AUTHENTICATED
U.S. GOVERNMENT
INFORMATION
GPO

FLU VACCINE: PROTECTING HIGH-RISK INDIVIDUALS AND STRENGTHENING THE MARKET

JOINT HEARING

BEFORE THE

SUBCOMMITTEE ON HEALTH

AND THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON ENERGY AND COMMERCE
HOUSE OF REPRESENTATIVES

ONE HUNDRED EIGHTH CONGRESS

SECOND SESSION

NOVEMBER 18, 2004

Serial No. 108–134

Printed for the use of the Committee on Energy and Commerce

Available via the World Wide Web: http://www.access.gpo.gov/congress/house

U.S. GOVERNMENT PRINTING OFFICE

97–274PDF WASHINGTON : 2005

For sale by the Superintendent of Documents, U.S. Government Printing Office
Internet: bookstore.gpo.gov Phone: toll free (866) 512–1800; DC area (202) 512–1800
Fax: (202) 512–2250 Mail: Stop SSOP, Washington, DC 20402–0001

COMMITTEE ON ENERGY AND COMMERCE

JOE BARTON, Texas, *Chairman*

W.J. "BILLY" TAUZIN, Louisiana
RALPH M. HALL, Texas
MICHAEL BILIRAKIS, Florida
FRED UPTON, Michigan
CLIFF STEARNS, Florida
PAUL E. GILLMOR, Ohio
JAMES C. GREENWOOD, Pennsylvania
CHRISTOPHER COX, California
NATHAN DEAL, Georgia
RICHARD BURR, North Carolina
ED WHITFIELD, Kentucky
CHARLIE NORWOOD, Georgia
BARBARA CUBIN, Wyoming
JOHN SHIMKUS, Illinois
HEATHER WILSON, New Mexico
JOHN B. SHADEGG, Arizona
CHARLES W. "CHIP" PICKERING, Mississippi, *Vice Chairman*
VITO FOSSELLA, New York
STEVE BUYER, Indiana
GEORGE RADANOVICH, California
CHARLES F. BASS, New Hampshire
JOSEPH R. PITTS, Pennsylvania
MARY BONO, California
GREG WALDEN, Oregon
LEE TERRY, Nebraska
MIKE FERGUSON, New Jersey
MIKE ROGERS, Michigan
DARRELL E. ISSA, California
C.L. "BUTCH" OTTER, Idaho
JOHN SULLIVAN, Oklahoma

JOHN D. DINGELL, Michigan
Ranking Member
HENRY A. WAXMAN, California
EDWARD J. MARKEY, Massachusetts
RICK BOUCHER, Virginia
EDOLPHUS TOWNS, New York
FRANK PALLONE, Jr., New Jersey
SHERROD BROWN, Ohio
BART GORDON, Tennessee
PETER DEUTSCH, Florida
BOBBY L. RUSH, Illinois
ANNA G. ESHOO, California
BART STUPAK, Michigan
ELIOT L. ENGEL, New York
ALBERT R. WYNN, Maryland
GENE GREEN, Texas
KAREN McCARTHY, Missouri
TED STRICKLAND, Ohio
DIANA DeGETTE, Colorado
LOIS CAPPS, California
MICHAEL F. DOYLE, Pennsylvania
CHRISTOPHER JOHN, Louisiana
TOM ALLEN, Maine
JIM DAVIS, Florida
JANICE D. SCHAKOWSKY, Illinois
HILDA L. SOLIS, California
CHARLES A. GONZALEZ, Texas

BUD ALBRIGHT, *Staff Director*
JAMES D. BARNETTE, *General Counsel*
REID P.F. STUNTZ, *Minority Staff Director and Chief Counsel*

SUBCOMMITTEE ON HEALTH

MICHAEL BILIRAKIS, Florida, *Chairman*

RALPH M. HALL, Texas
FRED UPTON, Michigan
JAMES C. GREENWOOD, Pennsylvania
NATHAN DEAL, Georgia
RICHARD BURR, North Carolina
ED WHITFIELD, Kentucky
CHARLIE NORWOOD, Georgia
Vice Chairman
BARBARA CUBIN, Wyoming
JOHN SHIMKUS, Illinois
HEATHER WILSON, New Mexico
JOHN B. SHADEGG, Arizona
CHARLES W. "CHIP" PICKERING, Mississippi
STEVE BUYER, Indiana
JOSEPH R. PITTS, Pennsylvania
MIKE FERGUSON, New Jersey
MIKE ROGERS, Michigan
JOE BARTON, Texas, (Ex Officio)

SHERROD BROWN, Ohio
Ranking Member
HENRY A. WAXMAN, California
EDOLPHUS TOWNS, New York
FRANK PALLONE, Jr., New Jersey
BART GORDON, Tennessee
ANNA G. ESHOO, California
BART STUPAK, Michigan
ELIOT L. ENGEL, New York
GENE GREEN, Texas
TED STRICKLAND, Ohio
DIANA DeGETTE, Colorado
LOIS CAPPS, California
CHRIS JOHN, Louisiana
BOBBY L. RUSH, Illinois
JOHN D. DINGELL, Michigan, (Ex Officio)

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

JAMES C. GREENWOOD, Pennsylvania, *Chairman*

MICHAEL BILIRAKIS, Florida
CLIFF STEARNS, Florida
RICHARD BURR, North Carolina
CHARLES F. BASS, New Hampshire
GREG WALDEN, Oregon
Vice Chairman
MIKE FERGUSON, New Jersey
MIKE ROGERS, Michigan
JOE BARTON, Texas,
(Ex Officio)

PETER DEUTSCH, Florida
Ranking Member
DIANA DEGETTE, Colorado
TOM ALLEN, Maine
JANICE D. SCHAKOWSKY, Illinois
HENRY A. WAXMAN, California
EDWARD J. MARKEY, Massachusetts
JOHN D. DINGELL, Michigan,
(Ex Officio)

CONTENTS

Page

Testimony of:

Coelingh, Kathleen, Senior Director of Regulatory and Scientific Affairs, Medimmune, Inc 106

Crawford, Lester M., Acting Commissioner, Food and Drug Administration 18

Fauci, Anthony S., Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health 24

Gerberding, Julie L., Director, Centers for Disease Control and Prevention 29

Heinrich, Janet, Director, Healthcare/Public Health Issues, U.S. Government Accountability Office 84

Mlotek, Mark E., Executive Vice President, Henry Schein, Inc 101

Olszewski, Janet, Director, Michigan Department of Community Health 77

Paradiso, Peter R., Vice President, New Business Development, Wyeth 94

Rosenbloom, Alan, President and CEO, Pennsylvania Health Care Association/Center for Assisted Living Management 90

Material submitted for the record by:

American College of Physicians, prepared statement of 119

FLU VACCINE: PROTECTING HIGH-RISK INDIVIDUALS AND STRENGTHENING THE MARKET

THURSDAY, NOVEMBER 18, 2004

HOUSE OF REPRESENTATIVES,
COMMITTEE ON ENERGY AND COMMERCE,
SUBCOMMITTEE ON HEALTH, JOINT WITH THE
SUBCOMMITTEE ON OVERSIGHT INVESTIGATIONS,
Washington, DC.

The subcommittees met, pursuant to notice, at 9:45 a.m., in room 2123, Rayburn House Office Building, Hon. Joe Barton (chairman) presiding.

Members present, Subcommittee on Health: Representatives Bilirakis, Upton, Deal, Whitfield, Shimkus, Wilson, Pickering, Ferguson, Rogers, Barton (ex officio), Eshoo, Green, Strickland, and Dingell (ex officio).

Members present, Subcommittee on Oversight and Investigations: Bilirakis, Stearns, Bass, Walden, Ferguson, Barton (ex officio), Schakowsky, and Markey.

Staff present: Chuck Clapton, majority counsel; Ryan Long, professional staff; Bill O'Brien, legislative analyst; Cheryl Jaeger, professional staff; Jeanne Haggerty, health policy coordinator; Eugenia Edwards, legislative clerk; Tony Cooke, majority counsel; John Ford, minority counsel; and Ashley Groesbeck, minority research assistant.

Chairman BARTON. The subcommittee joint hearing will come to order.

I want to thank our witnesses today for this important discussion. The flu vaccine shortage is vitally important and all of today's witnesses have a unique perspective on what is being done to address the problem.

I would assume all of the other members of this committee, have heard a lot about flu vaccines while we were back in our districts in recent weeks campaigning for the recently concluded election. I myself went to a nursing home and heard directly from the individuals in that particular nursing home that needed a shot and could not get the shot. I also visited senior centers and health care centers and met with doctors, nurses, clinicians, and in Texas there is and was a severe shortage for high risk patients.

I know that there are many, many people in my district and every other Congressional district in the country that want flu shots. They don't want a cheap political attack or demagoguery on this issue. There have been some that seem to view the current cri-

sis as an opportunity to score political points and to try to lay blame. I can assure my panelists that is not why we are here today.

The Energy and Commerce Committee is a committee that tries to find solutions to existing problems. This committee has a responsibility and I think the expertise to examine the issues surrounding the current shortage. The Energy and Commerce Committee today is going to be constructive. We hope to identify problems that led to the current shortage. We hope we can come to some conclusions about how to develop necessary solutions to, if at all possible, solve the problem this year, which is not likely to happen because of the severe shortfall, but at the minimum to come up with a matrix that prevents it from ever happening again.

Before October 5, the United States was expected to have on hand about 100 million doses of flu vaccine. With the announcement of Chiron's vaccine being contaminated, the United States' supply was effectively cut in half to about 50 million doses. But we have 300 million citizens approximately in the United States. 50 million does not go very far, doesn't go as far as it needs to in taking care of the percentage of the 300 million that need a flu vaccine.

The FDA and CDC have really, really tried in my opinion to work with other manufacturers to increase the current supply and we hope, because of those efforts, that it is going to be up to 61 million doses. The FDA is also working with facilities overseas to supply what they hope will be an additional 5 million doses. The CDC has developed and is implementing a plan to allocate 10 million doses of the flu vaccine to States that can then distribute those doses to high risk individuals.

One objective for today's hearing is to assess how successful this effort has been and what more can be done to provide high risk individuals with better access to flu vaccine.

Many of the witnesses on the second panel are on the front lines in delivering the vaccine, and I am going to be very interested in hearing of their perspective on the CDC plan and, if possible, if we can improve on that plan.

Ten years ago we had five suppliers in this country of injectable flu vaccines. Going into this flu season, we are down to two. You would think maybe we only have two because the demand has gone down. That is not right. Demand has gone up. The number of companies to meet that demand have gone down. The companies have continued to leave the market.

The lack of suppliers is a prime reason that we find ourselves in the situation that we have today. Without a diversity of vaccine suppliers, any problem turns into a major supply disruption. It is important that this committee examine the short-term solutions to address shortages for this year and possibly for next year, but we also should be prepared to address the generic weaknesses in the vaccine market and why companies are reluctant today to get into the flu vaccine business.

One company here today was a manufacturer of flu vaccine, but has decided to leave that market. We need to ask why the flu vaccine market has become so unattractive to manufacturers and, if

possible, what steps can be taken to encourage new producers to come back into the market.

I want to thank all of the witnesses today and their staffs that have worked to prepare for this hearing. It is hopeful that at the conclusion of the hearing, at a minimum the U.S. public is going to have a better understanding of what the situation is and a very, very positive outcome would be if we can come to agreement on some ways to help in the short term and prevent it from happening again in the long term.

Again, I want to thank our witnesses today and I look forward to hearing your testimony.

[The prepared statement of Hon. Joe Barton follows:]

PREPARED STATEMENT OF HON. JOE BARTON, CHAIRMAN, COMMITTEE ON ENERGY AND COMMERCE

Good morning. Let me begin by thanking all of the witnesses on both panels for being here today for this important hearing. The flu vaccine shortage is a vitally important health issue, and all of today's witnesses have unique perspectives on what is being done to address this problem.

I, and probably most other Members of Congress, heard a lot about flu vaccines while we were back in our districts in recent weeks. We heard the concerns of nursing homes, senior centers and health care providers about the problems they face getting doses of flu vaccine for their high risk patients.

I know that the people back in my district want flu shots, not cheap political attacks. There are some who seem to view the current crisis merely as an opportunity to score partisan points and try to lay blame. That is not why we are here today.

This is the Committee that has the responsibility and the expertise to examine the issues surrounding the current shortage. This Committee is going to be constructive—we will identify the problems that led to the current shortage and we will develop any necessary solutions to solve these problems. It is my hope that our efforts will not be diverted by attempts to assess blame, which are both ultimately futile and do nothing to improve any patient's access to flu vaccine.

Before October 5th, we expected 100 million does of flu vaccine would be delivered. With the announcement of Chiron's vaccine being contaminated, our supply was effectively cut in half. The FDA and the CDC have done an effective job in working with several manufacturers to increase our current supply to 61 million doses. The FDA is also working with facilities overseas to supply an additional five million doses of vaccine.

The CDC has developed and is implementing a plan to allocate 10 million doses of the flu vaccine to states that can then distribute these doses to high-risk individuals. One objective for today's hearing will be to assess how successful this effort has been and what more can be done to provide high-risk individuals with better access to flu vaccine. Many of the witnesses on the second panel are on the front lines in delivering flu vaccine, and I am interested in hearing their perspectives on the CDC's plan, and how we can improve the delivery of vaccine.

Ten years ago we had five suppliers of injectable flu vaccine. Going into this flu season we were down to two. Demand has increased over time, but companies continue to leave the market. The lack of suppliers is a prime reason that we find ourselves in the situation that we do today. Without a diversity of vaccine suppliers, any problem turns into a major supply disruption.

It is important that this Committee examines short-term solutions to address shortages for this and potentially next year. We must also be prepared to address the weaknesses in the vaccine market, and why companies are reluctant to get into the flu vaccine business. One company here today was a manufacturer of flu vaccine, but decided to leave that market. We need to ask why the flu vaccine market has become so unattractive to manufacturers and what steps can be taken to encourage new producers.

I would like to commend and thank all parties that have worked together to address this important public health concern. Thank you, and I look forward to your testimony.

Chairman BARTON. With that, I would ask the distinguished ranking member of the full committee, the Honorable John Dingell of Michigan, if he wishes to make an opening statement.

Mr. DINGELL. Mr. Chairman, thank you. I commend you for scheduling this hearing to respond to the questions related to the severe shortage of flu vaccine this year. All of us are hearing from constituents who are justifiably alarmed by this situation. They are alarmed for themselves and they are alarmed for their loved ones. We need to learn what got us to this point and, more importantly, we need to determine how to reduce the risk of repeating this mess.

I would observe that it appears to me that the watchdogs who are supposed to be diligent and vigorous in assuring the safety of the American people have been asleep or resting tranquilly instead of fully carrying out their responsibilities. There are questions into which this committee must go with considerable vigor.

As a preliminary matter, how and why did this immediate problem occur? What happened to Chiron? Did the Food and Drug Administration fully and wisely exercise its authority? Does the foreign inspection system work, or is it broken? Is it applied with sufficient vigor by the Food and Drug Administration?

It appears at first glance that answers to these questions are going to give our people little comfort. Chiron purchased a chronically troubled facility and was insufficiently aggressive in addressing shortcomings. FDA allowed the problems to fester and was laggard in reacting to bad news. Did FDA engage in sufficiently vigorous inquiry into the behavior of Chiron and did they provide the necessary inspections and inquiry into the functioning of that company?

Our hearings in 2000 showed that Food and Drug's foreign inspection system, which is often little more than an international honor system, is badly underfunded. Has that question been addressed? And it was in disarray at that time. Is this situation still the case?

Congress needs to get to the bottom of this and the Committee on Government Reform has already done important and useful work on what has happened here. But Congress must not wait to act on the underlying vulnerability of the vaccine supply that this sorry episode has revealed.

I recently announced my interest in developing bipartisan legislation aimed at ensuring an adequate and reliable supply of safe and effective flu vaccines. A number of elements are necessary to help achieve that goal: Guaranteeing adequate vaccine supplies, providing compensation for those injured, enhancing vaccine efforts in the area of research and other things, improving FDA inspection of flu vaccine manufacturing, improving FDA review process for new flu vaccines; authorizing emergency vaccine allocation procedures; and providing for continued monitoring and accountability; but also treating all vaccine manufacturers in the United States and elsewhere with equal care, intensity and vigor.

Mr. Chairman, I hope that in the best bipartisan tradition, this committee will be able to work together, as we have in the past, on this issue, and I would hope that we will be able to do so soon. It is not an exaggeration to say this is among the most important public health matters we face, now and in the future, and if we do a good job of addressing the matter of annual vaccines for influenza, then we may very well be improving our chances of mini-

mizing the damage that will be caused by the next influenza pandemic. A lot of work has been done to identify policy options. The Institute of Medicine, the Government Accountability Office, advisory committees and others have sifted through mountains of data and provided thoughtful analyses. It is now time for us to assess the policy options and to act.

Today's hearing is a good start, and we have an excellent array of witnesses. I am particularly pleased to welcome from the State of Michigan Janet Olszewski, the Director of the Michigan Department of Community Health. She is going to provide an important perspective from the State level on programs and policies used to manage this year's severe shortage of flu vaccine. She joins many other distinguished witnesses and I thank them all for appearing before us today.

I would note that the Food and Drug Administration should take small comfort about their appearance here today, because it appears that they have been tranquilly at rest where important responsibilities are needed to be addressed with vigor.

Thank you, Mr. Chairman.

Chairman BARTON. Thank you, Congressman Dingell.

We would now like to recognize the distinguished chairman of the Health Subcommittee, Mr. Bilirakis, for an opening statement.

Mr. BILIRAKIS. Thank you, Mr. Chairman.

Mr. Chairman, we all know I think what went wrong this year, but I am glad, and you pretty well said it, that we will not focus on what happened and who is to blame. That would be taking the easy way out of this problem. Too often in Congress we like to finger point, rather than take the more difficult road of finding real practical solutions. But today's hearing and the excellent panels of witnesses before us, I am really hopeful that members can focus on examining what is currently being done to get the flu vaccine to Americans and very importantly how we can prevent shortages in the future.

We have all heard from constituents, of course, many of them asking us if we have gotten our flu shot yet and that sort of thing. My son is a primary care physician, and for the first time he was not able to get any vaccine for his patients. Hopefully the witnesses here today will tell us what is being done to ensure that the people that we all represent will be able to get the vaccines they need.

What happened this year is, of course, extremely unfortunate, and we don't want to downplay that fact. However, Mr. Chairman, as a result of this shortage, several good things are happening. For example, because the flu vaccine is not as widely available this year, State and local health agencies have been working to target high risk individuals. In 2002-2003 flu season, only 43.6 percent of the high risk population was vaccinated. This year, due in large part to the focus on the importance of the vaccine and information about which individuals qualify as high risk, it is anticipated that percentage will be much higher.

Hopefully the problems experienced this year will encourage us, the Congress, to examine the barriers that currently exist to encourage participation in the flu vaccine market, and that examination will result in better policy.

There are some very real problems that exist in this market. For example, vaccines are difficult and expensive to make and the risk of failure in the development process is high. They require complex biological procedures and elaborate processing to keep them uncontaminated and yet effective. It can take a year to produce a vaccine, and each batch must be rigorously tested before it can be released to the U.S. market, which can take several additional months.

Also the demand for the vaccine is extremely unpredictable. There is a continuous struggle with how much flu vaccine to keep on hand, which often leads to irregular purchasing patterns. This in turn complicates production planning by manufacturers.

Additionally there is also the threat of litigation, as we know, which has played a role in driving companies out of the vaccine business.

It is tragic, Mr. Chairman, that there are barriers to market entry of vaccine companies. The flu vaccine is cost-effective, preventing not only the illness but also the far greater cost of treating the cases they prevent, yet the overall vaccine pricing structure that has evolved in the United States does not value a vaccine's role in holding down overall health care costs, sort of like what we experience with the Congressional Budget Office.

The fact that so few manufacturers remain is a clear indication that risks and rewards are askew. We are all anxious to hear answers to all of these questions, as so many others, from our witnesses.

Thank you, Mr. Chairman.

[The prepared statement of Hon. Michael Bilirakis follows:]

PREPARED STATEMENT OF HON. MICHAEL BILIRAKIS, CHAIRMAN, SUBCOMMITTEE ON HEALTH

Thank you Mr. Chairman. Good morning. I'm extremely pleased that we are holding this hearing on the flu vaccine shortage today. As I am sure you are all aware, this has been a topic that has been on the minds of most Americans as we enter into flu season this year.

Each year, millions of people in the United States get the flu. For many, this can be a life-threatening disease. About 36,000 people each year die and over 200,000 are hospitalized. Throughout our history, we have been plagued with epidemics and pandemics of influenza, "flu." The flu affects all age groups; however, infection is highest among children and the elderly. The flu vaccination is the primary method for preventing influenza and its severe complications.

Most of us are aware of what happened with regard to the flu vaccine this year. Currently, in the United States, there are only two manufacturers of the influenza, "flu" vaccine. When one of those two companies had their license to manufacture the flu vaccine suspended, preventing any release of this vaccine for this season, the expected supply of the flu vaccine available in the United States for this season was severely reduced.

As we all know what went wrong this year, I am glad that the hearing today will focus not on what happened and who is to blame. That would be taking the easy way out of this problem. Too often in Congress, we like to "finger point" rather than take the more difficult road of finding real, practical solutions. With today's hearing, and the excellent panels of witnesses before us, I am really hopeful that Members can focus on examining what is currently being done to get the flu vaccine to Americans, and how we can prevent shortages in the future.

First and foremost, I want to ensure that information is getting to the public about which individuals are considered to be "high-risk" and how we can get those individuals vaccinated. When I was home over the break, I had many of my constituents asking me about how they could get their flu shot. Hopefully the witnesses here today will tell us what is being done to ensure that the people I represent will be able to get the vaccines they need.

What happened with the flu vaccine this year is extremely unfortunate, and I don't want to downplay that fact. However, as a result of this shortage, several good things are happening. For example, because the flu vaccine is not as widely available this year, state and local health agencies have been working to target "high risk" individuals. In 2002-2003 flu season, only 43.6% of the "high risk" population was vaccinated. This year, due in large part to the focus on the importance of the vaccine, and information about which individuals qualify as "high risk," it is anticipated that that will be a much higher percentage.

The flu vaccine shortage this year highlights larger issues that plague the vaccine market, and I believe strongly that those issues need to be addressed. Ten years ago, there were 5 manufacturers of the influenza vaccine, over the past few years, more and more manufactures have ceased to produce vaccines, so we are down to two manufacturers.

Hopefully, the problems experienced this year will encourage Congress to examine the barriers that currently exist to encourage participation in the flu vaccine market, and that examination will result in better policy. There are some very real problems that exist in this market. For example, vaccines are difficult and expensive to make, and the risk of failure in the development process is high. They require complex biological procedures and elaborate processing to keep them uncontaminated yet effective. It can take a year to produce a vaccine, and each batch must be rigorously tested before it can be released to the U.S. market, which can take several additional months. Also, the demand for the flu vaccine is extremely unpredictable. Then there is a continuous struggle with how much flu vaccine to keep on hand, which often leads to irregular purchasing patterns. This, in turn, complicates production planning by manufacturers. Additionally, there is also threat of litigation has also played a role in driving companies out of the vaccine business.

It's tragic that there are barriers to market entry for vaccine companies. The flu vaccine is cost-effective, preventing not only the illness, but also the far greater costs of treating the cases they prevent. Yet the overall vaccine pricing structure that has evolved in the United States does not value a vaccine's role in holding down overall health-care costs. The fact that so few manufacturers remain is a clear indication that risks and rewards are askew.

I am anxious to hear from witnesses about what possible changes that could be made to encourage more participation in this area. As Chairman of the Energy and Commerce Subcommittee on Health, I do not intend for this hearing to be the extent of the Committee's examining this issue, rather the first step.

Thank you, Mr. Chairman.

Mr. UPTON [presiding]. I recognize Ms. Eshoo for an opening statement.

Ms. ESHOO. Thank you, Mr. Chairman. First let me say to all of my colleagues, congratulations on your reelections. I look forward to working with you in the next 2 years on the really major issues that come through this committee in the best traditions of the House Energy and Commerce Committee.

I want to thank the chairman for holding this critical hearing. I am pleased that it is Investigation and Oversight and the Health Committee. This issue deserves the attention of both of the subcommittees, and welcome to the distinguished representatives of really the premier agencies I think in the Federal Government, the FDA, the CDC and the NIH. It is a pleasure to see you here.

We all know what this issue is because it affected every single part of the country regardless of where anyone's Congressional district is. We knew it firsthand from our family. We understand it if we are of the age where we are supposed to get a flu shot. We understood it for ourselves. Most importantly, we understood it from the standpoint of our constituents.

For me, it was a sad sight to turn on the television and to see the news of seniors standing in line all over the country and exclaiming how could this happen in America? So that says more than one thing to me. What our system is, how this came to be,

what kind of fixes do we need to take a look at. Is there something wrong with the market? We have too few that are producing the vaccine. What can we do to enhance the private sector in producing a safe supply of vaccine, even though there are some rocks along the way in terms of the way they do it.

I also think we need to, through this hearing, take a very hard look at the FDA and its enforcement. Whatever we have on the books, the laws that we have had on the books, and I use the word premier organizations in my first few words this morning, I have always had a great deal of regard for the FDA. The American people have trusted the FDA to stand between them whatever it takes to guarantee consumer protection, consumer safety, and when that fails the American people are failed.

So one of the aspects of this hearing I think must zero in very professionally and in a surgical way, if I might say, what the enforcement of the FDA was. It is very disturbing to me to read about enforcement via the telephone. We all know that there isn't anything that takes the place of being in a plant. What happened during that timeframe? What kind of effect did it have to bring about on October 5 and what happened following that?

So I think, Mr. Chairman, we need to draw out of this hearing what I just described, the role of the private sector, where we can help to make that far more robust, where the private sector may need some help and some incentives.

At the end of the day we have the responsibility to guarantee a safe and full flow of vaccines available to those that need the vaccines the most without a rationing system, without having 80 and 85-year-olds standing in line in the cold and dismayed, and really disheartened and disappointed by what this Nation has to offer them.

It really was a public health mess. There wasn't any one of us that had a good answer to our constituents, except to say that the Public Health Service was doing everything that it could to double and triple up so that people could get their vaccines, those that needed them the most.

So I look forward to what we are going to learn from the experts today, but I do hope that we will not leave out that portion of a real probing look at the FDA, not for any political purposes. The FDA is not a political agency, and the public health of this country is not a political football either. The elections are over, so it is not a part of that. But I think we need to take a look at enforcement.

The chairman of the full committee and myself have worked on FDA issues. We know what those issues are and we know the importance of them and the relevance to the American people.

So thank you again for having this hearing, and welcome again to our distinguished guests here today. I look forward to what we are going to learn. Thank you.

Mr. UPTON. I recognize myself for an opening statement.

This is a very important hearing, exploring the lessons that we must learn from our current flu vaccine shortage and the steps that should be taken to ensure an adequate and reliable supply of vaccines in the future. This shortage has a very human face. I am hearing from many elderly and disabled folks who are shocked and frightened by the shortage.

Particularly poignant and troubling are the calls my office is getting from home-bound elderly folks who cannot get to their senior centers where flu shots may be given. Also very troubling are the calls from health professionals who care for our most vulnerable individuals and those who feel helpless in the face of the shortage to address their patients' fears and needs.

Clearly a major part of the problem is the fact that many pharmaceutical companies have withdrawn from the vaccine market, making us even more vulnerable to serious shortages, not only of flu vaccines, but also of childhood vaccines. For example, there is only one manufacturer in the United States that now produces the measles-mumps-rubella vaccine. There is only one producing the varicella vaccine, and only one that is producing the pneumonia vaccine. We need to figure out how to get more companies back into the production of those vaccines before we face even more critical trouble.

There is also a related issue that I think we should focus on today, the system for distributing vaccines. As you recall, we had a shortage for a month or so in the last flu season as well. I got a lot of calls from doctors and other health professionals who were angered and deeply frustrated by the fact that they could not get the vaccine they needed for their high-risk patients while right down the street people were getting flu shots at the supermarkets and drugstores, regardless of their risk status.

