

**2006 National Influenza Vaccine Summit**  
**(Sponsored by the American Medical Association and the Centers for**  
**Disease Control and Prevention)**  
**Atlanta, Georgia**  
**January 24-25, 2006**

**Minutes of Meeting**

**Welcome**

*Litjen (L.J) Tan and Raymond Strikas*

The 2006 National Influenza Vaccine Summit was held on January 24-25, 2006 in Atlanta, Georgia. According to meeting organizers, 226 people attended the Summit, representing a 46% increase in attendance over last year.

**Introduction**

*J. Edward Hill*

Dr. Ed Hill, President of the American Medical Association (AMA), provided Summit attendees with opening remarks. Dr. Hill expressed appreciation for the vaccine stakeholders who committed to participate in the 2006 Summit, noting that all stakeholders can work together to improve the distribution and use of vaccine. Physicians understand the incredible value of the influenza vaccine to the public's health and want to make these benefits available to all people, especially those in certain high-risk groups and those who face health disparities. The influenza vaccine is one of public health's most critical tools.

This year, despite efforts, physicians have had problems getting vaccine as a result of purchasing and distribution issues; some providers did not receive any vaccine, and others received it too late. This season, physicians have been worried about elderly persons living in rural areas who traditionally are vaccinated in a local physician's office. Vaccine distribution can be a problem for everyone involved, including patients, doctors, and distributors.

Vaccine shortages are a problem for all Americans, because regardless of demographics, all people are patients. However, certain groups are remaining under-vaccinated, including health-care workers, who often are left vulnerable to disease.

Of the U.S. population, 5%-20% become ill from influenza every year, costing billions of dollars. More than 200,000 of these people must be hospitalized, and 36,000 die each year. These incredibly high numbers must be lowered, which can be achieved only through the collaboration of diverse sectors and groups.

The AMA has made several proposals to help reduce the prevalence and impact of influenza in the United States. Specifically, the Association has proposed that a preorder period be established for small orders of vaccine and that postseason stockpile be converted to a preseason stockpile. The Summit will provide a forum for these issues to be further discussed.

## **Keynote Address**

*Julie Gerberding*

Dr. Julie Gerberding, Director of the Centers for Disease Control and Prevention (CDC), delivered the Summit's Keynote Address. Dr. Gerberding began by recognizing the remarkable group of stakeholders in attendance at the Summit, noting that she greatly respects each stakeholder's high level of commitment to collaboration. She also expressed gratitude for Dr. Hill's leadership and recognition of the importance of public health; she emphasized the importance of continued collaboration between CDC and AMA.

Summit participants were given background information regarding influenza-related issues that continue to face the United States. Seasonal influenza is a powerfully important infectious disease in this country and has a substantial impact that largely remains underappreciated.

Despite the challenges associated with influenza, many successes have been realized, particularly in the area of vaccination. For example, more manufacturers and scientists are beginning to focus their efforts on vaccine production, more supplies are becoming available, expanded influenza vaccine recommendations are being developed, more partnerships are being formed, and more groups are becoming engaged in directing and redirecting vaccine (e.g., manufacturers, health departments, and physicians). These successes can be attributed to a complex network of partners, including local and state health department professionals, representatives from the private sector and community-based organizations, animal health experts, and others. In addition, CDC has been closely working with other federal agencies (e.g., the Centers for Medicare and Medicaid Services and the Food and Drug Administration) in its influenza efforts.

Several challenges are associated with influenza vaccination. First, vaccine supply and demand are unpredictable from season to season; as a result, the number of doses distributed is always less than the doses produced, which creates a challenge for vaccine manufacturers and distributors in terms of timing, quantity, and geographic point-of-use distribution. This challenge becomes even more problematic in the face of expanding influenza vaccination recommendations. Second, influenza vaccine differs from other childhood vaccines, which presents additional challenges. Traditionally, all childhood vaccines have remained largely in the domain of the public sector; many lots of vaccine are purchased through the U.S. Vaccines for Children (VFC) Program; federally owned vaccine results in less financial risk to providers who are administering the vaccine. However, adult vaccinations are not typically purchased by CDC or other parts of the government, making it hard for federal agencies to weigh in on distribution and production practices. Finally, the influenza virus is unpredictable, which presents challenges to vaccine production. Each year, the circulating strain must be estimated, and season length and peak must be anticipated. Unfortunately, the ability of CDC to forecast these factors is limited.

Dr. Gerberding discussed the avian influenza situation facing the United States. The H5N1 virus has widespread prevalence in migratory birds and has a broad range of hosts (e.g., cats, pigs, and other mammals). The virus is also spreading geographically and is evolving as it spreads. Sporadic human cases have been identified mostly in young, healthy persons, and the virus has been associated with a high case-fatality rate (i.e., approximately 50%). Thus far, sustained and rapid person-to-person transmission has not been documented.

CDC is working to further develop a plan for dealing with an influenza pandemic based on the philosophy that an influenza threat anywhere is a threat to the United States. CDC supports the quenching of the first outbreaks of disease regardless of the countries in which they occur; funds have been dedicated for this type of activity. The U.S. pandemic plan lays out several activities that will be undertaken in the event of an influenza pandemic, including travel advisories, exit and entry screening, isolation, antiviral treatment, vaccination, quarantine, social distancing, and school closures. All community organizations and infrastructures will need to collaborate and communicate efforts to the public to ensure an effective response. Physicians in particular will need to assume responsibility for relaying timely and accurate public health messages.

Currently, CDC is trying to overcome challenges associated with developing and then distributing a pandemic vaccine. Expanded production of current egg-based vaccine is taking place, dose-sparing technologies are being investigated, non-egg vaccines are being evaluated, and new antigens are being targeted. All of these pandemic-associated activities will also be applicable to seasonal influenza.

CDC's pandemic flu efforts are being guided by several basic principles, including the need to understand and address viral unpredictability, be consumer oriented, remain focused by improving marketing and health communications, and have a greater health impact (e.g., through increased vaccine recommendations, increased indications for vaccination, stronger systems, continued collaboration, and better consumer habits). The agency also supports gaining a stronger research and vaccine safety budget to ensure that vaccine has a favorable adverse-event profile. Any vaccine perceived as being unsafe could derail any pandemic-associated efforts.

Several options exist for overcoming vaccine-related challenges. For example, the federal government could a) purchase more vaccine, b) purchase more early seasonal vaccine to increase distribution capacity and help direct vaccine, c) exert more control over the flu vaccine distribution process, d) expand vaccine recommendations, e) expand and promote vaccine recommendations, and f) promote or facilitate diversification in vaccine purchasing through cooperative buying.

## **Summit Overview, Meeting Objectives, and Charge for Session One**

*L.J Tan*

Dr. Tan gave an overview of the meeting agenda. Summit participants were informed that the meeting is organized into four sessions and four objectives. Session One sets the foundation for deliberations; during this session, perspectives from manufacturers, distributors, FDA, and other organizations will be presented. In addition, in Session One, participants will be presented with information regarding the 2005-06 influenza season and vaccine supply. Session Two will consist of organizing and prioritizing the issues identified in first session. During Session Three, the Summit will develop and prioritize recommendations, and during Session Four, the Summit will be charged with developing activities to address each identified recommendation.

Dr. Tan encouraged Summit attendees to provide feedback during the discussion portion of the meeting. In addition, participants were encouraged to write down any concerns or questions and to submit these thoughts to meeting organizers at the end of each day.

## SESSION ONE

### **Identify Issues Experienced during the 2005-06 Influenza Vaccination Season and Review Observed Trends**

*Raymond Strikas*

Dr. Strikas presented the Summit with information obtained from the 2005-06 Influenza Vaccine Supply Surveys. The objectives of the vaccine supply study were to a) better understand which providers were affected by influenza vaccine supply problems in 2005 and to what extent and b) assess the public's experience in seeking influenza vaccine.

Several groups were surveyed for the study, including physicians; local public health department staff; state and local immunization grantees; community, occupational, and pharmacy vaccinators; hospitals; federally qualified health centers; and the public. Pediatricians were selected for participation based on a random sample of 2,500 American Academy of Pediatrics members and 3,000 American College of Physicians members; other groups of participants were selected using various sampling methods.

The provider survey was conducted during mid- to late-November and included several core questions (e.g., "What was your experience with ordering influenza vaccine?" and "What occurred when your vaccine order was not accepted?"). Response rates were >50% for most groups. The survey revealed the following results.

