DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

Advisory Committee on Immunization Practices (ACIP)

Summary Report
August 5, 2010
Via Teleconference

Acronyms

AAP	American Academy of Pediatrics
ACIP	Advisory Committee on Immunization Practices
ACOG	American College of Obstetricians and Gynecologists
AMA	American Medical Association
ANA	American Nurses Association
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
FDA	Food and Drug Administration
GSK	GlaxoSmithKline
IDSA	Infectious Disease Society of America
ISO	Immunization Safety Office of CDC
IVATS	Influenza Vaccine Availability Tracking System
LAIV	Live Attenuated Influenza Vaccine
MMWR	*Morbidity and Mortality Weekly Report*
MMRV	Measles, Mumps, Rubella, Varicella
TIV	Trivalent Inactivated Vaccine
UK	United Kingdom
US	United States
VFC	Vaccines for Children Program
VIS	Vaccine Information Statements

FINAL – August 4, 2010

MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)
Centers for Disease Control and Prevention
1600 Clifton Road, NE, Atlanta, Georgia 30333 USA

Thursday, August 5, 2010
10:00 a.m. – 12:00 p.m. Eastern Daylight Time (U.S.)

TELECONFERENCE – ***dial in information for ACIP Members & Presenters***

Dial in number: Toll-free number (within U.S. and Canada)**:** 1-800-857-9623
Toll number: 1-773-756-4626

Passcode: 3908107

AGENDA ITEM	PURPOSE		PRESIDER/PRESENTER(s)
10:00	Welcome & introductions		Dr. Carol Baker (Chair, ACIP) Dr. Larry Pickering(Executive Secretary, ACIP; CDC)
10:05	Background on use of CSL trivalent inactivated influenza vaccine in Australia - 2010	Information	Dr. Tim Uyeki (CDC, National Center for Immunization and Respiratory Diseases, Influenza Division)
10:15	Influenza Work Group update: vote on use of CSL trivalent inactivated influenza vaccine in the United States, 2010-2011	Information Discussion Vote	Dr. Wendy Keitel (ACIP, WG Chair)
11:50	Public comment		Dr. Carol Baker (Chair, ACIP)
12:00	Adjourn		Dr. Carol Baker (Chair, ACIP

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ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

August 5, 2010
Teleconference

Summary Report

The Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC) convened an interim meeting of the Advisory Committee on Immunization Practices (ACIP) via teleconference on August 5, 2010. The following represents a summary of the proceedings.

Welcome and Introductions

Wendy Keitel, MD
Chair, ACIP Influenza Work Group
Baylor College of Medicine

Dr. Larry Pickering
Executive Secretary, ACIP / CDC

Dr. Carol Baker
Chair, ACIP

Dr. Keitel officially called the interim ACIP meeting to order.

Dr. Pickering welcomed those on the call to the interim meeting of the ACIP, and made administrative announcements. Slides presented during this meeting will be posted on the ACIP website within one week after the meeting. The meeting minutes will be available on the website within 90 days of the meeting. To ensure a quorum of voting members for this meeting, all *ex officio* members may be designated to vote as defined by the charter, which is posted on the ACIP website. With regard to disclosures, members who conduct clinical vaccine trials or serve on data safety monitoring boards may present to the committee on matters related to vaccines; however, they are prohibited from voting on issues related to those vaccines. Regarding other vaccines of the affected company, a member may participate in discussions with the proviso that he or she abstains on all votes related to the vaccines of that company.

With regard to meeting structure, open telephone lines were made available to ACIP members, *ex officio* members, Influenza Work Group members, other CDC staff involved in influenza, and representatives from CSL and Merck during the period of presentation and discussion of data. Participants with open lines were asked to place their telephones on mute during the presentations. All others on this call had dial-in access to listen only. When requested by Dr. Keitel or Dr. Baker, this line would be opened by the operator for general discussion and then public comment. Those who intended to make public comments were asked to give their name, organization if applicable, and declare any conflicts of interest. Time for public comments was

to be provided before the final vote. Given the time constraints, it was requested that each public comment be limited to two minutes.

Dr. Pickering reiterated that depending upon how many voting members were on the teleconference when conflicts of interest were called for, it may be necessary for *ex officio* members to vote as well.

Dr. Keitel the called for conflicts of interest, which were declared as follows:

Member	Conflicts
Dr. Baker	No conflicts
Dr. Chilton	No conflicts
Dr. Cieslak	No conflicts
Ms. Ehresmann	No conflicts
Dr. Englund	Receives research support from sanofi pasteur, Novartis, ADMA, and MedImmune. Dr. Pickering indicated that because other manufacturers may make influenza vaccines, Dr. Englund should not vote.
Dr. Judson	No conflicts
Dr. Keitel	Receives research support from Novartis.
Dr. Meissner	No conflicts
Ms. Rosenbaum	No conflicts
Dr. Sawyer	No conflicts

Dr. Pickering noted that there was a quorum, and that there was a sufficient number of voting members on the call so the *ex officio* members would not be required to vote.

Influenza Vaccine

Background on CSL Biotherapies Seasonal Influenza Vaccine in Australian Children, 2010

Tim Uyeki, MD, MPH, MPP
Influenza Division
National Center for Immunization and Respiratory Diseases

Dr. Uyeki reported that on April 22, 2010, seasonal influenza vaccination of children under the age of 5 years was suspended in Western Australia due to reports of febrile seizures that had occurred and been reported during a mass vaccination campaign. Of note, this seasonal influenza vaccination campaign with the target population of 6 months through 4 years of age was also conducted during the 2008 and 2009 seasons in Western Australia among a similar number of children in the same target population, with approximately 50,000 estimated to have been vaccinated. Febrile seizures were not reported during 2008 or 2009. On April 23, 2010, vaccination of children age 5 years and under was suspended throughout Australia pending further investigations [*Therapeutic Goods Administration, Australia, July 2, 2010*].