Further, when this year's shortage struck and we recognized that we needed to prioritize who was receiving the limited number of flu shots that were available, I don't think we had a handle on where the vaccines were. In Michigan, for example, our Department of Community Health officials estimated there were between half a million and a million flu shots in the State, but they weren't sure where those shots were distributed.

I would like to know how the current distribution system is organized and what changes need to be made to ensure that getting those vaccines to high risk individuals is a priority, particularly when shortages occur.

I look forward to working with my colleagues on both sides of the aisle on this committee and the administration to make sure we learn the lessons this flu vaccine shortage holds and take the steps needed to ensure that we have a stable supply for all vaccines.

I also want to lend a special welcome to a witness on the second panel, Janet Olszewski, who is the Director of the Michigan Department of Community Health. I look forward to her participation.

With that, I yield to the gentlewoman from Illinois, Ms. Schakowsky, for an opening statement.

Ms. SCHAKOWSKY. Thank you, Mr. Chairman. It is not just Congressional committees that are interested in getting to the bottom of this. Clearly the American public, people who are waiting in line for hours, who are searching around for flu shots, many who are unable simply to get them, even some of our most vulnerable people, are asking those questions.

I think the front page today of the Washington Post shows the great concern that a vast majority, that many, many people feel about it. One headline, FDA Is Flexing Less Muscle. Some question as to the relationship with drug questions. That is the headline.

The first paragraph begins, "In the past 4 years, the Food and Drug Administration has taken a noticeably less aggressive approach toward policing drugs that cause harmful side effects, records show," et cetera.

The other, U.S. knew last year of problems at vaccine plant. The Food and Drug Administration found serious problems of bacterial contamination at an influenza vaccine plant in England in 2003, 16 months before British regulators effectively closed the site and impounded its flu shots because of fears they were tainted. Not the FDA closed it, but the British regulators closed the plant.

So there are many, many answers that need to be had. Even in August of this year when the FDA was told again of additional contamination at the Chiron facility, it failed to act in a meaningful way to address the problem or to secure additional vaccine supply from elsewhere.

We have seen price gougers appear out of the woodwork to profit from a public health crisis. None of these problems occurred in other countries where the government plays a far greater role in assuring affordable access to health care. In fact, in Canada, they had enough flu vaccine supply to sell to those Americans who were close enough to the border to get it.

This is a big deal. 30,000 people die annually from the virus. Hundreds of thousands of others end up in the hospital. We need to answer these questions.

I was very disturbed when Vice President Cheney in kind of an explanation of what the problem is said that vaccine production just isn't profitable enough for private pharmaceutical companies. Is that going to be the consideration, that the profits of the pharmaceutical companies are going to take precedence over the health of the American people?

There is no question that had the FDA taken an appropriate course of action, that this year's vaccine shortage and perhaps the unnecessary sickness of many would be relieved.

I just want to end with this. The Governor of Illinois, Rod Blagojevich, who has been a leader in the fight for reimportation, has undertaken efforts to secure additional vaccine supplies for the most vulnerable people in our State, and is awaiting FDA authorization for those efforts. I want to hear more about the FDA's response, when we can get an answer to this, and why since we are still relying on foreign sources to meet our flu vaccine names, the Bush administration still is blocking Illinois' reimportation efforts of other lifesaving medicines.

Thank you, Mr. Chairman.

Chairman BARTON [presiding]. We would now like to hear from the distinguished Congressman from Florida, Mr. Stearns, for an opening statement.

Mr. STEARNS. Thank you, Mr. Chairman. Thank you for holding this hearing. It is timely even though we are in sort of a lame duck session.

We have a lot of seniors obviously in Florida, and when this occurred, I just want to give kudos to Governor Jeb Bush. He and his Secretary of Health immediately sprang into action. They issued directives implemented by DOH to help identify flu vaccines to ensure information on prevention measures, reach all these indi-

viduals who needed it. So immediately they stepped forward. They contacted the Florida nursing home industry, the Florida Medical Association, AARP, health care providers, the Department of Elderly Affairs and the Agency For Health Care Administration.

So, most importantly, our leaders in Florida sprang forth and said, hey, there is no need for panic. We are going to identify what we have, we are going to identify the highest risk, and we are going to give those individuals the flu shot that is needed so we will not have a health crisis.

Now, the flu vaccine is a unique case here. The length of its production can be up to 18 months, according to the GAO. There are so many strains of this flu and the virus seems to be always one step ahead of us, mutating its way to resistance. We may predict for the Hong Kong strain for next year and then we are pummeled by the Tokyo strain. It seems to me we hear there is a shortage not just this year but several in the past years in autumn, only to have vast unused quantities discarded the next March or so.

It is voluntary to get this flu vaccine and not necessarily lucrative to industry to produce it. Yet for their efforts and some of the lawsuits they have to undergo, which sometimes is the highest level, it makes them discouraged.

So why have we gone from just three or four manufacturers down to just one? Perhaps the manufacturers just decided, "I am going to throw up my hands and not deal with this. I don't want the litigation. It is too much hassle." We have to make sure this doesn't occur. Free market competition generally brings out choices, to which litigation and excessive regulation can be impediments.

So I would like to get out of this hearing tools to instill consumer confidence that the vaccine will be there, there will be choice and competition. Maybe the answer lies in liability protection or market incentives to get this going. Maybe we need some new innovative techniques that rely more on computer modeling, that cultures a better understanding of which flu vaccine is best. I don't know. But I am hoping to hear from our witnesses today some solutions and not just some bureaucratic explanation, some definite clearances.

Thank you, Mr. Chairman.

Chairman BARTON. We thank you, and would welcome our distinguished friend from Texas, Mr. Green, for an opening statement.

Mr. GREEN. Mr. Chairman, thank you for holding this hearing on the flu vaccine shortage. It is fitting this hearing is a joint effort by both the Health Subcommittee and the Oversight and Investigations Subcommittee.

The investigation work done by our Oversight and Investigations Subcommittee will no doubt be instrumental in helping us craft a government response to this problem and help prevent future shortages.

When the British government shut down production, the public health officials in my hometown of Houston learned they would not be receiving any of the flu vaccines they ordered for the adult population in Harris County.

As far as economics goes, the Harris County hospital district decision to go with Chiron was an easy one. It ordered over 60,000 doses from Chiron since it had established a business relationship with the firm, and Chiron offered the lowest price. It also has be-

come all too clear, however, that the reliance on economic rationale has failed us just as it failed our Harris County hospital district in Houston.

The current vaccine production market, which is controlled by the private sector, doesn't allow for the production of a vaccine supply adequate enough to further public health. The financial incentives simply are not there.

Unlike other vaccines, the makeup of the flu vaccine must change annually to respond to each year's dominant strains of the flu virus, which is to predict. The final product has a short shelf life that often yields surplus doses, which pharmaceutical firms must simply throw out and count as a loss.

These unfavorable market conditions have pushed all but one U.S. producer of flu vaccines out of market, which is little surprise considering the significant financial risk inherent in flu vaccine production. With only two flu vaccine manufacturers in the U.S. market, one U.S. based and one foreign, it is extremely difficult to ensure a supply adequate enough to meet the government's goal of widespread flu vaccination.

The shutdown proves without a doubt that any production disturbance has broad and serious ramifications, not only for flu vaccine supply but also for other potential vaccines.

In communities throughout the country the vaccine supply problems create long lines and fears in the ability of high risk individuals to get vaccinated. While this situation has forced public health officials to coordinate their efforts to provide the flu vaccine to those most in need, the shortage has also brought the worst out in some folks.

The Houston Chronicle puts it, "The invisible hand of the free market provides many benefits, but the suppression of greed is not among them."

This statement, unfortunately, hits close to home as price gouging has been uncovered as a result of not only a significant problem in Houston, but also around the country. According to a suit filed by our Texas Attorney General Greg Abbott, Houston Public Hospital has been a direct victim of price gouging as a result of restrictive flu vaccine supply. Ben Taub Hospital in Houston, one of our public hospitals, was scheduled to receive a portion of the 60,000 doses from Chiron for less than $80 a vial. Yet faced with no flu vaccine at all, Ben Taub paid nearly $400 a vial from a vaccine distributor which later tried to sell the addition vials to the hospital for $800 a vial, 1,000 percent markup. Again, this is a public hospital that either gets its public funding from the property taxes in Harris County or what they earn from Medicaid and some of our other public systems. This explanation is unacceptable and has to stop.

While I have every confidence that the judicial system will take care of the price gougers, we have to take the necessary steps at the Federal level to make sure this situation is not replicated today, and we rely heavily on the experience of our witnesses here today to help us understand what went wrong and where we can go from here, what legislative solutions we need to craft or where in the regulatory process we need to deal with it.

Again, Mr. Chairman, thank you and both of our subcommittees for holding this hearing.

Chairman BARTON. Thank you, Congressman Green.

We would now like to hear from the distinguished gentleman from Georgia, Mr. Deal, for an opening statement.

Mr. DEAL. Thank you Mr. Chairman. I thank you for holding this joint hearing, and I would especially like to welcome Dr. Gerberding from the CDC in Atlanta and the other distinguished panel members. I had the opportunity to hear their testimony yesterday in another committee, and I look forward to hearing additional evidence.

I think I am sort of like a lot of people. I didn't want a flu shot until I knew I couldn't get one. That wasn't true, however, of my 98-year-old mother and my 91-year-old father-in-law who live with me. They wanted one all along. To have a crisis like this come upon us obviously has dramatic effects. It is one of those reality tests that I guess Congress has to deal with from time to time.

All of us have identified as you will further identify for us that there are several components to trying to find a solution. One, and I think the information from the NIH is going to be very helpful with regard to the issue of research, what do we need to do further in terms of research to provide other alternatives? With no pun intended, certainly the egg-based life virus, we literally found us with all of our eggs in two baskets and one of those baskets taken away. That is alarming to all of us.

I think we need to know what can we do to stimulate additional entries into the marketplace and that may or may not be within the realm of anything you can give us advice about, but it is certainly a question that I think Congress must wrestle with.

The other area is one that has already been touched upon in opening statements and that is when a crisis of this nature emerges, do we need to have greater legislative authority given to our Federal agencies, whether it be the CDC or the FDA, in terms of controlling the distribution of limited resources in a time of crisis? That apparently is legislatively lacking at this point. At least it is only of minimal amount of authority given and conveyed at the current time. So I would be interested in hearing comments on all of those areas as to what your thoughts and feelings are on that.

Thank you, Mr. Chairman. I yield back.

Chairman BARTON. We thank the gentleman from Georgia and recognize the gentleman from Kentucky, Mr. Whitfield, for an opening statement.

Mr. WHITFIELD. Mr. Chairman, thank you very much. All of us are very much interested in this hearing on a matter of great importance. I don't think that we do anyone any good by trying to demonize anybody in this process, either the drug companies or FDA, but our goal here is to try to find some answers why there are only three vaccine manufacturers of influenza vaccine.

Two, will the new cell culture technology help improve the process and maybe encourage more companies to get into the process.

Three, I think we do have to acknowledge the cost of lawsuits today. I have been told that many of these companies, because of the volatility of lawsuits regarding vaccines, cannot obtain insur-

ance for liability and many of them are operating without liability insurance.

So I think there are many interesting questions here. I know that all of us look forward to the response of the witnesses and trying to come to a solution to this very important issue facing the people of the U.S.

I yield back the balance of my time.

Chairman BARTON. I thank the gentleman. I would ask the gentleman from Illinois, Mr. Shimkus, if he wishes to make an opening statement.

Mr. SHIMKUS. Mr. Chairman, in the interest of time and information, I waive.

Chairman BARTON. The gentleman waives. The gentleman from Oregon?

Mr. WALDEN. Mr. Chairman, just very briefly. I think this really boils down to two things: What did the FDA know, when did they know it, what did they do about it and what should they have done? Second, what is wrong with the current vaccine market and what should or can we do in the Congress to fix it?

That is what I really want to go to, is where were there breakdowns, either in the regulatory process or where were there breakdowns in the legislative process. We each have responsibilities here to fix the problems that exist. I look forward to the testimony.

Thank you.

Chairman BARTON. We recognize the distinguished gentleman from Michigan, Mr. Rogers, for an opening statement.

Mr. ROGERS. I yield, Mr. Chairman.

Chairman BARTON. Seeing no other members present, the Chair—I am sorry, Congressman Ferguson of the Garden State of New Jersey.

Mr. FERGUSON. Mr. Chairman, the Garden State and the medicine chest of the world, I might add. I thank you for this hearing.

Chairman BARTON. Do you have any extra vaccine?

Mr. FERGUSON. That is what we are going to find out today.

I appreciate, Mr. Chairman, your calling this hearing. Over the past week, committees on the Hill have been holding a number of hearings looking into what led us to the point that we are at today. I would prefer to look forward to take the opportunity today to examine why the vaccine market is so prohibitive to producers and subsequently what we can do in the future to ensure the American public is protected for flu seasons to come.

I would also like to discuss at some point what the CDC is doing to ensure we are protected against a future pandemic. Are we stockpiling antivirals for when the next pandemic strikes?

Vaccines are a difficult and risky product to make. Each year the FDA, in consultation with other agencies and organizations, reviews the flu virus strains that are prevalent and selects the three strains that are most likely to cause illness in the United States the following winter. Manufacturers then produce a vaccine that includes these three different strains which go into making that next year's unique flu vaccination.

The strain that the experts guess will strike varies from year-to-year, as does the number of people who will take the vaccine, which leads to a difficult guessing game.

Adding on top of that the myriad of regulations that the producers must adhere to and adding on top of that a mountain of liability concerns, and you find yourself in the position we have today: Only two companies, foreign companies, make flu vaccines for the U.S. Market.

The flu can be anywhere from an annoying to a debilitating illness that affects millions of people in the United States every year. On average, about 36,000 people a year die from the flu and over 200,000 people are hospitalized as a result of the flu.

These numbers highlight the importance of the flu vaccine, the role that it can play in protecting high risk individuals, particularly seniors and people who have diseases like diabetes. But what do we do when we are hit with a flu pandemic we are not prepared for? It is vital that we do what is needed to have the necessary stockpile of antiviral medications to address the needs of a population that becomes sick with the flu.

So I look forward to hearing the thoughts from our panel this morning on these and other questions. I thank you again for holding this hearing.

Chairman BARTON. We thank the gentleman for that statement and apologize for not recognizing him. I simply didn't see you. I apologize.

The Chair would ask unanimous consent that all members not present have the requisite number of days to put their statements in the record.

Hearing no objection, so ordered.

[Additional statements submitted for the record follow:]

PREPARED STATEMENT OF HON. HEATHER WILSON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW MEXICO

Thank you, Mr. Chairman, for holding this hearing today on the flu vaccine shortage. The flu vaccine shortage has had an effect on my constituents in New Mexico, just like in every other state.

New Mexico has historically had a higher proportion of citizens getting flu shots than other states. In 2003, 72.4 percent of seniors in New Mexico received a flu shot, greater than the national median of 69.9 percent, according to the Centers for Disease Control and Prevention. Sixty-one percent of New Mexicans age 18 to 64 who have diabetes received a flu shot last year, while the national median was 49 percent.

New Mexicans understand that flu vaccines are an important preventative health measure they can take to keep them healthy and save them on the costs of getting sick. People in New Mexico want to have the option to get a flu vaccine, and they are worried that some who want it may not be able to get a flu shot this year.

Tom Hopkins and his wife are seniors who live in Albuquerque. They waited in line for 3 hours before receiving their flu shots. Five-thousand seniors braved long lines to receive free flu shots at a two-day senior's expo in Albuquerque in October.

These instances are just a symptom of a larger problem—an unstable flu vaccine market with too few companies participating. While there were five flu vaccine manufacturers in 1994, there are only two today. It is our responsibility to ask why.

I believe we should focus on what we can do in the future to attract more manufacturers and prevent this from happening again. I look forward to hearing the testimony of the witnesses here today and hope it will help us in determining what Congress can do to improve the situation. It's an effort I believe Congress should and will address next year.

Thank you Mr. Chairman.

PREPARED STATEMENT OF HON. BART GORDON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TENNESSEE

Mr. Chairman, thank you for holding this important hearing. The shortage of flu vaccine this year highlights glaring problems with the vaccine industry. This is not a new problem. There have been flu shortages in 2000, 2003 and now 2004. We've seen similar shortages and distribution problems in recent years with vaccines for preventable childhood diseases including polio, whooping cough, and tetanus. This raises the question how prepared are we to combat a bio-terrorism threat if our public health system is ill-equipped to deal with the flu?

In 2002, I cosponsored legislation to establish a National Vaccine Authority, which would identify and ensure accountability for delays in vaccine production, supervise vaccine distribution and develop an emergency response and contingency plan to deal with shortages. I am encouraged that the committee is interested in developing bipartisan legislation to prevent future vaccine shortages. I look forward to working with my colleagues to ensure this legislation is not limited to the flu vaccine but looks at the entire vaccine production and distribution system, including childhood vaccines.

PREPARED STATEMENT OF HON. ELIOT ENGEL, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW YORK

Mr. Chairman, I want to thank you for holding this hearing. I have been concerned about the flu vaccine industry for many years now. It is the forth year of the new millennium—and we have had flu vaccine problems for three of these four years. Obviously, this is a health care system in need of doctoring itself.

The health toll on the American people due to the flu is terrible. Influenza can be very dangerous for people with heart, kidney, and lung conditions, including asthma. Young children and people over 65 are most at risk of flu becoming more serious, leading to hospitalizations and death. Influenza and pneumonia are the seventh leading cause of death among all Americans, resulting in over 62,000 deaths in 2001. The flu vaccine minimizes the dangerous consequences of influenza including pneumonia.

The annual cost to the U.S. economy is staggering. I have here an article from the CNN/Money website that states the annual cost is $13 to $15 billion per year. And, due to this year's shortage could rise about $20 billion. I ask unanimous consent that the article be made part of the record.

I believe that there is a general consensus that the economics of the industry are not very encouraging for manufacturers. Each year companies produce millions of doses that are eventually destroyed—this is one reason Wyeth, a company with a manufacturing plant in my district, got out of the vaccine production industry.

To me, it is obvious that the federal government can and should step in and have a positive role to play. I am a cosponsor of HR 3758, the Flu Protection Act of 2004, that would have the federal government contract with vaccine manufacturers to ensure adequate supply and that the shots are available throughout the flu season. It would also put federal funds into research for alternative vaccines with a faster production time. The cost to the federal government will be minimal in comparison to the cost of future hits to our economy.

My only regret is that the 108th Congress is to end so soon. I hope that when the 109th Congress convenes that we make this our first legislative priority. The Congress must move swiftly to ensure that we do not face millions of Americans who once again cannot get a flu shot.

I thank the Chair and yield back.

FLU SEASON COULD COST $20B

REPORT: LACK OF VACCINE COULD LIMIT SHOTS FOR EMPLOYEES; COST TO EMPLOYERS COULD BE UP NEARLY 50%.

October 18, 2004: 7:41 AM EDT

NEW YORK (CNN/Money)—A flu season made worse by a shortage of flu vaccine could cost the U.S. economy about $20 billion in health care costs and employee absences, according to a published report Monday.

The *Wall Street Journal* quotes David Cutler, a professor of economics at Harvard University, as saying the $20 billion estimate is up from the $13 billion to $15 bil-

lion in direct and indirect costs of a typical flu season. That would represent a rise in costs of between 33 to nearly 50 percent.

The U.S. is facing a shortage of flu vaccine after *Chiron Com. (Research),* which the U.S. government had counted on for about half the nation's supply, had its entire stock of the *vaccine pulled* because of problems discovered by British health authorities inspecting the Liverpool, England, plant that makes the vaccine.

U.S. public health authorities are urging that only those most at risk of health problems from the flu get flu shots this year. But many of those in the at-risk population, including the chronically ill, the elderly and infants age 2 and younger, are not in the work force.

Thus, many of those in the work force who normally get a flu shot will go into this year's flu season without their normal vaccine.

The *Journal* reports a recent study by ComPsych Corp., a Chicago human resources service firm, found 40 percent of people who don't get shots miss some time at work because of the flu, compared with less than 20 percent of people who receive flu shots.

"If we have a normal flu season and there are no shots available we're going to have a significant number of people miss work," CompPsych CEO Richard Chaifetz told the paper.

The paper reports that about 60 percent of employers had planned to offer flu vaccinations to their employees this year in an effort to cut illness and absenteeism among their work force. But the paper reported nearly all of those company programs are being put on hold or scrapped due to the vaccine shortage and the focus on using available vaccine on high-risk individuals.

Companies will focus on education and such measures as hand-sanitizer units instead of vaccine to do what they can to combat this flu season, the *Journal* said.

PREPARED STATEMENT OF HON. EDWARD J. MARKEY, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MASSACHUSETTS

Mr. Chairman, thank you for holding this important hearing on the flu vaccine shortage. Just yesterday, hundreds of seniors in my district stood in long lines at the Elks Lodge in Natick to put their name on a list for their upcoming flu clinic. In Massachusetts, we are hoping that registration programs like this one will help us target our scarce resources and ensure that the most vulnerable individuals get their flu shots first. But many of my constituents won't be able get the flu vaccine this year. They are worried and they want to know how the federal government and the pharmaceutical industry have allowed such a state of affairs.

Today we will hear from several witnesses about the problems at the Chiron manufacturing plant, and the events which led to the loss of half of the U.S. supply of flu vaccine. Today's news reports suggest that the FDA may have failed to properly exercise its responsibilities to ensure that Chiron's flu vaccine manufacturing facilities met appropriate safety and health standards. These reports are profoundly disturbing and I hope to learn why, if the FDA knew that Chiron had problems in June 2003, the agency they failed to promptly follow up with the company and ensure that the problems the FDA staff had identified at the plant were immediately corrected.

I am also concerned that the flu vaccine crisis is indicative of a larger problem at the FDA and in the pharmaceutical industry. Approximately 36,000 people die and 200,000 people are hospitalized every year due to complications from influenza. It is a disease that, while variable in its form, its yearly presence is as predictable as the changing seasons. Yet despite the ancient and cyclical nature of this threat, and despite repeated warnings and recommendations from the National Vaccine Advisory Committee, the Institute of Medicine, and the Government Accountability Office, the Bush Administration does not have a system is in place to protect the American public from the flu and the possibility of a flu epidemic. How is it that they allowed a problem at a single plant to eliminate half of our yearly supply of vaccine without a contingency plan to ensure that the American public has access to an adequate supply of flu vaccine? We need answers.

Ten years ago there were five suppliers of flu vaccine; today the US relies on two manufacturers to produce 95% of all our flu vaccine. This means that if a problem arises at one of the plants, it can significantly disrupt the supply of flu vaccine. Just as you shouldn't put all your eggs in one basket, the US should not grow all of its flu vaccine eggs at one company. We must find other companies who are willing to add to the future supply of the flu vaccine. Therefore, it is critical that we learn why companies have left the vaccine business and what steps we can take to change that trend.

The pharmaceutical industry tells us that the high cost of many prescription drugs is justified by the expenses associated with developing new drugs. But if the private sector has concluded that producing new flu vaccines every year is not something they wish to do because it is not sufficiently profitable, we must ask just what are they using their massive prescription drug profits for? If we cannot rely on private sector drug manufacturers to produce the flu vaccine we need in the U.S. each year, do we need to rethink the federal government's entire relationship with this industry in some very fundamental ways?

Today we are going to focus primarily on how we got here and what we can do to get the public through this upcoming flu season. However, it is my hope that the conversation will not end here. I look forward to further hearings on this subject and working with my colleagues to develop a comprehensive solution to the larger problem of guaranteeing a stable and adequate supply of vaccine.

Thank you.

Chairman BARTON. The Chair would also like to announce that a number of our Democrat members really, really wanted to come to this hearing, but former President Clinton is having the opening of his library in Little Rock and they already made previous arrangements to attend that ceremony. So their statements will obviously be in the record and will be very useful in our analysis.

We want to welcome our first panel. Our first panelist that is going to testify is the Acting Commissioner of the Food and Drug Administration, the Honorable Dr. Lester M. Crawford. Dr. Crawford, your statement is in the record in its entirety. We recognize you for 7 minutes to elaborate on it. Welcome to the committee.

STATEMENT OF LESTER M. CRAWFORD, ACTING COMMISSIONER, FOOD AND DRUG ADMINISTRATION

Mr. CRAWFORD. Thank you very much.

As has been said, FDA is responsible for the regulation and oversight of vaccines. I want to assure the committee and the public who are listening today that FDA takes these concerns about vaccine safety and availability very seriously indeed.

We have many important responsibilities related to vaccine safety. Before a vaccine is licensed, FDA monitors the safety of investigational vaccines. Later, when a manufacturer submits a vaccine license application to FDA, we conduct more extensive reviews. If we determine that a vaccine is safe, effective and that quality and consistency of manufacture have been demonstrated, we will license the vaccine.

In addition to a scientific review, we also inspect the manufacturing facilities every 2 years at a minimum.

Influenza vaccine is unique in that its active ingredients change almost every year. As you can imagine, this presents special manufacturing challenges. We began working with manufacturers at the earliest stages of vaccine development and continue to assist them further by conducting tests that assure the safety and efficacy of the vaccine.

Because of the complexity of the manufacturing process, FDA's Center for Biologics Evaluation and Research, or CBER, performs lot release on each lot of influenza vaccine manufactured prior to distribution of the product.

There has been a very significant increase in production over the past decade compared to approximately 20 million doses per year that were distributed in the mid-1980's. However, with the increas-

ing volume of doses needed each year and the decline in the number of influenza vaccine manufacturers, we have a very fragile infrastructure in the influenza market.

For the 2004-2005 flu season, only three manufacturers began production of influenza virus vaccine. Chiron Corporation and Aventis-Pasteur produced inactivated influenza vaccines. MedImmune Corporation manufacturers FluMist, a live influenza vaccine.

On the morning of October 5, 2004, the British Medicines and Healthcare Products Regulatory Agency, or MHRA, announced a 3-month suspension of Chiron's license to manufacture influenza vaccine. FDA immediately dispatched a senior team of scientists to the United Kingdom to meet with company officials and MHRA and to inspect Chiron's Liverpool manufacturing facility.

On October 15, 2004, after completing the inspection, FDA determined that it could not adequately assure that Chiron's vaccine met our safety standards. As a result, Chiron will not supply any influenza vaccine to the U.S. market for this season.

In coordination with others at the Department of Health and Human Services, we have actively explored all viable options to secure additional dosages of flu vaccine to provide more Americans protection against the flu. As a result of these efforts, we have been able to increase the available supply of flu vaccines for the U.S. population to 61 million doses for this season. Coupled with that initiative, we have been contacting manufacturers worldwide in an effort to identify increased supplies of antiviral medications that will provide further protection and treatment for Americans during this flu season.

Aventis-Pasteur believes that they have the capability of producing the same or more doses of influenza vaccine for the 2005-2006 season. In addition, MedImmune has indicated that it has the capability to produce 10 million doses of FluMist for the 2005-2006 season, as much as 40 million doses by 2007. We will continue to work to help Chiron address as quickly as possible the manufacturing problems they experienced during this year's production process. In addition, FDA has been encouraging foreign license manufacturers to apply for U.S. licensure and we are providing clear pathways to efficiently reach this goal.

Looking to the future, we must move science forward to help create more efficient ways to produce flu vaccine so we have greater flexibility to deal with shortages or unexpected problems. In each of the past two budgets, the Department has requested $100 million to shift vaccine development to new cell culture technologies as well as to provide for year-round availability for egg-based vaccines. We urge Congress to fully fund this $100 million request.

To help manufacturers overcome challenges in vaccine development, FDA has been investing its energy and resources in important initiatives such as the current good manufacturing practices for the 21st Century Initiative, also known as the CGNP Initiative. Under this initiative, FDA is working with industry to encourage the use of advanced technologies as well as quality systems and risk-based approaches that build quality into the manufacturing process and avoid the problems such as those Chiron experienced.

Once again, thank you for the opportunity. I look forward to the remainder of the hearing.