- Very few groups did not order vaccine (median: 4%).
- Most providers placed single or multiple orders that were accepted (median: 63%).
- Very few groups reported attempting to order but having no orders accepted (median: 2%).
- More pediatricians (60%) and hospitals (50%) reported ordering FluZone directly from their manufacturer.
- More community vaccinators and members of the Visiting Nurses Association than other groups reported ordering FluZone from a distributor.
- More community vaccinators and members of the Visiting Nurses Association than other groups reported ordering Fluvirin from a distributor.
- More community vaccinators and internists ordered from unknown distributors than other providers.
- Most community vaccinators, pediatricians, Federally Qualified Health Centers, and members of the Visiting Nurses Association ordered from at least two sources, whereas most respondents in all other groups ordered from only one source.
- At least 50% of providers in all groups reported receiving at least 40% of their orders, with the exception of family physicians.
- More government providers received >80% of their orders than providers in other groups.
- At least 50% of providers in all groups reported referring priority group patients to another location for flu shots as a result of inadequate vaccine supplies, with the exception of pediatricians and occupational health groups.
- Many groups complained that grocery stores and pharmacies were receiving vaccine when physicians were unable to obtain it.

Additional surveys were conducted among providers. The AMA Survey of Physicians on Influenza Vaccine Supply 2005-06, which had a low response rate of 12%, indicated that 78% of physicians could not vaccinate all of their high-priority patients. Only 24% of these providers received 81%-100% of their orders, and 30% received no vaccine. According to survey results, many physicians referred high-risk patients to other locations for vaccine (e.g., grocery stores, pharmacies, public health departments, and outpatient clinics). Of respondents, 38% indicated that this season was worse than the past season, and 38% indicated that it was better. Feedback from respondents revealed that most physicians feel that they should receive vaccine before pharmacies, supermarkets, and other commercial locations. The California Medical Society also conducted a vaccine supply survey. The Society e-mailed a survey to 14,000 physicians and had 299 respondents. Of respondents, 96% had ordered influenza vaccine; as of November 3<sup>rd</sup>, 29% had received some of their order, 23% had received all, and 46% had received none. Approximately 70% of providers were forced to turn away patients. Kaiser Permanente of Northern California also gathered vaccination data regarding the 2005-06 influenza season. These data indicated that of the 674,988 at-risk members, 632,328 members and employees were vaccinated.

Vaccine data were obtained from patients through the Gallup Survey. Approximately 900 participants (46% male and 54% female), most of whom were aged 18-49 years, answered questions about influenza vaccination (e.g., “How often do you get the flu shot?” and “Did you get a flu shot last year?”). Of participants, 38% received vaccine during the 2005-06 season, 48% did not want to be vaccinated, and 4% were unable to obtain vaccine from a provider. Most Gallup Poll participants received a flu shot from either a doctor’s office or HMO (39%), followed by the workplace (17%), other clinic or health center (10%), grocery store or pharmacy (10%), and health department (8%). When asked where they preferred to receive vaccine, most participants mentioned their physician’s offices (50%), followed by the workplace (17%) and other (11%).

The vaccination surveys had several limitations, including the use of different methods, the practice of convenience sampling, low response rates, and response bias. However, they revealed important information about vaccination practices for the 2005-06 season. In summary, data revealed that most provider groups refer patients to other providers when supplies are inadequate, most received >40% of their supply, and half received >80% of their needed supply.

Several issues emerged as needing to be addressed in surveys conducted in future influenza seasons. The following issues must be assessed: a) the best mechanism for acquiring information rapidly, b) determination of groups that should be included in surveys, c) the ideal timing of information collection, and d) the best types of information for collection.

#### *Discussion:*

- It was emphasized that the vaccine supply study involved a quick turnaround survey that represented 13,000 practice sites. A common concern raised by providers was the impact of shortages on their reputation; shortages caused patients to lose confidence and respect. Communication issues must be further discussed.

- Similar feedback was received from providers participating in the AAFP survey. Although many people sought vaccination, a loss of trust occurred when vaccine was unavailable. Patients could not understand why vaccine was not available at their medical homes. Patients who had difficulty organizing transportation were unable to travel to other sites to receive vaccine. The frustration level communicated by providers was “immense.”
- Clarification regarding future use of Gallop Survey data was requested. Dr. Strikas was asked whether these data would eventually be broken down by vaccine seeking behaviors. According to Dr. Strikas, these data also will be sorted out by the risk level of the patient.
- A representative from the American Healthcare Association (AHCA) noted that information from nursing homes was not collected in the survey. Nursing homes had great difficulty obtaining vaccine this year from Chiron. Many high-risk patients went unvaccinated until late into the season. Dr. Strikas explained that nursing homes were excluded from the survey because good data were already available through the AHCA.
- The issue of loss of patient confidence and trust was also raised by a representative from the California Medical Association. Patients of physicians who did not have access to vaccine were forced to obtain vaccine from mass vaccinators (e.g., grocery stores).
- Dr. Baxter from North Carolina Kaiser Permanente noted that the bird flu panic increased the public’s demand for vaccine; many patients asked whether the vaccine being offered would protect them against avian influenza. Vaccine supplies were exhausted within 3 weeks. Dr. Strikas added that according to the surveys, fear of avian influenza influenced vaccine-seeking behaviors in 15% of patients.
- It was noted that data are needed to substantiate the perception that stores and pharmacies had preferential access to vaccine. In addition, the expectation of vaccine providers should be better managed. Dr. Strikas agreed that the issue of perceived equity in ordering must be addressed by distributors.
- One participant discussed CDC’s October 24<sup>th</sup> cut-off date for vaccine tiering. He noted that the date was a compromise between needing to plan for vaccine administration and wanting to use all available vaccine. Immunization clinics can only be planned if a specific cut-off date has been selected.
- A meeting representative from Wisconsin inquired about whether the percentage of providers planning to offer vaccine in the 2006-07 is anticipated to decrease because of vaccine supply shortages and reimbursement issues. He was informed that because cumulative frustration has been expressed from providers this year, concerns exist that providers will stop administering vaccine. Dr. Tan added that the AMA received many telephone calls from frustrated providers who could not obtain vaccine, but no complaints were received regarding reimbursement. An attendee from the Task Force of the American Academy of Family Physicians clarified that in Texas, physicians have indicated that they will continue to vaccinate, but that their ordering volume may be decreased.
- It was voiced that the most telling evidence of the failure of the U.S. vaccine distribution system is the fact that shortages can be determined only after post-season surveys are conducted. This information should be available during the flu season to

ensure that vaccine can be properly distributed. According to Dr. Strikas, CDC is working on issues regarding vaccine tracking.

- According to a Summit participant from the Connecticut State Medical Society, the Connecticut State Department of Health tried to mediate redistribution of vaccine during last season's shortage. However, their efforts did not meet the needs of small practices. Difficulties were experienced regarding reimbursement and obtaining doses of vaccine.
- The October 24<sup>th</sup> cut-off date for prioritization was raised by a representative of the Minnesota Department of Health. She voiced the irony of being part of a system where before a certain date providers are unable to obtain vaccine, whereas afterwards, providers who finally have vaccine are unable to find patients willing to become vaccinated. A representative from the Immunization Action Coalition also discussed the cut-off date, noting that the date functioned poorly. It introduces another layer of complexity into the vaccine delivery process. In addition, the date created a huge demand for vaccine after it had passed.
- A representative from sanofi pasteur commented that his company provided 90% of the vaccine received by public health.
- Frustration was expressed regarding the practice of holding hospitals accountable for vaccinating specific populations even when vaccine is unavailable to them. Facilities should only be held accountable when vaccine is available.
- The perception exists that pharmacies had adequate supplies during the vaccine shortage, whereas hospitals experienced inadequate numbers of doses and delayed distribution.
- According to one state public health department representative, the state health department served as a distributor of vaccine during the 2004-05 season, which is an unusual role. The department was responsible for distributing 100,000 doses to physicians within 1 week. Is this to be a normal role of public health, as it is not currently defined as such?
- A Summit participant from Maxim Healthcare clarified that mass vaccinators also had problems obtaining vaccine. He stressed that his company strictly followed CDC's guidelines regarding priority vaccination before the October 24<sup>th</sup> date.
- The need to use health IT to better track vaccine was voiced. Electronic tracking of vaccine was done in the Louisiana hurricane response effort, and it was hugely successful. Another participant added that this type of tracking must be in place to ensure adequate response to a pandemic.
- A participant stressed that many vaccine-related challenges stem from insufficient supply and distribution. As more vaccine is produced, CDC should help push for universal immunization, which will help ensure that manufacturers have a successful market. It was noted that Emory and CDC sponsored a meeting to discuss the concept of universal influenza vaccination; ACIP also is deliberating issuing such recommendations.
- A Kaiser Permanente representative commented that Kaiser has tried to encourage late-season vaccination. Kaiser has data indicating that public awareness wanes before the end of December. Efforts to increase late-season vaccination resulted in a second wave of demand.

