ACIP meeting in February.

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This is - you should now be on Slide 22 by my count, and this is entitled National 2009 H1N1 Flu Survey, or NHFS. And this is a survey that looked at weekly national estimates of H1N1 and seasonal vaccine coverage, and some of the behavioral factors associated with when people chose to be vaccinated.

I've given you some of the methods here, which we probably don't need to go into. Let's skip to the next slide in the interest of time.

And just to give you a quick preview of the coverage results thus far, and also to let you know that probably within the next couple of weeks you'll see these updated in the MMWR; overall coverage for persons 6 months and older was 23.6% -- that's that bar on the far left; coverage among 6 month to 18 year olds was 33.8%, and so on down the line. You can see coverage according to age group, with 25 to 64 year-olds, for example, being a little less than 20% at 19.8%.

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This breaks out coverage according to the initial target groups. You remember when the vaccine first came out, there were certain groups targeted for that - those initial lots of vaccine.

And those included; six - children and young adults 6 months to 24 years old, you can see they ended up with 30% coverage thus far; persons with high risk for influenza complications of older age groups, 25 to 64 year olds, they had 29.1% coverage; and health care workers who, as we know, always have some difficulty getting vaccinated or are reluctant to get vaccinated in some instances, only had 39% coverage.

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This slide, I think, is important to illustrate that we continue to have problems with racial disparities and ethnic disparities, in terms of vaccine coverage. For example, during a regular season, there's - the difference in coverage for children is slight, it's only 1%. For H1N1 it was actually 7.5%. However that wasn't statistically significantly different.

For adults though, there was a significant difference in coverage -- both for seasonal vaccine and for H1N1. So adults who are African Americans had lower coverage than White Americans for the - both the types of vaccine.

And that is also true for adults who are Hispanic. Hispanic adults had lower coverage than Whites. And this is something we've seen both with seasonal vaccine and with H1N1. It's something we really do need to work on.

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So just to summarize the vaccine coverage data; by February 13, 86 million people had received 97 million doses of H1N1 vaccine, and that's of course because young children are supposed to get two doses.

Most of the doses went to the target groups. Coverage was higher in children than adults. About 39% of health care workers were vaccinated. Among those children less than 10 who are recommended for two doses, as many as 60% of those had actually gotten their second dose. H1N1 vaccine coverage among adults was significantly higher in Whites compared to Blacks or Hispanics, that didn't really - it was not really different by race or ethnicity among children.

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So why didn't some people get vaccinated? This question was posed to people in two months -- in January and in December - or rather I should say it the other way around I guess. And the leading reason, in both months, was that the vaccine is not needed. Now there also were significant proportions of people in both months, about 20%, who chose not to get vaccinated because they were concerned about side effects or being sick from the vaccine.

And as far as the vaccine availability goes, of course that was better in January as compared to December. And a few people also thought they hadn't had time to get vaccinated, or the vaccine did not work. And of course these are sorts of communication issues that we need to continue to deal with both for future pandemics, as well as for seasonal influenza.

Next slide please.

So, to give you a preview of what's coming up in the upcoming influenza season, I thought I'd report to you what went on at the Advisory Committee on Immunization Practices on February 24 in Atlanta.

The next slide please, and you should be on Slide 29 now. This is just - the next few slides I'm just going to describe to you what's happened over time with influenza vaccination recommendations. Before 2000, the recommendations were fairly restricted to persons 65 or older, those with medical conditions, pregnant women, their contacts, and health care workers.

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In 2000 there was a big step forward which recommended vaccination for all adults aged 50 or older. In 2003 another recommendation for children 6 months to 23 months old, their contacts and then the pregnancy recommendation was expanded a little bit. Now the rationale behind all these recommendations up to this point was to prevent influenza in groups that were at high risk for severe morbidity and mortality.

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You should be on 31 now. But over time there's been an expanding rationale for why people should get vaccinated against influenza. And I've listed some of this expanded rationale here. One is to prevent outpatient and emergency department visits. These are, in addition to preventing illness, also are costly and take people out of work and school and so are a worthy prevention goal.

We also began to think that we should provide protection to persons who are higher risk for - highest risk for infection, and that is school-aged children. Even though school-aged children in general have fairly mild disease, reducing infections in that group would also potentially -- and that's my third bullet here -- reduce transmission by protecting their contacts.

There's also a group of people who have an indication, who are unaware of their - of the vaccine recommendation as it currently - as it was phrased back then with all the different risk factors, people and their providers had trouble remembering all that. There's also the need to address the issue that severe morbidity and mortality still occur, rarely, but unpredictably, even among healthy persons. And finally, there was concern that we should move forward with providing better access for all to this potential health benefit.