[The prepared statement of Lester M. Crawford follows:]

PREPARED STATEMENT OF LESTER M. CRAWFORD, ACTING COMMISSIONER, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

INTRODUCTION

Mr. Chairman and members of the Committee, I am Dr. Lester M. Crawford, D.V.M., Ph.D., Acting Commissioner of the Food and Drug Administration (FDA or the Agency). As you know, the FDA is responsible for the regulation and oversight of vaccines in the United States. I want to assure the Committee, and the public who are here today, that FDA takes their concerns about vaccine safety and availability very seriously. I welcome this opportunity to describe FDA's ongoing efforts to ensure the safety, effectiveness, and availability of influenza and other vaccines licensed in the U.S.

VACCINE SAFETY

Vaccines have contributed greatly to the health and well being of the people of our nation; however, we must nonetheless be vigilant of any potential safety concern related to vaccines. I will briefly describe some of FDA's vaccine safety activities. In the pre-licensure phase, FDA monitors the safety of investigational vaccines as they are studied in clinical trials conducted under investigational new drug applications. When a manufacturer submits a license application to FDA, we review extensive information describing the manufacture and characterization of the vaccine, the safety and efficacy data from the clinical trials, and we typically inspect the manufacturing facility where the vaccine will be made. In addition, we usually seek advice from our Vaccines and Related Biological Products Advisory Committee on the safety and effectiveness of vaccine candidates. If we determine that a vaccine is safe, effective, and that quality and consistency of manufacture have been demonstrated, we will license the vaccine.

Post-licensure, we typically review the manufacturer's test results before the manufacturer can release new lots of vaccine to the market. We also inspect the manufacturing facilities every two years. In addition, FDA's Center for Biologics Evaluation and Research (CBER) and the Centers for Disease Control and Prevention (CDC) jointly manage the Vaccine Adverse Event Reporting System (VAERS), a cooperative program for vaccine safety. VAERS is a post-marketing safety surveillance program, collecting information about adverse events (side effects) that occur after the administration of U.S. licensed vaccines. Reports to the VAERS program are welcome from all concerned individuals: patients, parents, health care providers, pharmacists, and vaccine manufacturers. We review these reports on an ongoing basis and obtain additional information as needed.

INFLUENZA VACCINES

To increase our control of this very important disease, efforts are ongoing to increase the availability of influenza vaccine and increase coverage, especially of those individuals at increased risk of complications from influenza. Influenza vaccine is unique among vaccines in that its active ingredients change almost every year and thus presents new manufacturing challenges on an annual basis. Influenza viruses are continuously evolving or mutating, and the recommendations of which viruses to include in the vaccine each year are based on the surveillance data provided from laboratories worldwide. Early each year, public health experts evaluate the data to determine the strains of virus to be used in the manufacture of the influenza virus vaccine that will be administered in the fall. Currently, licensed vaccines contain three virus strains representing the strains predicted to be in U.S. circulation, as recommended by the U.S. Public Health Service (PHS) [including FDA, CDC, National Institutes of Health (NIH), and National Vaccine Program] for incorporation into the vaccine for 2004-2005. Because of the necessity to have a vaccine that matches the virus strains currently in circulation, vaccines manufactured for the previous year cannot be used.

FDA works closely to facilitate the rapid production of influenza vaccine each year. As soon as the strains are recommended, manufacturers begin to grow the virus strains in fertile hen's eggs. These strains of vaccine, known as "seed strains," used by each manufacturer are tested by FDA's CBER to assure they are the same as the recommended strains. FDA and manufacturers conduct tests to assure the safety and efficacy of the vaccine. Manufacturers submit the results of their testing

along with sample vials from each lot to CBER for our "lot release." Because of the complexity of the manufacturing process, CBER performs "lot release" on each lot of influenza vaccine manufactured prior to distribution of the product. "Lot release" consists of CBER's review of the manufacturers' test results, including tests on the lots of monovalent virus strains. Furthermore, to assure the safety and efficacy of these products, CBER performs additional testing as appropriate.

Although the manufacturing process and lot release is completed for some lots of influenza vaccine as early as July, the manufacturing of additional lots continues until September-October in order to manufacture and complete the testing on a very large number of vaccine doses. There has been a very significant increase in production over the past decade, as compared with approximately 20 million doses per year distributed in the mid-1980s. Because of the fragile infrastructure and decision of manufacturers to leave the market, the burden of production capacity and supply of influenza vaccine rested with thee manufacturers for the 2004-05 flu season. Chiron Corporation (Evans Vaccines Ltd.) manufactures Fluvirin, and Aventis Pasteur, Inc. manufactures Fluzone; both of these vaccines are inactivated influenza vaccines. MedImmune, Inc. manufactures FluMist, a live attenuated influenza vaccine.

2004-05 FLU SEASON

The loss of Chiron influenza vaccine supply remains a challenge. As you know, we are working hard to assure the safety and health of Americans as the flu season approaches. In coordination with other elements of the Department of Health and Human Services (HHS or the Department), we have been actively exploring all viable options to secure additional dosages of flu vaccine licensed for use in the U.S. that will provide more Americans protection against the flu. As a result of these efforts, I can report that we have been able to increase the available supply of flu vaccines for the U.S. population to 61 million doses for this flu season.

Coupled with that initiative, we have been contacting manufacturers worldwide in an effort to identify increased supplies of antiviral medications that will provide further protection and treatment for Americans during this flu season and are making progress in this area as well. In addition, we have already been working with our partners in the United Kingdom as well as with Chiron Corporation to complete our review of the problems encountered at their production facility in order to expeditiously determine what steps would be required to bring that facility into compliance.

As a matter of enforcement policy, FDA inspects U.S. licensed vaccine manufacturing facilities every two years. Based on this schedule, FDA inspected the Liverpool, U.K. facility where the Chiron vaccine is produced in 1999, 2001, and 2003. It should be noted that Chiron acquired the facility in July 2003 after FDA conducted the biennial inspection. During the 1999 inspection, FDA identified various concerns and, as a result, issued a warning letter regarding the Liverpool facility. The most significant issues identified in 1999 inspection were the lack of validation for its manufacturing processes, including establishing proper limits for bioburden (including bacteria) and issues related to assuring sterility in the manufacturing process. During the 2001 and 2003 inspections, although FDA found that the company made improvements, we also made observations related to current Good Manufacturing Practices (cGMPs). In each case, FDA reviewed the corrective measures and plans in response to these deficiencies. If fully implemented, the company's plans appeared adequate to correct deficiencies identified at the facility.

It is important to understand that, from the start of the manufacturing cycle, influenza vaccine manufacturing is not a sterile process because it involves the use of eggs, which are not sterile. Therefore, a certain amount of bioburden will be present in early stages of manufacturing. However, vaccine manufacturers must have effective measures, such as sterile filtration, to eliminate this bioburden. As a further safeguard, FDA requires a lot release and testing system for vaccines. This is a vital component of the multi-step safety assurance process for vaccines. It is also important to understand that new flu vaccine is formulated and produced for each flu season, so that concerns identified with vaccine from the prior year's supply do not necessarily relate to the current year's vaccine supply.

FDA'S 2004 COMMUNICATIONS WITH CHIRON AND MHRA

On August 25, 2004, Chiron informed FDA that the company had discovered bacterial contamination in eight lots of final vaccine product for this year's flu season supply and advised that they were investigating the problem. They shared with FDA an overview of their planned investigation to determine root causes of the problem as well as their plan to retest all other lots produced. Chiron quarantined

all influenza vaccine lots during its investigation, including those that had passed all required testing, and did not release any of the product.

In September 2004, FDA, CDC and Chiron scheduled weekly conference calls to discuss the status of the firm's investigation. Chiron stated to FDA that the company had identified the cause of the contamination and that the contamination was confined to the identified vaccine lots. The company indicated to FDA that it believed the cause of contamination in these lots could be traced back to one of two contaminated bulk lots used to formulate these final lots. Nonetheless, FDA concurred with the need for Chiron to thoroughly retest all final lots, complete a thorough investigation of the manufacturing process and provide a complete investigation report to FDA. While the investigation was ongoing, Chiron informed FDA that results of the retesting were negative and that the company would submit its final investigative report to FDA during the week of October 4-8.

In late September, Chiron advised that it would substantially meet its plans to supply influenza vaccine to the U.S. On September 28, Chiron's CEO affirmed this in testimony to the Senate Special Committee on Aging when he stated: "As of September 27th, it remains Chiron's expectation that between 46 million and 48 million Fluvirin doses will be delivered to the U.S. market beginning in early October as compared to the 50 million doses projected in July."

MHRA'S OCTOBER 5, 2004 ANNOUNCEMENT

On the morning of October 5, 2004, MHRA announced a three-month suspension of Chiron's license to manufacture influenza vaccine. FDA had no prior knowledge of the MHRA's intention to suspend the firm's U.K. license. MHRA's Chief Executive, Professor Kent Woods, indicated that MHRA did not have the legal authority to notify FDA about the suspension announced on October 5 until after MHRA instituted its administrative action. Dr. Woods has also stated that, "Contrary to some reported statements, MHRA, as the responsible regulatory authority in the United Kingdom, made the decision to suspend Chiron's license after an internal meeting on October 4 and first informed the company and the FDA of this decision on October 5. At the same time, we informed other drug regulatory authorities via an intergovernmental rapid information alert."

Upon learning of the MHRA's suspension on October 5, 2004, FDA communicated with both Chiron and the MHRA. While Chiron indicated to FDA that it believed it had satisfactorily addressed MHRA's inspectional findings and provided to FDA a copy of those findings and the company's response, MHRA expressed serious concerns about Chiron's vaccine stocks and the company's ability to assure the safety of the vaccine.

FDA OFFICIALS DISPATCHED TO THE U.K.

FDA dispatched a senior team of scientists, led by Dr. Jesse Goodman, the Director of FDA's CBER, to the U.K. on Wednesday, October 6, 2004, to gain further understanding of the MHRA's action. The team met with the MHRA on October 7, and met with Chiron on October 8.

FDA inspected Chiron's Liverpool manufacturing facility from October 10 through October—15, to evaluate the company's efforts to test for and assess the bacterial contamination detected in nine of the one hundred final vial lots of its influenza vaccine. FDA also evaluated Chiron's determination that the risk of bacterial contamination was confined to specific lots.

On October 15, 2004, upon completion of its inspection, FDA determined that it could not adequately assure that Chiron's vaccine met our safety standards. On October 15, we also provided Chiron with our inspectional observations (Form FDA 483) from our inspection and met with the company to discuss its compliance issues. FDA will continue to work with Chiron and the U.K. government to ensure that the company corrects the deficiencies in the Liverpool plant so that it can eventually resume production of a safe and effective influenza vaccine. In the wake of the October 2004 inspection, FDA will work closely with MHRA and Chiron to assess any proposed corrective measures that the company submits in response to the October inspection and the company's findings of contamination in final lots. FDA will analyze Chiron's responses for their thoroughness, accuracy, and their adequacy. Ultimately, however, the agency's final determination regarding the effectiveness of Chiron's corrective measures will be based on a comprehensive inspection that we anticipate will occur once the company has notified the agency in February or March 2005 of the proposed corrective measure.

FDA'S RESPONSE TO THE FLU VACCINE SHORTAGE

Assuring the safety and effectiveness of vaccines is central to FDA's mission. Our goal is to assist the health care community as they work to provide protection to more Americans against the flu. To assist in these efforts, both Aventis Pasteur and MedImmune have indicated to FDA that they will provide additional doses of influenza vaccine. As a result, we have increased the available supply of licensed flu vaccine for the U.S. population to 61 million doses for this flu season, Aventis Pasteur will produce a total of 58 million doses of Fluzone and MedImmune has scaled up production to produce a total of 3 million doses of FluMist. FluMist is recommended for healthy individuals 5 to 49 years of age, and therefore, provides an option for those who would not receive vaccine under CDC's priority guidelines as well as for certain categories within the CDC guidelines.

In addition to supplies of vaccine approved for use in the U.S., we have also identified about five million doses of influenza vaccine from foreign manufacturers that could potentially be available under investigational new drug applications (INDs). We have sent FDA inspectors to the manufacturing facilities of GlaxoSmithKline (GSK) in Germany and ID Biomedical in Canada to evaluate their manufacturing processes. These efforts could result in as much as 4 million doses from GSK and up to 1 million doses from ID Biomedical. Finally, in an effort to expand further the supply of vaccine to those with the greatest need, Secretary Thompson recently announced that military personnel will maximize the use of FluMist and Defense agencies will allow HHS to purchase 200,000 doses of injectable vaccine for which they had originally contracted so that we can make it available to the high-risk population in the U.S.

We have also been contacting manufacturers worldwide in an effort to identify increased supplies of antiviral medications. Antiviral medications are drugs that are approved to reduce symptoms and in some cases prevent onset of influenza if taken early after exposure has occurred. These drugs will help protect and treat for Americans during this flu season, and we are making progress in this area as well. There are enough antiviral medicines to treat influenza in 40 million Americans, if necessary.

To address the complications of those who experience the flu, Merck & Company plans to triple its production of pneumococcal polysaccharide vaccine from 6 million to between 17 and 18 million doses. Pneumococcal pneumonia is one of the most important and common serious complications of influenza, and the availability of this expanded supply during the current flu season will allow public health officials to lessen the possibility of this complication.

PREPARATIONS FOR NEXT YEAR

Aventis Pasteur believes they have the capability of producing the same or more doses of influenza vaccine for the 2005-06 flu season. In addition, MedImmune has indicated that it has the capability to produce 10 million doses of FluMist for the 2005-06 flu season and as much as 40 million doses by 2007.

We will continue to work with Chiron Corporation, in close collaboration with the UK regulatory authorities, to help Chiron address, as quickly as possible, the manufacturing problems they experienced during this year's production process. To this end, we have reached agreements with Chiron that allows for full sharing of information between the FDA and the MHRA as the company works to resolve the problems in Liverpool. In addition, FDA has also been encouraging foreign licensed manufacturers to apply for U.S. licensure, and is providing clear pathways to efficiently reach this goal.

LOOKING TO THE FUTURE

Immediately upon coming to HHS, Secretary Thompson under the leadership of President Bush began transforming the flu marketplace by investing in new technologies, securing more vaccines and medicines, and preparing stronger response plans. The largest investments ever made by the federal government in protecting against the flu have been made under President Bush's leadership.

In keeping with these unprecedented investments, we must move science forward to help create more efficient ways to produce flu vaccine so we have greater flexibility to deal with shortages or unexpected problems. In each of the past two budgets, the Department has requested $100 million to shift vaccine development to new cell-culture technologies, as well as to provide for year-round availability of eggs for egg-based vaccine. We received $50 million in the FY04 budget for this activity and urge Congress to fully fund the $100 million request in FY05 budget.

To help manufacturers overcome challenges such as the vaccine development problems Chiron is experiencing, FDA has been investing its energy and resources in important initiatives such as the Current Good Manufacturing Practices for the 21st Century (known as the cGMP initiative).

Under the cGMP initiative, FDA is working with industry to encourage the use of advanced technologies as well as quality systems and risk-based approaches that build quality into the manufacturing process. FDA is also using the same quality systems and risk-based approaches to modernize our manufacturing regulatory responsibilities. For example, we are providing advanced training for manufacturing investigators. This has led to greater inspection consistency and the ability to more readily identify manufacturing deficiencies. The cGMP initiative is also promoting better communication between manufacturers and the agency, which will enable manufacturers to anticipate and overcome production problems before they occur. Among the lessons we have learned from this year's events at Chiron is the need to enhance our international regulatory collaboration and harmonization efforts.

In the past year, we completed information sharing agreements with the European Medicines Agency, Health Canada, and SwissMedic, and most recently MHRA, to help assure that legal barriers do not inhibit critical communication between these agencies and FDA. FDA is undertaking an inventory of foreign manufacturing of U.S.-licensed products, such as flu vaccine, that are critical to public health, and will put into place information sharing agreements with other national regulatory authorities as needed. In addition, we recognize that public health needs and resources are increasingly global in nature and, in the hope that vaccines can be licensed in multiple regions of the world, FDA has been encouraging more internationally harmonized product development.

Recent events have highlighted how imperative it is that we support the U.S. and global vaccine manufacturing infrastructures and invest in more efficient, reliable and modern methods for producing influenza vaccine. With adequate supply and inoculation, influenza is manageable and we will be more likely to successfully face the challenge of future pandemics.

Once again, thank you for the opportunity to come here today and testify on this very important issue.

I would be happy to respond to any questions that members of the Committee may have for me.

Mr. BILIRAKIS [presiding]. Thank you very much.

Dr. Fauci, please proceed.

STATEMENT OF ANTHONY S. FAUCI, DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH

Mr. FAUCI. Thank you for giving me the opportunity to speak with you for a few minutes on the NIH research component of the departmental effort to address the many challenges that we face each year with flu and even in the eventuality of a possible pandemic flu, which is a serious issue we need to be looking at in the future, and I will address that in some of my comments.

Let me talk a little bit about the research. The research endeavor at the NIH is founded fundamentally on basic research with the thought of developing countermeasures against influenza, including diagnostics, therapeutics and vaccines. By basic research, we mean determining the mechanisms of how the virus causes disease, how it changes, how it genetically assumes the capability of jumping species, as well as the properties that allow it to spread from person to person. In addition, we do a bit of surveillance in determining the relationship between animal viruses and human viruses, and ultimately take all of this and put it in the mix of how we are going to develop the vaccines that are the subject of this particular hearing.

If you look at the resources that have been allocated to this endeavor, as you can see clearly from this poster, the amount of re-

sources that have gone into influenza over the past few years under the leadership of Secretary Thompson has been tripled from 2001 to 2005, from $20 million to over $65 million, as shown here.

With regard to the precise nature of the research, there are several things that have been done to facilitate the vaccine enterprise and to partner with industry to provide the scientific base for the kinds of things that they will need to do to continue to meet challenges. One of these in particular is the issue of reverse genetics. You may have heard of that. Let me explain what that is.

Reverse genetics creates a degree of consistency and predictability in how you isolate the initial virus that will go into your vaccine. Under most circumstances, we take a virus that we have worked with for many years, shown here on the right. That virus grows very well in egg-based cultures.

The virus that we want to have in our vaccine, let's take, for example, H5N1 that we are working with with pandemic flu, we don't know its capability of growing, so what we generally do is we grow them together with the thought that they will just spontaneously combine to give the properties of the virus that we want the vaccine for, but the growth properties of the others. This is a chance event.

With reverse genetics, you deliberately take the relevant genes from each of those viruses and insert them together to create a hybrid virus that will actually be the virus that will be the seed virus that will grow well in cultures. So with regard to what we can do in the future, this gives a consistency in our ability to isolate the virus and then go on and put it in the vaccine hopper.

We have heard a bit about egg-based cultures. These are tried and true and have served us well. But they have little surge capacity and there is a risk in them, as we have seen what happened with the contamination in the Chiron plant.

The two major endeavors that the NIH and our colleagues are doing to replace or get alternatives for the egg-based culture is what we call cell-based culture. This has the capability of being much more in your control and the ability to surge up if in the middle of the process you need more.

In addition, the powers of recombinant DNA technology to specifically make the antigens in question, all of these will push the vaccine field forward. In addition, we need therapy, something that isn't often discussed, but it is an important compliment to the armamentarium against influenza.

We have four drugs for treatment of influenza, three of which can also be used for prophylaxis or prevention. One of the NIH's goals is to keep the pipeline of these drugs robust, so that when we get to a situation where perhaps there may be the evolution of resistance to these drugs we will have alternatives to replace them.

Finally, how are we addressing the eventuality of a pandemic flu? Most of you, I am sure, are aware of the fact that we have a problem right now in Asia in that we have had several countries, particularly Thailand and Vietnam, in which there have been substantial chicken kills caused by avian influenza. More importantly, it has jumped species from the chicken to the human, and there have been 44 human cases and 32 deaths, a very high mortality rate. Fortunately, it has not acquired the capability of efficiently

spreading from person to person. There has been only one probable case of person-to-person transmission.

So the research enterprise has been working very aggressively to try and address this. What we have done so far is isolated the H5N1 virus by reverse genetics that I just explained to you a moment ago. We have developed pilot lots of vaccine that are in the process of being made right now and that anywhere from January up to March or April will ultimately go into clinical trials to determine both safety and what the proper dose is. In addition, we are continuing our screening for the development of new therapeutics.

So, in summary, the research approach to the comprehensive departmental approach toward influenza is a component that is essential to push the field forward so that we may be able to meet the challenges that we are facing right now and that we would inevitably face in the future, particularly with a pandemic flu.

Thank you, Mr. Chairman.

[The prepared statement of Anthony S. Fauci follows:]

PREPARED STATEMENT OF ANTHONY S. FAUCI, DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. Chairman and Members of the Committee, thank you for the opportunity to discuss with you today the role of the National Institutes of Health (NIH) in helping to ensure that the nation has a reliable supply of safe and effective influenza vaccines.

Because the influenza viruses in circulation change somewhat from season to season, the U.S. supply of influenza vaccine must be renewed each year—and often contains flu viruses that are different from those used the previous year. The current technology for vaccine manufacture requires that key decisions, such as which viruses will be included and the number of doses needed, be made many months before the arrival of the influenza season. The serious vaccine shortage that has occurred this year underscores the difficulties we face in annually renewing the influenza vaccine supply, and highlights the pressing need to move toward adoption of a variety of vaccine manufacturing techniques that include newer technologies that may decrease the risk involved in vaccine production as well as improve flexibility and the speed at which the vaccines can be made.

The National Institute of Allergy and Infectious Diseases (NIAID), a component of NIH, is the lead agency for the conduct of research on all infectious diseases, including influenza. In that capacity, NIAID provides the scientific input required to facilitate the development of both new influenza vaccine technologies and novel antiviral drugs against influenza viruses.

Under this administration we have made tremendous progress. Immediately upon coming to HHS, Secretary Thompson, under the leadership of President Bush, began investing in new technologies, securing more vaccines and medicines, and preparing stronger response plans. Total NIH funding for influenza research has grown more than three-fold in recent years, from $20.6 million in FY 2001 to a requested $65.9 million (320 percent) in the FY 2005 President's Budget. This is part of the largest investment ever made by the federal government in protecting against the flu.

NIAID INFLUENZA RESEARCH

NIAID pursues an ambitious basic and applied research agenda on influenza, including viral biology, pathogenesis, host immune responses, and epidemiology, which underpin our many programs that are aimed at developing new and improved influenza countermeasures such as vaccines, therapies and diagnostic tools. Because influenza vaccines are the primary public health tools available to limit the disease burden caused by annual influenza epidemics, vaccine research has a very high priority. NIAID also supports several research activities specifically focused on identifying and countering any future influenza pandemic.

Basic Research

The development of new and effective influenza countermeasures rests on a foundation of basic research. Some basic research focuses on specific questions regarding the biology of the virus such as how it enters cells, replicates, mutates, evolves into

new strains and induces an immune response, while other projects can be more broadly applied. For example, under a recent NIAID initiative called the Influenza Genome Project, NIAID will collaborate with researchers around the world to obtain the complete genetic sequence of several thousand human and animal influenza viruses. The resulting library of influenza sequences, some of which may be derived from samples collected decades ago, should add greatly to our understanding of what makes one strain more lethal than another, what genetic determinants most affect immunogenicity, and how the virus evolves over time. All of this is precisely the kind of information that will significantly enhance our ability to create more effective countermeasures.

Vaccines

Because influenza is such a highly transmissible virus, vaccines are essential tools for the control of influenza epidemics. The current system for the production of U.S. licensed influenza vaccines uses fertilized chicken eggs to grow influenza vaccine strains that have been selected to match the viruses likely to circulate in the coming influenza season. The viral particles are purified from the eggs, inactivated, and processed for distribution.

Although the egg-based technology has served us reasonably well for more than 40 years, there are several limitations to the current system that include: (1) a lengthy manufacturing process; (2) the need to forecast and select the virus strains to be used in the vaccine at least six months in advance of the influenza season; and (3) the annual need for hundreds of millions of fertilized chicken eggs to manufacture the vaccine. The decisions about which viral strains to include in the vaccine may not always be correct, but the long lead time required to acquire eggs for vaccine production makes mid-course corrective action virtually impossible. Additional limitations include the fact that some people are allergic to eggs and therefore cannot receive the classic vaccine. In addition, some influenza viruses do not grow well in chicken eggs and may in fact be virulent for the eggs, a circumstance that may result in delays bringing a vaccine to market and a possible decrease in the total number of doses available.

In each of the last two budgets, HHS has asked for $100 million to shift vaccine development from the cumbersome egg-based production to new cell-culture technologies, as well as to provide for year-round availability of eggs to provide for a secure supply and surge capacity. These new technologies will help produce flu vaccine more efficiently and provide more adaptability to unexpected problems or losses in production.

NIAID supports several research projects and other initiatives intended to foster the development of new influenza vaccines and manufacturing methods that are simpler, more reliable, yield more broadly cross-protective products, and provide more protection than those currently in use. For example, a technique developed by NIAID-supported scientists called reverse genetics allows scientists to manipulate the genomes of influenza viruses and to transfer genes between viral strains. The technique allows the rapid generation of seed viruses for vaccine candidates that exactly match the anticipated epidemic strain. By removing or modifying certain virulence genes, reverse genetics also can be used to convert highly pathogenic influenza viruses into vaccine candidates that are safer for vaccine manufacturers to handle.

To encourage participation by the pharmaceutical industry, NIAID supports Challenge Grants to fund the development of new influenza vaccine technologies. One approach under active development is the use of cell cultures to grow vaccine strains, rather than eggs. Another approach is to genetically engineer baculovirus, an insect virus not related to influenza, to express a gene that encodes an influenza coat protein such as hemagglutinin or neuraminidase. The engineered baculovirus is then grown in insect cell cultures, and the influenza protein that the virus produces is purified for use as a "recombinant subunit" influenza vaccine. A recent NIAID-supported Phase II clinical trial of a vaccine produced by Protein Sciences Corporation using this strategy showed that it is well tolerated and immunogenic; the company is conducting further clinical evaluation of this product. Other new pathways for producing influenza vaccines include DNA-based approaches and the development of broadly protective vaccines based on influenza virus proteins that are shared by multiple strains.

NIAID has been very successful in the past with ground-breaking vaccine research, including scientific advances that led to the development of hepatitis B, *Haemophilus influenzae b,* pneumococcal pneumonia, acellular pertussis, and live-attenuated intranasal influenza vaccines. I am confident that the approaches that we are currently pursuing with influenza will lead to a next-generation vaccine that improves upon the current egg-based technology.

In addition to developing influenza vaccine candidates, NIAID has developed an extensive capacity for clinically evaluating these products. For example, NIAID's Vaccine and Treatment Evaluation Units (VTEUs) comprise a network of university research hospitals across the United States that conduct clinical trials to test candidate vaccines for infectious diseases. These units can be accessed by both academic and industrial vaccine developers to evaluate the safety, immunogenicity, and ultimately, the efficacy of candidate vaccines.

Therapeutics

Antiviral medications are an important counterpart to vaccines, both to treat infection after it occurs and to prevent illness after exposure; four drugs are currently available for the treatment of influenza, three of which are also licensed for prevention. NIAID actively supports identification of new anti-influenza drugs through the screening of new drug candidates in both cell culture and in animals. In the past year, seven promising candidates have been identified. Efforts to design drugs that precisely target viral proteins and inhibit their functions also are under way. In addition, NIAID is developing novel broad-spectrum therapeutics against many influenza virus strains; some of these target viral entry into human cells, while others specifically attack and degrade the viral genome.

PANDEMIC INFLUENZA

Although the impact of influenza on morbidity and mortality in a normal epidemic year is substantial, much more serious influenza pandemics also can occur. As influenza viruses spread, they continuously evolve and accumulate small changes in their outer coat proteins, a process called "antigenic drift." This occurrence allows the virus to at least partially escape the human immune responses primed by vaccination or exposure to earlier versions of circulating influenza viruses. Influenza viruses can also jump species directly from certain animals such as chickens to human as well as swap genes with influenza viruses that infect birds, chickens, pigs, or other animals; the latter process is referred to as "reassortment." When such reassortment events occur, the result is the replacement of one or more of the outer coat proteins of the human virus with that of the animal virus, or an "antigenic shift." If the virus that has jumped species or the new reassorted virus evolves to be efficiently transmitted between people, a deadly influenza pandemic can result. As the population acquires immunity to the new strain over the next several years, the pandemic strain fades into the routine background of circulating viruses.