With regard to the findings of the investigation, vaccination of children age less than 5 years old with the 2010 trivalent inactivated vaccine (TIV) formulation produced by CSL Biotherapies (brand names Fluvax® or Fluvax® Junior) was associated with fever within 4 to 24 hours. A summary of the findings by the Therapeutic Goods Administration of Australia was released on July 2, 2010 indicating that in one cohort study, the risk of fever following Fluvax® vaccination was approximately 6.5 times higher than following a different TIV, Influvac®, made by Solvay / Abbott. Other studies indicated that the fever rate was approximately 8 to 10 times higher after receiving Fluvax® or Fluvax® Junior than Influvac® among children 6 months through less than 3 years old. In children 3 and 4 years old, the fever rate was 10 to 20 times higher after Fluvax® or Fluvax® Junior compared to Influvac®.

In terms of further data on fever, post-marketing surveillance reports in 2010 have indicated increased reports of fever in children age 5 years through 8 years following Fluvax® or Fluvax® Junior compared to the three previous seasons in Australia, although this is subject to reporting biases (e.g., lack of clarity about the vaccine coverage, influenza-stimulated reporting, et cetera). Nevertheless, there have been increased reports of fever in the 5 through 8 year old group following Fluvax® in 2010 compared to the three previous years. In addition, there are data from 2009 in which the CSL TIV was compared to another TIV in a clinical trial (both TIVs were the Northern Hemisphere formulation). This trial was conducted in the United States (US) and involved a 2-dose series for children aged 6 months through less than 8 years and 1 dose for children 9 through 18 years of age. The outcome for adverse events was fever occurring within 7 days of vaccination, which was found to be higher with CSL TIV (n = 229) versus the comparator (n = 228) for all age groups. In the group aged 6 months to less than 3 years, fever was 37% in CSL recipients versus 14% in the comparator. In children aged 3 to less than 5 years, fever was reported 32% of the times in CSL recipients compared to 11% in the comparator. In children aged 5 to less than 9 years, 16% reported fever with CSL versus 9% with the comparator. Again, this was only with the first dose of the vaccine. There was really no difference with the second dose of either vaccine in terms of fever reported [*Therapeutic Goods Administration, Australia, July 2, 2010*].

Substantially higher rates of febrile seizures have been reported in 2010 following vaccination with either Fluvax® or Fluvax® Junior among children 6 months through 4 years of age. Febrile seizure onset occurred a mean of 7.2 hours following vaccination, with a range of 5.9 to 8.4 hours. The overall rate of febrile seizures was estimated to be approximately 9 per 1,000 doses administered, which is roughly 9 times higher than the expected rate. In terms of the rates of febrile seizures for different age groups, for children aged 6 months through less than 3 years the rate was 7 to 10 per 1,000 doses administered. For children aged 3 years through less than 5 years, the rates were 1.5 per 1,000 for Fluvax® to 15 per 1,000 for Fluvax® Junior. For other vaccines that have been used (including Influvac®) the rate was 0 per 1,000 doses in children 6 months through less than 3 years of age and 3 years through less than 5 years. Compared to Influvac®, there was a substantially higher rate of febrile seizures with administration of Fluvax® or Fluvax® Junior [*Therapeutic Goods Administration, Australia, July 2, 2010*].

On April 26, 2010, the New Zealand Ministry of Health stopped the use of Fluvax® for ages less than 5 years also due to reports of febrile seizures. Prior to this stoppage, there were 9 cases of febrile seizures reported following Fluvax® in children aged less than 5 years. There was one case reported after vaccination with an unknown vaccine that was strongly suspected to be Fluvax®. A follow-up study revealed substantially increased febrile reactions in the 24 hours following Fluvax®, but this was not observed with Vaxigrip® manufactured by sanofi pasteur among more than 300 children aged less than 5 years. Another study revealed that no febrile seizures were reported in an estimated 5,000 to 7,000 children aged less than 5 years who had

received approximately 10,000 to 12,000 doses of Vaxigrip®. Similarly, no febrile seizures have been reported in New Zealand following administration of Influvac® [*Memo, from Immunisation Manager, New Zealand Ministry of Health, April 26, 2010; Australian Technical Advisory Group on Immunisation, July 30, 2010*].

No explanation has been identified to date for the observed increase in fever and febrile seizures in young children following administration of Fluvax® or Fluvax® Junior in 2010 in Australia or New Zealand. One limitation is that for persons aged 5 years and older, limited data are available on vaccination coverage with these or other TIVs. There was no increase in fever or febrile seizures noted with the monovalent 2009 H1N1 vaccination in Australia. On July 30, 2010, Australia allowed seasonal influenza vaccination of children to resume in those aged 6 months through 4 years using either Influvac® or Vaxigrip®, but not Fluvax® or Fluvax® Junior. Of note, the 2010-2011 Northern Hemisphere TIV strain composition is antigenically equivalent to what has been used in the 2010 Southern Hemisphere TIV in Australia and New Zealand [*Therapeutic Goods Administration, Australia, July 2, 2010; Dept. of Health and Ageing, Australian Government, July 30, 2010*].

In terms of the current policies on the use of CSL Biotherapies TIV, two countries in the Southern Hemisphere currently use CSL TIV (e.g., Australia and New Zealand). For Australia, Fluvax® and Fluvax® Junior are not recommended for use in children aged less than 5 years during 2010. In New Zealand, Fluvax® and Fluvax® Junior are not recommended for use in children aged less than 5 years during 2010. Three countries in the Northern Hemisphere use CSL Biotherapies TIV (e.g., Germany, the United Kingdom, and the US). The United Kingdom (UK) has recently published a recommendation regarding the use of Enzira®, which is distributed by Pfizer and CSL Biotherapies. The UK has recommended that these CSL vaccines not be used in children aged less than 5 years during the 2010-2011 influenza season [*Dept. of Health and Ageing, Australian Government, July 30, 2010; Memo, from Immunisation Manager, New Zealand Ministry of Health, April 26, 2010; Letter from Director of Immunisation, Dept. of Health, U.K., July 28, 2010*].

