

Written testimony of

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Before the

House Committee on Energy and Commerce

**Subcommittees on Health and Oversight and
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On behalf of Sanofi Pasteur, I would like to thank you for the opportunity to testify before the Subcommittees regarding a vital public health issue: the H1N1 influenza pandemic. As the world's largest and most experienced manufacturer of influenza vaccine, Sanofi Pasteur is committed to working in close cooperation with US and worldwide authorities to develop, produce and distribute a safe and effective Influenza A (H1N1) vaccine.

I. Background

Sanofi Pasteur is the largest company in the world devoted entirely to vaccines. Sanofi Pasteur offers the broadest range of vaccines protecting against 20 infectious diseases. In 2008, the company provided more than 1.6 billion doses of vaccine, making it possible to immunize more than 500 million people across the globe.

Sanofi Pasteur employs more than 11,000 employees worldwide and more than 3,200 here in the US. We have major facilities in Lyon, France, Toronto, Canada and Swiftwater, Pennsylvania. The Pennsylvania site is one of the company's four major integrated vaccine research and manufacturing centers. The site includes activities in research and development, production, filling and packaging, and distribution.

Sanofi Pasteur is the largest and most reliable manufacturer of influenza vaccine in the US and abroad, producing about 45 percent of the US annual influenza vaccine supply and about 40 percent of the worldwide supply. We are also the only domestic manufacturer of inactivated, injectable influenza vaccine. We have two licensed influenza vaccine manufacturing facilities

operating in Swiftwater, the second of which was licensed on May 6, 2009 by the Food and Drug Administration (FDA) and represents a 140,000-square-foot, \$200 million corporate investment by Sanofi Pasteur in domestic influenza vaccine manufacturing capacity, as well as a commitment to job creation in Pennsylvania. When running at full capacity, this new facility should produce approximately 100 million doses of the three-strain seasonal influenza vaccine per year. The original facility in Swiftwater is capable of producing 50 million doses of the three-strain seasonal influenza vaccine per year. Both facilities have been used to produce both seasonal and H1N1 vaccines and are now fully dedicated to H1N1 vaccine production. All seasonal and H1N1 vaccines for distribution by Sanofi Pasteur in the US are produced in Pennsylvania.

II. Pandemic Preparedness

Sanofi Pasteur has a long history of working collaboratively with both US and worldwide public health authorities on pandemic influenza. In 2004, we began working with the US Department of Health and Human Services (HHS) on early planning for a pandemic. We were the first to develop a proven large-scale manufacturing process for the H5N1 avian influenza vaccine, and we remain the only licensed manufacturer for H5N1 vaccine in the United States. Though at that time the focus was H5N1, otherwise known as bird flu, the groundwork laid has proven critical to our response to the H1N1 virus. For example, one of the most important steps toward preparing for an influenza pandemic was to put continuous egg supply contracts in place for vaccine producers. This has allowed the company to manufacture influenza vaccine on a year-round basis.

Unprecedented collaboration between industry and government has also been a hallmark of current pandemic response efforts. Sanofi Pasteur and all of the public health government agencies (HHS, FDA, BARDA, CDC and NIH) have worked to develop and produce a vaccine as rapidly and carefully as possible. Since April 30, 2009, Sanofi Pasteur has participated in weekly conference calls with these agencies in order to coordinate and plan for the testing, production and distribution of the H1N1 vaccine produced in Swiftwater. This collaborative approach can be credited with some early successes. For example, through close coordination with FDA and HHS, we were able to accelerate the licensure of two new filling lines in the new Formulation and Filling Facility at our Swiftwater location - one of which was not scheduled to be licensed until next year. Both lines are now operational and providing additional filling capacity. Licensure of a third line is pending, also on an expedited basis.

While the current H1N1 pandemic response has revealed key areas for improvement in public health infrastructure, our government agencies deserve recognition for their foresight and tireless effort in responding to the current pandemic. Sanofi Pasteur is committed to continued collaboration with key public health agencies and to remaining a consistent and reliable manufacturer of vaccines.