Three influenza pandemics occurred in the 20th century, in 1918, 1957, and 1968. The pandemic that occurred in 1918-1919 was the most severe, killing 20-40 million people worldwide, including more than half a million individuals in the United States. The pandemics that began in 1957 and 1968 killed approximately 2 million and 700,000 people worldwide, respectively.

One of the first internal committees Secretary Thompson created when he came to HHS was on pandemic flu. And last August, the Secretary unveiled the Department's draft Pandemic Influenza Response and Preparedness Plan. This plan outlines a coordinated national strategy to prepare for and respond to an influenza pandemic.

NIAID conducts research to understand the viral biology and epidemiology that underpinned past pandemics, and funds an extensive surveillance network in Asia to detect the emergence of influenza viruses with pandemic potential. In addition, the draft U.S. Pandemic Influenza Preparedness and Response Plan describes specific roles for NIAID should a pandemic occur. Foremost among these is to help develop and produce an effective vaccine as rapidly as possible. Specifically, NIAID will help to characterize the newly emerging influenza strain, isolate candidate vaccine seed viruses, develop investigational batches of candidate vaccines, and produce and distribute research reagents for use by vaccine researchers in academic and pharmaceutical industry laboratories. NIAID will also work with industry to produce and clinically test pandemic influenza vaccines at different doses and in different populations in our vaccine clinical trials sites, and will coordinate closely with CDC, FDA, and WHO to provide a safe and effective vaccine to the public as quickly as possible.

In recent years, several avian influenza virus strains that can infect humans have emerged. In 1999 and 2003, an H9N2 influenza strain caused illness in three people in Hong Kong. The H5N1 "bird flu" virus, first detected in humans in 1997, infected at least 44 people and killed 32 in 2004, and has spread widely among wild and domestic birds. There has been at least one documented case of human to human spread of an H5N1 virus. NIAID already has taken several steps to develop vaccines against both of these potential pandemic strains. To address the H9N2 threat, NIAID contracted with Chiron Corporation to produce investigational batches of an

inactivated vaccine, which will be evaluated clinically by NIAID early next year. For H5N1, Aventis-Pasteur, Inc. and Chiron are both producing investigational lots of inactivated H5N1 vaccine preparations; additionally, DHHS has contracted with Aventis to produce up to 2 million doses to be stockpiled for emergency use, if needed, to vaccinate health workers, researchers, and, if indicated, the public in affected areas. Development and evaluation of a combination antiviral regimen against these potential pandemic influenza strains are also now under way.

CONCLUSION

Given the disruption of the influenza vaccine supply that we experienced this year, and the inherent difficulties associated with the current manufacturing technology, it is clear that we must move toward next-generation influenza vaccines with all deliberate speed. NIAID's role in influenza vaccine development is to carry out the research upon which these new vaccines will be based, and to forge productive partnerships with private sector pharmaceutical and biotechnology companies to speed development and clinical evaluation of promising candidates.

In closing, Mr. Chairman, I would like to take a moment to remember John R. La Montagne, Ph.D., deputy director of NIAID, who died suddenly on November 2 while traveling to a meeting of the World Health Organization in Mexico City. Throughout his almost 30-year career at NIH, John's leadership and commitment to improving global health, particularly in the arena of influenza vaccine research, were remarkable. His generosity, wit, even-handedness and kindness made him a friend to all who knew him. Personally, he was a dear friend and one of the finest people I have ever known. He will be sorely missed.

I would be pleased to answer any questions you may have.

Mr. BILIRAKIS. Thank you.

Dr. Gerberding.

STATEMENT OF JULIE L. GERBERDING, DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION

Ms. Gerberding. Thank you. I do appreciate the privilege of being able to speak before the committee and subcommittees today. This is a very important issue for us at CDC, and we do have a vision of what we would like to end up with, and that is a modern influenza vaccine that is safe, affordable, effective and accessible and ideally one that was produced domestically from a reliable manufacturing process that would avoid the kinds of problems that we have experienced this year.

It is going to take some time and dollars to modernize that vaccine system, and it is going to take an improvement of the business climate for the manufacturers so that they have a stable market and a fair price and their liability issues are addressed. But it is also going to take a public that understands the need for a vaccine and a stable demand for that vaccine so that we can have a marketplace that doesn't have the vagaries that the current one does.

In the past several weeks, we have been working hard to get the doses of vaccine that we do have to the people who need it the most, and I want to really acknowledge and appreciate some health protection heroes in this regard.

First of all, we at CDC were also sad to see people standing in line to receive their vaccine. That was a heart-wrenching image, and we appreciate those who have been patient and persistent in trying to get their vaccine across all of your districts this year.

We also recognize and honor those who stepped aside to allow those who needed the vaccine to get it. We also are impressed with the incredible public health heroes at the local and State level, including the health official from Michigan who will be on the panel later this morning, who have absolutely risen to the occasion in a

way that I have never seen our public health system do before. This is truly the brightest star. So we are very grateful for the spirit of cooperation and altruism that has characterized this particular response.

At CDC, we are working in our Emergency Operations Center; I am mentioning this to illustrate that the investments that the administration and Congress have made in preparedness for a variety of emerging health threats are serving us well during influenza. We have several hundred people who are involved in a whole range of operational capabilities, but their bottom line is, right now, focused on helping to allocate the vaccine that we have in the fairest and most equitable way that we can.

We have for the first time ever developed a stockpile of vaccine and antiviral drugs. For the first time ever we have invested $50 million at HHS in developing year-round egg supply, and we hope to receive a $100 million investment for that and some other vaccine modernization efforts this year. And all together, CDC has benefited from a twentyfold increase in the investment in influenza preparedness over the last 4 years. So we have made a lot of progress, but as you can see from the situation we are in, we have a long way to go.

On the next graphic I have summarized where we are right now. At the current time, flu activity in the United States is not widespread. There are many States that still do not have flu activity. However, on the next graphic I am making a very important point, which is that flu is completely unpredictable. It is very early in the season right now. Most commonly flu peaks in February, so we are certainly not out of the woods. We don't know what severity the season will bring. We don't know what strain will ultimately predominate. We don't know yet when, where, and for whom flu will hit the hardest. So we still have a lot of work to do before we can rest.

On the next graphic I have also highlighted what is an extremely important principle. Yes, vaccine is the most important and the most effective way to prevent flu, but there are other things that we can do, and we are emphasizing all of these through our communication channels, in particular the common-sense respiratory hygiene and hand hygiene issues, but also staying home when people have flulike illness and not sending kids to school is actually very, very important. This sort of voluntary isolation really does help prevent the spread of flu in communities, and we want to emphasize that.

And I can't help but remind everyone that today is the Great American Smokeout Day, and while we don't usually associate tobacco with influenza, people who smoke tobacco are at risk for the complications of influenza, and now more than ever there is a strong reason to look at the opportunities for smoking cessation. So I just had to deliver that message as the CDC Director today.

Let me just mention very briefly some of the activities that are going on to assist our State and local health officials. Our goal is to have information about where flu is and what strain it is, where are the people who need vaccine, and where is the vaccine. So we have been using a number of traditional CDC methods to do this, including tracking the consequences of flu and using the laboratory

methodologies to know what strains are emerging in communities. On the next graphic I have listed a number of brand-new innovative strategies that we are using to track these issues this year, and for the first time ever we will have information at the county level in a very discrete way about people at risk, doses of vaccine delivered, and the specific information about flu.

We are taking advantage of a variety of things, but I want to point out just two very important ones. One is the vaccine tracking system which is a secure Web-based data base, which mwans that for the first time ever, State health officials have information about the specific details of where vaccine has been shipped in their jurisdictions, so they can use the latest information to make decisions about the on-going allocation process.

Since October, 13 million doses of vaccine were reallocated to high-priority people across our Nation with the full cooperation of Aventis, and over the last several weeks the remaining 12 million doses of vaccine have been apportioned to the States. State health officials are working in their jurisdictions to identify the gaps, the vaccine needs, and how they can do the very best job they can to get vaccine to the people who need it the most.

While we are very much focused on this flu season and the importance of protecting people's health this year, we have to recognize that there is an even more urgent imperative about solving the vaccine supply problem, and that is, of course, pandemic influenza. This next graphic is a picture of the last 100 years of influenza, demonstrating in the circles three very major global pandemics of flu, and on the far right-hand side the depiction of the emergence of these avian flu strains that Dr. Fauci mentioned. And the one, of course, that we are the most concerned about, the avian flu that exists in Asia right now. We have never had so much influenza circulating in birds and their contacts on the face of the globe at one time; and so not only do we need to deal with regular seasonal flu, but we have to speed up our whole intervention process to be prepared for what looks like a very serious incubator for the emergence of a potential global pandemic.

So, again, thank you for allowing us to be here, and we really do look forward to working with the committees and with the administration in a proactive way to solve this problem. Thank you.

[The prepared statement of Julie L. Gerberding follows:]

PREPARED STATEMENT OF JULIE L. GERBERDING, DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. Chairman and members of the committee, I am pleased to be here today to discuss the Centers for Disease Control and Prevention's (CDC) efforts to address the current influenza vaccine shortage. Vaccination is the primary strategy for protecting individuals who are at greatest risk of serious complications and death from influenza. In the face of this season's influenza vaccine shortage, CDC, state and local public health practitioners, and vaccine manufacturers have worked tirelessly to protect our most vulnerable populations. I want to especially recognize the good faith, cooperation, and the significant contribution of Aventis Pasteur to ensure that the available supply of influenza vaccine goes to those people who truly need it most this season. And we must not forget the important service of immunization providers on the front lines in doctors' offices, health clinics, grocery stores, and pharmacies working to prioritize, deliver, and administer vaccine so that it reaches high-risk individuals.

I also want to thank the nation's health protection heroes, those people across the country who are stepping aside and not getting vaccinated so that those at high-

risk will be protected this influenza season. I particularly appreciate the cooperative and collaborative spirit of Americans who have pulled together to help us meet this challenge head on.

I would be remiss, however, if I failed to mention the tremendous progress we have made. In the last four years, the Department of Health and Human Services has begun investing in new technologies, securing more vaccines and medicines, and preparing stronger response plans. We have made significant investments in protecting against the flu, including increases for CDC influenza funding ($17.2 million to $41.6 million, 242%) and creation of Strategic Reserves/Stockpiles ($0 to $80 million). These investments are further detailed as follows:

- **New Technologies:** In each of the last two budgets, HHS has asked for $100 million to shift vaccine development from the cumbersome egg-based production to new cell-culture technologies, as well as to provide for year-round availability of eggs to provide for a secure supply and surge capacity. These new technologies will help produce flu vaccine more efficiently and provide more adaptability to unexpected problems or losses in production.
- **Creating the Nation's First Stockpiles of Medicines:** For the first time ever, we have created stockpiles of both influenza vaccine and antiviral medications. The Department invested $40 million in 2004, and is planning to invest another $40 million in 2005, to stockpile influenza vaccine through the Vaccines for Children Program. We invested $87.1 million to stockpile 2.3 million doses of Tamiflu; we invested $34 million on Rimantadine capsules to treat 4.25 million adults and on Rimantadine syrup to treat 750,000 kids. These stockpiles give the government new ability to protect the most vulnerable, and respond effectively when there is a shortage of vaccine.
- **Pandemic Flu Plan:** In August, Secretary Thompson unveiled the department's draft Pandemic Influenza Response and Preparedness Plan. This plan outlines a coordinated national strategy to prepare for and respond to a flu pandemic. One of the first internal committees the Secretary created when he came to HHS was on the pandemic flu.
- **Improving Access by Covering Costs:** The Centers for Medicare & Medicaid Services (CMS) has more than doubled the payment rates for the vaccine and its administration since 2000. In 2004, CMS is paying $18.30 for the vaccine and administration—up from $8.92 in 2000. This is helping to ensure the vaccine is affordable for patients to get and cost-effective for providers to administer.

PREPARATIONS FOR THE 2004-05 INFLUENZA SEASON

Currently, three vaccine manufacturers are licensed to produce influenza vaccine for use in the United States; two produce inactivated vaccine delivered by intramuscular injection and one makes a live vaccine delivered by nasal spray. The inactivated vaccine, commonly referred to as the "flu shot," represents the majority of influenza vaccine available in the United States and is licensed for use in all individuals 6 months of age and older. The nasal spray vaccine is a new vaccine, introduced to the U.S. market for the 2003-04 influenza season, and is licensed for use in healthy persons between 5 to 49 years of age. All influenza vaccine is produced, and the vast majority is distributed and administered, by the private sector. Because of the time required to obtain adequate supplies of eggs in which influenza virus is grown, manufacturers must predict demand and decide how much of the vaccine to produce six to nine months before the influenza season begins. Because influenza vaccine production is a complicated process involving several steps over a long period of time, it was not possible to begin new production of influenza vaccine after the shortage was announced.

CDC and the Department of Health and Human Services (DHHS) took several steps to prepare for the 2004-05 influenza season, including specific action to prevent a late-season surge in vaccine demand such as the one experienced last year in which the demand for influenza vaccine in the United States exceeded what had been experienced in previous influenza seasons. In preparation for the 2004-05 influenza season:

- Vaccine manufacturers licensed to produce influenza vaccine for the U.S. market anticipated producing a supply of approximately 100 million doses of inactivated influenza vaccine for this year, significantly more doses than have ever been produced for the United States.
- CDC planned to establish a stockpile of 4.5 million doses of influenza vaccine for the nation's children. The primary purpose of the stockpile was to meet late-season, unmet pediatric demand as we are currently experiencing this year.

- CDC augmented domestic influenza surveillance this season with surveillance for pediatric hospitalizations and pediatric mortality reporting. In addition, CDC is expanding its capacity for rapid detection of new strains of influenza viruses and has funded a study to prospectively evaluate vaccine effectiveness during this winter's influenza season.

As noted previously, DHHS is supporting activities designed to ensure year round influenza vaccine capacity and to incentivize the accelerated development, licensing and domestic production of cell-culture influenza vaccines. The President's FY 2004 and FY 2005 budgets each proposed $100 million for these efforts. A contract for egg surge capacity worth about $10 million has already been awarded. Negotiations are currently underway for tissue culture vaccine research and development contracts.

In addition, DHHS has expanded biosurveillance activities so that scientists can more rapidly detect changes in circulating influenza viruses and determine potential strains for vaccines. DHHS is collaborating with the Department of Agriculture and the Department of State to further enhance surveillance efforts in Asia, in both human and animal populations

CDC RESPONSE TO THE 2004-05 INFLUENZA VACCINE SHORTAGE

On October 5, 2004, Chiron Corporation notified DHHS that none of its influenza vaccine (Fluvirin®) would be available for distribution in the United States for the 2004-05 influenza season. The company indicated that the Medicines and Healthcare Products Regulatory Agency (MHRA) in the United Kingdom, where Chiron's Fluvirin vaccine is produced, suspended the company's license to manufacture Fluvirin vaccine in its Liverpool facility for three months. This action prevented the release of its vaccine for this influenza season. This action reduced by approximately 46 to 48 million doses, or almost one-half, the expected supply of inactivated influenza vaccine available in the United States for the 2004-05 influenza season.

Following the Chiron announcement, DHHS and its agencies, including CDC, took immediate action in response to the loss of this vaccine supply. CDC responded quickly and effectively to the influenza vaccine shortage by activating the Director's Emergency Operations Center (DEOC) Influenza Task Force to coordinate the overall CDC response. CDC's immunization, infectious disease, and other experts are working collaboratively across the agency to address areas such as clinician policy and guidelines, vaccine supply and distribution, healthcare impact, logistics, influenza assessment and surveillance, informatics, and communications. These dedicated public health professionals have worked tirelessly to protect the nation's health during this influenza vaccine shortage.

CDC is working hard to target the distribution of the remaining inactivated vaccine towards the most vulnerable populations; identify available vaccine from other countries that might be used this season; reinforce the agency's supply of antiviral medications in the Strategic National Stockpile and provide recommendations for their use during this influenza season; develop strategic communication messages to facilitate the public health response to the shortage; enhance surveillance for influenza disease and outbreaks so that early, effective responses can be delivered; and implement a comprehensive monitoring and evaluation system to assess the effectiveness of the strategies to target vaccine to high-risk groups and the response to influenza outbreaks.

Interim Influenza Vaccination Recommendations for the 2004-05 Season

On October 5, in coordination with the Advisory Committee on Immunization Practices (ACIP), CDC issued interim recommendations for influenza vaccination during the 2004-05 season. The interim recommendations identify the priority groups of people that should receive the limited supply. These include people who are most vulnerable to develop serious complications and even death from influenza: adults 65 years of age and older, children 6 to 23 months of age, individuals with certain chronic underlying medical conditions, pregnant women, residents of nursing homes and long-term care facilities, and children on chronic aspirin therapy. In addition, the ACIP recommended vaccination for individuals who might otherwise spread influenza to high-risk individuals, including household contacts of infants under 6 months of age and healthcare workers providing direct, hands-on patient care. These interim recommendations take precedence over earlier recommendations.

Influenza Vaccine Supply and Allocation Plan

Following the Chiron withdrawal, Aventis Pasteur announced that it would work with CDC to develop a plan to target the remaining available influenza vaccine toward providers serving the populations at greatest risk for serous complications

from influenza. I commend Aventis Pasteur for its leadership and willingness to join us in addressing this public health concern. In addition, state and local health officials have worked together with the CDC and Aventis Pasteur to assure the most equitable and efficient means of distribution of the remaining, limited supply of vaccine across the Nation. The significant contributions and leadership of these public health professionals has enabled our nation to respond effectively to this public health challenge.

As of October 5, Aventis Pasteur had planned to produce over 50 million doses of inactivated influenza vaccine for the 2004-05 influenza season. At that time, approximately 33 million doses had already been shipped to pediatricians, primary care and other office-based physicians, public health providers, and other community-based vaccine providers. Approximately 14.2 million of the remaining 22.4 million doses of unshipped vaccine were allocated for redistribution through Aventis Pasteur contracts with providers serving the high-priority populations. On October 19, 2004, Aventis Pasteur announced that it would produce an additional 2.6 million doses of vaccine that would be available in January 2005. With these additional doses, their total of inactivated influenza vaccine for this season is expected to exceed 58 million doses, of which 10.3 million are still to be produced and distributed in the coming weeks, as of November 9, 2004.

CDC and Aventis worked to identify a number of orders placed with Aventis Pasteur and the seven distributors through which Chiron vaccine is shipped, that were intended for providers known to serve substantial numbers of high-risk patients. These included doses ordered by:

- State and local health departments;
- The Vaccines for Children Program;
- Children's providers;
- Healthcare providers for Aventis Pasteur's preservative-free influenza vaccine (licensed for use with children 6-35 months of age);
- The Department of Veterans Affairs and the Indian Health Service;
- Long-term care facilities and acute care hospitals;
- The Visiting Nurses Association of American (VNAA); and
- The Department of Defense.

Every effort has been made to provide vaccine to as many providers serving high-risk populations as possible in a timely fashion.

CDC, state and local health officials, Aventis Pasteur, and Chiron vaccine distributors worked together to canvass the orders placed with the seven Chiron distributors, with an emphasis on orders placed by providers likely to be serving a high number of priority patients; and surveyed long-term care facilities to identify those facilities that ordered Chiron vaccine, either directly or via a sub-distributor or intermediaries such as pharmacies.

The CDC implemented a secure web-based application, the Flu Vaccine Finder that is available to state health officials to identify all doses of inactivated influenza vaccine shipped to their state during the 2004-05 season. State health officials and CDC have worked together, in consultation with local health departments, to develop a formula for the equitable distribution of the remaining influenza vaccine to be shipped. This formula took into account the population of high-risk individuals in each state and the number of influenza vaccine doses that have already been shipped to each state.

Of the limited number of licensed doses of vaccine that remains to be shipped, there is agreement that all public sector orders that were submitted on federal, state, and multistate contracts will be filled. CDC estimates this to be approximately 11.9 million doses total, with 3.4 million of those doses to complete the public sector orders that were submitted on federal, state and multistate contracts. CDC has asked state health officials to work collaboratively with local health departments and private immunization providers to guide the final allocation of the remaining approximately 7.2 million adult doses. State and local health officials are best suited to develop and implement this second phase of the vaccine allocation plan. Another 1.2 million doses of pediatric vaccine will be allocated to states using the same approach. State and local health officials have the most accurate and comprehensive understanding of the needs within their jurisdictions, the necessary relationships with public and private health care providers to target vaccine to reach the most vulnerable populations in their states, and the authority to ration in times of shortage.

Price Gouging

Finally, there is the issue of alleged price gouging. CDC is very concerned to learn of reported incidences of price gouging during this particularly challenging time. In response to the reports of alleged price gouging, the Secretary sent a letter on Octo-

ber 14, 2004, to each state urging them to thoroughly investigate reports of price gouging involving influenza vaccine and to prosecute to the full extent of the law those found to be involved. CDC is also collecting reports on price gouging and sharing them with the National Association of Attorneys General and state prosecutors.

Additional Sources of Influenza Vaccine

Approximately 3 million doses of the intranasally administered, live, attenuated influenza vaccine, FluMist, are being produced for the 2004-05 season. This vaccine is encouraged for use among healthy persons ages 5-49 years who are not pregnant. This includes healthcare workers (except those who work with severely immunocompromised patients in special care units) and household contacts of infants less than 6 months of age. CDC is making people aware of this alternative to inactivated influenza vaccine.

Several manufacturers of influenza vaccines licensed for use in Europe and Canada have vaccine, which is under review for use in the United States as Investigational New Drugs (IND). Because these vaccines are not currently licensed in this country, they will have to be administered under special protocols with written consent. CDC is studying the feasibility of use of IND vaccine as it is developing protocols for vaccine use and the U.S. Food and Drug Administration (FDA) is inspecting the manufacturing plants. As many as 5 to 6 million doses of vaccine may be available from these manufacturers, although even if approved for an IND, we would not expect delivery of most of this vaccine until December and January.

Antiviral Medications and Pneumococcal Vaccine

Influenza antiviral medications are an important adjunct to influenza vaccine in the prevention and treatment of influenza. CDC has developed interim recommendations on the use of antiviral medications for the 2004-05 influenza season. The interim recommendations were developed to reduce the impact of influenza on persons at high risk for developing severe complications secondary to infection. The recommendations are not intended to guide the use of these medications in other situations, such as outbreaks of avian influenza.

Influenza antiviral medications have long been used to limit the spread and impact of institutional influenza outbreaks. They are also used for treatment and chemoprophylaxis (prevention) of influenza in other settings. In the United States, four antiviral medications—amantadine, rimantadine, oseltamivir, and zanamivir—are approved for treatment of influenza. When used for treatment within the first two days of illness, all four medications are similarly effective in reducing the duration of illness caused by Strain A influenzas by one or two days. Only three antiviral medications (amantadine, rimantadine, and oseltamivir) are approved for prevention of influenza.

CDC encourages the use of amantadine or rimantadine for prevention and use of oseltamivir or zanamivir for treatment of those who are ill from influenza, as supplies allow. People who are at high risk of serious complications from influenza may benefit most from antiviral medications.

The United States has a supply of influenza antiviral medications for both adults and children stored in the Strategic National Stockpile for emergency situations. There are 1,336,380 regimens of rimantadine tablets, 60,000 regimens of rimantadine syrup, 859,993 regimens of oseltamavir capsules, and 110,336 regimens of oseltamavir suspension. DHHS has procured additional supplies of antiviral medications, and shipments are arriving weekly. By the end of December, the federal stockpile of antiviral drugs will include enough doses of rimantadine for 4.25 million adults and 750,000 children and enough oseltamivir for 2.3 million people. Rimantadine will be made available to states and territories for use in outbreak settings, as might occur in a hospital or long-term care facility, if commercially available supplies become depleted nationwide. Because oseltamavir is the only antiviral drug known to be effective against avian influenza, we will work to maintain the supply of oseltamavir in reserve to be used in the event of an influenza pandemic.

In addition, Merck & Co. is tripling its production of pneumococcal vaccine used to prevent pneumococcal disease, which is a common complication of influenza. Pneumovax is not a substitute for the influenza vaccine, but can help prevent influenza complications. Many people who fall into the priority groups for the influenza vaccine should also get the pneumonia vaccine.

Communicating the Public Health Response

Since the release of the interim influenza vaccination recommendations, CDC has used a variety of channels to communicate comprehensive information about the influenza season, the recommendations for priority groups for vaccination, the status of the vaccine supply, and alternative methods of reducing the transmission and severity of disease. Relevant and timely communications with the public, health care

professionals and policy makers is a critical component of the public health response to the current influenza season and the vaccine shortage.

CDC's influenza web portal (http://www.cdc.gov/flu) features updated information and materials for the public and clinicians. Materials are available in ten languages (in addition to English) as well as in low-literacy formats. As the public health response to the vaccine shortage has evolved, this website has become a vital resource receiving 300,000 visits per day at its peak, leveling off at over 150,000 visits per day over the past few weeks.

In addition to communications via the Internet, CDC established a new toll-free hotline number, 1-800-CDC INFO, to respond to public and clinician inquiries related to the influenza season and the vaccine shortage. This automated hotline includes selections in English and Spanish, and provides callers with timely and relevant information regarding the influenza season and the vaccine shortage. Since the announcement by Chiron on October 5, 2004, CDC has responded to several thousand inquiries from the public and clinicians through its hotlines.

In collaboration with the non-profit Ad Council, CDC recorded and distributed two audio public service announcements to over 9,000 AM and FM radio stations across the nation. In addition, two video public service announcements are being developed for distribution before Thanksgiving, and plans are underway to run print ads and articles in the nation's newspapers over the next several weeks.

CDC has also made specific efforts to reach business and educational institutions with critical information about the priority populations recommended for vaccination and alternative methods for preventing transmission of disease in the workplace and educational settings.

THE 2004-05 INFLUENZA SEASON

Influenza seasons are unpredictable. Although epidemics of influenza occur virtually all every year, the particular viruses and the beginning, peak, severity, and length of the epidemic can vary widely from year to year. Before a season begins, it is not possible to accurately predict what the season will look like. However, as of the week ending October 30, 2004, influenza activity in the United States has been low. Forty (0.8%) of 4,736 respiratory specimens tested by U.S. World Health Organization (WHO) and National Respiratory and Enteric Virus Surveillance System (NREVSS) collaborating laboratories were positive for influenza. The proportion of patient visits to sentinel providers for influenza-like illness (ILI) and the proportion of deaths attributed to pneumonia and influenza were below epidemic levels. One state has reported regional influenza activity, one has reported local activity, and 26 states and New York City have reported sporadic influenza activity. Twenty states and the District of Columbia have reported no influenza activity.

CDC has characterized three influenza viruses collected by U.S. laboratories since October 1, 2004. All were influenza A (H3N2) viruses and were characterized as A/Fujian/411/2002-like, which is an influenza component included in the 2004-05 influenza vaccine.

CONCLUSION

Thank you for bringing additional attention to this important public health issue. CDC is committed to protecting and promoting health for all Americans, preventing disease and disability through public health research and public outreach, and support of important interventions including vaccination. Recognizing the important role of vaccines in protecting the health of all Americans and in preparing for future threats, we will continue to work with our partners to manage the current influenza vaccine shortage and to address our nation's need for access to a safe, reliable supply of influenza vaccine in the future.

Thank you for your interest in this issue and your support of CDC's immunization programs. I will be happy to answer any questions.

Mr. BILIRAKIS. Thank you, Doctor.

And you have indicated, all of you, your willingness to work with the committee. The committee would invite your comments, your recommendations; basically, you know, what can Congress do in order to help out the situation and whatnot. So there will be specific questions in writing that will be furnished to you after we finish up.

Ms. GERBERDING. Thank you.

Mr. BILIRAKIS. But whether those questions go into what can we do further, please feel free to keep in mind that we can only help if we get input from you.

Dr. Fauci, first, you have chosen to mention Dr. La Montagne in your written statement, and so you obviously were very close to him. Our sympathies, sir, for your loss and the country's loss, health care's loss, of Dr. La Montagne.