- Because VFC has been effective in childhood immunization worldwide, perhaps the Summit should consider whether such a program should be implemented for adults.
- It was emphasized that not only are distribution data important to states, but also prebooking data. Prebooking data would enable the determination of whether providers are dropping out of the supply network.
- One Summit attendee stressed that providers who had a hard time obtaining vaccine this year ordered vaccine from Chiron. Chiron needs to have vaccine available on time this season.
- The issue of partial shipments was raised. The result of partial shipments for physicians was that no provider was able to provide vaccine to all his/her patients.
- The concept of “holding back” vaccine distribution until a critical number of doses is available was proposed.
- The need to communicate to providers regarding when they should expect vaccine shipments was voiced. This concern was echoed by several Summit participants. Dr. Strikas stressed that because influenza vaccine is a biological, it is never predictable.
- Summit participants were updated regarding the AAFP concept of prioritizing the shipment of small orders of vaccine. Full shipments of small orders would ensure that small practices receive vaccine. Sanofi pasteur mentioned that they actually did ship out orders of less than 500 doses in their entirety.
- It was emphasized that many of the vaccine shortage-associated problems stemmed from Chiron’s inability to produce vaccine on time and in projected quantities.
- Several participants echoed the sentiment that a distribution problem is unavoidable in the face of a vaccine shortage.
- An occupational health representative noted that this year, her company is experiencing excellent late-season vaccination rates, most likely because of concerns of pandemic influenza. As avian influenza concerns rose, employees increased seasonal vaccine-seeking behaviors.
- The AMA experienced communication issues this season despite making great strides to ensure consistent messaging. A disconnect occurred: the public received the message that plenty of vaccine would be available, but when they sought immunization, physicians did not have vaccine.
- A representative from the Utah Immunization Program noted that partial shipment distribution worked effectively in that state.

## **2005-06 Licensed Vaccine Manufacturers’ Perspectives**

### **Chiron**

*Peter A. Galiano*

Peter Galiano, Chiron Corporation’s Vice President for U.S. Sales, provided Summit attendees with information regarding the manufacturing activities that took place during the 2005-06 influenza season and provided them with insight into the upcoming season. He began his presentation by expressing gratitude to Summit members and stakeholders for their patience, cooperation, and encouragement over the past year.

During the 2005-06 influenza season, Chiron completed unprecedented remediation activities to ensure a successful return of Fluvirin vaccine to market. These efforts demonstrate Chiron's commitment to patients, healthcare providers, and customers. The success of the remediation efforts was made possible through the exceptional efforts by colleagues across the global Chiron organization (e.g., the United States, Germany, Italy, the Netherlands, and India), extensive cooperation between U.S. and U.K. regulators, six MHRA inspections, and a 9-day FDA inspection. During 2005, Chiron met its goal of returning to market within one season and sustaining vaccine supply for the future. On March 2, the company announced license reinstatement in less than 5 months, on August 31<sup>st</sup>, Chiron announced favorable results from the FDA inspection, and on October 17<sup>th</sup>, the company announced the first delivery and release of Fluvirin to U.S. customers.

Chiron is dedicated to ensuring adequate influenza vaccine supplies into the 2006-07 influenza season. Thus far, the corporation is on track for a standard manufacturing season; approximately 40 million doses are anticipated. Chiron also is engaging in pandemic preparedness efforts. The company is working through the traditional seasonal manufacturing "break" to contribute to pandemic vaccine stockpiling efforts. Specifically, collaborations are underway with the U.S. government and with several other countries based on results from NIH avian influenza studies.

Efforts to educate the public and providers have become a priority for the Chiron Corporation. The company is planning to issue an electronic newsletter throughout the 2006-07 influenza season to ensure timely supply updates, and it is supporting national and grassroots education initiatives to increase the awareness of the importance of influenza vaccination.

## **GlaxoSmithKline**

*Andrew MacKnight*

Mr. MacKnight updated participants regarding GlaxoSmithKline's (GSK's) 2005-06 influenza prevention efforts. He outlined last season's distribution activities and discussed plans for the 2006-07 influenza season.

During the 2005-06 influenza season, GSK was committed to preventing influenza disease. The company launched an expansion of its Dresden Plant with the goal of doubling production capacity by 2008. In addition, GSK acquired both the ID Biomedical Corporation and an additional U.S. manufacturing facility located in Marietta, Pennsylvania that would be used to produce cell-culture-based vaccines for both pandemic and inter-pandemic influenza strains. Finally, GSK announced its development of an improved influenza vaccine using a novel adjuvant.

GSK ensured that its vaccine product, known as Fluarix, was made available for providers and distributors in a timely manner during the 2005-06 season. Approximately 7.5 million doses of Fluarix were distributed, most of which were made available in September and all of which were available by the end of October. Distribution was made primarily through supply houses serving immunizers of high-priority patients (e.g., hospitals and long-term care facilities).

Regarding the upcoming influenza season, GSK has a goal of distributing 20-30 million doses pending the 2006 expansion of vaccine recommendations and FDA licensure of Fluviral. Specifically, the company plans to manufacture 7-9 million doses of Fluarix in pre-

filled syringes (licensed for use in persons aged  $\geq 18$  years of age and containing only residual amounts of thimerosal resulting from the manufacturing process); in addition, the company's objective is to gain licensure of Fluviral for the 2006-07 season and manufacture 15-20 million doses in 10-dose vials (thimerosal would be used as a preservative). FDA has granted GSK "fast-track status" for vaccine approval and is currently working with the company to obtain a pediatric indication for its new product.

GSK has outlined its 2006-07 vaccine distribution objectives and has identified several guiding principles. The company will focus on offering vaccine to a wider breadth of customers through its manufacture of two forms of vaccine. These vaccines will be distributed to public health departments, office-based physicians, long-term care facilities, hospitals, and mass immunizers. The following guiding principles have been identified by GSK for the upcoming influenza season: a) GSK will be a leader in influenza vaccine and respond to global public health needs; b) GSK will continue innovation to improve vaccine effectiveness and production processes; c) GSK is committed to sharing information with public health; d) GSK is committed to looking at avenues for improving the influenza vaccine system; and e) GSK has made significant investment and is committed, long term, to the influenza market.

## **MedImmune**

*Kathleen L. Coelingh*

The MedImmune update was given by Kathleen Coelingh. She first provided Summit participants with background information regarding live, attenuated influenza vaccine (LAIV). Several drivers of LAIV supply have been identified: label indication, policy, and public health partnerships. Regarding demand, an expanded LAIV indication to children aged  $< 5$  years, which is expected in 2007, would increase demand, along with an expansion of the Advisory Committee on Immunization Practices (ACIP) recommendations, increased public awareness (e.g., of the seriousness of both seasonal and pandemic influenza), and improved LAIV formulation (i.e., refrigerated versus frozen vaccine).

MedImmune is working to develop an LAIV formulation that is refrigerator-stable. Several studies have been conducted, including a phase three study comparing frozen and refrigerated LAIV. The phase three study involved 26 clinical sites and 980 participants; it focused on two formulations (i.e., frozen and refrigerated) comprised of the same attenuated master strains. The study has revealed that both formulations have similar safety, reactogenicity, and immunogenicity profiles. A total of 22 other studies of refrigerator-stable vaccines have been conducted. These studies have involved 40,000 participants and have demonstrated that refrigerated LAIV has similar efficacy to frozen vaccine in placebo-controlled trials. In one substantial trial that compared the safety and relative efficacy of LAIV and TIV, a 44% reduction in cases caused by antigenically matched flu and a 58% reduction in cases caused by antigenically mis-matched flu was observed. MedImmune expects that on the basis of these clinical trials, a new indication for a refrigerator-stable formulation will be issued in the near future. The manufacturer has set a goal of launching a new refrigerator-stable vaccine with expanded indication for the 2007-08 influenza season.