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So in 2006, the recommendations were expanded through 59 months of age for children and their contacts. In 2008, the school-aged children recommendation, a great big one. And at that point, for this past influenza season, it meant that about 85% of the population had an indication for vaccination.

Now, at the ACIP meeting in February there was - as you know, there was a vote put forward and passed, for a simple recommendation -- one that recommended vaccine for all persons aged 6 months or older. And this was the rationale behind it.

These are fairly dense bullets here, and I'm not going to read them all for you. But basically it could be summed up as saying that influenza vaccination is safe and effective. That mortality occurs in all age groups, including those adults who didn't currently have a recommendation.

And of course, already 50% of those middle-aged adults had a recommendation that some persons have influenza complications but don't realize it. They don't have risk -- they either don't realize that their risk factor

makes them eligible, or they don't even know they have the risk factor. And we also had this issue with possible newly identified risk factors, which included things like morbid obesity and race/ethnicity.

And then finally, the hope that a recommendation that all people ages 6 months or older would eliminate the need to determine whether each person had an indication for vaccination, they would emphasize the importance of preventing influenza across the population spectrum, and perhaps begin to reduce some of the barriers to people getting - to getting increased numbers of people vaccinated against this.

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And of course, this is where the recommendations are now. In the 2010-2011 season, the recommendation has been moved forward to include all adults, which means, all persons 6 months and older are recommended to annually receive the influenza vaccine.

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And I'll wrap it up with these next few slides, just to give you a preview of the types of vaccines that we expect to be available in this upcoming influenza season. A number of the companies have made changes in the types of vaccines available.

And I'll just kind of run through them here. I've - hopefully you can see on your screen, I've highlighted those changes in red. First of all, there's a high dose vaccine now for seniors that Sanofi Pasteur will have available in this upcoming season. This vaccine gives you higher antibody levels in that age

group. But it remains to be seen whether this translates into better protection. Studies are underway.

But this is another option for seniors. It's not preferred for seniors; it's another option for providers and seniors who want to take advantage of the higher antibody levels that this vaccine can engender. Novartis has a new vaccine for adults called Agriflu. It's made in the same way as Fluvirin is, but it's just another option for adults.

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CSL has changed their age indication so that now it's all the way down to 6 months. That means CSL vaccines can be given across the age spectrum and that increases your options for young children. Similarly Fluarix from GSK is now licensed down to 3 years and older. So again, more options for younger children.

And of course we will continue to have the vaccines that you're used to from previous years, including the live attenuated vaccine, Flumist, which of course was quite useful during the pandemic in mass immunization clinics, particularly in schools. So with that, and having run over my time a bit now, I apologize to Dr. Broder and turn it back over to her.

Loretta (Jackson) Brown: Thank you Dr. Fiore. Please welcome our second speaker, Dr. Broder. Dr. Broder?

Dr. Karen Broder: Good afternoon. I appreciate the opportunity to provide an update on H1N1 influenza vaccine safety monitoring in the U.S. I would like to remind people

that this topic was presented earlier in September. If anybody would like to review that, I believe it's available on the COCA Web site.

And during this talk, we'll review the systems that are in place to monitor the safety of H1N1 vaccines, especially the Vaccine Adverse Event Reporting System, or VAERS. And I will also present some preliminary H1N1 vaccine safety data from VAERS.

So we'll start with some background about influenza vaccine safety and vaccine safety monitoring systems. I believe I'm on Slide 39 now. Seasonal influenza vaccines have an excellent track record for safety that is supported by numerous studies.

The most frequent reaction after inactivated influenza vaccines, which are administered by injection, is injection sight pain. And up to 64% of people who receive these vaccines experience some pain after vaccination. And the most frequent reaction after the live attenuated influenza vaccine administered intranasally, is rhinitis. And up to about half of people who get the intranasal vaccine have rhinitis.

Vaccine components in seasonal influenza vaccines -- for example the egg protein -- may rarely trigger severe allergic reactions or anaphylaxis. And as this group probably knows, influenza vaccines are contraindicated in persons with severe allergies to eggs or to other components of the vaccine.

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Now there has been long-standing interest about the potential risk of Guillain-Barré Syndrome, or GBS, after influenza vaccine. GBS is an immune-

mediated acute demyelinating polyneuropathy affecting the peripheral nervous system. It's characterized by various degrees of weakness, sensory abnormalities, and autonomic dysfunction of the nerves due to damage of the peripheral nerves and nerve roots.