Afluria® is manufactured by CSL and is distributed by Merck in the US. This vaccine was approved in adults in 2007 by the Food and Drug Administration (FDA). In November 2009, it was approved by FDA for use in children 6 months and older. The 2010–2011 package insert for Afluria®, which was recently approved, includes additional information in Section 5: Warnings and Precautions, Section 6: Adverse Reactions, and Section 8: Use in Specific Populations. Basically, the additional language pertains to information about the experiences in Australia and New Zealand. Section 5.1: Fever and Febrile Seizures now reads as follows:

> Administration of CSL's 2010 Southern Hemisphere influenza vaccine has been associated with increased post-marketing reports of fever and febrile seizures in children predominantly below the age of 5 years as compared to previous years [*Afluria package insert, July 30, 2010*]

ACIP Influenza Work Group Update: Vote on Use of CSL Biotherapies Trivalent Inactivated Seasonal Influenza Vaccine (Afluria) for the 2010-2011 Influenza Season

Wendy Keitel, MD
Chair, ACIP Influenza Work Group
Baylor College of Medicine

Dr. Keitel thanked the members of the Work Group who have been devoted to this issue over the previous several months, as well as their colleagues at the FDA and CSL for their input into the Work Group's deliberations. She also acknowledged the tragic and untimely death of their fellow Work Group member, Dr. Carol Friedman, and extended the Group's condolences to her family, friends, and colleagues.

As summarized by Dr. Uyeki, Dr. Keitel reiterated that a number of investigations have been performed to ascertain the etiology of the increased occurrence of febrile reactions associated with seizures in younger children. The vaccine is at its range for potency, and there is no evidence of endotoxin contamination. The vaccine passed the rabbit pyrogenicity assessment. There is no evidence of failure of complete inactivation of the virus, nor is there currently any evidence to suggest that there is incomplete disruption of whole viruses, which clearly has been associated with reactions and seizures in past influenza vaccines. There are currently a number of on-going investigations being used to evaluate the manufacturing processes and reagents related to the destruction of whole virions to determine what role they could possibly play; however, the cause of this increased reactogenicity remains unknown. The workgroup deliberated over a number of potential options. After extremely careful consideration, the majority opinion was that the following recommendation should be made:

- Afluria® should not be used in children aged 6 months through 8 years, except for children aged 5 years through 8 years old who are considered to be at high risk for influenza complications, if no other seasonal TIV is available.

- Other age-appropriate, licensed seasonal influenza vaccine formulations should be used for prevention of influenza in children aged 6 months through 8 years.

Although this verbiage may require some word smithing if embraced byACIP, Dr. Keitel pointed out that this conclusion was predicated on the fact that there is a suggestion of increased reactogenicity in children aged 5 through 8 year olds; there is clearly an increased risk for febrile seizures in children under the age of 5 years; an increased fever response has been observed in prior CSL seasonal vaccines; and other options are available for prevention of influenza in the US.

The following minority alternative option was favored by several Work Group members, including Drs. Keitel and Neuzil (who was not able to join the call), due to the simplicity of the messaging from a public health standpoint, and because other age-appropriate licensed seasonal influenza vaccination formulations could be used:

- Afluria should not be used in children aged 6 months through 8 years.

- Other age-appropriate, licensed seasonal influenza vaccine formulations should be used for prevention of influenza in children aged 6 months through 8 years.

Discussion Points

Dr. Uyeki noted that Dr. Fiore thought there may be some grammatical confusion with the way the recommendation was worded. With that in mind, Dr. Fiore suggested the following wording:

- Afluria® is not recommended for children age 6 months through 8 years.
- Use of Afluria® can be considered if no other TIV is available for children aged 5 years through 8 years with chronic medical complications because the risk for influenza complications is likely to outweigh the risk for febrile seizures in this group.

Dr. Pickering noted that a recommendation could be approved, with word smithing generally permitted by the committee members afterward. This is a well-recognized practice that has been utilized in the past.

Dr. Baker indicated that she would first invite discussion from ACIP members which would be followed by discussion from liaison members and a public comment session prior to the vote.

Dr. Sawyer requested further information regarding the strange signal in the older age group of 5 through 8 years of age on slide 4. The only information he saw during this presentation was a 16% rate of fever compared to 9% rate, which he assumed was a subset of the sample of 229 children.

Dr. Keitel responded that the information on that slide referred to the 2009 CSL vaccine.

Dr. Sawyer inquired as to what, in general, the strength of information was about fever in children aged 5 through 9 and whether there was a breakdown of rates of febrile seizures in that age group. While fever of any cause at that age group is rare, he wanted to be comfortable extending through age 8 in the US as opposed to what was done in Australia and New Zealand.

Dr. Keitel responded that the work group understood based on spontaneous reporting, that there was a marked increase in the number of reports of adverse events. These were generally fever, but there was also a small increase in reports of "central nervous system abnormalities." The caveat is that this may have been stimulated reporting albeit at a much higher frequency than in the three preceding years. With regard to febrile seizures, her understanding was there are anecdotal reports of febrile seizures among children in that age group, with at least one of these children having a history of past febrile seizures.

Dr. Uyeki added that to clarify on slide 4, the 2009 data were from the clinical trial of the CSL TIV compared to a different TIV. In all three of those age groups, including 5 to less than 9 years, there was a higher frequency of fever. However, that outcome was for fever. The study lacked sufficient power to find febrile seizures. In terms of the post-marketing surveillance, their understanding was that in the three seasons prior to 2010, there were approximately 10 to 20 reports of fever in the 5 through 8 year old age group; whereas, in 2010, the rate was substantially higher. He deferred to CSL for the exact data, with the caveat that vaccine coverage in the 5 through 8 year old group is unknown. Also unknown is whether vaccine coverage was the same in 2010 as it was in the three previous seasons. The number of febrile convulsions and the rate is definitely lower, but in children 5 through 8 years, the rate is typically much lower. There were at least two reports for children aged 5 and one for a 9-year old who had febrile seizures following vaccination of Fluvax®. He believed both had a history of febrile

seizures. He requested that a representative from CSL further comment on the questions regarding fever and febrile seizures in this age group.

Dr. Jane Leong (CSL) responded that they observed increased spontaneous reporting in the 2010 Southern Hemisphere season. However, as Dr. Uyeki said, this was with a background of fairly significant media reporting so it is believed that reports were hyper-stimulated. Nevertheless, increases were observed in febrile reactions. Few febrile convulsions were observed because these typically do not occur in children older than 5. No febrile convulsions were observed at all in the 5 to 8 year old children.

Dr. Sawyer inquired as to whether this information indicated that above age 8, even an anecdotal suggestion of fever was not observed, and whether that was how they came to the conclusion that the cutoff should be age 8.