Regarding supply, MedImmune currently has the capacity to manufacture approximately 15 million trivalent doses of vaccine for a single influenza season; current fill capacity is approximately 35 million doses. Future capacity, however, has been estimated to

exceed 80 million doses of vaccine. Supply issues are priority for MedImmune. To ensure appropriate supply of vaccine into future influenza seasons, MedImmune supports the creation of a universal influenza vaccination recommendation. This type of recommendation would help sustain public health, ensure a predictable supply, encourage a stable and innovative vaccine industry, and facilitate pandemic response efforts. MedImmune also has identified a need to establish a clear road map for strategy, age groups, and timeframes. In addition, public and private partnerships must be established to facilitate strong, evidence-based recommendations; develop infrastructure for school-based vaccination programs; coordinate supply planning; and ensure adequate demand for increased supplies.

**Sanofi pasteur, Inc.**

*Philip H. Hosbach*

Phil Hosbach updated Summit participants regarding sanofi pasteur's manufacturing activities during the 2005-06 influenza season and discussed the manufacturer's future plans and projections. Despite the 2005-06 vaccine shortage, sanofi pasteur continued to be a consistent and reliable supplier of influenza vaccine. The Company produced a record 63 million doses---13 million more than originally planned. Vaccine shipments began in early August, and 58.2 million doses were distributed by the end of November. All prebooked requests were filled 6 weeks ahead of schedule, and no orders were reduced or cancelled. Although sanofi pasteur supplied 90% of the nation's public health need, the company currently does not have the capacity to meet all of the U.S. influenza vaccine demand.

The shipping plan employed by sanofi pasteur proved to be effective and timely. By the end of October 2005, all sanofi pasteur customers had received at least a partial delivery of their orders, which allowed them to begin immunizing their priority patients. Although it was costly, sanofi pasteur initiated a split-delivery distribution process in response to CDC's recommendation for immunization prioritization. Vaccine was shipped equitably across all customer segments throughout the shipping season (i.e., one third to private physicians, one third to the public sector, one-tenth to alternative access points, and one third to other customer segments). The pediatric dosage of vaccine (containing no preservative) was considered a priority, as most recipients of this formulation required two doses administered 1 month apart.

Sanofi pasteur considers 2005-06 vaccine-related challenges to have resulted from supply rather than distribution inadequacies. Sanofi pasteur can not supply the entire market, and despite the company's equitable and timely distribution, vaccine supply during the 2005-06 influenza season did not match demand.

Sanofi pasteur supports the practice of vaccine prebooking and recognizes that prebooking is a necessary part of the influenza ordering process. Prebooking helps determine production forecasts, allows for the proper planning of customers' immunization campaigns, is an essential part of the normal influenza market landscape, and mitigates the financial risk inherent in the influenza vaccine market. Sanofi pasteur has implemented a prebooking program for the 2006-07 influenza season. Prebooking will begin for all customers on Tuesday, January 31, 2006 at 12:00 noon EST. This year, only one request for vaccine will be needed.

Regarding the 2006-07 influenza season, Sanofi pasteur projects that influenza vaccine supply for next season will be ample; therefore, ways to increase demand must be

identified. To increase immunization coverage, sanofi pasteur recommends that universal recommendations be phased in and that the two separate age groups of 50-64 years and  $\geq 65$  years be reclassified into one priority age group (i.e.,  $\geq 50$  years). The company also proposes that ACIP and CDC create a modification to existing recommendations that would serve as a transition step towards universal influenza vaccination recommendations.

## **Food and Drug Administration Perspective on the 2005-06 Influenza Season**

*Jerry Weir*

The U.S. Food and Drug Administration's (FDA's) perspective on the influenza vaccine supply during the 2005-06 season was conveyed to the Summit by Dr. Jerry Weir, Director of the Division of Viral Products, Center for Biologics Evaluation and Research, FDA. He began by giving background information regarding the currently available inactivated influenza vaccines. Trivalent vaccines are comprised of influenza A H1N1, influenza H3N2, and influenza B; the strains included in these vaccines are chosen on the basis of circulating viruses. Each dose contains at least 15  $\mu\text{g}$  of each HA. The efficacy of trivalent vaccines relates to vaccine potency (i.e., immunogenicity). Efficacy is based on the match of vaccine HA and NA with circulating strains.

Because the influenza virus continuously drifts, several questions must be answered by FDA before selecting strains to be included in vaccine for an upcoming season. The agency must consider whether a) new (drifted or shifted) influenza viruses are present; b) new viruses are spreading from person-to-person; c) current vaccines induce antibodies against the new viruses; and d) strains exist that are suitable for vaccine inclusion. The strains selected for the 2005-06 influenza vaccine were A/New Caledonia/20/99 (H1N1)-like; A/California/7/2004 (H3N2)-like; and B/Shanghai/361/2002-like.

Dr. Weir discussed FDA's timeline for vaccine production after strain change and for distribution. Six weeks must be dedicated to obtaining a reference virus, and an additional 6 weeks is required for developing reference reagents. During this 12-week period, seed virus preparation is taking place, along with monovalent production. Trivalent production begins 12 weeks after the start of the process and lasts for approximately 2 weeks. Vaccine distribution begins approximately 20 weeks into the vaccine production process.

Dr. Weir presented Summit participants with examples of questions that likely will need to be addressed by FDA to ensure the availability of more timely and effective vaccine. The following paragraphs outline these questions and FDA's responses.

- **Is FDA willing to look at influenza vaccine processes with the intent of finding ways to achieve earlier testing and release of vaccine?** The agency is considering making several changes, including modifications to the current procedure for monovalent potency assignment. FDA will not make any changes to the vaccine production process that would negatively impact the upcoming vaccine supply. The agency plans to periodically re-assess all aspects of the testing/release/support process to ensure the timely release of vaccine and continued high standards of product safety, efficacy, and potency.
- **Does FDA have plans to increase the resources devoted to influenza vaccine testing and release in preparation for the 2006 season?** The resources devoted to

influenza vaccine testing and release at FDA are expected to increase in preparation for the 2006-07 influenza season. New resources have been dedicated for pandemic influenza-related efforts for FY '06.

- **Would earlier availability of potency reagents allow earlier formulation and release of vaccine and can the FDA produce potency reagents earlier in the process?** Earlier availability of potency reagents could lead to earlier monovalent potency assignment and trivalent formulation, but in practice, this activity might have minimal effect because of staggered monovalent production. In addition, antisera production begins when antigen is available, and antigen becomes available only when a reference virus is available. However, the agency has identified investigations into new methods of antigen and antisera production as being a research priority.
- **Does the FDA test and approve monovalent bulk lots immediately upon receipt when manufacturers produce lots at risk early in the season?** The agency conducts this testing and approval process early in the season (e.g., January and February), although these activities are met with competing demands for serology studies that are necessary for strain selection. In general, no waiting period for monovalent testing is implemented; testing is continuous from February through November. The current procedure for monovalent potency assignment is being examined by FDA to determine whether changes can be made to improve the process.
- **Would limiting the option for vaccine formulation to a single virus for each strain type lead to increased efficiency (e.g., fewer potency reagents)?** Although limiting the viruses included in the vaccine requires fewer resources, FDA currently is not considering limiting options because a) multiple options provide manufacturers the opportunity to maximize yields in their systems and b) increased diversity in antigens might have a positive impact on disease prevention.
- **Is increasing the size of lots technically feasible and if so, what are the disadvantages?** Although feasibility of lot size is a manufacturing issue, FDA has worked with various sizes of lots from manufacturers and anticipates being able to do so in the future if resources permit. Larger lot sizes require the pooling of harvests, and therefore, any potential problem with a larger monovalent lot would impact a proportionally larger number of vaccine doses.
- **Can the FDA make any of all of these suggested changes so that the timetable for vaccine availability will shift and will manufacturers follow suit?** Changes to monovalent testing procedures are under consideration by FDA. The agency is investigating alternative methods of producing reagents and trying to identify improved test methods. However, some aspects of the vaccine production timeline will be difficult to alter (e.g., the strain selection process).

## **Vaccine Distributors' Perspectives**

### **Health Industry Distributors Association (HIDA)**

*Jennifer M. Alfisi*

As a representative with the Health Industry Distributor's Association, Ms. Alfisi provided the Summit with the vaccine distributors' perspective on influenza vaccine distribution. She began by defining the role of distributors, noting that distributors are wholesale customers of the manufacturers, and they therefore experienced the same shortages as other customers during the 2005 season. Along with health-care providers, vaccine distributors experienced more influenza vaccine being delivered directly to customers by manufacturers, had less than their full allotment of vaccine sent from manufacturers, had staggered delivery, and received complaints from physician customers. Despite these challenges, distributors have stated that they adhered closely to the CDC guidelines by targeting primarily the office-based practitioner.