The estimated annual incidence of GBS is about one case per 100,000 population. And the reason, I think, that there is this concern about GBS is because in 1976, the swine influenza vaccine that was used at that time was causally associated with GBS, with about one additional case occurring per 100,000 persons vaccinated.

So since that time, subsequent studies of seasonal influenza vaccines have either found a very small increased risk for GBS after vaccination or no increased risk for GBS at all. And the conclusion has been that if there is a risk of GBS from seasonal influenza vaccines, it would be no more than about one additional case per million people vaccinated.

With this in mind, let's just review the timeline for the H1N1 vaccines. As you know, the pandemic started in the spring of 2009. And the vaccine was really rapidly developed and produced and distributed in a very fast timeline to meet public health needs.

In September 2009 the FDA licensed the monovalent vaccines for injection, which we refer to in this talk as monovalent inactivated vaccine or MIV, and as a live product which is referred to as LAMV. And the licensure and manufacturing process for these H1N1 vaccines were the same as those used for seasonal vaccines for the injection and for the live nasal product.

And so it was really anticipated that the safety profile of the H1N1 vaccines would be similar to that of seasonal influenza vaccines. And as we already talked about, the profile for safety for seasonal influenza vaccines is very good.

In July, as I believe Dr. Fiore reviewed -- CDC's Advisory Committee on Immunization Practices recommended this vaccine for target groups. And then in October 2009 the first doses of H1N1 vaccine became available to the public.

At that same time, very comprehensive vaccine safety monitoring was implemented in the United States. And numerous partners across the Federal government, State Health Departments, industry, academia, as well as the clinical community, collaborated to conduct this extensive monitoring.

The goals of the vaccine safety monitoring this - during this program were to identify clinically significant adverse events following receipt of the 2009 H1N1 vaccine in a timely manner; to rapidly evaluate serious adverse events after this vaccine and determine the public health importance of these events; to evaluate if there is a risk of GBS associated with the 2009 H1N1 vaccine; and then importantly, to communicate vaccine safety information about the H1N1 vaccine in a clear and transparent manner to health care providers, public health officials as well as the public.

This slide is a busy slide, but it shows the numerous components of the comprehensive monitoring effort. The systems above the dotted black line are those that were really designed to detect potential vaccine safety signals. And we use this term to mean an event that could be temporally occurring more often after vaccine receipt than anticipated by chance. And the main system

used in this above the line set of systems is the Vaccine Adverse Event Reporting System or VAERS, which I'll discuss shortly.

The systems below the line are designed to be able to verify any potential signals of concern. And I won't go through all of them. I just want to highlight one of the systems, which is the Vaccine Safety Datalink -- I think it's shown in the second box on the left -- that's VSD. And VSD is a collaboration between CDC and eight managed care organizations in the U.S. that covers over 9 million people.

What VSD does is it collects information about vaccination and health outcomes. And it can be used to actually look for risks of adverse events after vaccination - by comparing risks after vaccination with other groups or time periods, to actually look at risk. VSD is also currently being used to look for potential associations between H1N1 vaccine and certain pre-specified adverse events, such as anaphylaxis.

Now with such a big monitoring system in place, it was very important to have a group that was kind of overseeing it and coordinating these systems, and looking at the data. And this group was formed, and it is the H1N1 Vaccine Safety Risk Assessment Working Group, which is out of the National Vaccine Advisory Committee.

This group was formed to conduct independent, rapid reviews of the available safety monitoring data for the 2009 H1N1 influenza vaccines. It includes eight members from Federal Advisory Committees, as well as representatives from the Institute of Medicine and the public. And the National Vaccine Program Office coordinates these activities.

Importantly, this workgroup has been meeting routinely during the H1N1 response to review data. And has been posting reports on their Web site that are available to the public and to anyone to review.

So with this background in mind, we'll now switch gears and we'll spend a few minutes talking a little bit more about VAERS, which is hopefully a system that many of you are familiar with. VAERS is the Nation's frontline, early warning system to detect potential vaccine safety problems for licensed vaccines in the United States -- and I emphasize potential, because it really is a system that's designed just to look for possible concerns, but not to actually verify the concerns. That needs to be done, usually, through other systems.

VAERS is a volunteer reporting system that's jointly managed by CDC and the Food and Drug Administration. It's national in scope. It encourages reports from health care providers, and accepts reports from vaccinees and other people.