Dr. Jane Leong (CSL) replied that in the children older than 8 or 9 in Australia, the cutoff was 9 years. While there were increased reports, the numbers were not as great as in the younger children. Therefore, increased reports were attributed to stimulated reporting. In the 8 to 9 year old group, the reports included fever, the majority was non-serious, and they were consistent with previous experience.

To summarize, Dr. Baker said it seemed that in children over 5 through under 9 years of age, based on limited data, there was definitely more fever but no indication of more febrile convulsions.

Dr. Meissner noted that if the CSL vaccine was not used in children under 36 months, that left just Sanofi Pasteur to provide vaccine to children age 6 through 35 months. This raised the issue regarding whether there would be adequate supply.

Dr. Baker added that MedImmune's live attenuated influenza vaccine (LAIV) can be used beginning at age 24 months.

Dr. Uyeki responded, and Dr. Leong affirmed, that CSL made a decision not to distribute the 0.25 mL product. They were not planning to distribute vaccine that would be eligible for 6 months through less than 3 years of age. CDC understands that Sanofi Pasteur and MedImmune would be able to provide sufficient vaccine for the young, vulnerable age group.

Dr. Santoli added that she thought the other manufacturers would be participating in this call and could speak for themselves with regard to vaccine supply. She reported that the total projected number was about 12.7 million doses. Given that CSL decided not to produce the 0.25 mL doses for the US market, it was her understanding that more than half of the was in the 0.5 cc syringe, and a smaller amount was in the multi-dose vials. That meant US would have about 6 million doses using half as a rough estimate. She requested that someone from CSL or Merck speak further about supply.

Dr. Leong (CSL) responded that it was correct that CSL would *not* supply the 0.25 mL doses. They informed the ACIP Influenza Work Group that morning that they had made a decision not to supply the multi-dose vials. CLS continues to explore how this will impact the complete numbers in the end, and they will report back to ACIP with further information about this and the exact number of single dose syringes of 0.5 mL will be supplied.

Dr. Santoli added that with the total number of CSL doses completely removed, there were currently about 145 to 150 million doses across the other manufacturers. For comparison, the most that has been distributed in a single season was about 114 million doses. The current number of doses is significantly higher than that, even without adding in the CSL doses. However, that is a different question than what manufacturers actually have available to sell immediately.

It remained unclear to Ms. Ehresmann whether the other manufacturers would be able to meet the demand for the younger age groups. In addition, she wondered whether contingency plans had been established for providers who ordered CSL exclusively for that age group to ensure that they have access to vaccine.

Dr. Baker indicated that at least one manufacturer had shipped to the US Vaccines for Children (VFC) program, for which about 50% of children are eligible. It seems that the VFC supply might be a priority and might drive vaccine availability for that age group from the other manufacturers.

Dr. Santoli reported that the VFC had received some doses, as had the private sector. The product is multi-dose vials and it is not the pediatric formula.

Dr. Keitel clarified that based on what they had just heard, it did not appear that CSL had any plans to distribute a vaccine that could be used in a less than 36 month old child. There is no 0.25 mL and there is no multi-dose vial from which to draw 0.25 mL.

Dr. Ed Bresnitz (Merck) commented that the number of doses in the multi-dose vial, that are not going to be delivered now based on CSL's decision, was about 5 million. They had said that approximately 12 million doses would be available prior to this decision, which left approximately 6 to 7 million doses of a single dose 0.5 cc that possibly could be available and is for ages 3 and up. Those numbers are not finalized, given that CSL and Merck must discuss this.

Dr. Chilton pointed out that ACIP had discussed febrile seizures previously in the context of measles, mumps, rubella, varicella (MMRV) vaccine. He did not recall the frequency or incidence of febrile seizures following administration of MMRV, but ACIP made a somewhat different recommendation regarding that vaccine based on that frequency.

Dr. Keitel responded that it was 1 out of 2500 MMR and 2 out of 2500 MMRV, which is about 25 times more common.

Dr. Karen Broder (Immunization Safety Office, CDC) clarified that for MMRV, 1 in 2500 was a rough estimate for the attributable risk of febrile seizures, meaning the additional febrile seizures experienced 5 to 12 days after vaccination with MMRV compared with the young children who received the MMR and varicella vaccines separately. If memory served her correctly, it was something on the order of about 8 febrile seizure events per 10,000 vaccinees for MMRV versus MMR + varicella vaccine. One of the issues was that the MMR and varicella vaccine option was available and at the time, the MMRV vaccine was not available. There was a lot of discussion about the risks and benefits of weighing the options for the MMRV and the varicella. Parents and providers were permitted to use the MMRV product for those young children provided that they clearly describe the risks and benefits.

Dr. Meissner noted that another question that arose in the MMRV discussion regarded the use of antipyretics. Obviously, it would not work so well for MMRV because the fever occurs more than a week after the vaccine. However, the influenza vaccine the seizures seemed to occur with a peak at 7 to 8 hours after the administration of vaccine. He wondered whether consideration had been given to prophylactic use of antipyretics post-immunization.

Dr. Uyeki responded that there was brief discussion about this among the Work Group members, with the feeling that because there are plenty of alternative vaccines, this should not be considered as an option for recommendation.

Ms. Ehresmann had concerns similar to Dr. Sawyer's about what was driving the 5 through 8 year old recommendation. While she understood what was described in terms of post-marketing surveillance, in the absence of febrile seizures, she did not feel that the evidence was compelling enough for her. In terms of the current recommendations, 9 and under is the age group for 2 doses of seasonal influenza vaccine. In 2009, 10 and under was added for H1N1. Now they had the potential to make a recommendation not to use a certain product for 8 years and under. She found this to be very confusing and without compelling evidence, it seemed that they should align more with Australia's recommendation.

Dr. Keitel clarified that it was under 9 years, namely age 5 through 8 years. In fact, that was a public health issue that it was consistent with the two doses, which is under 9.

As a member of the Work Group, Dr. Englund reported that simplicity and straightforwardness were very important factors that the group considered when they wrote the proposed guidelines that were put forth for a vote. In terms of whether the Work Group had any concerns about the ages 5 through 8 group, it is quite clear that there is an increased risk of fever. The Work Group thought that since these vaccines would be used in pediatric practices, simplicity was a very important factor. Keeping it out of children in the less than 9 year old age group is a very important factor that equals the lack of good data.