I would ask you, sir, first of all, all of the vaccine that is out there now in use is egg-based; is it not?

Mr. FAUCI. Yes. The vaccine that we make now and have made in the past is made in eggs.

Mr. BILIRAKIS. Okay. When you talked about these alternatives, cell-based, et cetera, when might we anticipate? Is there a time line, an anticipated time line, when we might anticipate those being on line and ready to be used?

Mr. FAUCI. It is a gradual phase-in process, Mr. Chairman, that will be measured in years, probably anywhere from 3 to 5 years. There are some companies who are more aggressive in the sense of already transferring most of what they are doing vis-a-vis their production into cell-culture based in a semiexperimental way. We are funding and others are funding—both independently at the company level, as well as through the NIH—ways of looking at the real questions that arise. Is the cell culture adequate to grow the virus? Does the virus change when it grows in that cell? What are the safety issues?

All of these things need to be done before you can with confidence essentially turn over your process to cell culture. So I think it is important to make clear that although we have great hopes for it, it is not going to be something that next year or the year after is going to replace eggs. It is going to be a gradual over several years.

Mr. BILIRAKIS. Okay. And you have indicated in your charts that there have been great increases in funding provided for research in this regard. And so it is not a lack of resources, then, in terms of trying to speed up the process?

Mr. FAUCI. Well, it is a scientific issue at first. But also, we have asked the Department for $100 million in the previous year, and we hope that we will get that this year for not only increasing the egg surge capacity, which we do still need, but also making the transition to cell-based culture. So there is a two-pronged way of addressing the problems that the committee members mentioned in several of their opening statements. Not only do we need to phase into a cell-based culture, but we also need to provide a greater surge capacity for the egg-based culture. And, in fact, there has been investment just this year of $10 million to do that; in other words, to have eggs year round so that if we have an emergency where we need to surge up, we will not be in a position where the eggs are already gone because that phase of the process has already been passed.

Mr. BILIRAKIS. Thank you.

Dr. Crawford, would the FDA have stopped use of the drug, the vaccine, if the United Kingdom hadn't taken action?

Mr. CRAWFORD. Yes, we would have.

Mr. BILIRAKIS. You would have definitely?

Mr. CRAWFORD. Yes. With our lot release program, we would not have allowed it into circulation or to be marketed.

Mr. BILIRAKIS. You were aware that the U.K. Was going to pull their manufacturing?

Mr. CRAWFORD. We were not aware. They—in a statement released by the British Government, they said because of vagaries in their law related to confidential commercial information, they could not inform the United States or several other countries that were not going to get flu vaccine because of that particular problem. We had been made aware of a potential problem on August 25, and at that point we asked the company to quarantine all doses of the vaccine. So none of it was used. And we would have made the same determination we unhappily and sadly had to make 10 days later.

Mr. BILIRAKIS. So you would have made that determination even before the U.K. Did?

Mr. CRAWFORD. No. We asked that the company give us its final data by October 5, and that conference was scheduled later the morning that the U.K. Announced its results. So we would have been a few hours later, due to the time change.

Mr. BILIRAKIS. All right. I guess my time has expired.

Mr. Dingell to inquire?

Mr. DINGELL. Mr. Chairman, thank you.

Mr. Crawford, on October 3, 2000, this subcommittee held hearings that were focused in good part on the multitude of problems FDA has been experiencing with the policing of foreign firms sending drug products to the United States for domestic consumption. At that time we discussed the time limits with regard to how often these facilities could be inspected in other countries. I will be submitting to you a letter requesting further information on that. And I also ask unanimous consent that that letter, Mr. Chairman, be inserted into the record, and also the previous correspondence between the chairman of the Oversight Subcommittee and the ranking minority member of the Oversight Subcommittee with the Food and Drug Administration, because there are a number of questions that show that things are not going as well as they could down there.

Mr. BILIRAKIS. Without objection, that will be the case.

[The information referred to follows:]

W.J. "BILLY" TAUZIN, LOUISIANA
RALPH M. HALL, TEXAS
MICHAEL BILIRAKIS, FLORIDA
FRED UPTON, MICHIGAN
CLIFF STEARNS, FLORIDA
PAUL E. GILLMOR, OHIO
JAMES C. GREENWOOD, PENNSYLVANIA
CHRISTOPHER COX, CALIFORNIA
NATHAN DEAL, GEORGIA
RICHARD BURR, NORTH CAROLINA
ED WHITFIELD, KENTUCKY
CHARLIE NORWOOD, GEORGIA
BARBARA CUBIN, WYOMING
JOHN SHIMKUS, ILLINOIS
HEATHER WILSON, NEW MEXICO
JOHN B. SHADEGG, ARIZONA
CHARLES W. "CHIP" PICKERING, MISSISSIPPI
VITO FOSSELLA, NEW YORK
STEVE BUYER, INDIANA
GEORGE RADANOVICH, CALIFORNIA
CHARLES F. BASS, NEW HAMPSHIRE
JOSEPH R. PITTS, PENNSYLVANIA
MARY BONO, CALIFORNIA
GREG WALDEN, OREGON
LEE TERRY, NEBRASKA
MIKE FERGUSON, NEW JERSEY
MIKE ROGERS, MICHIGAN
DARRELL E. ISSA, CALIFORNIA
C.L. "BUTCH" OTTER, IDAHO
JOHN SULLIVAN, OKLAHOMA

BUD ALBRIGHT, STAFF DIRECTOR

ONE HUNDRED EIGHTH CONGRESS

U.S. House of Representatives

Committee on Energy and Commerce

Washington, DC 20515–6115

JOE BARTON, TEXAS
CHAIRMAN

JOHN D. DINGELL, MICHIGAN
HENRY A. WAXMAN, CALIFORNIA
EDWARD J. MARKEY, MASSACHUSETTS
RICK BOUCHER, VIRGINIA
EDOLPHUS TOWNS, NEW YORK
FRANK PALLONE, JR., NEW JERSEY
SHERROD BROWN, OHIO
BART GORDON, TENNESSEE
PETER DEUTSCH, FLORIDA
BOBBY L. RUSH, ILLINOIS
ANNA G. ESHOO, CALIFORNIA
BART STUPAK, MICHIGAN
ELIOT L. ENGEL, NEW YORK
ALBERT R. WYNN, MARYLAND
GENE GREEN, TEXAS
KAREN MCCARTHY, MISSOURI
TED STRICKLAND, OHIO
DIANA DEGETTE, COLORADO
LOIS CAPPS, CALIFORNIA
MICHAEL F. DOYLE, PENNSYLVANIA
CHRISTOPHER JOHN, LOUISIANA
TOM ALLEN, MAINE
JIM DAVIS, FLORIDA
JAN SCHAKOWSKY, ILLINOIS
HILDA L. SOLIS, CALIFORNIA
CHARLES A. GONZALEZ, TEXAS

November 18, 2004

Lester M. Crawford, D.V. M., Ph.D.
Acting Commissioner of Food and Drugs
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Crawford:

As part of its continuing oversight of matters of public health, the Committee is examining issues surrounding the recent loss of nearly half of the flu vaccine needed by the United States this year as a result of contamination at the Liverpool, UK manufacturing facility of Chiron Corporation ("Chiron"). We are deeply troubled by this sudden shortage of U.S. supplies of flu vaccine.

Of particular concern is the question of whether Chiron and/or the U.S. Government had sufficient notice from available evidence to take additional steps to safeguard against this sudden shortage. According to news reports, in late August 2004, Chiron discovered bacterial contamination in its Liverpool UK plant where it makes Fluvirin, the commercial name of the flu vaccine on order from the U.S. The U.S. Food and Drug Administration ("FDA") learned of the situation shortly after its discovery and coincidentally had a team at Chiron at the time on another matter and they were able to begin a review of the issue. This was not the first time, however, that the FDA had encountered problems at this Chiron facility. In June 2003, shortly after Chiron purchased the Liverpool plant, the FDA conducted an inspection of the site and found quality-control problems and contamination at an early stage of the production process, but these issues were reportedly resolved.

Another question of interest is whether Chiron and the U.S. Government should have taken immediate steps when the contamination came to light to ascertain better the precise scope of the problem and to react more effectively to protect the public health. On August 26, 2004, Chiron publicly disclosed its discovery of contamination of some flu vaccine lots and shortly thereafter received inspectors from the UK Medicines and Healthcare products Regulatory Agency ("MHRA") to assess the situation. MHRA

suspended Chiron's license on October 5, 2004, thereby revealing more widespread contamination of the vaccine lots. It is our understanding that the U.S. Government has claimed that it was not aware of the more widespread contamination until about the time the MHRA took action in early October 2004.

We are concerned that the situation presented here may have common roots in problems this Committee has already identified for the FDA. For example in our earlier hearings on Counterfeit Bulk Drugs, this Committee presented instances of flaws in the FDA's ability to track and inspect foreign firms that send drug products to the U.S. We are troubled by the prospect that the many management concerns and resource constraints raised by this Committee already to the FDA may still plague the agency today and affect its ability to oversee this key sector of drug manufacturing.

The safety and availability of the medicines needed for public health in the U.S. are of paramount concern to this Committee and, as such, we request that, pursuant to Rules X and XI of the U.S. House of Representatives, you provide us the information requested below by Wednesday, December 1, 2004:

1. A timeline beginning with Chiron's acquisition of the Liverpool facility to the present, which includes all the following events:

   a. Any and all events related to the safety of and/or any potential, possible or actual contamination of flu vaccines, at any stage of manufacture, at the facility;
   b. All communications with Chiron or any regulatory authority relating to either the safety of or any potential, possible or actual contamination of vaccines, at any stage of manufacture, at the facility;
   c. All inspections of the Chiron facility by the FDA or any other third party;
   d. All public statements or communications made by the FDA relating to Chiron; and
   e. All public statements or communications made by the FDA relating to the adequacy and/or availability of influenza vaccine to the U.S. public for the 2004 – 2005 flu season.

   Please produce any records relating to the information identified in this timeline, unless otherwise produced in response to this letter.

2. All records relating to any potential, possible or actual contamination of flu vaccines, at any stage of manufacture, at Chiron's Liverpool facility.

3. The dates, purpose and findings of all FDA inspections of Chiron's Liverpool facility.

4. All records relating to any inspections by you, or any regulator, of Chiron's Liverpool facility, including, but not limited to:

a. The June 2003 inspection by the FDA including, but not limited to, all records relating to any action contemplated, proposed or undertaken with respect to Chiron as a result;
b. The August 2004 inspection by the FDA;
c. The September 2004 inspection by the MHRA; and
d. The October 2004 inspection by the FDA.

5. What specific issues did the FDA identify at Chiron in the June 2003 inspection and what specific actions did Chiron take in response to each such issue?

6. Did any problems or concerns with the process, practices, techniques, standards, facilities, equipment or personnel associated with the manufacture of vaccine at Chiron's Liverpool plant identified in the FDA's June 2003 inspection contribute, in any way, to the matters leading to the October 2004 scrapping of Chiron's vaccine production?

7. All records relating to communications between the FDA and Chiron, from May 2003 to the present, related to the Liverpool facility.

8. All records relating to communications between the FDA and any other party, including, but not limited to, the MHRA, relating to Chiron, from May 2003 to the present, related to the Liverpool facility.

9. For each foreign country in which there are facilities or firms which the FDA must inspect for current good manufacturing practices, please state the following:

a. A list of all subject facilities within each foreign country and the date of the last FDA inspection of each such facility;
b. The foreign regulatory body (bodies) in each foreign country with relevant jurisdiction over matters of product safety;
c. Describe the manner in which the FDA receives all necessary and relevant information and reports about each such facility;
d. Is there any formal information exchange process with the relevant foreign regulators, such as in the form of a Memorandum of Understanding or other such agreement and, if not, why not; and
e. What procedures must be followed for the FDA to visit and inspect any subject facility?

10. With respect to the FDA's inspections of foreign facilities, as discussed above, please state the following:

a. What is the average cost of each such foreign facility inspection;
b. What is the total amount the FDA has spent on such inspections in the past 5 years;

c. What is the total budget at the FDA for such inspections; and
d. What is the number of inspectors currently available for such inspections?

Please note that, for purposes of responding to this request, the terms "records" and "relating" should be interpreted in accordance with the attachment to this letter. If you have any questions about this matter, please contact either Anthony M. Cooke of the Majority Committee Staff at (202) 226-2424, or Chris Knauer of the Minority Committee Staff at (202) 226-3400.

Sincerely,

Joe Barton
Chairman

John D. Dingell
Ranking Member

Attachment

ATTACHMENT

1. The term "records" is to be construed in the broadest sense and shall mean any written or graphic material, however produced or reproduced, of any kind or description, consisting of the original and any non-identical copy (whether different from the original because of notes made on or attached to such copy or otherwise) and drafts and both sides thereof, whether printed or recorded electronically or magnetically or stored in any type of data bank, including, but not limited to, the following: correspondence, memoranda, records, summaries of personal conversations or interviews, minutes or records of meetings or conferences, opinions or reports of consultants, projections, statistical statements, drafts, contracts, agreements, purchase orders, invoices, confirmations, telegraphs, telexes, agendas, books, notes, pamphlets, periodicals, reports, studies, evaluations, opinions, logs, diaries, desk calendars, appointment books, tape recordings, video recordings, e-mails, voice mails, computer tapes, or other computer stored matter, magnetic tapes, microfilm, microfiche, punch cards, all other records kept by electronic, photographic, or mechanical means, charts, photographs, notebooks, drawings, plans, inter-office communications, intra-office and intra-departmental communications, transcripts, checks and canceled checks, bank statements, ledgers, books, records or statements of accounts, and papers and things similar to any of the foregoing, however denominated.

2. The terms "relating," "relate," or "regarding" as to any given subject means anything that constitutes, contains, embodies, identifies, deals with, or is in any manner whatsoever pertinent to that subject, including but not limited to records concerning the preparation of other records.

Mr. DINGELL. In the meantime, though, what have you done about this matter? How can you assure us that you are securing the necessary data on the firms, their inspection status, and that these matters are not still a problem at the Food and Drug Administration?

Mr. CRAWFORD. Thank you, sir. I look forward to working with you with respect to the letter and so forth.

What we are doing is this particular plant in Liverpool, England, that was not able to produce vaccine that we could assure the safety of, we are working with the British Government and also with that company and trying to figure out what we can do to get them relicensed.

Mr. DINGELL. How often does the Food and Drug Administration send in inspectors over there? What arrangements do you have with regard to the inspections that the Food and Drug Administration should be making there? What cooperation do you have with the British agency on these matters? It looks to me like we have here a faith-based initiative.

Mr. CRAWFORD. What we have is an agreement now with the British Government because the corporation Chiron has agreed to jointly share all the information including the confidential information with both governments that we get every 2 years unless there is a problem. As you know, we were in this plant August 25, we were back in it after, from October 8 through October 10, and then a little bit beyond. We will go back in with the British Government before the determination is made as to whether or not they are going to relicense the plant. That decision has to be made by January 5.

Mr. DINGELL. Well, you have two problems. One is if they can't make safe vaccine, if you don't catch them and don't prevent it, then they can send it over here. If they can, and you can properly investigate them, they may not be able to send it, so we continue our flu vaccine shortage. What do we do about that?

Mr. CRAWFORD. Well, we will know this time early enough to where we—which will be, as I mentioned, by January 5, whether or not they are going to be able to produce vaccine. At that point we will confer with CDC and others in HHS to see where we can get the vaccine from, and it will be early enough at that point to get it from other sources.

Mr. DINGELL. I am going to ask you for a table of time and frequency on these inspections of all of your overseas suppliers; how often, when, and how many people do you have to perform the inspections that are needed. That—you can't respond to it at this particular time, but that is my concern, and that will be in the letter here.

Now, I also want you to tell us here, Mr. Crawford, at the time of the earlier hearings, the Food and Drug Administration said that it was attempting to determine how much resources would be required to conduct good manufacturing practices inspections for all firms shipping drug product to the United States at least every 2 years. Do you have the capacity now, the resources, and the money necessary to inspect these plants at least every 2 years?

Mr. CRAWFORD. Yes, sir, we do. What is a problem for us is that every 2 years, as you know from the hearing, is a routine inspec-

tion if we need to go back on a regular basis, and that takes more money that isn't appropriated, so we are building into our request for the future enough funding to allow these continuing inspections. We do have more inspectors now than we did in 2000.

Mr. DINGELL. I am going to ask you to submit to us a description of all of the resources which you have, the frequency during which you may make these inspections, and the effectiveness of your achieving these inspections. Now, understand what I want from this table. I am not going to be deceived, nor are you, about how these inspections will necessarily accomplish our purposes of assuring safety, because it is more than just the frequency of the inspections. There is the quality of the work which is done, the capability of the inspectors, the need and the ability of the inspectors to go back to the place where there are troubles; and, last of all, the ability of the Food and Drug Administration to address the relationship with the foreign government regulatory agencies. And so the questions that you are to be getting from me on these matters will focus on this.

And I ask unanimous consent, Mr. Chairman, that that correspondence be put in the record together with the response at the appropriate time.

Mr. BILIRAKIS. Without objection, that would be the case.

The gentleman's time has expired.

Mr. Upton to inquire.

Mr. Barton.

Chairman BARTON. We all get our chance. Thank you, though, Mr. Chairman.

My first question is fairly basic. But when we decertified the—was it 50 million doses that Chiron had manufactured? Is that correct?

Mr. CRAWFORD. That is correct. Yes.

Chairman BARTON. Are any of those salvageable, or have they already been destroyed?

Mr. CRAWFORD. No. We had to make the determination based on our inspection and the information that was given over to us by Chiron that none of it could be used.

Chairman BARTON. So what has happened to it? Is it still in storage?

Mr. CRAWFORD. There were 6 million doses that had already been shipped to the United States that we had previously had under quarantine. The remainder was in the United Kingdom. They are being systematically destroyed.

Chairman BARTON. I don't know how you do your inspections, but if the doses—are they stored in big vats or gallons or little vials? How is it?

Mr. CRAWFORD. They are stored in a variety of ways. There are what are called tank car vials, which are big vials. They also—they hadn't completed the production run, so some of them were still in bulk, which would be large amounts of vaccine.

Chairman BARTON. But there is medically and scientifically no way that any of that vaccine is usable?

Mr. CRAWFORD. It is not usable. And that was one of the roughest decisions that I had ever had to make and the FDA had to make. But it cannot be used, none of it.

Chairman BARTON. Because that would be obvious, if there was some way to go through and inspect it batch by batch. You know, every little bit counts, because that is a lot that is destroyed. But that is off the table.

I don't know if it is Dr. Gerberding or Dr. Fauci—and I think Congressman Bilirakis asked this question. Is there any availability of new technology to manufacture a vaccine that we could fast-forward that might actually produce some this year by using a different methodology than traditionally has been used?

Mr. FAUCI. Let me take a crack at it first. Not at this point. Certainly not egg-based, because the egg-based is a process that really goes over many months. The decision is made in January sometime about what virus, what seed virus, what reference virus you are going to put in the eggs. You have got to get the eggs from the chickens, you have got to inject them, you have got to get them grown up, you have got to harvest it, kill the virus, and then go through the process of putting it in the vials that is necessary to distribute it.

Chairman BARTON. And there is no way? There is nothing we can do?

Mr. FAUCI. I sense your frustration with that, but we have struggled with this: Is there anything we can do vis-a-vis producing more versus some of the things that I will yield to Dr. Gerberding because she has worked with the Aventis company about and other companies about how to get more doses. But from a production standpoint, we can't take the clock back and start the process over at this point in time for this flu season.

Ms. GERBERDING. I would just say that both Aventis and the manufacturers of FluMist, the nasal vaccine, have pushed their manufacturing processes beyond where we thought we would be this year. So Aventis was able to identify additional doses in part because their yield was higher than expected, and in part because they were able to extend the production cycle a bit longer.

But one of the additional complications is that if we push on the system this year, it cuts into production for next year. That is how tightly coupled these cycles are. So anything we do now will mean less vaccine for whatever strains emerge next year. It is a very fragile system.

Chairman BARTON. So we can't salvage any of the doses that were already manufactured, and we can't change the process because of a lot of different reasons. So the next alternative for this year would be to go overseas to other nations that have vaccines that have not been approved for use in the United States and see if we can somehow, first, get them to agree to ship it to us, and second, make sure that it does meet the standards that are necessary for safety and efficacy. How much of that type of vaccine might be available on the world market?

Mr. CRAWFORD. We have contacted every country and every manufacturer in the world to see if we can't get some additional doses. We have identified now three companies in three overseas countries that are willing to ship vaccine from the amount that they have left over from sales. Now, that amount will be approximately 5 million, perhaps as much as 6 million doses, and we are very close to some announcements with respect to that. We have to

identify the company, talk them into it, get the data from them, and then visit the plant, inspect the plant, and then come back and make a determination.

Chairman BARTON. Well, is the general attitude overseas we are going to take care of 100 percent of our population, and if we happen to have a few extra doses, we might let you have them? I mean, I would think if we really needed 100 million, I am going to guess the world market is a billion? I don't know what it is, but——

Mr. CRAWFORD. I think Dr. Gerberding and Dr. Fauci know that particular amount. We consume about a third of it, I believe.

Chairman BARTON. So the world market is about 300 million. So there is 200 million floating around in the rest of the world. Is the attitude, when you talk to your international compadres, once we have taken care of everybody that we think might potentially need one, then we might let you have some? Or are they trying to actually trying to find ways to help?

Mr. CRAWFORD. I think there is a feeling that they want to help the United States, but there are multiple reactions that we get. These companies certainly want to help, and they are doing what they can do. In some countries influenza immunization isn't particularly emphasized, so they don't have any particular national interest in it. Other countries, there are some barriers to sale because we can't be sure of how it was stored and so forth, and some of them really don't want to get involved in the U.S. Market.

Chairman BARTON. Thank you, Mr. Chairman. Before I yield back, I want the audience to know, I did not get a flu shot.

Mr. BILIRAKIS. Nor did I, Mr. Chairman.

Mr. Green to inquire.

Mr. GREEN. Mr. Chairman, I don't know if this is confession time or not, but I would like to ask some questions, and I appreciate the opportunity. It looks like there is a concern, and I know, Dr. Crawford, you talk about the FDA, after they discover a problem, and then according to the testimony we have is that most of that was dealt with by conference calls. And you don't have the budget available to go back in particularly a foreign location and investigate to see if they actually did correct the deficiencies?

Mr. CRAWFORD. Yes. What happened is we were, in fact, in the plant doing another task on August 25 when the company found that it had a problem. So we were able to consult with them onsite in August of this year. At that point we put them under notice that we wanted a report on a weekly basis of their progress. And then the other thing we did is we quarantined all the vaccine that had been produced or would be produced from that plant and then later had to make the decision to destroy it.

Mr. GREEN. So that was in August?

Mr. CRAWFORD. That was in August.

Mr. GREEN. And it seemed like it was early October, October 7 or something like that——

Mr. CRAWFORD. October 5.

Mr. GREEN [continuing]. That the release was made. And I assume there was activity between the end of August and October 7 before it was released to the public trying to find alternative sources for the production?

Mr. CRAWFORD. Actually, it was too late to find alternative sources for the production, because it starts right after the first of the year, and we could not have gotten any at that point.

Mr. GREEN. Does the administration, that you know of, have plans to submit legislation aimed at sharing the adequate and reliable supply of flu vaccines? And not only flu, but there are some of us who also have additional concerns.

Mr. CRAWFORD. I am not aware of such legislation, but I wouldn't necessarily be at this point.

Mr. GREEN. Okay. I just noticed, you said you were there in August, and that was not for an inspection, it was for some other reason that you were in the United Kingdom?

Mr. CRAWFORD. Yes. As I said, we were doing another task, as I just mentioned.

Mr. GREEN. Okay. Is there interest in the FDA, and do you need legislative authority to—other than just appropriations, to expand that? If somebody has a problem—and, again, this should be with lots of Federal programs—if instead of just relying on a conference call to say, yes, we corrected it, and here is our documentation, do you need legislative authority to be able to expand that ability to go back in?

Mr. CRAWFORD. No. We have the legal authority to do it. What we don't have are FDA offices overseas, so we have to dispatch people from here, which is a logistical and a financial problem for us. We did find violations within the plant for the 2001, 2002 season, and we sent a team over to reconcile that in the middle of the summer of 2003. That all was done directly. And if there are violations and we need to go back, then we do have to go back.

Mr. GREEN. Mr. Chairman, I have a lot of questions, and will we have the opportunity to submit questions to our panels?

Mr. BILIRAKIS. Yes. I have already mentioned that certainly, as per usual, we will do that.

Mr. GREEN. Thank you.

Dr. Gerberding, in our second panel we will hear from Alan Rosenbloom, who is on behalf of the American Health Care Association. He specifically requested guidance from CDC on how best to handle partial orders and how to allocate scarce vaccines within high-risk groups. Has the CDC provided that to not only that association, but our public health agencies?

Ms. GERBERDING. On October 5, CDC initially worked with the Advisory Committee on Immunization Practices to announce the high-priority risk groups, so that that was blasted out to all of the clinicians and public health agencies around the country through our health alerting system. Since that time, health care providers at the local level have had to make difficult choices about who to vaccinate first. The ACIP and CDC considered whether or not subprioritizing people in those high-risk categories would be useful or helpful, and on October 5 the decision was no because there was no science on which to base that subprioritization.

Since that time, I initiated a consultation with several renowned ethicists to ask their advice. If science couldn't tell us about the importance of subprioritization, was there a way we could think about this using the tools of ethicists to make a fair and equitable distribution process? While the input from the ethicists was extremely

helpful, it did not lead us to conclude that it was realistic for the Federal Government to tell local health officials how to make those decisions at the local level.

And what we have really been seeing is that they have done a great job of making tough decisions, including Minnesota, which has done such a good job of encouraging the public to defer vaccination that they are actually not getting the people who need it the most to step up and receive it. So we have deferred and have supported the decisions that the hospitals and local health officers are making with authorities and statutes that——

Mr. GREEN. I am almost out of my time. I am out of time. But my concern is that you are leaving it to the local community, and in most cases we like that. But if we have 85 million high risk and only 61 million vaccines, do you have to prioritize in that high-risk group somehow? And the guidance from the CDC, because, again, it is a national problem, it wasn't my local hospital district, that they need that guidance, and whether it is the health care providers or the public health care and anyone else.

But, Mr. Chairman, like I said, I have a whole lot of other questions I would like to submit.

Mr. BILIRAKIS. Thank you.

Mr. Upton to inquire.

Mr. UPTON. Thank you, Mr. Chairman. I, too, have a lot of questions. And as much as we would like to turn back the clock on this flu season, obviously we can't. We have got to learn from the experience. And so in that mode, let me ask a number of different questions.

Dr. Fauci, you indicated at some point along the line that there was a study that was going on on half doses, their effectiveness on the non-high-risk population. I just wonder a question; when you expect the results of that study to come back, and if you can give us an early indication of what that may be, what those findings may be.

Mr. FAUCI. Yes. Thank you, Mr. Upton. Those studies have actually been done. The first study was done comparing intramuscular full dose with a half dose, and was done with healthy individuals from 18 to 49 years old and showed that, in fact, these individuals had comparable responses between a half and a full dose. I will get back to in 1 second why that is not particularly helpful right now for us, because this study was done in very healthy individuals and not in the people who would be in the risk groups.

The studies that were just published in the New England Journal of Medicine actually used the technique of injecting the vaccine intradermally, or directly into the skin, not underneath the skin, which is subcutaneous, or into the muscle, which is intramuscular. And the finding is that you can inject anywhere from one-half to one-fifth of the dose if you give it intradermally. Because the cells in the skin are particularly attuned to responding to antigens that you stick into the skin. you would get comparable responses.

Now, that was seen fundamentally best in young people again, to a lesser extent in people over 60, 65, but still it was an advantage. So what we take away from that study is that, given the logistics of what it would take to switch over to that now, it probably is not going to help us this year for a number of reasons: Because

the vaccine is not approved for usage intradermally, and it would again require doing it under, quote, experimental conditions. But what we do learn from that is that this is a way that is going to be explored in future evaluations of vaccine, to see whether or not you can actually get comparable responses or even better responses with appropriate doses intradermally. So it is an important scientific observation, it will be pursued, but we don't feel from a practical standpoint it is going to bail us out for this year.