During the H1N1 response, VAERS was enhanced by increasing its staffing to be able to process and review reports more rapidly. And also taking steps to try to increase awareness about VAERS, and improve reporting to VAERS from health care providers.

Before spending any more time on VAERS, it's important to just highlight some limitations. And it's always important to keep these limitations in mind when you're looking at VAERS data.

First, VAERS usually cannot assess causality between a vaccine and the adverse event. Some adverse outcomes will happen after vaccination just by

chance, some may be caused by the vaccine. But VAERS usually cannot distinguish between the two.

The quality of data on the VAERS report is variable. There's no un-vaccinated comparison group. The denominator data is lacking. And VAERS both - data may be - reports may be stimulated, for example, if there's an event in the media that's publicizing a particular outcome. At the same time, people may not report all events that happen after vaccination, so there may be some under-reporting.

I'd like to now take a few minutes and remind you about how and what to report to VAERS. So we often get asked the question about what should be reported to VAERS. We suggest that providers report any clinically significant adverse event to VAERS that you think is important to you or your patients. And you don't need to know whether the event was caused by the vaccine to do this.

When you're reporting to VAERS it's important to include as much information as you can. The form has fields, and it's important to fill out this as much as you can.

In addition, the National Childhood Vaccine Injury Act requires that health care providers report any adverse event listed by the vaccine manufacturer as a contraindication to further doses of the vaccine, or specific events listed in the VAERS Reportable Events table that occur within the specified time period after vaccination. This information is available at the VAERS Web site.

I do want to highlight that the National Childhood Vaccine Injury Act does not specifically apply to the H1N1 vaccines. However, we do encourage reporting for clinically important adverse events.

And there are three ways to report to VAERS; you can either report online through the secure Web site; you can download a form and fax it in; or you can mail it in. And if you need assistance completing a form, the 800 number is provided on this slide as a reference.

We are also often asked how VAERS defines a serious report. The way that serious reports are defined in VAERS is actually based on the code of Federal regulations. Most of the time, this corresponds to a severe adverse event. But sometimes a report may not be that severe and may be coded as serious. And sometimes a report may be involving a severe outcome and may not be coded as serious.

And the way reports are coded as serious is if they are a report involving death, hospitalization or prolongation of hospitalization, a life-threatening illness as determined by the reporter, a permanent disability, or congenital anomalies. And most of these are listed in Box 8 on the VAERS form.

And this is just to remind you again, slide was in twice about how to report to VAERS.

Now let's look a little bit at some data. And I do want to let you know that the next couple of slides coming up have a lot of numbers on them and are there for your reference. So I'm just going to pull out the ones that I think are worth discussing.

In this slide, we see the VAERS report following seasonal influenza vaccine and H1N1 influenza vaccine, as received by February 16, 2010. The seasonal vaccinations are shown in yellow, and the H1N1 vaccinations are shown in the other color. And you'll see that we received almost 10,000 reports, after H1N1, about 9881 reports. And over 6000 reports after seasonal influenza vaccine.

I would like to highlight that most, more than 90% of these reports, were not considered serious in either group. And the proportion of serious reports was not higher after H1N1 vaccines compared with the seasonal vaccines. So for example, for the inactivated vaccines, about 7.2% of the inactivated vaccine reports were classified as serious. And about 7.8 of the seasonal inactivated vaccine reports were classified as serious.

And moving on to the next slide, this shows the age breakdown. Again, there is a lot of information on this slide. But most of the reports are non-serious. I think it's interesting that for the live vaccine, more than half of the reports were in the pediatric group -- younger than 19. And the proportion of non-fatal serious reports is similar or lower in the H1N1 group compared with the seasonal group for all the age groups represented here.

And then if we look at the last complicated data slide for the inactivated products, again we see the age breakdown. This is a little bit older - more reports are in the older age group as expected here than we saw for the live vaccine.

For the H1N1 reports, about 24% are in the 50 and older age group. About 36 reports are in the - 36% of the reports are in the 50 and older age group for the seasonal vaccine. Again, the proportion of non-fatal serious reports is

generally similar or lower in the H1N1 group compared with the seasonal vaccination group for all the age groups seen.

This is a graph that we thought would help you see how the VAERS reports are following the doses distributed. So the blue bars represent the VAERS reports received each week beginning in the week ending at the end of October 23, 2009. And the red line shows the doses distributed by week. And you see that both the red and the blue, the doses distributed and the number of reports were at their peak in November and then they have declined.

And you do see that there was a - the decline happened a little earlier with the doses distributed than with the VAERS reports. And that's what we expect, because people continue to report adverse events after vaccination for several weeks after vaccination. So we expect that the VAERS reports to take a little longer to come down.