Speaking as a pediatrician, Dr. Baker noted that for this season, the recommendation was for children less than 9 years of age who have not previously been vaccinated to receive 2 doses. The work group was recommending, both for the hard data in the less than 5 year olds and for the fever data, be it not completely convincing, that children less than 9 years of age would not receive the CSL vaccine. In terms of simplicity for family practitioners and pediatricians, all they would have to think about is whether a child is less than 9 when thinking about which vaccine and how many doses are needed. The work group contemplated many programmatic considerations.

Dr. Keitel responded that the simplest message would be the alternative option, which is not to use CLS vaccine in children under 9 years of age. The majority vote of the Work Group was to include the caveat about using the CSL vaccine in high risk children if no other vaccine was available, after weighing the risks and the benefits.

Dr. Lett requested that Dr. Uyeki discuss the email exchanges he had with Dr. Stanley Gall regarding his concern about pregnant women.

Dr. Uyeki responded that there does not appear to be any data to inform a recommendation about the use of this vaccine in pregnant women in the Southern Hemisphere. Vaccine coverage among pregnant women in Australia and New Zealand is not known, nor has CDC heard anything from its colleagues in Australia and New Zealand about reports of fever following

seasonal influenza vaccination of pregnant women. While coverage in pregnant women with this vaccine is completely unknown, it is thought to be very low. The issues that have been raised for discussion with pregnant women are that, theoretically, if a pregnant woman has a post-vaccination febrile reaction, this could have implications for the health of the fetus. Theoretical concerns have been raised amongst a tremendous uncertainty about whether there is any fever signal in adults or even older adolescents of reproductive age. Dr. Gall is a liaison member for American College of Obstetricians and Gynecologists (ACOG) to the ACIP Influenza Work Group. He mentioned if there was post-vaccination fever, certainly that would have implications for the fetus. Again, there are no suitable data to inform this question.

Dr. Baker added that based on Phase I controlled trials, pregnant women in general seem to have less febrile responses to vaccines than non-pregnant women receiving the same dose and the same vaccine. Pregnant women were studied in 2009 with respect to 2009 H1N1 vaccine, and using the results of the trial the year before for seasonal influenza. She wondered whether there were any data available from these larger studies on the rate of fever in pregnant versus non-pregnant women.

Dr. Englund responded that she did not have data, but knew that for 2009 H1N1 vaccination, the rate of fever overall in adults and in pregnant women was very low.

Dr. Keitel's understanding was that there was almost no fever at all.

Dr. Gorman confirmed that there were very few febrile reactions in adults. While they did not statistically test this, the "eyeball test" suggested that there was no difference between the rate in the general adult population and the rate in pregnant women.

Dr. Keitel noted that CSL vaccine per se was not studied.

Dr. Baker felt that in the absence of data suggesting concern, she thought they should stick to what was known.

Ms. Rosenbaum inquired about the availability of alternative vaccines for children 5 through 8 years of age, and what the level of concern was about other vaccines that could be used for this population.

Dr. Santoli replied that the challenge was that there are a number of vaccines that can be used in multiple populations, and it is not clear who purchased what. The multi-dose vial from Sanofi Pasteur can be used in any age. CDC does not know which providers have purchased the Sanofi Pasteur multi-dose vials or for what age groups they intended to use this product. Other than knowing that the pediatric product is used in only one group, it is very difficult to talk about what product is available for children more than age 3 years because it is available for children over 3, but it is also available for older children and adults.

Dr. Keitel reiterated that there is definitely live attenuated influenza vaccine (LAIV). Whether providers have ordered this product remains unknown, and it is indicated only for healthy children 2 years or age and older. LAIV is not currently indicated for asthmatics, who represent the largest risk group. She reminded everyone that the first option included a proviso that if no other vaccine is available and a child is high risk, the child may be vaccinated with CSL vaccine.

Dr. Baker noted that in general, if everything proceeded as planned this year, and certainly as occurred in previous years, Sanofi Pasteur has provided the largest number of doses, followed by GlaxoSmithKline (GSK) and Novartis. Hoping for the best and with nothing occurring before vaccines start being shipped, the vaccines currently available should supply a small proportion of children 5 through 8 years of age. However, there is the matter of who orders what product.

Dr. Cieslak said he liked the Work Group's recommendations, but like Ms. Ehresmann was concerned about pediatricians who had placed all of their orders with CSL in terms of the likelihood that they would be able to acquire vaccine from another source at this point.

Drs. Baker and Pickering noted that as soon as the lines were opened to all parties on the teleconference, the manufacturers would be invited to comment further.

Ms. Ehresmann requested that Dr. Santoli follow up with the manufacturers and that CDC coordinate with the American Academy of Pediatrics (AAP) in terms of whatever information they had been able to obtain.

Dr. Santoli replied that CDC works with the National Influenza Vaccine Summit. There is a tool on the American Medical Association (AMA) website called the Influenza Vaccine Availability Tracking System (IVATS). Manufacturers and distributors submit information to IVATS that is updated on a weekly basis to let others know what is available for sale. The website address is: www.preventinfluenza.org/ivats

Dr. Tan (AMA) added that the IVATS tool is available and will be up in 2010. Now that the manufacturers have all started shipping vaccines, AMA will be ramping up the system and planned to have it operational in the next week or so. This tool will allow anybody who visits the site to identify who is selling vaccine.

Dr. Sawyer expressed his support of the majority opinion of the work group to allow flexibility in the 5 through 8 year old group with regard to product, given the shipment information just discussed. He reminded everyone that febrile seizures are extremely unusual in that age group, and that the data are fairly soft about fever in that age group. He stressed the importance of maintaining flexibility because of supply, though it may be at the expense of making the recommendation slightly more complex.

Dr. Tan again raised the question regarding the alignment of the ACIP recommendation with the recommendations from the UK, Australia, and New Zealand, which actually specify below 5.

Dr. Keitel replied that there is suggested evidence that there is an increased level of reactogenicity, the underlying cause of which is not known, and there are alternative vaccines available. Therefore, the Work Group felt that it would be prudent to limit use in this age group.