Distributors have identified several effects as being associated with vaccine supply shortfalls. Providers and customers are confused about supply and are wary about prebooking vaccine. In addition, some smaller distributors have indicated that they will not carry influenza vaccine in the future.

The 2006-07 influenza vaccine supply has been discussed by distributors. If vaccine supply during the upcoming season is ample, distributors have processes in place to deliver vaccine to all priority groups. In addition, distribution supports efforts to guarantee that there is sufficient supply of influenza vaccine for the 2006-07 season and beyond.

### **Healthcare Distribution Management Association**

*Scott Melville*

Mr. Melville provided additional information regarding the distribution of influenza vaccine. He spoke as a representative from the Healthcare Distribution Management Association, which represents primary healthcare distributors across the country; members of the association deliver 9 million prescription drugs every day.

Dr. Melville provided background information about the nature of the healthcare distribution business in the United States. He echoed Ms. Alfisi's perspective that distributors can only distribute what suppliers have provided them. Vaccine supply was insufficient during the 2005-06 year, which resulted in distribution problems. Distributors supply providers on a daily basis, and the goal of distribution companies is to engage in consistent vaccine delivery to their customers. Distributors must purchase influenza vaccine before the doses are purchased by providers, which places them at financial risk, particularly because the influenza vaccine has a limited shelf life and expires after each influenza season. Therefore, each season, distributors must anticipate the demand that they will receive from their customers. Distributors face challenges when providers enter into purchasing contracts with multiple distributors and don't follow through on purchases; in light of these practices, distribution companies must be careful not to purchase excess product. The implementation of federal buy-back programs for influenza vaccine would ensure that excess inventory risk would be financially assumed by the government—not distributors.

Distribution companies are becoming concerned about the growing trend to create state-based regulations for vaccine distribution. These regulations could be an impediment to timely delivery of vaccine. Although the current distribution system is efficient and enables vaccine to be moved around from state to state in a timely manner, implementation of unique and inconsistent state regulations likely would negatively impact distribution response time.

## **SESSIONS TWO, THREE, AND FOUR: Organize and Prioritize Issues Identified in Session One; Develop and Prioritize Summit Recommendations; and Develop Activities to Address Summit Recommendations**

On the basis of discussion by Summit attendees, several influenza vaccine-related issues were identified in Session Two as needing to be addressed either in the immediate future (e.g., before the 2006-07 influenza season) or in the long-term. After these priority vaccine-related issues were identified, thorough discussion took place during Session Three regarding each topic. In that session, Summit participants were charged with addressing the timing and prioritization of each topic and developing recommendations. Finally, during Session Four, participants were charged with defining specific activities needed to help the Summit address each topic and recommendation. The following priority issues, recommendations, discussion points, and bulleted action items represent feedback from Summit participants expressed during the 2-day meeting. The ideal timing for addressing each priority issue is listed in parentheses following the issue heading.

### **Issue 1. Vaccine Supply and Distribution (Short-, Mid-, and Long-term)**

#### ***Recommendations:***

#### *1. A strategic vaccine plan for the United States must be created*

The issue of inadequate vaccine supply was identified as being a primary contributor to vaccine-related challenges. According to many Summit participants, sufficient supply is integral to effective distribution efforts; distribution difficulties are inherent when supplies are limited, and therefore both issues must be addressed in parallel. Supply and distribution issues should be dealt with on two levels: a) consumer access to vaccine from their providers and b) provider access to vaccine through distributors.

#### *Activities:*

- The Summit should define its vision for influenza vaccination in the United States

#### *2. The issue of the timing of distribution and supply must be addressed and effectively communicated to providers, the public, and the media in a timely manner.*

Summit participants noted that even when an adequate supply of vaccine is produced, it must be delivered in a timely manner to providers to be effective; timing is closely linked with consumer demand. Knowledge regarding when vaccine is available is extremely valuable to providers; this information should be conveyed to providers via the manufacturers and distributors several weeks before doses become available. Even if the supply issue is dealt with, there is value in having better knowledge about when vaccine will become available; this should be done weeks in advance.

*Activities:*

- The Summit could create a ListServe or a communications tool to convey vaccine supply timing issues
- Communication to providers is needed now regarding vaccine supply; the message should be delivered by CDC
- The Summit should call on distributors and manufacturers to communicate with providers regarding which vaccine is ordered and the status of vaccine order. The Summit Exec Committee and Communications Workgroup should follow up with distributors and manufacturers
- CDC must coordinate and develop a system to ensure that accurate and current data by region are available
- Data flow from CDC to state and local health departments should be improved
- Zip code data is not ideal; CDC could provide more detailed and accurate data to state and local health departments regarding vaccine supply.
- The Summit should formally ask vaccine manufacturers to fully communicate with the public regarding vaccine status
- Later discussion on issues pertaining to distribution and supply prompted the Summit to consider the formation of a Task Force to monitor the issues

*3. The vaccine distribution system must be made more transparent to ensure that distribution is perceived as being equitable.*

Confidence and trust in the vaccine distribution system must be gained from providers and consumers. To achieve greater confidence, health-care professionals and their patients must be provided with a transparent perspective of the distribution of influenza vaccine. The health-care community must be informed about where the vaccine is going and why. Data from the 2005-06 season demonstrate that distribution was uneven because some vaccine manufacturers could not provide adequate amounts of vaccine; preferential distribution was not intended or planned for. Instead, inconsistencies in distribution occurred as a function of where providers ordered vaccine.

*Activities:*

- Providers should be given data regarding vaccine distribution to ensure that distribution is equitable.
- The Summit should work to ensure that distribution is equitable (e.g., comparable percentages of orders are filled regardless of practice size or setting at a comparable time)
- Manufacturers and FDA should better communicate timing of vaccine availability to providers
- The Exec Committee and Communications Workgroup should form a Task Force to develop a plan for the Summit
- The public should be educated regarding the feasibility of conducting equitable distribution of vaccine in the event of a shortage. The Summit could decide whether equitable distribution is possible.

- Tiering recommendations must be followed consistently regardless of provider to ensure “reasonable” distribution
- The Summit should develop a communications plan for educating providers and the public regarding last year’s vaccine supply issues

*4. Vaccine manufacturers must be ensured that a certain amount of vaccine will be purchased each season.*

To ensure adequate production of vaccine from manufacturers, they should be guaranteed that a certain amount of vaccine will be purchased each influenza season. This type of guarantee would reduce the economic uncertainty and variability faced by flu vaccine manufacturers.

*Activities:*

- The role of the federal government in stabilizing vaccine supply should be elucidated
- Vaccine is both a commercial and public health product. Both of these perspectives should be represented.
- The federal government could assume the role of purchaser in the event of over-supply of vaccine. The feasibility of this should be explored. The IOM could be asked by the Summit to do a report on the role of the federal government in stabilizing vaccine supply. Congressional action likely will be required.
- The Summit could serve as a resource for legislators. The National Conference of State Legislatures is involved in educating legislators and could be participants in the Summit.
- A federal “buy back” program could be reinforced
- The Summit Exec Committee should explore collaborations with secondary stakeholders

*5. A “roadmap” of groups in need of vaccine prioritization is needed to help illustrate and link supply and demand issues.*

Participants identified the need for a roadmap of supply and demand issues that could be used to chart the ideal course of vaccine production. This roadmap would clearly link together the issues of supply and demand; without this type of linkage, supply will never meet demand.

*Activities:*

- The Summit did not address this point.
- As more providers administer vaccine in alternative settings, this administration must be communicated to the patients’ medical home
- The Summit could work with ACIP to gain knowledge regarding school-aged vaccination and support recommendations. The evidence-base must be put in place. **A strategic plan should be developed that addresses specific populations.**

*6. U.S. production and distribution of vaccine should be completed in September of each year.*

The production of vaccine is complicated and unpredictable. Summit participants concurred that ideally, influenza vaccine production should be completed well in advance of the influenza season (i.e., during September). Earlier availability of vaccine will help facilitate allocation and increase demand. FDA and manufacturers must collaborate to find ways to decrease production time.

*Activities:*

- The Summit could explore the best way to streamline the process.
- Communication with manufacturers should be improved regarding strain changes and decisions
- Research and development should be conducted to reduce the reliance on egg-based technologies
- Manufacturers should provide information about which proportion of doses is available in September; the Summit can ask this of manufacturers.
- The influenza season could be extended; attention should be given to the beginning and end of the season.
- Clarification is need from FDA regarding vaccine release

*7. Increased demand must accompany increased vaccine supply.*

This topic is discussed in great detail in later sections of this report.