Next slide please.

This is a slide just showing, looking at the numbers in a different way. We can look at the total number of H1N1 doses distributed, which is about 126 million doses as of February 16. And we can look at the total VAERS reports. And we can calculate a reporting rate for VAERS reports received per million doses distributed.

And so for the H1N1 vaccines, you can see there were 78 overall reports received for - to VAERS, per million doses distributed, but a much smaller amount -- only five per million doses distributed were of the serious category.

And now we'll get into part of the talk that might be interesting to some of you on the call which is, "What do these reports look like when you review them?" And I want to take a moment just to explain what happens after the reports are received.

The data I showed you earlier was based on the data that comes in on the report as it's filled out. The next set of data is based on review of medical records. VAERS staff requests medical records for any serious reports, and reports with certain conditions -- such anaphylaxis or Guillain-Barré Syndrome. And in the H1N1 response, clinicians reviewed these reports and looked at them a little more closely. And we present some of those data here.

After H1N1 vaccines, out of all the doses we talked about, there were 46 reports of death that were temporally associated with vaccination. Six of these were after the live product, and 40 of these were after the inactivated product. The age range was from 16 months to 94 years. And the onset interval from vaccination to death ranged from 0 to 37 days.

When we looked at these reports, and we looked at the death certificate and the autopsy, and we looked at the reported cause of death just reported out on these forms, this is the way they were distributed; cardiac, there were 22 had that as a reported cause of death; eight had infectious causes as the reported cause of death; five had neurologic outcomes; four multiple systems; two respiratory; one trauma; one pregnancy complication; and three unknowns.

I do want to take a moment just to say that here we're listing the reported cause of death as assessed by the Medical Examiner, or person who completed the death certificate. But in our review of these VAERS cases, we don't

generally assess for causality. We look to understand and describe the cases, and to look for patterns.

And the next slide shows what we found so far with respect to the Guillain-Barré Syndrome and the anaphylaxis. In these cases, clinicians looked at the total possible number of cases based on what came in through the automated data and what they saw in the manual review of reports. And then looked at these more closely, looking at the medical record for a physician diagnosis and using some case definition criteria from collaboration. (I wish to clarify that the collaboration is the Brigthon Collaboration, which is an international group that develops case definitions for adverse events after immunization).

And you'll note that these numbers are in flux because these data continue to be reviewed. But at the time these slides were made, as of January 31, there had been 123 possible GBS reports received; 64 of these have been verified, one was inconclusive, one was pending, and 57 had been ruled out and they were other conditions. And for the anaphylaxis, reports 268 of them had potential anaphylaxis, 115 reports were verified, and three were pending, and 150 were ruled out.

So with this in mind, let's look a little more at the overall assessment of the H1N1 vaccine safety. These VAERS data that I showed fed into a larger system. CDC provided initial data regarding the safety of H1N1 vaccines after the first two months of the program in an MMWR, which came out in early December 2009.

The conclusions at this time were that there were no substantial differences noted between H1N1 and seasonal influenza vaccine adverse events. And no safety signals were seen. And that continues to be the conclusion today.

Next slide.

These next two slides just show the data that the Vaccine Safety Risk Assessment Working Group looked at in making their assessment. These data are from their site and are available for your review. So I will not go into these slides in detail.

And the next slide shows the assessment from the Vaccine Safety Risk Assessment Working Group at their last report. As of February 26, (clarify this was 2010) the working group concluded that the data are adequate to assess the presence or absence of a signal.

Additionally, the working group concluded that the data do not favor a signal between the outcomes examined and the H1N1 vaccines. As signal is defined as an event that could be temporally occurring more often after vaccine receipt than anticipated by chance alone.

It's important to take a step back and recognize that although we have a very comprehensive federal monitoring system in place for H1N1, clinicians really play an important part in ensuring vaccine safety. And this starts at the time you're visiting with the patient, and even educating or drawing up the vaccine.

And as people on this call probably know well, you have a lot of responsibility. And we really appreciate your effort.

Clinicians need to properly store and administer the vaccine in a safe manner. They need to screen for contraindications and precautions. They need to

educate the vaccinee or caregiver about risks and benefits of the vaccine and this is helped by the Vaccine Information Statement.

For the H1N1 response, there were Influenza Vaccination Record cards that were completed. If there is an adverse event after vaccinations, the clinician is responsible for taking care of that and reporting clinically significant adverse events to VAERS. So this is not a small task, and we recognize the importance.