Mr. UPTON. You indicated in your testimony that you had tripled the funding for influenza research. I am wondering if your 2006 budget request continues on that same path as we look at perhaps a pandemic down the road.

Mr. FAUCI. As you know, the budget requests for the Department and the NIH is not a lot, not a major increase, it is a couple of percent, but within that framework we are giving high priority to a number of issues. Influenza is one of them. So we would predict that within the small increase that we are having, since we are going to be preferentially favoring influenza, we will be continuing that upswing.

Mr. UPTON. Thank you.

Dr. Crawford, I want to go back through these dates for a second. You indicated that the FDA thought that there was going to be some problem on, I think you mentioned, August 25, and yet at what point did you trigger a response to the CDC that, in fact, there may be some trouble? Did you wait until October 5? I mean, was there some communication between then?

Mr. CRAWFORD. Actually when we went into the mode following notification by the plant on August 25 of double-checking with the plant on a regular basis, CDC joined us in that initiative. So they were on those.

Mr. UPTON. So they knew back in August that there could be a problem, which you confirmed?

Mr. CRAWFORD. Well, we both believed that the problem was solvable, and we did not expect that the vaccine was going to be unusable at that point. But they were alerted to what we were alerted to.

Mr. UPTON. And then you came to the final conclusion then on October 5 that it was not salvageable and that we have a problem?

Mr. CRAWFORD. Actually what happened is that the British made their announcement on October 5. We had the final meeting and presentation of data from Chiron Corporation also on October 5. We sent a team over on—they were functioning by October 8, and on October 15 I made the decision that it could not be used.

Mr. UPTON. And, Dr. Gerberding, just as the CDC was beginning to become aware of this and looking at a seriously limited supply of vaccine, obviously one of the first things that comes to everyone's mind is that we need to prioritize so that those that really need it get it versus folks in a nonrisk department. At what point did you actually—did the CDC begin to formulate notices to the States and others that they should be prepared for this problem?

Ms. GERBERDING. In August, when the contamination of the 6 to 8 lots out of the 48 million doses of vaccine, Chiron was not——

Mr. UPTON. That is not Mr. Bilirakis telling me that my time was expired. Go ahead.

Ms. GERBERDING. In August, when we learned about contamination of a few lots of Chiron's vaccine, we immediately conferred with FDA to determine what this meant for the ultimate supply. And we were reassured by Chiron as well as FDA that we should expect a delay in shipment, but that overall, we would still be expecting to receive 48 million doses from Chiron. So the likely scenario was that we would have the full 100 million dose total that we had been expecting; but we had to be prepared for the worst-case scenario, and so we took some additional steps.

First of all, we increased our stockpile purchase of vaccine, so we bought 2 million more doses of vaccine from Aventis, which is the first time we have ever been able to do that. We also increased our purchase of oseltamivir, which is the drug to treat influenza. And we also initiated a survey of States to determine prioritization, and contingency plans that were in place should we not receive our Chiron vaccine. We considered what could be done at this time to try to reallocate the vaccine supply in the best possible way if needed.

Of course, in October when we learned the news, we were actually in the middle of another House hearing. I think when that information became known to Chiron and to us, we immediately began to initiate the reallocation scheme that we had in our back pocket.

Mr. BILIRAKIS. The gentleman's time has expired.

Did any of the bad vaccine get out there?

Ms. GERBERDING. Absolutely none of the bad vaccine has been used.

Mr. BILIRAKIS. Ms. Eshoo to inquire.

Ms. ESHOO. Thank you, Mr. Chairman.

And thank you to the witnesses again. Dr. Fauci and Dr. Gerberding, I have a great deal of regard for what you have done for our country, and I salute you for it.

Dr. Crawford, I want to go back to what I expressed as some of my concerns in my opening statement, and that is the quality of the work and the inspections, and what brought us to really losing at least half of our Nation's vaccine supply just as the season for giving the shots began, and the role of the FDA in this.

Last evening, maybe some would think there is something really wrong with me, instead of watching other things on TV, I tuned into the hearing, the House hearing that took place yesterday. And you were there, you testified. There were at least—I think at least 100 pages, detailed reports, of the problems that came out and the FDA's role in that, and that is what I want to pursue.

There seems to be a disconnect, as I heard it, between what happened in August, the follow-up to the 2003 determinations of contamination in the plant. You seem to be insisting that there is not any nexus between what was found in 2003 in contaminations and what happened in 2004. Is that correct?

Mr. CRAWFORD. That is absolutely correct.

Ms. ESHOO. And you still stand with that?

Mr. CRAWFORD. Yeah. If I could explain about 2003.

Ms. ESHOO. Well, I heard your testimony, and that is that what was reported seemed to be corrected, and that it doesn't have any

connection to 2004. And yet it was the British Health Service that shut the plant down, and that is what I want to pursue.

In August 2004, as I understand it, Chiron announced publicly that there were at least of the supply about 5 million contaminated. The British service convened very high-level meetings. They got copies of Chiron's—of what Chiron was doing. The FDA was nowhere to be found in this; is that correct?

Mr. CRAWFORD. That is absolutely incorrect.

Ms. ESHOO. All right. Tell me what the FDA actually did.

Mr. CRAWFORD. We were in the plant doing another duty on August 25 when we were informed by——

Ms. ESHOO. What was that duty?

Mr. CRAWFORD. They were introducing a new line, which basically is a subdivision of the plant.

Ms. ESHOO. Was that FDA inspection?

Mr. CRAWFORD. Yes.

Ms. ESHOO. Or was it—and was it, FDA inspection, related to the 2003?

Mr. CRAWFORD. Well, what happened in 2003 was——

Ms. ESHOO. I know what happened in 2003.

Mr. CRAWFORD. I don't think you do. What happened in 2003 was—is that we finished our investigation of the 2001, 2002 production. The 2003 production was perfectly all right. Nothing went wrong in 2003. That is the misconception that the newspaper got.

Ms. ESHOO. Well, you know, there is an old adage, and it does apply to many, many people, that—and Alcoholics Anonymous is famous for it—that you first have to acknowledge that there is a problem. And I would use that analogy, and I am sorry to say that about the FDA, because it seems to me that the British have beaten us to the punch on this.

Mr. CRAWFORD. No. We actually found out about it first.

Ms. ESHOO. What did you do about it?

Mr. CRAWFORD. On August 25 we quarantined all the doses of the vaccine——

Ms. ESHOO. Let me just read into the record, and I will place it in the record, the FDA's October 2004 inspection report. Your own inspectors said: Failure to adequately address root causes during failure investigations noted during the inspection of year 2003 have not been adequately corrected.

Did you read their report, number one?

Mr. CRAWFORD. Yeah, I approved that report.

[The report follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA/OE/DIVISION OF COMPLIANCE MANAGEMENT AND OPERATIONS 5600 FISHERS LANE, ROCKVILLE, MD 20857 USA TEL: (301) 827-0391/FAX: (301) 827-0342	10/10-15/2004 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: ANDY SNEDDON, VICE PRESIDENT OF MANUFACTURING, UK SITE DIRECTOR

FIRM NAME	STREET ADDRESS
EVANS VACCINES an affiliate of CHIRON CORPORATION	GASKILL ROAD
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
LIVERPOOL L24 9GR, UK	VACCINE MANUFACTURER

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT, CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (WE) OBSERVED:

1) Regarding Fluvirin Sterility Investigation #R/0198/10/04 dated October 9th 2004:

A) The Fluvirin Sterility Failure Investigation Report states (in part) that [redacted] fumigation took place on May 17, 2004 as a corrective action to increased levels of Gram negative organisms (including *Serratia spp*) during April and May. The area fumigated was the formulation suite. The firm deemed that the fumigation "was successful, as confirmed by ongoing environmental monitoring" and that "it should be noted that there are no confirmed isolates of *Serratia spp.* within the Grade [redacted] LAF unit where aseptic connections are made." The firm further deems this as "a key assessment criteria for further batch processing as part of the Quality Assurance Process". This investigation conclusion is not supported and information reported is inaccurate, in that:

1) the firm does not report that Gram negative rods, oxidase negative, were actually isolated in the formulation areas after the fumigation, further Gram negative rods identified as *Serratia spp.* were also isolated, and

2) there is no evidence that the firm took further action to correct continued excursions of alert and action levels in formulation rooms [redacted] and [redacted] from May 2004 through September 2004. The firm continued to experience alert and action level excursions for Gram negative organisms, including but not limited to, *Serratia spp.*

B) Regarding retest performed on the sterility test failures for four of nine final vial product lots, there is no investigation into the mixed pass and fail sterility test results for the original two lots and two "sister" lots associated with the failed monovalents.

The original two failed lots [redacted] were retested [redacted] times the normal test sample size (normal test sample size is [redacted] vials). The "sister" lots [redacted] of the two original failed lots were also retested [redacted] times the normal test sample size. Results are as follows:

Lot#	Re-Test Date	Results of each set of 40 vials
[redacted]	22 Jul 04	[redacted] set of [redacted] vials passed sterility test [redacted] sets of [redacted] vials failed sterility test
[redacted]	22 Jul 04	[redacted] sets of [redacted] vials failed sterility test
[redacted]	28 Jul 04	[redacted] sets of [redacted] vials failed sterility test

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Charlotte G. Oxenstierna, CSO Paula A. Trosti, CSO John D. Finkelstein, Ph.D. Supv. Chemist David S. Cho, Ph.D., Microbiologist Mark A. Elengold, Deputy Director Oper., CDER	15 October 2004

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA/OE/DIVISION OF COMPLIANCE MANAGEMENT AND OPERATIONS 5600 FISHERS LANE, ROCKVILLE, MD 20857 USA TEL: (301) 827-0391/FAX: (301) 827-0342	10/10-15/2004 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: ANDY SNEDDON, VICE PRESIDENT OF MANUFACTURING, UK SITE DIRECTOR

FIRM NAME	STREET ADDRESS
EVANS VACCINES an affiliate of CHIRON CORPORATION	GASKILL ROAD
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
LIVERPOOL L24 9GR, UK	VACCINE MANUFACTURER

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT, CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (WE) OBSERVED:

[redacted] 29 Jul 04 [redacted] sets of [redacted] vials passed sterility test
[redacted] sets of [redacted] vials failed sterility test

C) SOP M198, Sterility Investigation Report (Version 06), was not followed during the Fluvirin Sterility Failure investigations in that, the SOP required a Non-Conformance Report (NCR) be initiated in accordance with the NCR SOP. This was not done for the nine filled vial lots that were contaminated with *Serratia spp.* Regarding filled vials, the first failure occurred on 8 July 2004. The 9th failure occurred 2 August 2004. There is no documentation to show that root cause, immediate corrective action, or product impact was addressed at the time of each failure (as per the firm's SOP). One NCR (dated 28 September 2004) was generated to cover all nine sterility failures as well as monovalent blend failures and serves only to refer to the final Fluvirin Sterility Failure Investigation dated 9 October 2004.

D) No documentation of rationale in the Fluvirin Sterility Investigation #R/0198/10/04 dated October 9th 2004 indicating that all three (3) monoblend batches of the Fluvirin trivalent strains with sterility failures are the B/Jiangsu strain.

E) The investigation of the root cause analyses, corrective/preventive actions, conclusions and recommendations did not include B/Jiangsu bulk batch [redacted]. The first of the three (3) monoblend batches implicated in the nine (9) Fluvirin final filled vials sterility failures with bioburden level of 67cfu (specification of [redacted] cfu/ml) but failed sterility at the bulk stage (isolate: *Serratia marcesens).* (Was referenced in the Investigation Report)

F) The investigation did not specifically state that high bioburden levels were noted in the Fluvirin B/Jiangsu strain at the [redacted] /Pre filtration step in [redacted] (83%) of [redacted] monoblend batches manufactured for year 2004 campaign with 170-39,000,000cfu/ml bioburden levels per batch (alert level [redacted] cfu/ml). This is higher bioburden than noted for any of the other two Fluvirin monoblend strains.

G) No documentation in the investigation report of the effect of keeping the monoblend/trivalent formulations at [redacted] for up to [redacted] during processing was considered. Fluvirin finished vials are labeled for shipment at 2-8°C and Fluvirin monoblend/trivalent bulks are stored at temperature of [redacted] °C.

H) There is a lack of scientific data to support the statistical rationale for the retest sampling and testing plan.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Deborah G. Deuenevel, CSO Paula A. Trost, CSO John D. Finkelstein, Ph.D. Supr. Chemist David S. Cho, Ph.D., Microbiologist Mark A. Ellenpeld, Deputy Director Oper., CBER	15 October 2004

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA/OE/DIVISION OF COMPLIANCE MANAGEMENT AND OPERATIONS 5600 FISHERS LANE, ROCKVILLE, MD 20857 USA TEL: (301) 827-0391/FAX: (301) 827-0342	10/10-15/2004 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: ANDY SNEDDON, VICE PRESIDENT OF MANUFACTURING, UK SITE DIRECTOR

FIRM NAME	STREET ADDRESS
EVANS VACCINES an affiliate of CHIRON CORPORATION	GASKILL ROAD
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
LIVERPOOL L24 9GR, UK	VACCINE MANUFACTURER

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT, CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (WE) OBSERVED:

2) Regarding clean room design and operations for Formulation Room [redacted] (Filtration) and Formulation Room [redacted] (Trivalent Blending): The Class [redacted] (Class [redacted] area where post filtration aseptic connections take place is equipped with [redacted] curtains in the form of strips approximately [redacted] inches wide and are arranged so as to overlap each other and are attached at the ceiling surrounding the HEPA filter. The curtains separate the Class [redacted] area from the Class [redacted] (Class [redacted] area.

A) The curtains are approximately [redacted] from the floor some of the [redacted] strips are bent leaving gaps between each strip. There is lack of assurance that airflow would not be disrupted. Available smoke videos do not provide assurance that there is no disruption.

B) The room is arranged so that operators are required to reach into curtains or beneath the curtains and vigorously manipulate equipment only 6 to 12 inches inside the curtains. During a mock demonstration of operations, one operator was observed making aseptic connections approximately [redacted] from the floor which is [redacted] below the bottom of the curtains and was required by the design of the equipment to disrupt the curtains that separate the Class [redacted] and Class [redacted] areas.

C) The equipment configuration within the Class [redacted] environment is such that operators must crouch in the airflow stream sweeping towards the critical area where multiple aseptic connections are made

D) Available smoke studies do not demonstrate the ability to maintain integrity of laminar airflow within the critical area when operator is present. Furthermore, the operator moves from a Class [redacted] environment into the Class [redacted] environment on multiple occasions during aseptic operations

3) Filtration occurs in Formulation Room [redacted] and trivalent blending occurs in Formulation Room [redacted] Activities involve operators making aseptic connections at pre and post filtration sites. These operations routinely encompass between [redacted] in which operators are performing critical operations. Regarding air environmental monitoring in virus formulation areas, there is a lack of assurance that microbial contamination during critical operations would be adequately detected in that:

A) The firm does not routinely monitor active air while critical operations are taking place. Viable active air sampling is tested using a [redacted] L sample which takes between [redacted] for [redacted] of growth media (a total of [redacted] air sampling).

B) Viable active air sampling that is performed in the Class [redacted] area is not performed in the area where most critical operations are occurring but rather, the air sampler is placed on tables [redacted] different locations at [redacted] different times) near the corners of the Class [redacted] area.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Omotunde O. Ownusami, CSO Paula A. Trost, CSO John D. Finkbeiner, Ph.D. Supv. Chemist David S. Cho, Ph.D., Microbiologist Mark A. Stengold, Deputy Director Oper., CBER	15 October 2004

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA/OE/DIVISION OF COMPLIANCE MANAGEMENT AND OPERATIONS 5600 FISHERS LANE, ROCKVILLE, MD 20857 USA TEL: (301) 827-0391/FAX: (301) 827-0342	10/10-15/2004 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
TO: ANDY SNEDDON, VICE PRESIDENT OF MANUFACTURING, UK SITE DIRECTOR

FIRM NAME	STREET ADDRESS
EVANS VACCINES an affiliate of CHIRON CORPORATION	GASKILL ROAD
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
LIVERPOOL L24 9GR, UK	VACCINE MANUFACTURER

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT, CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (WE) OBSERVED:

C) Settling plates are not placed in areas where the most activity is occurring and not in areas of critical operations.

D) There is a lack of assurance that the current sampling volume for non viable particulate of [redacted] cu ft/[redacted] is adequate in relation to the time required to perform operations [redacted] Sampling is not routinely performed in the area of critical process at the time of critical process.

4) Regarding Control of Bioburden in the Manufacturing Facility:

A) [redacted] (60%) out of [redacted] Fluvirin monoblend batches used in the formulations of the trivalent batches manufactured for year 2004 Fluvirin Campaign were out of bioburden alert level of [redacted]fu/ml with bioburden levels as high as 39,000,000cfu/ml.

B) Out of Specification (OOS) batches of Fluvirin monoblends: A/Wyoming, B/Jiangsu and A/New Caledonia were noted as a result of the high bioburden levels in Observation 2A above and total of 26 out of [redacted] monoblend batches resulted in OOS results for endotoxin levels of up to 5052 Eu/ml (alert level specification for US [redacted] Eu/ml). The monoblends with high endotoxin levels were not used for USA Fluvirin market.

C) Approximately 80% of all microorganisms' growth in the Fluvirin filling room, monoblend aseptic filtration, and trivalent formulation room excursions were not identified to the genus level.

D) Per Non-conformance Report #2004/1071/07 dated July 5th, 2004 Mycoplasma growths were confirmed for Fluvirin A/Wyoming Master Seed batch [redacted] and Working Seed batch [redacted] Also, per M/2004/1029 dated March 15th 2004, Mycoplasma growth was also confirmed on A/Wyoming Working Seed batch [redacted] The contaminated seed lots were used in five Fluvirin monoblend batches that were later rejected.

E) Bioburden investigation is incomplete in that there is a lack of documentation that water quality was directly investigated as a potential for contribution to bioburden though purified water does have direct contact with the egg product mixture. For example, purified water is used to clean equipment, including the [redacted] Centrifuge, the [redacted] Centrifuge and [redacted] Machine which come into direct contact with product.

F) Besides the nine (9) batches of Fluvirin that were rejected for sterility failures (Investigation # R/0198/10/04 dated October 9th 2004), additional four (4) batches of finished Fluvirin vials were also rejected due to environmental excursions. For example:

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (PRINT OR Type)	DATE ISSUED
		Osasbunde O. Omoruyemi, CSO Paula A. Trowl, CSO John G. Finkbeiner, Ph.D. Supv. Chemist David B. Cho, Ph.D., Microbiologist Mark A. Ziengold, Deputy Director Oper., CBER	15 October 2004

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA/OE/DIVISION OF COMPLIANCE MANAGEMENT AND OPERATIONS 5600 FISHERS LANE, ROCKVILLE, MD 20857 USA TEL: (301) 827-0391/FAX: (301) 827-0342	10/10-15/2004 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: ANDY SNEDDON, VICE PRESIDENT OF MANUFACTURING, UK SITE DIRECTOR

FIRM NAME	STREET ADDRESS
EVANS VACCINES an affiliate of CHIRON CORPORATION	GASKILL ROAD
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
LIVERPOOL L24 9GR, UK	VACCINE MANUFACTURER

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT, CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (WE) OBSERVED:

1) Per Non-Conformance Report #2004/1632 dated September 9th, 2004 lot [redacted] was rejected due to growth of *Micrococcus spp* on Fluvirin filling needle swab. In addition, two alert levels with microbial growths identified as Gram positive cocci/Gram negative rods were also identified in the [redacted] change room" and within the grade [redacted] area outside of the filling room sterile corridor respectively.

2) Per Non-Conformance Report #2004/1852 dated October 2nd 2004, batch [redacted] *Staphylococcus spp* growth was identified on Fluvirin filling needle swab and on hand plate sample of one aseptic filling room operator. Also alert level growth of *Staphylococcus aureus/Moraxella spp* was detected in the [redacted] change room".

3) Per Non-Conformance Report #2004/1863 dated October 4th 2004, batch [redacted] microbial growth of gram positive cocci were noted in the grade [redacted] aseptic filling room (Class [redacted] Micrococcus spp were noted on hand plate of one operator. Gram negative rod oxidase negative and gram positive cocci/rods were also isolated from setting plates in the changing room.

4) Per Non-Conformance Report #2004/1625 dated September 8th, 2004 batch [redacted] microbial action limits were reached by two (2) Fluvirin filling Operators working in the grade [redacted] aseptic filling area (Class [redacted] In addition, growth of *Brevibacillus brevis, Bacillus subtilis, Micrococcus spp* and Gram negative rods were noted at vial in-feed on the [redacted] filling machine.

G) Although individual investigations were conducted into the following Fluvirin aseptic filling room excursions, no formal overall investigation was conducted to assure adequate corrective and preventive actions.

5) Failure to adequately address root causes during failure investigations, noted during the inspection of year 2003 has not been adequately corrected. For example the previous inspection observation noted:

A) The most recent sterility failure Investigation #R/0198/10/04 for nine (9) filled vials of finished Fluvirin batches concluded that inadequate aseptic technique during aseptic connections was the cause. During the 2003 inspection, the firm was cited for failure to evaluate the reduction in aseptic connection to reduce the possibility of contamination. There is no documentation that adequate corrective action has been conducted.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Gwendolyn G. Gwaunsami, CSO Paula A. Trout, CSO John D. Finkelstein, Ph.D. Supv. Chemist David S. Cho, Ph.D., Microbiologist Mark A. Elengold, Deputy Director Oper., CDER	15 October 2004

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA/OE/DIVISION OF COMPLIANCE MANAGEMENT AND OPERATIONS 5600 FISHERS LANE, ROCKVILLE, MD 20857 USA TEL: (301) 827-0391/FAX: (301) 827-0342	10/10-15/2004 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
TO: ANDY SNEDDON, VICE PRESIDENT OF MANUFACTURING, UK SITE DIRECTOR

FIRM NAME	STREET ADDRESS
EVANS VACCINES an affiliate of CHIRON CORPORATION	GASKILL ROAD
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
LIVERPOOL L24 9GR, UK	VACCINE MANUFACTURER

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT, CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (WE) OBSERVED:

B) Control and failure investigations into bulk Fluvirin monoblend/lots at the [redacted] step with high bioburden levels is deficient, in that lots were noted with total high bioburden volumes of 9.66×10^8 cfu, 7.07×10^7 cfu & 1.26×10^7 cfu in year 2000/2001 and 2001/2002 campaigns and no "effect" investigations has been opened to find the root causes of the high levels of bioburden in these lots. **(Not corrected from previous inspection of 2003 in that similar occurrences noted during this inspection)**

6) Regarding Aseptic Media Fills Simulation:

A) Media fill simulations are not representative of actual aseptic fill processes in that, interventions that occurred during aseptic filling processes are not evaluated and considered for incorporation into the media fill simulations. **(Not corrected from previous inspection of 2003)** For example;

Media fills conducted as part of the sterility failure Investigation Report #R/0198/10/04 into nine (9) filled vials of Fluvirin batches and routine aseptic media fill simulations per protocol #PQR/0142/04 &PQP/0146/02 failed to include the review and evaluation of batch records for syringes and vials for unusual interventions that occurred during routine aseptic filling processes for incorporation into aseptic fill simulations per: SOP #SCP029 dated October 26th 2003 titled: General Procedure for Routine Monitoring of Aseptic Manufacturing Processes by Process Simulations Utilizing Sterile Media Fills.

B) Deficiencies were noted in the routine aseptic media fill simulations for Fluvirin monoblend aseptic fill /trivalent aseptic formulation simulations, and trivalent media fill simulation investigation into Fluvirin nine (9) filled vials sterility investigation #R/0198/10/04. Aseptic simulations were not representative of actual aseptic fill conditions: Specifically:

1) No Batch record reviews of previously manufactured lots were conducted

2) No documentation that interventions were conducted during the media fills

3) The routine aseptic media fills for the monoblend and trivalent stages do not encompass all interventions normally performed during production.

4) No documentation that worst case challenges were conducted during the aseptic media fills simulations.

7) Regarding quality operations:

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Omobande O. Oruwusomi, CSO Paula A. Trask, CSO John D. Finkelstein, Ph.D. Supv. Chemist David S. Chu, Ph.D., Microbiologist Mark A. Ebingold, Deputy Director Oper., CBER	15 October 2004

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA/OE/DIVISION OF COMPLIANCE MANAGEMENT AND OPERATIONS 5600 FISHERS LANE, ROCKVILLE, MD 20857 USA TEL: (301) 827-0391/FAX: (301) 827-0342	10/10-15/2004 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: ANDY SNEDDON, VICE PRESIDENT OF MANUFACTURING, UK SITE DIRECTOR

FIRM NAME	STREET ADDRESS
EVANS VACCINES an affiliate of CHIRON CORPORATION	GASKILL ROAD
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
LIVERPOOL L24 9GR, UK	VACCINE MANUFACTURER

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT, CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (WE) OBSERVED:

A) Monovalent blend pools produced during the 2004 production campaign that have exceeded the alert limit have been forward processed to final product on multiple occasions, even when bioburden results have exceeded alert limit by multiple orders of magnitude. For process stream excursions of the alert limit that have occurred in the downstream processing steps where purification of desirable components may be completed, it is not clear that the investigation assessed potential product quality impact in terms of microbial metabolites, microbial degradation of the desired vaccine components, or introduction of sensitizing agents into the product.

B) In twenty-four (24) incidences during the 2004 Fluvirin campaign, cultures were used in egg inoculation that exceeded bioburden levels, i.e., [redacted] cfu (alert of [redacted] cfu/[redacted] ml). This resulted in the inoculation of approximately [redacted] eggs per batch which were used in the manufacturing of Fluvirin Vaccine with high bioburden containing cultures. Although the firm was aware that the live virus inoculum contained high bioburden, the eggs/batches were not rejected but allowed to continue through the Fluvirin manufacturing process.

C) Technical Report Reference Number R/0123/06/04, revision one, accepted August 12, 2004, states on page 24, "During 2003, no adverse events investigations were performed due to 5 occurrences from one batch." This indicates that no independent review of adverse event reports by batch was performed as a quality control procedure.

8) Regarding zonal centrifugation operations:

A) There is no written procedure or cleaning validation for the manual cleaning of the upper and lower assemblies, which are part of the flow path for the process stream.

B) The written procedure for cleaning of the main body of the zonal centrifuge rotor describes the flushing of process stream contact parts for a period of [redacted] There are no directions describing the surfaces to be flushed.

C) Validation studies for the zonal centrifugation operations characterize material based on [redacted] assays but do not characterize egg proteins, or other specific process or product related impurities.

9) Regarding [redacted] processing tanks utilized in the [redacted] production area where purification operations, sterile filtration, and aseptic formulation operations are conducted:

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Oseelamide O. Osunkoya, CSO Paula A. Trosil, CSO John D. Finkbohner, Ph.D. Supv. Chemist David S. Chu, Ph.D., Microbiologist Mark A. Elengical, Deputy Director Oper., CBER	15 October 2004

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA/OE/DIVISION OF COMPLIANCE MANAGEMENT AND OPERATIONS 5600 FISHERS LANE, ROCKVILLE, MD 20857 USA TEL: (301) 827-0391/FAX: (301) 827-0342	10/10-15/2004 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: ANDY SNEDDON, VICE PRESIDENT OF MANUFACTURING, UK SITE DIRECTOR

FIRM NAME	STREET ADDRESS
EVANS VACCINES an affiliate of CHIRON CORPORATION	GASKILL ROAD
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
LIVERPOOL L24 9GR, UK	VACCINE MANUFACTURER

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT, CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (WE) OBSERVED:

A) Prior to August 2004, there was no periodic preventative maintenance program or written assessment of aspects potentially effecting tank integrity such as damage to sealing surfaces, sealing gaskets, valve assemblies, or sterile vent filter assemblies. Difficulties with [redacted] valves and integrity of sterile vent filters have been noted in processing.

B) Tanks are usually double door passed through the autoclave into the Class [redacted] formulation areas; however, on some occasions, the vessels have been single door passed back into the vessel preparation area [redacted] and transferred via materials airlock and wiped down into the clean zone.