Dr. Carolyn Bridges (CDC) added that these other countries do not have a universal pediatric influenza vaccine program. If they do target children, it is children less than age 5 years. One of the issues is that the denominator data for 5 through 8 year olds is unknown. Therefore, it is not clear what the risk actually is. Due to the fever signal for 5 through 8 year olds, and because the US pediatric vaccination program through age 18 years, the Work Group's suggested recommendation and alternative do not align with the recommendation of the other countries.

Dr. Baker stressed that an important component of parent messaging would be to explain why the US recommendations differ from other countries. At this point, she requested that the lines be opened to liaison members, and invited any representatives from FDA to speak first.

Dr. Baylor (FDA) indicated that FDA had been involved in discussions with the Work Group, and understands the rationale regarding the recommended options that were before the full ACIP, although they differ from the package insert. FDA understands the differences between its mandate and the ACIP's, and has no objections to the recommended options.

Dr. Hachey (DoD) noted that complex messaging had consistently been their "Achilles Heel" in attempts to increase immunization rates. After every influenza season, one of the common complaints has been complex messaging. Given that, he supported the alternative option of making things as simple as conceivably possible.

Dr. Baker pointed out for anybody who had not be listening the entire time that people favoring the alternative option included the current ACIP Influenza Work Group Chair, Dr. Keitel, and the former Chair, Dr. Neuzil.

Dr. Lewin (Novartis) reported that Novartis has begun shipping vaccine. They project to have approximately 40 million doses available over the season. Most of the doses have been allocated already, but they will work with CDC and the Influenza Summit to make additional doses available or to allocate supply. Influenza virion is indicated in individuals aged 4 years and above, so this product will cover only 4 through 8 year olds.

While Dr. Brewer (ANA) appreciated the conversation and the decisions ACIP had to make, as a liaison she advocated for simpler messaging and trying to alleviate some of the burden on the providers of having to figure out the levels of complexity.

Dr. Katz (IDSA) supported the simpler approach as one who frequently receives calls from practicing physicians. He stressed that the simpler the approach, the more effective it would be. He agreed that the complexity of the divided approach was a negative liability, and suggested sticking with the assets of everything up through age 8.

Dr. Kathleen Coelingh (MedImmune) offered an update on vaccine availability of FluMist®. MedImmune committed to producing about 15 to 16 million doses of the intranasal vaccine that is approved for healthy children 24 months and older. Most of that vaccine has been allocated and they have begun shipping; however, she anticipated that they could probably make an extra 2 million doses available if needed for the 2 to 3 year old age group. MedImmune will work with CDC or the Summit, to summarize the additional doses. She requested a contact to whom this information should be transmitted.

Dr. Santoli replied that it would make the most sense to submit the information directly into the IVATS tool, given that this is the tool that CDC and AMA use together to communicate to the public.

Dr. Tan (AMA) added that the AMA would be soliciting that tool. Once all of the information is in, they will make an announcement through the Summit so that people can visit the site to learn what vaccines are available.

Dr. Cory Robertson (Sanofi Pasteur) reported that they too had begun shipping vaccine doses, and expect to deliver 70 million doses this season. With respect to the supply issue, Sanofi

Pasteur has pediatric doses that are yet to be reserved. They are in the process of assessing their manufacturing capacity to determine whether they can meet the void left by CSL not being able to provide doses to the US market this season. The number of doses available for young children is being assessed. They will work with CDC and the Influenza Summit to make sure that information is available.

Dr. Meissner explained that his major reservation with the alternative option was the issue of supply. ACIP has now recommended the vaccine for everyone, and it remained unclear whether there would be adequate supplies for children in the older age group if ACIP stated that the CSL vaccine should not be used for 6 months through 8 years. There could be some children in the 5 through 8 year old age group for whom a vaccine would not be available.

Dr. Baker stressed that the answer remained unknown. Every year, different amounts of seasonal vaccine have been available. Last year, all pediatric age groups were recommended but all were not covered because they simply do not get their vaccines. This was not based on supply. While in part this had to do with supply and distribution in specific practices or locations, in general for the country, it has never been a problem and doses are always thrown away, which is very sad. Dr. Baker surveyed the largest practices in Houston, and no CSL vaccine has been ordered for children.

Dr. Englund added that many pediatricians have no control over what vaccines are ordered or what is available. She thought the first option reflected the fact that for the 5 through 8 year old age group, there was a risk-benefit consideration. While it was a more complicated option, it appeared that very few sites were ordering the vaccine, and that the first option offered more leeway for the practicing physician despite being slightly more complicated.

Ms. Ehresmann said that having heard from Sanofi Pasteur and Novartis, each of which indicated that they were considering the possibility of increasing the availability of vaccine in some of the key age groups, she was feeling more comfortable with the supply issue for providers who may have ordered CSL and with the more streamlined recommendation.

Dr. Baker declared the line open for public comment.

Luke Noll (FFF Enterprises) asked everyone to keep in mind that last year, the CSL product was only approved in individuals under the age of 18, so 2010 would mark the first full year that the product would have been approved for use in the under 18 age group, which may make a difference in supply. FFF Enterprises anticipates having vaccine available to cover the CSL orders that have received.

Dr. Baker indicated that she would entertain a motion from an ACIP member.

Motion: Use of CSL Trivalent Inactivated Influenza Vaccine in the US

Dr. Sawyer made a motion to adopt the majority opinion, Option 1, that Afluria® should not be used in children aged 6 months through 8 years, except for children aged 5 years through 8 years who are considered to be at high risk for influenza complications, if no other seasonal TIV is available. Dr. Meissner seconded the motion.

The motion carried with 8 affirmative votes, 2 abstentions, and 1 negative vote.

Dr. Baker thanked everyone for a wonderful discussion during this teleconference, as well as their diligence in doing their homework in terms of the background materials.

Dr. Pickering noted that members of the press and / or others with questions could contact Mr. Tom Skinner.

Kristine Sheedy (CDC) indicated that CDC would work as quickly as possible to finalize questions / answers, summarize this discussion, place information on the website by the end of the day. The goal would be to make this information prominent on www.cdc.gov/flu. She indicated that if the press reached an ACIP member who had the time and was willing, they were free to make comments on the teleconference and the vote. CDC will be doing the same, with Director Melinda Wharton handling the CDC inquiries.