So in closing, during the 2009 H1N1 vaccine safety response, there was comprehensive Federal monitoring that was implemented very quickly. This was a robust system that involved the collaboration with many partners. And it included both new and existing systems. With more than 125 million doses of H1N1 vaccines distributed in the United States, no safety concerns have emerged.

Clinicians play an important role in vaccine safety monitoring and education, and played an important part in the H1N1 safety monitoring effort. And vaccine safety monitoring will continue to be important during future influenza vaccination seasons, especially as recommendations expand.

And I would like to close with a few resources that might be of interest to this group, on the next couple of slides. And then acknowledge the many partners, including health care providers, for their contribution for the vaccine safety monitoring. Thank you.

Loretta (Jackson) Brown: Thank you so much for that presentation. We will now open up the lines for the question and answer session. Operator?

Coordinator: Thank you. We will now begin the question and answer session. If you'd like to ask a question, please press star 1 on your touchtone phone. Please un-mute your phone and record your first and last name. Your name is required to introduce your question. To withdraw your question, you may press star 2.

Once again, to ask a question, please press star 1. One moment please for the first question. First question comes from Dr. (Norman Castau).

Dr. (Norman Castau): Yes, I have a couple of questions. One, on the slide that showed the new vaccines for the upcoming year, I saw times three for every kind. Are we supposed to get three shots?

And two, if the nasal mist causes rhinitis, does that cause a loss of vaccine and lower antibody levels?

Dr. Anthony Fiore: All right, thanks for that question. This is Tony Fiore answering that question.

First of all, the times three does not refer to how many shots you get. The number of shots you get is the same as is usual for seasonal vaccines and that's older children and adults get one shot; children under the age of 9 who have never been vaccinated before get two shots. And children under the age of 9 who have a previous history of having seasonal vaccine get one shot.

That's the current plan. So it's the same as usual. The times three refers to the number of different strains that are in the vaccine. And so, as usual, it's a trivalent vaccine.

As far as rhinitis goes, we don't advocate that people be revaccinated if they get some runniness of the nose afterwards. We believe the vaccine does give a good take - that you - we're talking about the live attenuated vaccine you squirt up the nose now, that - some of that is - some of that runny nose is a reaction to the vaccine; viruses replicating and interferon being produced. And as a result, runny nose occurring.

No, we don't see a need to be vaccinated. And the vaccine, the live attenuated vaccine, the one you squirt up your nose, actually works quite well in stimulating a local immune response.

Dr. (Norman Castau): Okay. Is there any chance that the government will provide the vaccine, as they did this year? I participated via my local Medical Reserve Corps, and we vaccinated 70,000 people -- mostly children. And I suspect, a lot of those would not have gotten vaccinated if they had to go to a clinic or their local physician.

Dr. Anthony Fiore: Well, we're certainly hoping that we'll build on some of the momentum that was generated with the pandemic response. I think a number of Health Departments have learned a lot about partnering with local groups, with schools, with local physicians, about doing mass clinics.

But there's not planned, at this time, a large-scale purchase by the Federal government with distribution of vaccine the way it was done for the pandemic response. We'll go back to the previous model, with the hopes that some of that momentum from this mass immunization clinics carries over and occurs again.

And it has been occurring more in recent years. Even before the pandemic we were seeing more of that kind of thing.

Dr. (Norman Castau): Okay, thank you.

Coordinator: Next question comes from Dr. (Robert Ball).

Dr. (Robert Ball): Nice shot Tony and Karen. Tony, question for you; on your Slide 17, the pie chart of deaths by age group, do you have any data showing Years In Potential Life Lost, YIPPLL -- or probably wouldn't apply dailys -- regarding the deaths in the younger age groups from H1N1 compared to seasonal deaths in the older age group.

I suspect that even though the numerator numbers of deaths is lower from 2009 H1N1, the Years Life Lost will be significantly higher. Any data? Any slides coming?

Dr. Anthony Fiore: I don't have their slides, but our modeling group is busy on those sorts of calculations. And they'll be - they will be using statistics like quallies to compare the pandemic impact to the seasonal flu. And as you point out, death at any age due to flu are tragic, and potentially preventable. But of course death in children and younger adults have, in some ways, a larger impact on society due to lost work, and to life lost, and so on.

Dr. (Robert Ball): Very good. Thank you.

Coordinator: Next question comes from (Elizabeth Bancroft).

(Elizabeth Bancroft): Hi, it's (Elizabeth Bancroft) from Los Angeles County. And again, I found the epidemiology presentation very interesting. And my impression is -- and I'm just wondering if it'd be a reasonable impression -- is that essentially folks who are under 65 lived through a true pandemic with a higher rates than usual of death.