*8. Plans should be developed to address excess late-season vaccine.*

Options for reducing excess late-season vaccine include a late-season return policy for providers (accompanied by a specific deadline); CDC “buy back” of vaccine for distribution to underserved populations; tax breaks for providers who use excess vaccine to vaccinate underserved populations; and a sharing of the financial implications of excess vaccine by CDC, manufacturers, and providers.

If a late-season return policy for providers is implemented, an exact deadline would be needed; Summit participants suggested using either December 1<sup>st</sup> or January 1<sup>st</sup> as deadlines. Although the Summit supported this policy, it was noted that manufacturers must also be protected against the economic impact of having excess vaccine returned to them. It was suggested that CDC buy back excess influenza vaccine and assume the economic risk that otherwise would be experienced by manufacturers.

Discussion took place regarding whether Congress should be approached about giving tax breaks and other incentives to providers who administer unused vaccine to underserved persons.

*9. Manufacturers and distributors should make partial shipments of vaccine in the event of vaccine shortages, but the projected status of the complete shipment must be properly communicated; this practice should be avoided when vaccine supplies are sufficient.*

It was agreed that the practice of making a full shipment of small orders should be addressed, as some manufacturers are already engaging in this activity.

*Activities:*

- The Summit will form a task force to examine this issue

*10. Distributors and manufacturers must develop a consistent and universal policy regarding partial shipment of vaccine.*

Summit participants were divided regarding whether distributors should continue making partial shipments, although it was agreed that the Summit must take a position on this practice. It was emphasized that partial shipments are only acceptable when providers can be assured that the full shipment will eventually be made.

*Activities:*

- Each distributor and manufacturers should have consistency in their own shipment policies
- CDC/Summit could provide guidelines of distributor expectations
- Policies change inherently; they should remain flexible but should be clearly communicated to providers and public health
- A document could be created for distributors that outlines customer concerns
- Ideally, distributors could inform stakeholders about which sector is receiving vaccine and when
- The Summit should collaborate with CDC in developing a task force to examine data issues and determine what types of data are needed; manufacturers and distributors must also be included.
- The Summit/CDC could convene a meeting to discuss what types of data are needed and which data are available. This would lead to a better understanding between public health, manufacturers, and distributors.

*11. Distributors should “hold back” vaccine from providers until a critical mass of doses is obtained (e.g., 1,000 doses).*

The concept of holding back vaccine from providers was discussed by participants. Although some view this practice as being beneficial, the majority of Summit participants do not endorse or support this activity because it would lead to a decrease in vaccine use and therefore less protection against influenza. Although this practice was initially suggested as being a potential Summit recommendation, the Summit agreed that recommending such a practice would be inappropriate.

*Activities:*

- Groups should be prioritized to receive vaccine as it becomes available
- Note: Summit deems inappropriate

*12. The corporate sector must be further engaged in the vaccine delivery system. Employers should be persuaded that it is beneficial to offer employees vaccine.*

*Activities:*

- Better return on investment data are needed regarding the value of flu vaccination in the corporate sector
- Corporate campaigns could be held later in the influenza season, but this minimizes return on investment for businesses. In addition, resistance exists regarding late-season vaccination. Financial implications to corporations must be considered.
- Employers should be encouraged to ensure that health insurance plans cover vaccination
- Employers should be further educated
- The ideal timing of workplace clinics must be investigated

*13. CDC should focus on creating a preseason stockpile to replace the late-season stockpile.*

The reasoning behind CDC's creation of a late-season stockpile was to supplement VFC patients as vaccine supplies run short. Several Summit attendees proposed that a preseason stockpile would serve to buffer the flow of vaccine through the influenza season when necessary. A preseason stockpile could be a large-scale solution to almost every short-term vaccination issue. The stockpile would be created by obtaining vaccine from all manufacturers before distribution of vaccine occurs for the season. Such a preseason stockpile could be released if not needed by mid-November, and possibly earlier. The creation of such a stockpile would help ensure that providers in small practices receive vaccine. However, concern was also expressed that in the event of a shortage, it may not be best to have vaccine sitting in a stockpile and that a preseason stockpile does not encourage manufacturers to make more vaccine or providers to immunize further into the season. It was clear that the Summit was not in consensus on this issue.

*Activities:*

- Summit should encourage that resources be given to CDC for the stockpile. These resources should not be diverted from the VFC or childhood vaccination program (317 Program).
- The Summit should consider scenarios of vaccine supply and how these scenarios will be affected by the stockpile
- Creation of a preseason stockpile could potentially reduce the amount of vaccine available to the public at the start of the season; stockpiling should not occur in the event of a vaccine shortage.
- Past-year vaccine with closely matched strains could be held for the next season's preseason stockpile. However, many regulatory issues would need to be addressed, and strains rarely are closely matched.

*14. Health insurance coverage for the influenza vaccine should be increased.*

Traditionally, third-party payers have considered vaccinations to be a voluntary health benefit. Many third party HMOs do not reimburse for flu vaccinations, particularly when these vaccinations are given at other sites (i.e., outside the patient's medical home). Cost-benefit analyses must be conducted regarding vaccines and other preventive health measures; these data could be used to influence insurance companies to pay for vaccinations.

*15. Education should be increased regarding the safety of influenza vaccines (including thimerosal-containing vaccines) and the science showing no association between these vaccines and autism and other developmental disorders*

*Activities:*

- The Summit could prepare a press sheet regarding the dangers of these laws. The Summit could follow up with the National Conference of State Legislatures
- The Summit could work with manufacturers regarding the supply of T-free vaccines
- CDC will be working on a contract for these vaccines for states that have legislation
- Summit recommendations must be consistent with recommendations from other organizations (AAP and ACIP)

## **Issue 2. CDC's tiering recommendations (Short-term)**

***Recommendations:***

*1. The tiering structure should be used for vaccine distribution only in the event of a vaccine shortage. Healthcare providers should be aware of which populations should be offered vaccine if provider supplies are limited locally. However, even when vaccine supplies are sufficient, providers should emphasize the vaccination of priority groups.*

Summit participants were divided regarding the practice of tiering. The practice of tiering would be useful in a pandemic or in the case of a vaccine shortage, and it represents a rational prioritization of resources, which is a critical role of public health. In addition, tiering defines the way in which people should inquire about vaccine availability: tiered groups inquire earlier, which minimizes overload. However, this practice also can be problematic. Tiering recommendations can be confusing to both providers and the public and can create the perception of inequitable vaccine distribution. Prioritizing vaccine groups also can result in communication barriers between providers and their patients.

Much discussion took place regarding whether tiering practices should be in place by default (to be overridden in the case of ample supply) or whether these practices should be implemented in the event of a shortage. ACIP recommendations suggest that tiering be the default.

Other feedback was received, including discussion about whether expansion of the priority vaccination groups would help the public's perception of tiering practices.

*Activities:*

- A document should be created to define tiering recommendations; this should be available in advance of the influenza season. The default plan could be non-prioritization (the Summit generally favors this option). This should be communicated to CDC and ACIP. In the case of a shortage, priority vaccination would occur
- Priority groups should be consistent
- Clarification is needed regarding when non-priority populations should begin to receive vaccine
- When constraints are put on the vaccine delivery system, less people receive vaccine
- The efficacy of prioritization should be investigated
- CDC could assess coverage in prioritization vs. non-prioritization influenza seasons
- The issues of distribution and prioritization must be differentiated

*2. Priority recommendations should be well communicated to providers, the public, and the media.*

Tiering, or priority, recommendations can be confusing to providers and patients; to avoid confusion, increased effort should be given to public health communication when vaccine tiering recommendations are implemented.

It was suggested that the term “tiering” be replaced with “priority vaccination” to help minimize confusion.

*Activities:*

- Communications with the public should be kept as simple as possible.
- Only one date should be used
- Regular and timely communication about planning process to summit partners

*3. Ideally, vaccine prioritization should be voluntary, not mandated.*

In addition, Summit participants suggested that tiering practices be defined via guidelines versus recommendations.

*Activities:*

- The Summit should remain silent regarding this issue.

*4. CDC must clarify whether tiering should continue after vaccine supplies increase or after the deadline is reached.*

CDC must communicate when tiering practices can be stopped for the season; the ideal tiering “end date” should be further investigated and identified, and this deadline should be clearly communicated to providers in a stand-alone document. It was emphasized that

when tiering recommendations are implemented, a plan must be developed to pull recommendations once sufficient vaccine supply is achieved.