Dr. Pickering suggested that if members did not feel like commenting or did not have time, they could refer inquiries to Tom Skinner who would ensure that they were directed to the right person for a rapid answer.

Dr. Keitel asked whether there were any issues related to the Vaccine Information Statements (VIS).

Kris Sheedy responded that CDC staff would be discussing this further, with the hope that the VIS would be posted no later than early the next week.

Dr. Pickering added that typically mention would not be made about a specific vaccine in the VIS. Part of CDC's deliberations would address whether to include a specific statement about the CSL vaccine in the VIS. He also indicated that the draft Policy Note had been written and would be distributed to ACIP members for comments. It was making its way through the clearance process, and he requested an update on this from Dr. Uyeki.

Dr. Uyeki reported that the Policy Note draft was going through clearance, with the expectation that there would be a publication in the *Morbidity and Mortality Weekly Report (MMWR)* the following week to summarize and report on the background and the ACIP recommendation.

Dr. Tan inquired as to whether he could submit the slides from Dr. Uyeki's presentation to the Summit.

Dr. Pickering replied that this would be premature because there may be some final wording, and the slides must go though CDC clearance. Therefore, he requested that the slides be kept everything confidential until they were officially posted on the ACIP website. This will be on the fast track, so the final version will be posted as soon as possible.

Dr. Tan requested clarification regarding whether the vote was public, and whether they could state that ACIP voted on the use of CSL vaccine.

Dr. Pickering responded that the vote was public as are all ACIP votes. Because ACIP is an advisory committee, this vote will be submitted to Dr. Frieden for his approval and publication in the *MMWR* before it is finalized. While a statement could be made about the ACIP vote, the caveat was that it was not yet official CDC policy.

Certification

With no further questions / comments raised or business posed, Dr. Baker officially adjourned the ACIP teleconference.

I hereby certify that to the best of my knowledge, the foregoing Minutes of the August 5, 2010 ACIP Teleconference are accurate and complete:

_____
Date

_____
Dr. Carol J. Baker, Chair
Advisory Committee on
Immunization Practices (ACIP)

Attendance Roster

FTS CDC NCHSTP Conference Call
Leona Mitchell - Conference Leader
Aug 5 2010 @ 09:00 AM CT
Confirmation # 3462584

Speakers:

Carol	Baker
Norman	Baylor
Beth	Bell
Joe	Bresee
James	Cheek
Lance	Chilton
Paul	Cieslak
Ruben	Donis
Kris	Ehresmann
Janet	Englund
Anthony	Fiore
Demetria	Gardner
Bruce	Gellin
Richard	Gorman
Michael	Greenberg
Wayne	Hachey
Stephanie	Henry-Wallace
Frank	Judson
Wendy	Keitel
Chet	Kitchen
Susan	Lett
Gladys	Lewellen
Cody	Meissner
Sara	Rosenbaum
Cindy	Ruff
Jeanne	Santoli
Mark	Sawyer
Tom	Skinner
Frank	Stefano
LJ	Tan
Terry	Tumpey
Tim	Uyeki

	First Name	Last Name	Company
1	Jon	Abramson	Wake Forest University
2	Bethany	Anderson	CDC
3	Phyllis	Arthur	BIO
4	Lynn	Bahta	MN Dept of Health
5	Jack	Balrymple	Balrymple & Associates
6	Allyn	Bandell	MedImmune
7	Linda	Bantell	Central CT Health District
8	Jennifer	Bender	Alembic Health
9	Henry	Bernastein	AAP
10	Gus	Birkhead	National Vaccine Advisory Committee
11	Nichole	Bobo	National Association of School Nurses
12	Mick	Bolbuc	CT DPH
13	Michael	Brady	American Academy of Pediatrics
14	Katie	Brewer	American Nurses Association
15	Sheila	Burke	CSL
16	Erin	Burns	CDC
17	Stephanie	Cadavillo	Wintrop University Hospital
18	William	Callaghan	CDC
19	Doug	Campos- Outcalt	American Academy of Family Physicians
20	Cristi	Carlton	MI Dept of Community Health
21	Heather	Carman	Cooney Waters
22	Donna	Cary	Sanofi Pasteur
23	Mike	Chaney	American Academy of Pediatrics
24	Sharon	Chin	Merck
25	David	Cho	US FDA
26	Marcy	Cleaver	Merck
27	Kathleen	Coelingh	MedImmune
28	Nancy	Cox	CDC
29	Stephen	Dachowski	Merck
30	Dack	Dalrymple	Dalrymple & Associates
31	Reetu	Dandora	Merck
32	Christine	Danka	Presbyterian Senior Care
33	Joy	Dasgupta	GlaxoSmithKline
34	Kathleen	Derr	Worcester County Health Dept
35	Stephen	Dolak	United States Navy
36	Sara	Duvall	NY State Dept of Health
37	Pam	Eisele	Merck
38	Kimberly	Elmore	Premier Inc
39	Alexis	Elward	HICPAC ACIP
40	Geoffery	Evans	HRSA
41	Mark	Feinberg	Merck
42	Sandor	Feldman	MS State Dept of Health
43	Angela	Fhen	HHS
44	Bob	Finn	International Medical News Group
45	Ashley	Fishburn	HIDA
46	Laurel	Fowler	CDC
47	Jen	Frantz	American Academy of Pediatrics
48	Stanley	Gall	American College of Obstetricians
49	Ann	Gapper	McKesson