C) Documentation of sprayball coverage for processing tanks is not found in cleaning validation studies or I/OQ studies for these processing tanks. In addition, the written documentation for visual determination of cleanliness is non-specific relative to assessment of soiling on most difficult to clean surfaces.

D) Cleaning validation for the CIP process for Vessel [redacted] which is utilized in the aseptic formulation of trivalent bulk influenza vaccine, did not include an assessment of sprayball coverage for the vessel. In addition, the study did not include swab sampling of the transfer lines used in the transfer of monovalent blend pools into the mixing vessel [redacted], and for transferring the aseptic trivalent formulated bulk back into a sterilized [redacted] liter tank in formulation room [redacted]

10) Manufacturing instructions (batch production record) do not always capture important processing information. For example, processing tanks are not traceable within the batch production record. In addition, it is not possible to consistently trace processing tanks to specific unit operations for a specific lot.

11) The specified replacement schedule (annual replacement) for the [redacted] filtration [redacted] is not supported by production history accumulated since January 2003. For example, [redacted] sets of [redacted] have been used in the 2003 production campaign, and [redacted] in the 2004 campaign. The stated reason for change after initial annual installation is fouling of the [redacted] resulting in longer processing times.

12) Regarding equipment supporting manufacturing operations in the Egg Virus Unit (EVU):

A) There is no spray ball coverage cleaning studies for the harvest tank, bulk holding tank, inactivation vessel [redacted] and inactivation vessel [redacted]

B) There are no studies to determine the swab sampling sites for the harvest tank, bulk holding tank, inactivation vessel [redacted] and inactivation vessel [redacted]

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Gowthamchandra G. Casaravelli, CSO Paula A. Trost, CSO John D. Finkbohner, Ph.D. Supv. Chemist David S. Cho, Ph.D., Microbiologist Mark A. Ebersole, Deputy Director Opns., CDER	15 October 2004

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
ORA/OE/DIVISION OF COMPLIANCE MANAGEMENT AND OPERATIONS 5600 FISHERS LANE, ROCKVILLE, MD 20857 USA TEL: (301) 827-0391/FAX: (301) 827-0342	10/10-15/2004 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED
TO: ANDY SNEDDON, VICE PRESIDENT OF MANUFACTURING, UK SITE DIRECTOR

FIRM NAME	STREET ADDRESS
EVANS VACCINES an affiliate of CHIRON CORPORATION	GASKILL ROAD
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
LIVERPOOL L24 9GR, UK	VACCINE MANUFACTURER

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS, AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT, CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

DURING AN INSPECTION OF YOUR FIRM (WE) OBSERVED:

13) There is no documentation that a manufacturing quality review was conducted in a timely manner on adverse event reports received for twenty-two batches of Fluvirin manufactured in the 2003/2004 campaign where one or more criteria for manufacturing investigation were met per SOP MPD-0022 (Section 7.7), SOP MPD-024 (Section 7.5), and (Section seventeen page 41) of the June 27, 2003 response to the June 10 FD483).

For example:

A) Seven adverse event reports received for injection site type reactions to batch number 765484

B) Ten adverse event reports received for injection site type reactions to batch number 765751

C) Five adverse event reports received for injection site type reactions to batch number 766053

(Incomplete corrective action to the previous inspection of 2003)

14) Regarding product equipment compatibility study:

The [redacted] Tubing used throughout the Fluvirin manufacturing process to transfer centrifuged, formulated and finished product for filling was out specification of [redacted]mg for USP Non-Volatile Residue with result of 1327mg per [redacted] test result. No investigation, corrective and preventive action has been conducted and no justification/rationale is provided for the lack of investigation. **(Incomplete corrective action from previous inspection of 2003)**

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Dominique G. Dupuisanet, CBO Paula A. Trost, CBO John D. Reibsteiner, Ph.D. Supv. Chemist David S. Cho, Ph.D., Microbiologist Mark A. Elengold, Deputy Director Oper., CBER	15 October 2004

The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under unsanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."

Ms. ESHOO. And did you agree with your own inspectors?

Mr. CRAWFORD. That was about the 2001, 2002 production. The 2003 production was all right. The 2004 production was quite correctly condemned by FDA.

Ms. ESHOO. Dr. Crawford, let me ask you this: Did you agree with what the British Health Services did, or did you think that they were absolutely off on the wrong foot and that what they discovered you did not agree with?

Mr. CRAWFORD. We sent a team in and we authenticated what the British did, and that is why I made the decision to destroy the vaccine production.

Ms. ESHOO. You made that decision after October 5, or before October 5?

Mr. CRAWFORD. After, when we sent the team of inspectors in.

Mr. BILIRAKIS. The gentlewoman's time has expired.

Ms. ESHOO. If I might just finish my sentence, Mr. Chairman.

We have a problem, in my view, with the FDA. The FDA has been slow, the FDA has not been effective, the FDA has not been on the beat. And what Dr. Crawford just said is that they made a decision, essentially started singing off the same page as the British Health Service, after they shut the plant down.

Mr. CRAWFORD. I have to respond to that.

Mr. BILIRAKIS. Very quickly now.

Mr. CRAWFORD. Actually, the FDA did not cause the contamination. What the FDA did was order destroy the production; it couldn't be used, so the FDA did precisely what it was supposed to do.

Mr. BILIRAKIS. Mr. Deal to inquire.

Mr. DEAL. Thank you, Mr. Chairman.

Dr. Gerberding, you have a program known as Vaccines For Children, and I believe this past—this year you ordered like 4½ million doses under that program and got less than half of that. Do we have a similar stockpiling program for senior citizens? And if we do not, should we have one? And what kind of cost factor would there be?

Ms. GERBERDING. This was the first time that we had a stockpile of flu vaccine for children, and we originally had put our eggs in both baskets and ordered some from Chiron and some from Aventis. But when we could not receive the Chiron doses for the stockpile, we then purchased additional doses from Aventis. So we have about 4½ million doses of vaccine in that stockpile that have been used to support the immunization of at risk children and also children between the ages of 6 and 23 months.

We don't have a stockpile of vaccine for adults at this point in time, and I think that is one of the issues that needs to be thought about when we are trying to find solutions to the vaccine supply change. Would a stable market or would a purchase or guarantee of not having doses go to waste, or what are some of the ideas on how we could stabilize the market for the manufacturers and ensure that we had some reserves that could be distributed or allocated equitably if we had another crisis like this.

Mr. DEAL. As I indicated in my opening statement, the distribution issue is of concern to me and I think to a lot of people. The apportionment process that you participated in from the CDC I as-

sume was a voluntary approach by participating agencies who allowed you to be intervenor, if the word is correct, to make a distribution. Do you feel that we need to give statutory authority to your agency or some Federal agency that in a time of crisis you had that statutory authority to be an intervenor?

Ms. GERBERDING. We have been relying on statutory authority of the State health officials and local health officials, and I can't tell you yet whether we could improve upon that with a Federal authority or not. Our State health officials developed the criteria for the apportionment before they knew what that would mean to each of them in terms of doses, which was a very fair and equitable way of arriving at those decisions. So the apportionment was formula-based, and now they are in the challenging phase of allocating their apportionment to people who need it most. We will be assessing the success of this effort as it goes forward.

Mr. DEAL. I would like to ask that if you—in that assessment process if you could make recommendations in that regard. I think we would be interested in hearing that.

Ms. GERBERDING. Thank you.

Mr. DEAL. Dr. Crawford, with regard to the—one of the delays here was the fact that the British authorities under their law apparently could not, because of confidentiality rules, reveal to FDA some of the information that they had at an earlier stage. My question to you would be can FDA, in dealing with certification of manufacturers, especially foreign manufacturers, can you as a condition of certification require that they waive any national confidentiality rules such as the one here to avoid this in the future?

Mr. CRAWFORD. We are working with that with our attorneys, and I don't have an answer yet, but we are working on it.

Mr. DEAL. That would appear to me to be one of the things that you could put as a reasonable criteria for certification.

Mr. CRAWFORD. Thank you.

Mr. DEAL. And I forget who made the comment, but as somebody from the poultry capital of the world, where I have got at least one or two farmers that have got more chickens that I have people in my entire congressional district, somebody said something about you couldn't do it because of the availability of eggs. Dr. Fauci, was that you? Have we got an egg problem? I am accustomed to dealing with avian flu in my district, and we are more concerned sometimes about the chicken flu than we are the human flu. But this is a reversal here.

Mr. FAUCI. We don't have an egg problem in general, but when you start the process of getting chickens and then getting eggs that are prescreened eggs that you then use to inject the virus in to grow, it is a process that has to start off with a company getting the chickens, ordering them, getting them to lay the eggs, get the eggs, and then going through the process.

Mr. DEAL. Do we have to have special chickens to lay these eggs?

Mr. FAUCI. No, you don't have to have special chickens, but you can't just go running around the field and get chickens to start laying eggs.

Mr. DEAL. I am going to volunteer some of my poultry producers if that is the problem.

Mr. FAUCI. The fact is, Mr. Deal, that it is a process that takes months of sequential steps. So when you get to step 7 and something goes wrong, you can't just recreate the process. You have to go back again and start over, get new eggs, inject virus into the eggs, grow it up, kill the virus, process it, and put it into the vials.

Mr. DEAL. So I am assuming that if you make the determination of the species that you are going to go after in January, and it is only available until later in the fall of the year, it is in excess of a 6-month process?

Mr. FAUCI. Yes, it is in excess of a 6-month process. And that is the reason why one of the other Members had asked the question, let us say we knew in August or September, whatever it is, that we, in fact, needed to have more production, we couldn't just turn the clock back and start from square one. That is the issue at hand that sometimes gets lost in the process.

Mr. DEAL. Thank you.

Chairman BARTON [presiding]. The gentlelady from Illinois is recognized for 5 minutes for questions.

Ms. SCHAKOWSKY. Thank you, Mr. Chairman.

Dr. Crawford, Illinois Governor Rod Blagojevich sent a letter to the FDA on October 25 of this year asking the agency what needed to be done to get your approval to bring the vaccines that have already been committed now to Illinois, hundreds of thousands, into the State as soon as possible. I understand the vaccines have been manufactured by Aventis and GlaxoSmithKline. I also understood that earlier this week you indicated that the FDA will have a decision as to whether Illinois and New York actually will be able to bring these vaccines into the country within 2 or 3 weeks. So I wanted to ask you when Illinois can expect the decision, if you have any hint of whether or not we are going to be able to do that. And I would like to ensure today that the schedule is going to remain as you said and not longer.

Mr. CRAWFORD. As you may know, we immediately met with the Governor's staff, and we started the process. They shared with us some important information. We had to get the lot numbers. We have now verified the lot numbers with the production companies. Then we also had to accumulate what is called the pedigree, where all the vaccine had been, whether it had been in other countries, whether it had been kept under refrigeration or not. And then the final thing is we had to get information which is called a master file from these companies.

Ms. SCHAKOWSKY. You are talking about both companies?

Mr. CRAWFORD. Yes. And we have got all the data we need at this point, and we are sifting through it, and we should have a decision very soon. I might add that both that Governor and a number of others and the mayor of New York have been very cooperative with us.

Ms. SCHAKOWSKY. And have you been getting full cooperation from both the drug companies in providing the data that you need?

Mr. CRAWFORD. We have. We absolutely have. They are worried a little bit because they don't know where all the vaccine has been. There were rumors that it had been to other countries and then shipped back to England, where it had been amassed. But we have

assured the companies that we will know what that pedigree or history of the vaccine after it left their plant is.

Ms. SCHAKOWSKY. So they are fully cooperating?

Mr. CRAWFORD. They are fully cooperating.

Ms. SCHAKOWSKY. I wanted to go back to that document and your response to it that Ms. Eshoo had referred to on how—what you found in 2003 is nowhere related to 2004. And I am confused, and I want to again read this and the sentence that followed that wasn't read.

During the 2003 inspection, the firm was cited for failure to evaluate the reduction in—something—connection to reduce the possibility of contamination. There is—this is now from the 2004 report. There is no documentation that adequate corrective action has been conducted.

So if in 2004 you are finding that the corrective action that was expected was not taken, how is it that you can say that none of the previous problems that were detected affect what happened in 2004?

Mr. CRAWFORD. The citation that that refers to was for the 2001, 2002 production, and we closed out that investigation in 2003. And that is why 2003 shows up. But the 2003 production was fine. That vaccine was okay.

Ms. SCHAKOWSKY. There is no documentation that adequate corrective action has been conducted. Why is that noted during the—that adequate corrective action has not been taken? So I don't understand that.

Mr. CRAWFORD. What happened, they were referring to not 2003, but to 2002. And we did—what happened was they made the corrections, and then it seemed to have happened again. It is important to point out that Chiron did not own the plant until mid-2003, so they were not involved in their earlier violations.

Ms. SCHAKOWSKY. So there is no systemic underlying problem that you feel was identified?

Mr. CRAWFORD. No.

Ms. SCHAKOWSKY. Okay. Let me ask one quick question also. On October 5, have you gone back and gotten the British inspection reports that indicated the problems for—before you found out about them?

Mr. CRAWFORD. We are now—due to an agreement between the British Government, Chiron, and the U.S. Government, we are now able to share that information. So we have all that, yes.

Ms. SCHAKOWSKY. You have the full reports, and you have looked at those?

Mr. CRAWFORD. We do.

Ms. SCHAKOWSKY. Thank you very much.

Chairman BARTON. We thank the gentlelady.

The gentleman from Illinois Mr. Shimkus is recognized for 5 minutes for questioning.

Mr. SHIMKUS. Thank you, Mr. Chairman.

I think what we have learned today so far is this is a very capital-intensive business. It takes a long time, there is a lot of risk. There is just a risk in being able to identify the strain. And even though you put three strains in, who knows if it is the strain that is going to hit. Again, a lot of capital investment, risk in identifying

the influenza. There is risk in the liability concerns. All of this, it is when people invest capital dollars to hopefully at a minimum break even or make a profit, probably speaks to why we had five at one time and now have two. So if the government is going to be involved, we need to really ask the questions of how to encourage these businesses to continue to assume the risks, this capital expense in being in this business.

And there is a supply and demand equation. And I think since now we don't have the supply we need, there is also the debate and the discussion on demand; how do we work on restricting or identifying the individuals in need so that we can decrease the overall demand. We have done a good job of saying to the U.S., everybody get a flu shot. But when the supply is less, then we have to refocus. And I think of my friend Gene Green's question on help in getting information to States to help get that word out so that those most vulnerable, we are ensuring that they are the ones that have access to that.

I also find it curious in the FDA debate, and, Director Crawford, you are receiving the brunt of it, is that we applaud you for being able to find the bad batch before it was used. Safety and efficacy is the important thing. We have the same people not wanting you to do your job on the reimportation issue on safety and efficacy. I am sure you feel like a Ping-Pong ball; you can't do anything right sometimes. When you do a good job of finding the safety and efficacy, you get beat up on it, and then when you say you want to ensure safety and efficacy, you get beat up on it there. So isn't it great to be in public service and to your country?

Two questions. One is to Dr. Gerberding, and it deals with, again, the demand side, as I did in the little brief opening before the question. And since I represent a rural area of 30 counties in southern Illinois, there is always a concern that rural areas, smaller communities, and as we try to restrict demand to those who need, but then the population is oh so small, we don't want to be left out. I think we are fine if we know we have got a fair shot like everybody else, but there is always a fear that rural areas get left out in the apportionment of goods and services because our voice isn't—the 30 counties is not—my population in 30 counties is probably the same as a couple-block area in downtown Chicago. I mean, who do you hear more? So can you speak to that for a second?

Ms. GERBERDING. Just a quick frame. Of the people in high risk categories in normal years who should be vaccinated, we generally do not even vaccinate 50 percent. So we cannot, no matter how hard we push, create the demand even for the people who are the most vulnerable. That has been most frustrating. Actually, manufacturers have thrown away 35 million doses of vaccine in the last 3 or 4 years.

Mr. SHIMKUS. So another issue of return on investment, if you are making a product in a good year and you don't have the use.

Ms. GERBERDING. That is right. We generally have a surplus of vaccine, yet we are not vaccinating 100 percent of the people who need it.

With respect to the rural areas, in addition to making the very detailed information about who is receiving vaccine doses in the State available to the State health officers, we are in the process

of making that information available to the county health officials, so they will know how many high-risk people are in their county, what their needs are, and they can then work with the apportionment to the State and try to make sure they get a fair share of the State's vaccine allotment.

Mr. SHIMKUS. Dr. Fauci, can you explain briefly the difference between the live and the killed vaccine? We are going to hear from FluMist in the second panel. It is my understanding, and it may not be correct, does the military receive the live vaccine now? And from the NIH perspective, can you kind of explain what advantages that might have?

Mr. FAUCI. Well, the killed vaccine is thoroughly killed. As Dr. Gerberding mentioned at yesterday's hearing, there is no chance with a killed vaccine that there will be any replication or any chance of a person getting infected from it. It is a good vaccine, and it induces a good response.

The attenuated vaccine or live, weakened vaccine, the MedImmune FluMist, is also a very good vaccine. It has been attenuated by cold adaptation, which means it is grown out in the cold so that it can get into the nose and replicate a bit and produce a very robust immune response, but it doesn't have any chance because of how it has been selected, for example, to go into the lower respiratory tract and replicate there. So it is very safe.

There are theoretical possibilities that the replicating virus can be transmitted to someone else, but that is only a theoretical possibility. In fact, as a scientist who has been involved in attenuated vaccines for some time, I would predict that when further studies are done, it is going to be shown to be very safe and not having a problem of being transmitted inadvertently to someone else.

It has some distinct advantages. First of all, a live attenuated vaccine is almost invariably a more potent vaccine than is a killed vaccine because it mimics the natural infection better. In fact, we have some preliminary data from last year that people who were vaccinated with the attenuated vaccine, the FluMist, had a broader immunological response that covers cross-reacting viruses better than a killed vaccine.

So although there is a theoretical issue of it being able to be spread from person to person, in fact, I believe it is only theoretical, and I believe, in the long run, it will be shown to be a very good vaccine.

Mr. SHIMKUS. Thank you. I am going to be respectful of my time. I am going to just throw this out. I am not asking for an answer.

In the United States, have we done a job of educating so much on the need for flu vaccines that we have? I know we are not getting all the high-risk, but are we getting a lot of people taking the flu vaccine that probably you could argue did not need it?

Ms. GERBERDING. This year, we have early information about the low-risk people who have been vaccinated, and right now, it looks like less than 5 percent, which is not bad considering that we normally really make a push for everyone to receive a vaccine, and the first 33 million doses went out before the high-priority list was demonstrated.

Mr. SHIMKUS. Thank you, Mr. Chairman.

Chairman BARTON. We thank the gentleman from Illinois and recognize the distinguished gentleman from Florida, Mr. Stearns, for 5 minutes.

Mr. STEARNS. Thank you, Mr. Chairman.

I have a question I really want to ask for all three of you.

Dr. Crawford, I think I will start with you.

In my opening statement, I mentioned the unpredictability of this flu vaccine, whether it is the Tokyo flu or whether it is the Beijing flu, and all the strains and how they change as they move, so there is a nap shot that America tries to take of this flu vaccine, and they said, yes, we think in high probability that is the one that we should inoculate everybody for 18 months later or a year later.

So how does the unpredictability in the flu vaccine market hinder efforts to prepare for such a potential public health disaster? That is for each of you.

I will start with you, Dr. Crawford.

Mr. CRAWFORD. Well, as you mentioned, the Department of Health and Human Services does determine which strain or strains are most likely to be a problem. In my view, one of the things it does commercially is, that means you have to produce a new kind of vaccine every year, and that has got to be a strain on the companies.

Mr. STEARNS. For them to do that, that is more investment, with the possibility of——

Mr. CRAWFORD. That is my belief, yes.

Mr. STEARNS. Dr. Fauci?

Mr. FAUCI. I don't think that that is the most relevant area of risk for the company, because the determination is made by WHO, together with the CDC and the FDA, about what is going to go into the vaccine. Ninety percent of the time they are correct. It is usually based on which strains have been circulating, usually in the southern hemisphere.

Mr. STEARNS. So they are 90 percent correct every year?

Mr. FAUCI. They are usually quite good, anywhere between 80 and 90 percent.

Mr. STEARNS. So the evidence comes in after the flu vaccine season, and they say, by golly, it helped 90 percent of the people. How do they come up with the 90 percent? How do they come up with the 90 percent?

Mr. FAUCI. No, it doesn't help 90 percent of the people. What they do, when I say 90 percent correct, usually the decision that is made around January based on strains that have been circulating the previous season in the southern hemisphere, which is usually a good indication of some strains we might see in our own hemisphere toward the end of the season, you can make a pretty good determination, a guesstimate, about what is going to happen the following year. Based on that, the decision is made as to what goes into the vaccine.

When I say about 80 to 90 percent, I am not saying 80 to 90 percent effective. I mean 80 to 90 percent of the time, it is a correct match, that what you decided would go into the vaccine is actually——

Mr. STEARNS. Not efficacy, but match.

Mr. FAUCI. Right, and Dr. Gerberding can address that even more cogently since she is involved in that process.

Ms. GERBERDING. I just want to mention this is a global effort, because these strains emerge usually in other parts of the world. In the 2005 President's budget, there is a specific initiative to enhance our global detection capability so we can get our hands on the viruses that are emerging in Asia or in the Middle East or wherever the new flu strains are coming out.

So we are creating a network of laboratories that circumvent the globe and get those strains to Atlanta so they can be sequenced, and then we can utilize them in the NIH laboratories to create the seed virus.

But this is a system that is not complete yet, so we are making additional investments. We hope to make more investments in making sure that we are getting the strains in surveillance, and we are getting them sequenced so that we have a better chance of getting a 100 percent match between the likely viruses and what the manufacturers are creating.

Mr. STEARNS. So if you only get 90 percent, that sounds like a good figure. But if you get a 90 percent match, and you miss it by 10 percent, that means 10 percent of a lot of people are getting something they don't need or it is the wrong type of match for their flu.

Mr. FAUCI. No, that is 10 percent of the time.

Mr. STEARNS. Can I extrapolate to population? So if we had 36,000 people die because of a lack of flu shot, they had the flu and they didn't have the flu shot, 10 percent it wouldn't have mattered.

Mr. FAUCI. No, I am sorry. Ten percent of the time, you will have made a wrong match. So, for that year, 100 percent of the people who are getting the vaccine are not getting a correctly matched vaccine.

Ms. GERBERDING. I just need to clarify one thing, though. There are three strains.

Mr. FAUCI. I am sorry, that is correct. There are three in there. I didn't want to get too detailed about it, but there are three. For example, this year's vaccine has an H3N2, an H1N1 and a B, so there are three components, in that particular flu vaccine.

The one you are generally referring to is the one that gives the most trouble, is the A. Right now, the circulating virus we are seeing in the population is fundamentally a Fujian H3N2. There are others also there, but that is the predominant one right now, which is also contained in the vaccine.

So apropos of your question, it looks like this year is actually one of those 9 out of 10 correct matches.

Mr. STEARNS. Thank you.

Chairman BARTON. We welcome our distinguished member from Massachusetts, the home of the World Champion Boston Red Sox, to the hearing, and look forward to his questions.

Mr. MARKEY. Also the World Champion Boston Patriots, and the next president—no, no, that is different.

Thank you, Mr. Chairman. And the ranking minority member of the Telecommunications Subcommittee.

Dr. Crawford, I understand that in your response to an earlier question, you indicated that the contamination discovered in the

June 2003 inspection was corrected. However, the FDA's October 2004 report states that, during the 2003 inspections, the firm was cited for failure to evaluate the reduction in aseptic connections to reduce the possibility of contamination.

There is no documentation, Doctor, that adequate corrective action has been conducted.

That is the FDA. Is that report wrong?

Mr. CRAWFORD. The inspection took place in 2002. The report was closed out in 2003. The 2003 production of vaccine was perfectly all right. There were no violations. What happened was—they are talking about the 2002 problems surfaced again in part in 2004, 2 years later.

Mr. MARKEY. So you don't think that this is a case, a clear case, that it is not just a question of specific isolated problems at this plant, but a weakness in the overall system that created a risk of contamination?

Mr. CRAWFORD. The 2004 problem was a systematic breakdown. That did not occur in 2002 because we were able to salvage vaccine. We thought, at one point, we would be able to salvage 91 percent of this particular vaccine, and that was not the case. We had to make a decision that all of it was destroyed.

Mr. MARKEY. But your own report says that the problem has not been corrected.

Mr. CRAWFORD. No, the problem resurfaced. The 2003 vaccine was perfectly all right.

Mr. MARKEY. That is not what it says. It says there is no documentation that adequate corrective action has been conducted.

Mr. CRAWFORD. Well, yes. Yes, what happened was, in the 2002, we found violations, and then that was closed down in 2003. The 2003 production was okay. That proves they had made the corrections. They resurfaced in 2004, which is disturbing, and that is why we had to make the decision we did to destroy it.

Mr. MARKEY. So if there are contaminated connections between tanks in the production process that were identified in 2003 and not corrected in 2004 and which the company concluded was the cause of the contamination this year, why won't you admit that?

Mr. CRAWFORD. That was not 2003, that was 2002. The bio-burden, that is, the bacteria that were present in 2002, don't live long enough to be in the 2004 production. So what happened is the same kind of thing happened again.

Mr. MARKEY. If the problem hasn't been corrected, then it is going to come back.

Mr. CRAWFORD. It was corrected.

Mr. MARKEY. The report says it was not corrected.

Mr. CRAWFORD. In 2002, we had a problem with the fill. We made a report. We closed that report out in 2003. Some of the same kinds of problems did occur again in 2004. What happened in 2002 is not relevant to 2004.

Mr. MARKEY. Do you agree with that, Dr. Fauci? Is he correct in what he is saying?

Mr. FAUCI. I don't think I have enough knowledge of that report.

Mr. MARKEY. Dr. Gerberding, is he correct in what he is saying?

Ms. GERBERDING. This is the first I heard—yesterday and today—about connections and bio-burden, and I have not seen the reports.

Mr. MARKEY. You have never seen the reports. I am just afraid that the FDA has become the Mr. McGoo of the flu. You don't see things that everyone else sees, that there is obviously a problem that was identified, and it is still not being admitted by the FDA.

Mr. CRAWFORD. The FDA is a regulatory agency. What we did in August of this year is we caused all the production to be quarantined so it could not go into production, and then we ordered it destroyed. So we did precisely what we are supposed to do. And about Mr. McGoo, I don't agree with that.

Mr. MARKEY. You cited this problem in 2003 for this very same company.

Mr. CRAWFORD. No, it was 2002.

Mr. MARKEY. But you cited them in 2003.

Mr. CRAWFORD. No, we closed out the 2002 report in 2003.

Mr. MARKEY. So, in 2003, you gave them a clean bill of health?

Mr. CRAWFORD. Yes, the vaccine was fine in 2003. It was actually used in the United States, 48 million doses.

Mr. MARKEY. And you don't believe there was any reason then to pursue any further a vigorous investigation of whether or not there was contamination going on in the supply?

Mr. CRAWFORD. We did the no-release system, which is a painstaking process, for the 2003 lot, and the vaccine was perfectly okay, not a problem.

Mr. MARKEY. Thank you, Mr. Chairman.

Mr. WALDEN [presiding]. I now recognize myself for 5 minutes.

Dr. Crawford, I just want to make sure I understand this. In 2002, there was a problem. You identified the problem. You investigated the problem. The report came out in 2003, correct?

Mr. CRAWFORD. That is correct.

Mr. WALDEN. In 2003, you are keeping an eye on this situation. There was no problem. The vaccine was safe, and it was distributed properly.

Mr. CRAWFORD. Yes.

Mr. WALDEN. For the 2004 batch of vaccine, there was a problem similar to that in 2002?

Mr. CRAWFORD. Yes. It was much worse than 2002 because we had contamination in the final vials. That is the first time we had experienced that.

Mr. WALDEN. So what happened in 2004 is not what happened in 2002.

Mr. CRAWFORD. Not at all.