III. Production

Sanofi Pasteur's goal is to produce the largest number of H1N1 vaccine doses in the shortest amount of time while ensuring vaccine safety and compliance with the legal and regulatory requirements of public health authorities. (See Exhibit A for vaccine development process.) We have been working in close cooperation with key US government agencies including HHS, CDC, FDA, NIH and BARDA to accomplish this goal. We have devoted

extraordinary resources to the production of both seasonal and H1N1 vaccine this year. Today, more than 2,000 people at our Swiftwater facilities are in some manner involved responding to the pandemic through development, production, testing and distribution of the H1N1 vaccine. Our production facilities are running at their full licensed capacity, 24 hours a day, 7 days a week, with many of our employees making exceptional personal sacrifices to develop, produce and deliver vaccine as quickly and carefully as possible.

We have moved quickly to produce the vaccine to meet demand, but have taken no shortcuts. Sanofi Pasteur expects to produce and distribute over 125 million doses of influenza vaccine this fall in the United States— 50.5 million seasonal and 75.3 million doses of H1N1 vaccine.

IV. Egg-Based Technology

This level of production is achieved by employing a proven, well-tested method that uses egg-based technology. Recent reports of H1N1 vaccine shortages have spurred some to question whether the egg-based manufacturing technology might be out-dated. Ironically, it is largely because the vaccine manufacturing process is so well-established that the vaccine's safety profile is so well defined. Contrary to popular perception, cell culture technology does not necessarily increase yields and there is no evidence that cell culture derived vaccine is more efficacious than egg-derived vaccine.

Historically, chicken eggs have provided the most advantageous and reliable method for producing influenza vaccine. More than 95 percent of the world's influenza vaccine production uses egg-based technology and this method is anticipated to provide the majority of the world's

influenza vaccine for the foreseeable future. Currently, there are no cell culture H1N1 influenza vaccines licensed in the US.

The egg-based vaccine production method we currently utilize is a technologically sophisticated process that has proven adaptable to emergency situations like the current pandemic. In fact, this year provided us with an opportunity to directly compare the availability of influenza vaccines produced with egg-based and European cell culture-based production for a novel pandemic strain. Each of the methods produced clinical lots within similar timeframes. Large-scale production was initiated in nearly the same timeframe. More importantly, the US was the first country to start a nationwide influenza immunization program, receiving all of its vaccine from egg-based production.

The production of an influenza vaccine is a complicated process, involving many steps that typically take about six months to complete from the time a seed virus is received. Many steps in the process are the same regardless of the technology used. For example, growing antigen on any medium can only begin after the seed virus is isolated and is sent to manufacturers by the US Food and Drug Administration. Additionally, no matter which production method is used, all vaccines must undergo rigorous quality control and safety testing. This testing is done for each individual vaccine production lot and accounts for approximately 85 percent of the production timeframe. The testing is comparable for both egg-based and cell-culture technologies.

V. Timeline Delays

As mentioned above, the timeframe to produce influenza vaccine typically takes about 6 months. With H1N1, Sanofi Pasteur was able to accelerate the timeframe which enabled delivery

of the first doses of vaccine only 4 months after the company received the seed virus from the CDC. This remarkable effort could not have been accomplished without our expertise and the dedication of our employees. Additionally our close coordination and collaborative work with FDA allowed Sanofi Pasteur to make vaccine in an accelerated fashion, while still ensuring vaccine safety and compliance with the legal and regulatory requirements of public health authorities. There has been a great deal of information and misinformation about vaccine delays and the reasons for such delays. (See Exhibit B for detailed timeline of Sanofi Pasteur pandemic actions.) Sanofi Pasteur began shipping H1N1 vaccine on September 29, 2009, which was earlier than forecast. As of November 13, 2009, Sanofi Pasteur has shipped 20 million doses and expects to ship several million more each week in November and December. We have orders for 75.3 million doses of bulk antigen for anticipated delivery between October and the end of December. Although we are still awaiting final direction from HHS on the formulation and fill of the final portion of these 75.3 million doses of bulk antigen, we are on track and fully anticipate we will be able to deliver all the 75.3 million doses as filled product by the end of December.

Notwithstanding that Sanofi Pasteur has largely succeeded in producing the H1N1 vaccine as initially projected, there were some factors that affected the delivery schedules for H1N1 vaccine, albeit only marginally.