And folks over 65 essentially had a relatively mild season for themselves and actually didn't really live through a pandemic. They just lived through, you know, a season that they had seen pre-1957. Or seasons they had seen pre-1957.

Would that be sort of a reasonable way of looking at things?

Dr. Anthony Fiore: Yes, I think that is a reasonable way to looking at things. I haven't heard it expressed that way, but I think it is quite reasonable now. And I don't mean at all to minimize the serious influenza infections we did see, even in seniors, they did occur. But they did not occur in the same sorts of - they did occur, rather, in the same sorts of numbers one might see in a typical seasonal H1N1 season...

(Elizabeth Bancroft): Right.

Dr. Anthony Fiore: ...perhaps even less than an H3N2.

(Elizabeth Bancroft): Well, what I've seen is that for seniors, they actually had a higher death rate than the 0 to 4, for example. It's just that their death rate - the 0 to 4 death rate was higher than you normally see, and the seniors death rate was so much lower than you normally see, that even though their death rate was higher, it still - it just was so inverted.

Dr. Anthony Fiore: Yes. Okay, I would agree.

(Elizabeth Bancroft): Thank you.

Coordinator: Next question comes from Dr. (Beth Shortridge).

Dr. (Beth Shortridge): Hello. The - will continue to immunize young babies with H1N1 vaccine, and the next seasonal vaccine will have H1N1 in it. And caregivers are asking whether they should postpone the H1N1 -- which I'm not advocating, now that it's almost April -- anticipating that they'll be getting the vaccine in the fall. And I just want to know how we should counsel the caregivers regarding the advisability of giving H1N1 now and again in six months?

Dr. Anthony Fiore: Well, I don't think we're concerned from a - and Karen Broder can chime in here, but we're not particularly concerned about that from a safety standpoint. I think there's benefit still to advocating vaccination, in that - particularly in that age group, because we think that age group is probably going to need two doses of that antigen to get a good response. That's one reason.

Another reason though, is that we don't know what's going to happen over this next few months. If the pandemic virus...

Dr. (Beth Shortridge): That is how I've been counseling parents, but I am not an epidemiologist. I didn't know if there was any material coming out, or available to give them?

Dr. Anthony Fiore: I think there's some communications material. It's a tricky balance about how to counsel them. You don't want to over-scare people. You know, it does

appear that this pandemic wave is - has slowed down considerably at this point. But there is still disease; particularly in the Southeast. There is still the potential for people that are traveling or something to walk into a winter influenza epidemic in the Southern hemisphere, for example.

And finally, this pandemic virus is - showed us last summer and spring it didn't really respect the whole, "Warm weather, flu goes away," paradigm. And so it's possible we'll continue to see smoldering infection rates through the summer -- perhaps more so than we do in a normal summer when we really see very little flu.

So I think you're on solid ground saying, "It's still a good idea to be vaccinated."

Dr. (Beth Shortridge): Thank you.

Coordinator: Next question comes from (Jeanine Williams).

(Jeanine Williams): Yes, I had a question about the VAERS report. I was wondering if you had any data concerning children that were administered H1N1 outside of FDA approved age ranges?

Dr. Karen Broder: Hi, this is Dr. Broder. Well we do know that this happened. You're talking about children that were given the vaccine, for example, a product that was approved for an 18 and older product that went into the arm of a child who might have been 3 or something like that?

(Jeanine Williams): Right.

Dr. Karen Broder: Is that - that's your question?

(Jeanine Williams): Yes.

Dr. Karen Broder: We do know that that happened. I'll defer to Tony, to maybe talk about the - I believe there were some adjustments in the CDC recommendations that allowed for use off-label when there weren't licensed products available. And I'll defer to Tony.

But we haven't seen any signals of concern for safety in general. And we've reviewed every serious report that's come in after H1N1. So I think that given those two activities together, if there was something that was, you know, especially severe that was likely to happen in that group, we should have seen it.

And the data that we have from VAERS would - I would say, we're not seeing a particular concern with that. Although it's - it wasn't a focus of study.

(Jeanine Williams): Okay. Thanks.

Dr. Anthony Fiore: Yes. I think Dr. Broder offered that I should add a bit to that. I guess two points I'd make would be that; the - many of the vaccines that even when they're - even - were studied even in age groups for which they are not currently licensed. And we did not see any safety signals. And admittedly, that's, you know, that's a few hundred people in a study, and not a large scale safety assessment. That's one thing to consider.