*5. Tiering recommendations should be made at the federal level. Implementation should take place at the state and local levels.*

*6. Tiering recommendations must be applicable to all providers, regardless of practice size and patient population.*

Consistent implementation of recommendations will help minimize vaccine distribution inequities.

### **Issue 3. Communications (Short-, Mid-, and Long-term)**

#### ***Recommendations:***

*1. CDC and local and state public health agencies must work to regain public trust regarding vaccine supply. Misconceptions must be addressed and clarified (e.g., the perception that some providers received vaccine preferentially over others).*

It was emphasized that the public's trust must be regained. Both providers and patients turn to state and local health departments for clear public health messages, and these agencies must be perceived as trustworthy sources of information. To further regain public trust, CDC should clearly communicate 2005-06 vaccine-related issues to help clarify perceptions of distribution inequity and explain vaccine shortages.

#### *Activity:*

- A public campaign could be developed

*2. CDC and state/local public health agencies should better update providers, the public, and the media regarding influenza vaccine-related issues (e.g., distribution and supply by region).*

A suggestion was made that CDC could develop a website that would provide providers, the public, and the media with live, real-time information regarding vaccine distribution and supply. Web-based communications would need to be region-specific, as different areas of the country face different situations at different times.

#### *Activity*

- *CDC could develop a website*
- *Local PH could develop a blast fax and/or email list or a two-way communication system to send press releases and emails to practitioners, hospitals, HMOs, and nursing homes.*

3. *CDC must provide influenza vaccine-related materials to health departments in a timely manner.*

In the past, CDC's informational materials have been published too late in the influenza season to be of use to public health officials and providers.

4. *Consistent messages must be delivered to the public regarding seasonal versus pandemic vaccination.*

Much of the public is confused about whether vaccination against seasonal virus is effective against a pandemic strain.

5. *Providers and the public must be informed about the unpredictable nature of influenza vaccine production and educated about other aspects of influenza vaccination.*

Patients often have anxiety that stems from the perception that the influenza vaccine situation is controllable; it would be beneficial if people realize that influenza vaccine production is unpredictable. In addition, patients should receive accurate information regarding the effectiveness of flu vaccine in the elderly (i.e., inactivated flu vaccine does work, but it is not clear how well it works in the older elderly population).

*Activity*

- Invite the advocacy group "Families Fighting Flu" to Summit to put a face to the disease

6. *For the long-term efforts, communications packages for different circumstances should be developed.*

It was suggested that providers be characterized as small providers (eg, physician offices) and large providers (eg, community immunizers).

*Activity:*

**Issue 4. Process of vaccine testing and release (Short-term)**

***Recommendations:***

1. *Manufacturers and FDA should work to reduce the time required for vaccine testing and release to ensure that appropriate supply can be distributed before the start of the influenza season. FDA has indicated interest in expediting release of monovalent lots.*

**Issue 5. Communicating ordering and shipping policies (short-term)**

***Recommendations:***

*1. Inaccurate perceptions that certain providers only serve certain populations should be corrected.*

*2. Prioritization of vaccine shipments to certain customer/customer segments by distributors must be addressed and communicated to vaccine providers, the public, and the media.*

Summit participants stressed the importance of addressing how customers are being classified and perceived. A misconception exists about which populations are served by certain providers; there is an assumption that certain providers don't serve certain populations and that facilities with larger orders are more likely to receive vaccine. Manufacturers have stated this type of preferential distribution does not take place, but it is unknown whether distributors engage in this type of activity. However, according to a Summit participant representing a distributor, most distributors use CDC guidelines to decide where vaccine is needed.

Perceptions should be addressed regarding whether it is a "bad practice" to ship vaccine to large practices and to providers who place large orders. Summit participants suggested that if the goal of vaccination efforts is to protect as much of the public as possible, this type of practice may be beneficial. In addition, in certain situations, it may be beneficial to vaccinate certain priority groups of people (e.g., Hurricane Katrina relief workers).

*3. Distributors must keep providers informed about the timing of shipments and other distribution issues.*

A representative from Chiron noted that his company plans to create a website that will include information about vaccine supply and availability. An additional website could be developed that includes a list of contact information for distributors and manufacturers; such a website could be created by the Summit.

*Activities:*

- A website could be developed that includes a list of contact information for distributors and manufacturers. Information on which distributors and manufacturers have restrictions on provision of vaccine should be posted.

*4. Policies and procedures regarding the ordering of vaccine should be communicated early to providers and manufacturers/distributors should develop establish consistent system for ordering and distribution.*

The Summit could collaborate with distributors to develop these policies.

**Issue 6. Health and long-term care facility residents (including home-health care recipients) (Short-term)**

***Recommendations:***

*1. The disconnect regarding the need for these facilities to meet quality standards in the face of a vaccine shortage must be addressed (see role of federal government)*

One example of a population experiencing this disconnect is nursing home residents. Nursing home administrators were told that they would be judged by their provision of influenza vaccine, but they were not able to obtain vaccine. Quality standards for health-care facilities are hard to reach during vaccine shortages. Summit participants suggested that home-health providers also be held accountable for meeting quality standards.

#### **Issue 7. Knowing the location of influenza vaccine**

##### ***Recommendations:***

*1. Prebooking data should be made available for identifying gaps in vaccine availability.*

It was noted that distribution data for the 2005-06 season are available.

*2. Distribution data must be improved to facilitate understanding of where vaccine goes and to improve manipulation of vaccine supplies.*

Prebooking information for the 2005-06 influenza season has not been made available.

*3. There is a need to identify which provider has vaccine and which provider needs vaccine.*

#### **Issue 8. Government's role in a vaccine supply issue**

##### ***Recommendations:***

*1. The federal government must ensure that influenza vaccination remains in the public's consciousness.*

*2. Prebooking and its implications must be examined soon by the federal government.*

*3. CDC should work to create promotional marketing materials in support of influenza vaccination.*

Summit attendees discussed the need for CDC to take a major role in marketing vaccine across the country, which would create increased demand. CDC should create materials and make them widely available for use at the local level.

*4. CDC should provide clarification to other federal agencies regarding vaccine supply quality measures.*

*5. Uniform federal guidelines regarding vaccine distribution should be developed and used by all states.*

Much discussion took place regarding the development of consistent guidelines. Concern was expressed that many states are looking at legislation to control distribution of vaccine; legislation that differs from state to state would hinder the timely delivery of vaccine. In California, the Legislature is considering implementing these regulations in response to an enormous frustration in supply levels. It was felt that the Summit and CDC should take the lead on this issue and encourage states to follow standardized federal guidelines.

*Activities:*

- The summit should take a stance and encourage states to follow federal guidelines, because different regulations across states could cause problems.

*6. The role of state and local health departments in vaccine distribution and reallocation should be recognized. Many are involved in answering state legislature questions.*

In the event of a vaccine shortage, state and local health departments are required to engage in a resource-intensive effort to decide how vaccine should be allocated. Vaccine distribution decisions should be delegated to state and local agencies by the Summit. The issue of whether state and local health departments should serve as vaccine providers also must be further discussed.

*Activities:*

- Create Summit fact sheets for state and local PH departments

*7. State PH should determine what went well and what needs improvement for the upcoming season.*

*Activities:*

- Conduct a survey of local public health departments

### **Issue 9: Anti-thimerosal legislation**

*1. The Summit should get involved in state legislative efforts on influenza vaccine and thimerosal*

Overall, participants felt the need for the Summit to support state efforts regarding thimerosal legislation. Anti-vaccine advocates likely will become more vocal as a move is made towards recommending universal influenza vaccination. Currently, legislation is going to the House. Six states have laws enacted; three have taken effect. Many states have introduced legislation this year. An assumption exists that if state-based legislation is enacted to limit thimerosal in vaccine, thimerosal-free vaccine will be available for use in that state. However, this likely is a false assumption.

*2. Summit should provide materials to help partners on educating the patients on the issue*

Inquiries about thimerosal-containing vaccines increasingly are being received from the public, and negative propaganda is affecting vaccine acceptance. It was felt that the Summit should take the lead in providing the public and media with accurate information regarding this preservative. The science behind thimerosal-containing vaccines must be made known.