50	Diana	Gaskins	Retired
51	Anita	Geevarughese	NY City Dept of Health
52	Nancy	Gemeinhart	BJC Healthcare
53	Joanne	Geoegelis	GlaxoSmithKline
54	Jane	Gidudu	CDC
55	Gino	Girardi	NIAD
56	Kathleen	Glassner	Merck
57	Sharon	Greene	Harvard Medical School
58	Stan	Grogg	AOA
59	Chris	Ground	FFF Enterprises
60	Swati	Gupta	Merck
61	Jacqueline	Haas	Coram
62	Penina	Haber	CDC
63	Stephen	Hadler	CDC
64	Christine	Hahn	CSTE
65	Neal	Halsey	Johns Hopkins University
66	Erik	Halstrom	FFF
67	Kimberly	Harrington	New Hampshire Hospital
68	Janice	Hashimoto	Novarts Caccines
69	Jamar	Hawkins	HHS
70	Vincent	Haynes	Medimmune
71	Greg	Healy	CSL Dehring
72	Guillermo	Herrera	GSK
73	Jan	Hicks-Thomson	WA State Dept of Health
74	Malaika	Hilliard	CDC
75	Jette	Hogenmiller	Truman Medical Center
76	Wayne	Hogrefe	Focus Diagnostices
77	Warner	Hudson	UCLA
78	Mark	Hummel	Premier
79	John	Iskander	CDC
80	Liz	Izaguirre	TCPH
81	Anna	Jacobs	OGC
82	Robert	Janssen	DynaVax Technologies
83	Will	Jernigan	Merck
84	Rosemary	Johann-Liang	HRSA
85	Barbara	Jones	Cabell Huntington Hospital
86	Lynn	Jones	Wellpoint
87	Doug	Jordan	CDC
88	Steve	Kalmeyer	N/A
89	Lori	Kamimoto	CDC
90	Randy	Katsoyannis	CDC
91	Samuel	Katz	Infectious Disease Society of America
92	Harry	Keyserling	SHEA
93	Alena	Khromava	Sanofi Pasteur
94	Linda	Kinsinger	Veterans Health Admin
95	Dmitry	Kissin	CDC
96	Tom	Kuchenberg	HHS
97	Caroline	Lagoy	CDC
98	Nancy	Lawler	The Joint Commission
99	Marie-Michele	Leger	AAPA

100	Terence	Leopold	Medimmune
101	Zanie	Leroy	CDC
102	Gladys	Lewellen	CDC
103	Clement	Lewin	Novartis
104	Paige	Lewis	CDC
105	Patrick	Liedtka	Merck & Company
106	Joanne	Luedtke	IBM
107	Jan	Markowitz	Baltimore County Dept of Health
108	Mary	Marolla	Alembic Health Communications
109	Marie	Mazur	CSL
110	Courtnay	McFeters	MI Dept of Community Health
111	William	McKinney	University of Louisville
112	Barbara	McLean	Baltimore County Health Dept
113	Marco	Melo	HHS
114	Toby	Merlin	CDC
115	Kelly	Moore	TN Department of Health
116	Riyadh	Muhammad	SC Dept of Health
117	Flor	Munos	Baylor College of Medicine
118	Oidda	Musdrau	CDC
119	Mike	Neal	Olgelby Public Relations
120	Mirjana	Nesin	NIH
121	Luke	Noll	FFF Enterprises
122	Elizabeth	Parilla	MN Dept of Health
123	Kathy	Parrish	Merck
124	Shital	Patel	Baylor College of Medicine
125	Lindsay	Paul	Alembic Health
126	Chandra	Pendergraft	CDC
127	Georgia	Perdue	Eastern Shore Hospital Center
128	Diane	Peterson	Immunization Action Coalition
129	Rhonda	Pikart	NIH DMID
130	Kristin	Pope	CDC
131	Kumar	Rallapalli	Pfizer
132	Lisa	Randall	Immunization Action Coalition
133	Sonja	Rasmussen	CDC
134	Marykate	Reeves-Hoche	Sanofi Pasteur
135	Margaret	Rennels	GlaxoSmithKline
136	Judith	Richards	Talbot County DPH
137	Heather	Richmond	Medimmune
138	Cory	Robertson	Pasteaur
139	Bob	Roos	CidRap News
140	Sara	Rosenbaum	George Washington University
141	Mitchel	Rothholz	American Pharmacists Association
142	Mary	Rubin	DVIC
143	Cindy	Ruff	CMS
144	Nicki	Sabin	Visiting Nurses Assoc
145	Mark	Sanyour	Novartis
146	William	Schaffner	Vanderbuilt University School of Medicine
147	Robert	Schechter	CDPH
148	Tim	Schnaare	GlaxoSmithKline
149	Laura	Scott	Family Fighting Flu

150	Abbey	Shefer	CDC
151	Judith	Shindman	Sanofi Pasteur
152	BJ	Shoptaw	Delmar VA Foundation
153	Barbara	Slade	CDC
154	Laura	Smith	CDC
155	Stephen	Smith	Sanofi Pasteur
156	Dixie	Snider	CDC
157	Sandra	Snow	AR Dept of Health
158	Patsy	Stinchfield	NAPNAP
159	Mike	Stobbe	Associated Press
160	Jeffery	Stoddard	Novartis
161	Kathleen	Stratton	IOM
162	Raymond	Strikas	National Vaccine Program Office
163	Leora	Suprun	Merck
164	Mark	Thompson	Thompson Pharmacy Medical
165	Ruth	Thompson	Baltimore County Dept of Health
166	Stephanie	Thompson	CDC
167	Terri	Thornton	IA State Health Dept
168	Lynn	Trefren	Tri-County Health Department
169	Vivienne	Treharne	FL Department of Health
170	Theadore	Tsai	Novartis
171	William	Tsang	Ruder Finn
172	Margaret	Verrico	UPMC Medical Center
173	Peter	Vigliarolo	Cooney Waters
174	Edward	Wake	NYC Dept of Health
175	Terethia	Walker	Exxon Mobil
176	Jeremy	Ward	Ofstead & Associates
177	Theda	Watson	St Vincents Hospital IN
178	Robert	Weibel	Vacine Injury Compensation Program
179	Rick	Welsh	SMQAI
180	Mirian	Wenworth	Merck
181	Patricia	Whitley-Williams	University of Medicine & Dentistry of NJ-Robert Wood Johns
182	Meredith	Whittaker	Sommers County ARH
183	Austin	Wilder	CDC
184	Cynthia	Williams	Lorenzo Health Clinic
185	Skip	Wolfe	CDC
186	Eileen	Yamada	CA Dept of Public Health
187	Terry	Yamauchi	AK Children's Hospital
188	Sandra	Yarn	GAAAP
189	Zhiping	Ye	FDA
190	Janice	Zalen	AHCA
191	Jane	Zucker	NYC Dept of Health