- The production yield of this strain was initially significantly lower than standard. Lower yielding new strains are not unusual, even for seasonal flu vaccine; however, the initial yields for H1N1 were exceptionally low. Utilizing its expertise, the company was able to optimize the productivity of the seed virus such that yields are now approaching those traditionally seen for the annual seasonal vaccine. Going forward, we do not anticipate H1N1 yields to be a significant factor impacting future production schedules.

- By early August 2009, a series of clinical trials were initiated by both the NIH and Sanofi Pasteur in adult, elderly and pediatric populations. The initial data from these studies became available in early September. The first data came from NIH trials using H1N1 vaccine produced by Sanofi Pasteur. In part, this clinical information was necessary to finalize the language with CBER on the H1N1 vaccine packaging and the product insert. There was a delay of 2-3 weeks in obtaining final product labeling approval which was needed in order to complete product labeling and packaging. Initial supply projections were based on earlier receipt of this final labeling.
- Sanofi Pasteur originally anticipated that nearly all H1N1 vaccine orders would be for multi-dose vials. While the majority of orders are for multi-dose vials, a larger than expected number of single-dose and syringe presentations were also ordered, requiring some adjustments to filling and finishing schedules. To increase production throughput, Sanofi Pasteur worked with FDA to accelerate the approval of two new filling lines. In addition, the company identified and secured contract filling and packaging capacity to supplement its own internal resources. Throughout this process, the company has been in constant communication with HHS to discuss production and delivery schedule issues and has conducted 30 weekly telephone conferences with HHS agencies.
- The company faced an unprecedented and complex challenge of producing, testing, packaging, filling and distributing two influenza vaccines simultaneously.

In producing a complex biological product there is always an element of uncertainty regarding the production schedule. This is true regardless of the technology. In terms of bulk antigen production, the company is on schedule to deliver as per the original commitments made to HHS. As noted above, several unforeseen delays have contributed to an approximate 2-4

week delay in the delivery of finished and released vaccine in accordance with the order issued by HHS on August 21, 2009. These delays were communicated in early September to HHS, through our weekly phone calls, and delivery schedules were formally revisited and revised several times throughout September and October as new information became available. Even with the unforeseen delays, we are well-positioned, based on long standing experience in influenza vaccine production, to continue to fulfill our agreements with HHS. We are on track to make all 75 million H1N1 doses of vaccine available to HHS by the end of December. At the same time, Sanofi Pasteur stands firm on its original commitment to deliver all 50 million doses of seasonal vaccine to all customers who hold reservations. Seasonal distribution is expected to be completed by the end of November, which is still well ahead of the historical peak of seasonal influenza season.

VI. Sanofi Pasteur Vaccine Production Highlights (Exhibit B)

Specific timeline related to the production of H1N1 vaccine:

- On May 27, 2009, we received the A (H1N1) seed virus from the CDC which is an International WHO influenza reference center.
- Sanofi Pasteur began large-scale production of the vaccine on June 23, 2009.
- We began clinical trials of the vaccine in the US on August 6, 2009.
- The vaccine was licensed by the FDA on September 15, 2009.
- We began shipping vaccine to HHS on September 29, 2009 and shipments are ongoing as lots become available.
- We anticipate that we will be able to fill all 75.3 million doses of bulk antigen by the end of December, pending HHS orders for formulation and fill of the remaining bulk antigen.

VII. Vaccine Safety

In deciding to license the H1N1 vaccine, the FDA followed the same regulatory process by which it approves strain changes for the annual seasonal influenza vaccine. The H1N1 vaccine is produced by the same manufacturing process and in the same facilities used for seasonal vaccine.

Additionally, clinical trials were initiated and followed to evaluate the immunogenicity and safety of the vaccine. Data from several independent trials indicate that the H1N1 vaccine is similar in terms of immunogenicity and safety to seasonal influenza strains. The safety profile of the vaccine will be carefully and continually monitored in ongoing follow-up to the clinical trials for six months post immunization and by health officials as the public immunization campaign continues.

Conclusion

Sanofi Pasteur appreciates the opportunity to testify before the Subcommittees and to provide information on the vaccine production process for the 2009 H1N1 influenza vaccine. We are committed to working in partnership with the federal government and public health community to provide the American public with access to the H1N1 influenza vaccine as quickly as possible. We are confident that we are taking every step to produce a safe and effective product. I look forward to answering any questions.