*3. Summit partners should sign onto IAC's letter to Congress on federal anti-thimerosal legislation*

IAC is putting together a letter to send to Congress with signatures from medical organizations and other groups stating that anti-thimerosal legislation is opposed and why. Additional signatures are needed. Perhaps a statement issued from CDC's immunization program also would be helpful. The Summit also could provide Congress with information regarding the impact of such legislation should it be passed.

Summit members also must be aware of the legislative proposal that any unused vaccine be considered a toxic substance. Summit members should be aware of the proposed legislation in their own states and discourage legislators from passing it. Some states are considering a compromise by mandating the use of thimerosal-free vaccine only when this type of vaccine is available.

**Issue 10: Improving vaccine demand**

*1. Summit should encourage progress towards universal immunization*

*2. Summit should help educate on the issues of vaccine effectiveness in the elderly and vaccine utilization in other high risk populations.*

*Activities:*

- Summit reach out to specialty societies to educate and target high priority populations
- All providers need to recommend vaccine to their patients, and should role-model by receiving vaccine themselves.
- Improve attendance of minority physician groups and other consumer groups that represent minorities

*3. Summit should engage third-party payers to pay for influenza immunization*

Influenza immunization for adults tends to be less covered by insurance companies, which likely reflects employees' tendency to not ask for coverage. Messages regarding the importance of flu vaccination must be better communicated to members of the U.S. workforce.

4. *An adult immunization program is needed. Scope varied from partner to partner from total federalization of vaccine to federal procurement of vaccine only for uninsured adults*

The Utah Immunization coalition representative said that there is a disconnect between state pediatric influenza immunization programs and adult influenza immunization programs.

*Activity*

- A campaign for high-risk adolescents should be considered
- State campaigns to improve pediatric outreach for influenza vaccine

5. *Influenza disease must be given a face*

*Activities:*

- Summit should work to get Oprah interested.

6. *Allow patients to be directly involved in vaccine ordering by creating a system where they reserve their own vaccine through their healthcare provider.*

Study the feasibility of a consumer-driven vaccine reservation system permitting a user to reserve and prepay for vaccine prior to production. This would ease consumer fears and provide more definitive production targets for manufacturers.

7. *Improve “late” season immunization*

*Activities:*

- Sell vaccine at cost
- Local PH to establish lists of providers who still need vaccine
- Summit to encourage “outbreak” focus for “late” season immunization

8. *Health-care worker vaccination plans must be further elucidated.*

9. *Don’t get stuck on “shortage;” need plan for handling abundance of vaccine*

**Issue 11: Prebooking of vaccine**

1. *Small orders should be given a period to preorder vaccine ahead of the crowd*

Much discussion has taken place regarding providers who need only a small number of doses. It has been proposed that manufacturers allow these providers to reserve vaccine during a special prebooking period. Currently, the AMA is working with manufacturers on this issue. Another participant recommended that priority pre-booking and priority partial delivery of vaccine be developed to those providers ordering small quantities of vaccine.

Some manufacturers and other partners in the Summit did not agree with this idea, saying that preferential treatment of any sector of vaccine providers would be difficult to justify to the sector(s) not receiving the preferential treatment. No consensus was achieved with this issue.

*2. Assist small providers to create purchasing cooperatives*

Using a “mass-purchaser” to consolidate small orders of vaccine likely would increase vaccine availability for solo practitioners.

## **Summit Activities and the HHS Pandemic Plan**

*Bruce G. Gellin*

The Director of HHS's National Vaccine Program Office, Dr. Bruce Gellin, discussed HHS's pandemic preparedness activities, including pandemic vaccine goals, antiviral goals, and budget priorities. He began his presentation by emphasizing that activities put into place for pandemic influenza preparedness will benefit seasonal influenza preparedness, and vice versa.

Estimates have been made regarding pandemic influenza vaccine supply, capacity, and need. Currently, only a few million courses of pandemic vaccine (i.e., two doses per person at 90µg/dose) have been produced and added to the stockpile; the annual domestic capacity to produce vaccine is not much higher, at only about 10 million courses. However, in the event of an influenza pandemic, approximately 300 million Americans would need to become vaccinated. In light of this gap in vaccine capacity, HHS has established the following pandemic vaccine goals:

- Acquire a stockpile of 20 million courses of vaccine against the most likely pandemic threat
- Create a domestic influenza vaccine manufacturing capacity sufficient to produce 300 million courses within 6 months of the onset of a pandemic
- Collaborate with industry to accelerate the development of dose-sparing techniques
- Collaborate with industry to develop broad spectrum influenza vaccine

HHS also has established goals for the production of influenza antivirals. The agency aims to create a stockpile of antivirals that would treat 25% of the U.S. population (i.e., approximately 75 million treatment courses). In addition, a reserve capacity of 6 million treatment courses is needed, which results in a total antiviral stockpiling goal of 81 million treatment courses. The federal government plans to provide funding for 50 million of these courses and to provide subsidies to states for 25% of the 31 million courses. To ensure that antivirals are as effective as possible against a pandemic strain, HHS is facilitating the advanced development of new antiviral agents. The agency posted a request for information (RFI) on January 20, 2006 in hopes of gaining interest from researchers capable of identifying potential prophylactic/therapeutic agents likely to be effective in preventing or reducing influenza virus infection. HHS has asked researchers to consider the following vaccine characteristics: treatment/prophylaxis, shelf life, efficacy, bioavailability/half life, and oral/parenteral delivery.

State, local, and federal budgets must reflect the need to improve pandemic preparedness. To ensure state and local preparedness, \$350 million was included in the recent Congressional emergency appropriation for combating pandemic influenza. Each state will receive a minimum of \$500,000, with an additional allocation of funds based on population. The remaining \$250 million will be awarded later in 2006 in accord with guidance that will require progress and performance. States and municipalities can use these funds to accelerate and intensify current planning efforts and to exercise their plans.

Additional budget priorities have been identified for the federal level. FDA's regulatory science base must be expanded, the Strategic National Stockpile must be enhanced, CDC's influenza laboratory capacity must be increased, domestic surveillance (e.g., Biosense) must be expanded, and vaccine tracking and registry must be improved.

The U.S. government also is committing funds for combating avian influenza at the global level. The United States has pledged \$334 million to global avian influenza efforts to ensure that the following activities take place:

- countries threatened by the virus receive grants and technical assistance
- national preparedness plans are developed and exercised;
- surveillance and response systems are improved;
- the use and distribution of animal vaccine is monitored and evaluated;
- vaccines are tested and used;
- local rapid-response teams and medical personnel are appropriately trained;
- communications and public awareness campaigns are supported;
- international research activities are supported; and
- the influenza-related work of international technical agencies, private-sector partners, and non-governmental organizations is supported.

## **Summit Activities and the 2006 ACIP Meeting**

*Nicole Smith*

Dr. Nicole Smith with CDC's Influenza Branch updated Summit participants regarding potential changes that may be made to the ACIP influenza recommendations at the February ACIP meeting. She began by discussing the criteria ACIP is using to determine whether influenza vaccination recommendations should be expanded, which includes a) safety, b) efficacy and effectiveness, c) feasibility of implementation, d) economic evaluation, e) prevention of reassortment, and f) levels of demand and supply. ACIP also has identified gaps in the science of influenza and its prevention that must be closed to ensure optimal protection from the influenza virus if the vaccine recommendations are expanded. The following activities must be undertaken: a) an optimal influenza vaccine must be developed, b) the influenza disease burden and program impacts must be assessed, and c) cost-effectiveness and prevention effectiveness must be measured.

Several changes likely will be made to existing influenza vaccine recommendations at the upcoming ACIP meeting. The recommendations likely will reiterate the importance of providing two doses of vaccine to children <9 years of age receiving vaccine for the first time. In addition, antiviral recommendations likely will be revised on the basis of recent findings of influenza A (H3N2) viruses that are resistant to amantadine and rimantadine. Recommendations will also update information about coverage levels, vaccine strains, vaccine products, and references. Finally, the new recommendations likely will revise a) the timing of eliminating tiered recommendations and b) phrasing regarding the timing of vaccination.

Other changes to the influenza vaccine recommendations may be made by ACIP at future meetings. For instance, the Committee may extend routine influenza vaccination recommendations to include a) children 2-6 years of age and their household contacts and caregivers and b) persons at risk of non-human influenza (e.g., poultry or swine industry workers and travelers to affected areas). The committee also could potentially expand the list of priority groups for vaccination. Finally, ACIP likely will identify next steps related to recommendations for universal vaccination (i.e., identify decision-making criteria, assess available and needed data, and establish a time-line for phasing in recommendations).