We have in past seasons, and continued during the pandemic, here at CDC to be somewhat permissive when it came to using vaccines outside their age

indications - for example a child who needs a dose comes into the clinic, and you don't have available the vaccine licensed for that age group. Rather than miss the opportunity to complete the vaccination, that you go ahead and use a vaccine that's outside of its age indication.

But we would not really want to encourage it at this point. We do allow providers to go off license like that when it's not practical to schedule another appointment. So we've been sort of permissive, but not encouraging of it.

(Jeanine Williams): Okay. And can I just ask another question related to it? Would you like for us to continue to report, even though it's not a reaction that the client may necessarily have to the vaccine, but if we find out that they had the vaccine out of age range, to report VAERS?

Dr. Karen Broder: This is Karen Broder. This question came up many, many times during the response.

And for purposes of the H1N1, we actually would say that if there was (clarify the response if for about using vaccines out of the recommended age ranges. - if the - the reasons to report would be; if you had a special safety concern; if there was an adverse event that happened after the vaccination, even if you're not sure it's related; or if this was something related to the live product, then we would encourage a report, because the live vaccine has just been around less and there's a smaller number of doses distributed.

And there's some opportunity for people to bet getting it who have health issues where they're not supposed to get it. We thought it was simpler to go ahead and - and - and - ask for reports around that vaccine without restrictions.

But if you have an inactivated product that was administered off-label, just by age range, and there's no safety concern in your mind, and no adverse event happened, at this point we're not specifically requesting that for VAERS.

(Jeanine Williams): Okay.

Dr. Karen Broder: Does that clarify your.

(Jeanine Williams): It does. Thank you.

Dr. Karen Broder: Thank you.

Coordinator: Next question comes from (Bill Hals).

(Bill Hals): Hi. This question's come up several times, then maybe you can help clarify something. We noticed that there seemed to be somewhat of an early deteriorations of some of the vaccines, and therefore some early expirations and recalls on some of the vaccines. It caused a little bit of a wrinkle within our community, and within our population as well as to the, you know, the safety issues.

And we assured everyone, of course, that it, you know, it was perfectly safe. That in - and per your all recommendations, you didn't need to come back for additional immunizations. But is that an artifact of the rapid development of this vaccine? Or is that commonplace with these types of vaccine?

And the second part of my question is, are - do you have some contingencies set aside in the event that the H1N (sic) decides to ramp up again?

Dr. Anthony Fiore: Hi, this is Tony Fiore. I think I can field that question and welcome Dr. Broder to pitch in if she has other thoughts.

As far as whether this is unusual, we have had in past seasons occasions when potency had fallen below specification and vaccines were recalled or were short dated. Field correction, I think is the term for when the expiration dates moved up. So it has happened before.

It did seem, I think to everyone's perception was that it seemed to have occurred more often with this particular 2009 H1N1 vaccine antigen. And it might reflect our inexperience with this antigen and maintaining stability. I think the manufacturers are working on whether - working to figure out whether there's something they can do to make this antigen more stable, and less likely to be subjected to one of those recalls.

Again, it's not a safety issue, it's the fact that the amount of antigen in the vaccine fell below specification. But it has happened in past years. And whether we will face it again in the fall, I'm not sure. I know that they have a lot of - they'll have time to play with the specifications over the summer when they're working on the Southern hemisphere vaccine...

(Bill Hals): Good.

Dr. Anthony Fiore: Again in the fall.

(Bill Hals): Okay, good. Well thank you very much. I appreciate that. There's a lot of folks that may not have voiced that question, but I think we here are more clear on it. Thank you.

Coordinator: There are no further questions at this time.

Loretta (Jackson) Brown: This is Loretta (Jackson) Brown. I want to thank our presenters for providing our listeners with this information. And I would also like to thank our participants for joining us today.

If you have additional questions for any of our speakers, please email the Clinician Outreach Communication Activity, COCA, at coca@cdc.gov. Please indicate the speaker's name in the subject line of your email and we will ensure that your email is forwarded to the appropriate person for a response. Again, the email address is C-O-C-A@cdc.G-O-V.

The recording of this call and the transcript will be posted to the COCA Web site at emergency.cdc.gov/coca within the next week. You have a year to obtain continuing education for this call. All continuing education credits and contact hours for COCA conference calls are issued online through the CDC training and continuing education online system at www.2-a.cdc.gov/T-C-E-online/.

Thank you again for participating and have a great day.

Coordinator: This concludes today's conference. Please disconnect at this time.

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