Mr. WELDON. Is it a problem with cleanliness in the lab? I don't know——

Mr. CRAWFORD. Some of the same kinds of things happened, but they were unrelated to what happened in 2002. There was a different company that was using the plant in 2002, so I don't think it was related.

Mr. WALDEN. Can you describe what it is specifically thought that occurred that might be similar?

Mr. CRAWFORD. Well, we——

Mr. WALDEN. The vials are not clean? Are they not purified?

Mr. CRAWFORD. With the flu vaccine, because of the eggs that they come from, there is this accumulation of bacteria, not only in the plant, but in the vaccine. And it is the role of the company to decontaminate both as they go through the production process.

In 2004, they were not able to do that, and so the plant was contaminated, and also the final doses of vaccine were contaminated. So that is what happened.

Mr. WALDEN. So what is it you can do or the company can do to ensure that the vaccine for 2005 doesn't face the same challenge? Are there good practices? You have put out a report, right, on the practices?

Mr. CRAWFORD. Yes.

Mr. WALDEN. What does that report say? What are we going to do to make sure this doesn't happen again, to the best of our ability?

Mr. CRAWFORD. What we are doing is we are working with Chiron, the company, and also the U.K., the regulatory agency there, to make a final decision on whether or not this plant can be relicensed. That has to be done under British rules and also for the company's benefit to produce vaccine for next year by January 2005. So we are working with them on that. We will know early enough.

Mr. WELDON. What happens if that plant can't be reauthorized?

Mr. CRAWFORD. Then we will have to seek sources from elsewhere for the vaccine.

Mr. WELDON. And what is the time line to secure that source?

Mr. CRAWFORD. Well, the vaccine production generally begins about the time we will know about this plant. We should be able to adequately seek additional sources.

Mr. WELDON. There are companies that would step in to the void and plants that could make the vaccine?

Mr. CRAWFORD. Dr. Gerberding might want to comment on that, but there are other manufacturers. They just do not choose to be in the U.S. market.

Mr. WALDEN. Dr. Gerberding?

Ms. GERBERDING. We know from the three companies that Dr. Crawford and FDA are investigating internationally right now that we may be able to get up to 5 million additional doses into the United States this flu season, so we would go first to those companies. But it would depend on whether or not they can increase their production and whether or not their product can be licensed in the United States, because bringing it in as an investigational drug is a lot more complicated than bringing it in as a fully licensed vaccine.

Mr. WALDEN. So what do we face? What are you all doing in the worst case scenario, which would be that Chiron cannot be reauthorized and this plant cannot be used? What is the backup? What is plan B here?

Ms. GERBERDING. Plan B will be to get any vaccine that we can from international sources into the country, whether it is licensed or not.

But setting aside that issue, obviously we are in communication with the two existing manufacturers in the United States to see

what can be done to maximize their production. They are not going to be able to fill in the gap.

Mr. WALDEN. That was my question. Can they produce 46 million or 48 million doses?

Ms. GERBERDING. 61 million. And even if they push it up by 10 percent, that is not necessarily going to solve the problem.

Mr. WALDEN. What do you think they could produce?

Ms. GERBERDING. Well, we are in conversations to see what is the best they can do with their existing production facilities. One thing we don't want to do is push so hard that we end up with the same kind of bio-burden problem that we have had with Chiron. So we have to be respectful that good manufacturing processes and safety have to be the overriding concern. So we have to then do what we are doing right now, which is, from the very beginning of the flu season, prioritize the vaccine and work with the manufacturers and the health officials and the jurisdictions to target immediately at the beginning of the flu season and to make sure that we have that plan in place before flu hits.

Mr. WALDEN. All right. My time has expired.

Now, I would like to recognize the gentleman from New Jersey, Mr. Ferguson, for 5 minutes.

Mr. FERGUSON. Thank you.

A number of the points and issues I wanted to talk about have been addressed, liability in particular and others. I do have a couple of questions for Dr. Gerberding, a couple of observations.

The focus that we have been talking about in terms of preventing a crisis in the future, obviously, that is a big part of the focus of today. But it doesn't take much imagination to consider a very serious scenario of another pandemic. The New York Times Magazine on November 7 talked about that a little bit. From what I understand, the prospect of a pandemic flu is not a question of really if, it is really more a question of when.

We had these disastrous flu pandemics in the past. In 1918, 500,000 people died in the U.S. alone. We have had subsequent pandemics in the fifties and seventies.

My friend, Mr. Markey, I am sure would remind us that 1918 was the last time the Boston Red Sox won the World Series before this year. We have had more frequent flu pandemics in this country than we have had Red Sox World Series championships. So the fact that the Red Sox won again this year may, in fact, be a signal that other things are in store.

But, in particular, I know there is a pandemic influenza preparedness and response plan that has been completed and provided to the public for a response. Planning, of course, is good, and it is important. But I am most interested in the actions we are taking in terms of the implementation of that plan.

Given the potential lack of a match between the available vaccines and a particular strain of influenza that could cause a pandemic, this means, obviously, that antiviral stockpiling is very important, something that I referred to in my opening statement and that we have discussed a little bit here.

How many antiviral medications do we currently have in our strategic national stockpile?

Ms. GERBERDING. Right now, we have enough of the Tamiflu for 2.6 million treatment courses, and we are in the process of purchasing enough Rimantadine, which could be used for treatment—but we are mainly focusing on that drug for prophylaxis—for about 5 million people.

This is the first time we have ever had these drugs in our stockpile, and we do look forward for opportunities to scale up that stockpile as we go forward in time, particularly of the Tamiflu, which is the drug that we would need to use if we had an avian problem.

Mr. FERGUSON. Is 2 million-something, it is a nice stockpile, but is that enough? Is that a large enough stockpile? I know that HHS has indicated through lots of different sources they think they could stockpile as much as for 40 million cases. We are talking about 2 million of Tamiflu; several million from other sources. We are talking about a country of almost 300 million people.

Ms. GERBERDING. Currently, today, our manufacturers estimate that they have the production capability to treat 40 million people for influenza. That would be a pretty big outbreak, if not a domestic pandemic, that would require us to need to treat 40 million people. Because, remember, even though there are many people who suffer complications from flu, the vast majority of us have an annoying illness and a couple days lost from work, but we don't need treatment, because we are not that ill and not vulnerable to the serious complications.

We would like to have enough capacity to assure that anybody who needed a dose could have it, and one of the ways of doing that is to expand our stockpile in the same way that we do drugs for terrorism events. So we would certainly prefer to have a larger stockpile.

Mr. FERGUSON. How are the essential personnel, military, health care workers? Do we have enough for essential personnel purposes in the stockpile? I am specifically speaking of the antivirals now.

Ms. GERBERDING. Yes, the antivirals can be used for treatment—in which case, it is a small number of tablets necessary—or for prophylaxis. In the case of prophylaxis, the need is much greater, because you have to take the prophylactic drugs as long as there is influenza in your community or in your setting. So that means that people could need to be on prophylactic drugs for longer periods of time.

Part of the planning for a pandemic includes some of the lessons that we learned from SARS, where we had no drug and we had no vaccine, but we had very serious and dangerous outbreaks. And we learned that other kinds of more traditional interventions also will need to play a role, like isolation and voluntary quarantine or even quarantine, if necessary.

Also, we are working with education systems to identify at what point would schools need to be closed, when would we set aside certain hospitals as flu hospitals and so on and so forth.

So the planning here is very complicated, but we are planning from the lessons learned from SARS. I think that was a very valuable help to us in recognizing the seriousness of what we face.

Mr. FERGUSON. Just very quickly, because my time is pretty much over, Tamiflu, much of the Tamiflu or all of the Tamiflu that we stockpile is made in Switzerland. Is that correct?

Ms. GERBERDING. I believe so.

Mr. FERGUSON. What provisions or thoughts or plans have been made for some sort of domestic production of antivirals that work?

Ms. GERBERDING. The same issues we are dealing with, with regard to vaccines, really apply to many antimicrobial agents as well, where the domestic market is small relative to the international market. And we face this problem with some of the countermeasures for terrorism threats as well where the drugs are actually not produced domestically. So I think many of the ideas and opportunities to solve the vaccine problem may have relevance to looking at these other antimicrobial agents as well.

Mr. FERGUSON. Well, I would just close by saying, I appreciate the work that you are doing, particularly with the stockpile. I happen to believe that antivirals are in many ways at least as important as the vaccine issue, and if we are going to be able to address the potential crisis, we need to make sure that we have an adequate stockpile. I would urge you and your colleagues to increase your work on that.

Thank you.

Mr. WALDEN [presiding]. The Chair recognizes the gentlewoman from New Mexico for 5 minutes for questions.

Ms. WILSON. Thank you, Mr. Chairman.

And I appreciate your willingness to come here today. This has affected all of us tremendously.

I have a question both for the FDA and the CDC. New Mexico, as well as New York City and Illinois, have joined together in trying to purchase 150,000 additional flu vaccine doses directly from companies in France and Germany. This is part of an effort that was initiated I think in the State of Illinois. What is the position of the CDC and the FDA on this effort?

Mr. CRAWFORD. We have been working with the Governors of those States to get them to do a couple of things in conjunction with FDA. One is to get the serial numbers. The other is to get the production information and distribution information.

We now have all of that in hand, and we are moving forward to a decision very quickly. I cannot say how we will decide at this point, but they have been very cooperative. They have helped us a great deal, as we have been on our quest to get as many doses as we can safely introduce into the U.S. So it is moving forward.

Ms. WILSON. When you say it is be moving forward quickly, how fast is this being expedited? And when can we expect a decision?

Mr. CRAWFORD. We should have a statement on it within the next few days. I wouldn't want to say exactly when, because we may actually need a bit more information about what countries the vaccine has been in, and we do need to go back to the primary manufacturers and make sure they will help us with some production information.

But we made those preliminary visits. Everything looks like it is great. I just can't say exactly when. But it will be sooner rather than later.

Ms. WILSON. Is it likely there will be any conditions placed only those vaccines if they are approved for importation?

Mr. CRAWFORD. Those vaccines are not approved in the U.S., so we will have to go into a special approval system, which is what we use for experimental products. It will require consenting on the part of the people that receive the vaccine, in all probability. We are working through that also, and that is part of what we are up to.

Ms. WILSON. Is the CDC involved in this, or is it strictly the FDA?

Ms. GERBERDING. The warrantee of the safety of the vaccines is an FDA responsibility, and we are very impressed how high safety is valued by the FDA. We want to be able to get safe doses of vaccine from any source we can. So once we know they are safe and they can be legally brought into the country, we will work with appropriate people to help allocate them from wherever they come from. We are interested in getting as many doses of safe and effective vaccine available to Americans as we can.

Ms. WILSON. Are there other sources of this vaccine? I know the States are pursuing this directly. But is the CDC pursuing purchasing other doses of vaccine for more distribution from the same sources?

Ms. GERBERDING. I believe Dr. Crawford has his eye on about 5 million doses of vaccine from three international markets, and we are working with Secretary Thompson and the Department to figure out how we can procure any of those that are determined to be safe and how we can then distribute them under this investigational drug status, which is a large scale effort that we have not undertaken on such a large scale before in our country.

It is not a simple process to deliver investigational drugs, but we have a whole team of people who are working on this and are already developing the human subjects process. So we are taking all the steps we can to deal with the regulatory requirements in advance of even the purchase of the drug.

Ms. WILSON. Let me shift gears here for a second and ask you, looking forward to how we can avoid this problem in the future. In 1994, as I understand it, we had 5 manufacturers of flu vaccine, at least that is the information I have been given, and we are now down to only two today supplying the American market.

How do we change this? Are we underpaying or undercompensating the people taking the risk to manufacture this stuff? Is that driven by the Federal Government, because we are buying so many doses of it that we really do control the market? Or is it a liability issue? We obviously need more sources of supply, and I would like your view on how we fix this.

Mr. FAUCI. Well, there are several that we all have been discussing for some time, and it has to do with everything from incentivizing the companies to get involved to, in some manner or form, reducing the risk that one has to face, risk of a very uncertain market, risk of the actual manufacturing process itself.

As we have often said, an important analogy is, if a company has an opportunity of making major investments in trying to develop a blockbuster drug versus a major investment to get into the vaccine field, most of the time, if you make a pure business decision,

it is going to be to go with less risk and more profit. So what we can do is everything from the research that I have discussed to some of the things about getting the awareness and the culture in this country of more vaccines for more people.

We are increasing the numbers of people to be vaccinated approaching close to if not 150 million people, as opposed to what it has been in the past, which has been much less.

Liability issues clearly are important. Perhaps tax incentives would be important. As I mentioned, the research. Taking the risk out and making this something that is an incentive for the companies to get involved.

So we have to partner with the companies. It all comes down to partnering with the companies.

Ms. WILSON. Thank you.

Mr. WALDEN. Thank you for your question.

I want to thank the panel for being here today. We certainly appreciate your input on this important issue, the public health. There are many more issues we need to discuss about how to fix the problem for the future and how we can partner with you to do that. So we appreciate your enlightened testimony today. You are now excused.

I would now like to call up the second panel, if you want to make your way forward. We have with us on the second panel Ms. Janet Olszewski, she is the director of the Michigan Department of Community Health; Mr. Mark Mlotek, the Executive Vice President of Henry Schein, Inc.; Mr. Alan Rosenbloom, President and CEO, Pennsylvania Health Care Association/Center for Assisted Living Management; Ms. Janet Heinrich, Director, Healthcare/Public Health Issues, U.S. Government Accountability Office; Peter Paradiso, Ph.D., Vice President, New Business Development, Wyeth; and Cathleen Coelingh, the Senior Director for Regulatory and Scientific Affairs, MedImmune, Inc.

We welcome you all here.

We will start with Janet Olszewski. Thank you for being here today. We look forward to your testimony. You will have 5 minutes. Of course, your full written testimony is in our record for us to read. Thank you.

STATEMENTS OF JANET OLSZEWSKI, DIRECTOR, MICHIGAN DEPARTMENT OF COMMUNITY HEALTH; JANET HEINRICH, DIRECTOR, HEALTHCARE/PUBLIC HEALTH ISSUES, U.S. GOVERNMENT ACCOUNTABILITY OFFICE; ALAN ROSENBLOOM, PRESIDENT AND CEO, PENNSYLVANIA HEALTH CARE ASSOCIATION/CENTER FOR ASSISTED LIVING MANAGEMENT; PETER R. PARADISO, VICE PRESIDENT, NEW BUSINESS DEVELOPMENT, WYETH; MARK E. MLOTEK, EXECUTIVE VICE PRESIDENT, HENRY SCHEIN, INC.; AND KATHLEEN COELINGH, SENIOR DIRECTOR OF REGULATORY AND SCIENTIFIC AFFAIRS, MEDIMMUNE, INC.

Ms. OLSZEWSKI. Thank you. Good afternoon, Mr. Chairman and distinguished members of the subcommittees. My name is Janet Olszewski, and I want to thank you for this opportunity to share Michigan's experience related to this year's influenza vaccine shortage.

Governor Granholm and I are committed to keeping Michigan's citizens safe and informed throughout this process and to assure that this situation does not repeat itself.

I am the director of the Michigan Department of Community Health, the State agency that houses the public health responsibilities for the State of Michigan. Today, I represent both the State of Michigan as well as the Association of State and Territorial Health Officials.

I would like to share Michigan's experience with the current flu vaccine shortage and then highlight three areas where we believe the Federal Government must provide effective leadership to avoid problems like those we are facing today.

These areas include ensuring a safe and adequate supply of flu vaccine every year; creating an adult immunization program; and maintaining and enhancing the infrastructure necessary for an optimal emergency response.

On Tuesday, October 5, 2004, after Chiron announced it was unable to deliver any vaccine to fill this year's orders, staff from our department and health departments across the country participated in an emergency call with the Association of State and Territorial Health Officials and the Centers for Disease Control to discuss possible strategies to manage the sudden vaccine shortage.

One of the responses that came from CDC, in consultation with the Advisory Committee on Immunization Practices, was to recommend that the vaccine that we have only be administered to individuals in a set of high-priority groups.

In Michigan, as in many States, most vaccine is purchased privately by physicians, hospitals, nursing homes and even major grocery and retail chain stores through distributors or directly from manufacturers such as Aventis. We knew this fact would make the job of tracking inventory and assuring that only people in priority categories achieve the vaccine extremely challenging. We also knew that we could not do it alone.

Using information from the CDC recommendations and other estimates, we determined that roughly 3.4 million or one-third of Michigan's citizens would be eligible for vaccination in the high-priority groups. Our first inventory after October 5 indicated we had approximately 500,000 doses in the State. We now know we will have just under 2 million doses of Aventis flu vaccine to vaccinate that high-risk group. This includes the 340,000 doses of redistributed vaccine that we expect to receive. And this would allow us to vaccinate only 58 percent of the high-risk groups if we knew that all doses were only going to high-risk groups. And as Dr. Gerberding indicated, there was some vaccine distributed before October 5, and that could have gone to other groups as well.

By Friday of that first week, we had engaged the leadership of the Michigan Association of Local Public Health—we have a robust local health department community in our State—to discuss how they would participate with us in responding to this crisis.

During that first week, we also made calls to grocery, retail and pharmacy associations to request that vaccine only be administered to individuals within the priority groups and to request that their members advise us of any vaccine supply they had.

As the situation unfolded, the State's response included tracking inventory and disease; establishing mechanisms for routine communications with our public and private partners and the general public; and developing a reallocation plan, which included a rapid response team made up of individuals from the State and local public health teams to allocate vaccine supply.

At the start of this event, outside of the vaccine that the State purchases for the Vaccine for Children Program, we had no method to track inventory. Therefore, in the week following the Chiron announcement, Michigan's 45 local health departments began the laborious task of calling all private physicians in their jurisdictions to identify who had extra vaccine and who was in need of vaccine.

To reach the broader public, the department sponsored a large press conference on October 13 that included representatives of all the major health plans, medical, osteopathic, pharmaceutical, and local and public health association, and we have continued those activities on a regular basis.

Because tracking vaccine was proving to be extremely challenging and we had anecdotal evidence that a few groups considered the CDC priority-group information to be advisory, the department took another step and issued a public health order that legally restricts vaccination to those in the priority populations. Several other States have also used their authority to issue such orders.

The flu vaccine shortage has stretched our staff within the department as well as the staff in local health departments to capacity and beyond. We have fielded numerous calls and e-mails from corporations administering vaccine, health-related organizations, private providers, consumers, all of whom are trying to get vaccines, all of whom are trying to get high-priority populations vaccinated.

Recently, the CDC and Aventis released information regarding where vaccine in Michigan has been distributed using the secure data network that Dr. Gerberding referenced in her testimony. In addition, they soon followed this information with information about how much more we could expect.

Although the details of how the States will physically receive and finance the remaining vaccine have not been fully explained, our task of smoothing out the distribution gaps should become easier now that we have this information.

We are very appreciative of the public-private partnership that the CDC and Aventis have forged during these trying times. Likewise, we are appreciative of the help we have received from all of our colleagues in local public health, provider offices, health-related institutions and agencies, major corporations and the general public.

However, I cannot stress enough how important it is for Congress to take steps now to prevent a similar shortage from occurring again. The Federal Government must start now to ensure that we have a reliable public health infrastructure to combat the flu, year in and year out. I will emphasize three components.

The Federal Government must take responsibility for ensuring a safe and adequate supply of flu vaccine every year. We now see States and municipalities individually scrambling to secure their

own additional supplies from Canadian and European sources because it is our obligation to take care of our citizens. This is not an effective approach to vaccine supply.

Only the Federal Government has the ability to assure an adequate and safe influenza vaccine supply each year. This is not the only supply crisis we have faced in recent years. However, it is the most significant.

The Federal Government should take whatever steps are necessary to ensure a stable supply. Relying simply on market forces does not work when it comes to flu vaccine. In order to assure the manufacture of adequate supply of vaccine, you may have to offer some types of financial guarantees to manufacturers, contract directly with suppliers, even if it means some years our supply exceeds actual demand.

We also need to develop the capability to produce vaccine throughout the year and to encourage additional manufacturers to enter the market.

Also, NIH research into new technologies to produce vaccine in more expeditious and efficient ways are necessary.

Finally, the recent news that intradermal injection of inactivated flu vaccine could produce an immune response in selected populations using fractional doses would also help the supply issue, if it is pursued, and we believe it should be.

Also, it is important that the Federal Government should help in creating an adult immunization program. Ninety percent of the 36,000 influenza-related deaths that occur each year in the U.S. are among those 65 and older. Due to influenza's profound impact on older adults' health, the ACIP broadened the recommendations for flu vaccine in 2002 to include adults age 50 to 64 in addition to older adults.

One objective of Healthy People 2010 is to achieve 90 percent coverage of non-institutionalized adults. However, as you have heard, we often vaccinate less than 50 percent.

There is no specific Federal CDC funding available to States or the private sector for adult vaccination programs. All immunization grants are intended to serve childhood vaccination programs before serving adults, and the grants have been insufficient to meet both needs.

Funding for adult immunization programs would not only assist in achieving our objective of vaccination, but it would decrease morbidity and mortality from influenza and pneumonia and also therefore reduce health care costs.

Finally, the Government must help us maintain and enhance the infrastructure necessary for optimal emergency response. We must better address the issues of both communication and the ability to redirect allocation of supply. A decentralized ordering and distribution system, such as the one we have now, requires strong provisions for communication regarding the location of existing supply and the ability to redirect allocation.

CDC's Secured Data Network has worked well in disseminating vital information these last couple of weeks and has made the reallocation during Phase II far less burdensome than Phase I. We recommend that it be used regularly throughout the flu season to

communicate flu vaccine allocation patterns to public health officials.

We have also depended on our emergency preparedness network during this shortage. Both State and local health jurisdictions have used their emergency preparedness contact system, known as the Help Alert Network, to send and receive information. This system was built after 9/11 to address cases of bioterrorism, but the vaccine crisis demonstrates the importance of this infrastructure to an adequate and timely response to a wide variety of public health events.

Continued and enhanced Federal support for Michigan and other States' emergency preparedness is absolutely vital. Likewise, our public health order served our citizens well by restricting the use of flu vaccine. We advocate that the Department of Health and Human Services have similar authority to potentially restrict the use and to manage allocation of flu vaccine during severe shortages.

Thank you for the opportunity to speak with you today.

[The prepared statement of Janet Olszewski follows:]

PREPARED STATEMENT OF JANET OLSZEWSKI, REPRESENTING MICHIGAN DEPARTMENT OF COMMUNITY HEALTH AND THE ASSOCIATION OF STATE AND TERRITORIAL HEALTH OFFICIALS

Good morning Mr. Chairmen and distinguished members of the Subcommittees. My name is Janet Olszewski and I want to thank you for this opportunity to share Michigan's experience relating to this year's influenza vaccine shortage. Governor Granholm and I are committed to keeping Michigan's citizens safe and informed throughout this process.

I am the Director of the Michigan Department of Community Health (MDCH), the state agency that houses the public health administration responsibilities for the State of Michigan. I earned my master's degree in social work from the University of Michigan and obtained my undergraduate degree from Boston University. I have worked for the State of Michigan, in a variety of public health roles for over 25 years, and also served as Vice President for Government Programs and Regulation at M-CARE, a managed care company owned by the University of Michigan.

Today I represent both the State of Michigan as well as the Association of State and Territorial Health Officials. I would like to share Michigan's experience with the current flu vaccine shortage and then highlight three areas where we believe the federal government must provide effective leadership to avoid problems like those we are facing today. These areas include:

1) Ensuring a safe and adequate supply of flu vaccine every year;
2) Creating an adult immunization program; and
3) Maintaining and enhancing the infrastructure necessary for an optimal emergency response.

BACKGROUND/MICHIGAN EXPERIENCE

On Tuesday, October 5, 2004, after Chiron announced it was unable to deliver any vaccine to fill this year's orders, staff from MDCH and health departments across the country participated in an emergency call with the Association of State and Territorial Health Officials (ASTHO) and the Centers for Disease Control and Prevention (CDC) to discuss possible strategies to manage the sudden vaccine shortage. One of the first responses came from the CDC, who in consultation with the Advisory Committee on Immunization Practices (ACIP), recommended inactivated flu vaccine be administered only to individuals within the following priority groups this flu season:

- all children aged 6-23 months;
- adults aged >65 years;
- persons aged 2-64 years with underlying chronic medical conditions;
- all women who will be pregnant during the influenza season;
- residents of nursing homes and long-term care facilities;
- children aged 6 months-18 years on chronic aspirin therapy;

- health-care workers involved in direct patient care; and
- out-of-home caregivers and household contacts of children aged <6 months.

In Michigan, as in many states, most vaccine is purchased privately by physicians, hospitals, nursing homes, and even major grocery and retail stores through distributors or directly from manufacturers such as Aventis. We knew this fact would make the job of tracking inventory and assuring that only people in priority categories receive the vaccine extremely challenging. We also realized we could not do it alone.

Using information from the CDC recommendations and other estimates from the CDC, our staff determined that roughly 3.4 million "priority" Michigan residents would be eligible for vaccination, representing over one third of Michigan's population. Our first inventory after October 5 indicated we had approximately 500,000 doses within the state. We now know we will have just under 2 million doses of Aventis flu vaccine, which will be available to vaccinate those 3.4 million residents. This includes the 340,000 doses of redistributed vaccine that Michigan expects to receive from Aventis.

By Friday of that first week, MDCH had engaged the leadership of the Michigan Association of Local Public Health, an organization of county health departments, in discussions to determine the role of local public health in responding to this crisis. We also convened a meeting of public health and academic physicians to make recommendations about further prioritizing within the CDC priority groups.

During the first week, calls were also made to grocery, retail and pharmacy associations to request that vaccine only be administered to individuals within the priority groups and to request that their members advise us of any vaccine supply they had. As the situation unfolded, the State's response included tracking vaccine inventory and influenza disease, establishing mechanisms for routine communications with private and public partners and the general public, and developing a reallocation plan, which included establishing a "rapid response team" made up of individuals from state and local public health agencies to allocate vaccine supply.

At the start of this event, aside from the vaccine that the State purchases for the Vaccines for Children Program, there was no method to track vaccine inventory. Therefore, in the week following the Chiron announcement, Michigan's 45 local health departments began the laborious task of calling all private providers in their jurisdictions to identify who had extra vaccine and who was in need of vaccine. To reach the broader public, the Department sponsored a large press conference on October 13th that included representatives of major health plans and medical, osteopathic, pharmaceutical, and local public health associations and have continued those activities on a regular basis. Because tracking vaccine was proving to be extremely challenging and we had anecdotal evidence that a few groups considered the CDC priority group information to be advisory, the Department took another step and issued a public health order that restricted vaccination to those in the priority populations. Several other states have also used their authority to issue public health orders.

The flu vaccine shortage has stretched the Michigan Department of Community Health's Division of Immunization to capacity and beyond. In addition to countless emails from the public, local public health agencies, health-related organizations and other corporations administering vaccines, staff have received numerous calls from individuals and agencies with requests for detailed information, such as locating vaccine sources, explaining the priority groups and how they were determined, and discussing the public health order. We are pleased to note that most providers have welcomed the order as a way of explaining to patients the rationale for adhering to the CDC's priority groups. And, to our knowledge, all providers have willingly followed the order.

In addition to the Immunization staff, the flu vaccine shortage has required the involvement of all of our senior-level management, public information personnel and some of our emergency preparedness personnel to manage state level planning, logistics, communication and coordination of activities.

Recently the CDC and Aventis released information regarding where vaccine in Michigan has been distributed using the CDC's Secure Data Network. In addition, they soon followed this information with data about how much more vaccine Michigan could expect this flu season. We will receive 340,000 doses, as I mentioned previously. Although the details of how the states will physically receive and finance the remaining vaccine have not been fully explained, our task of "smoothing" out the distribution gaps should become easier.

We are very appreciative of the public-private relationship that the CDC and Aventis have forged during these trying times. Likewise, we are appreciative of the help we have received from our colleagues in local public health, provider offices, health-related institutions and agencies, major corporations and the general public

in Michigan during this flu vaccine shortage. However, I cannot stress enough how important it is for Congress to take steps now to prevent a similar shortage from occurring again.

RECOMMENDATIONS

The federal government must start now to ensure that we have a reliable public health infrastructure to combat the flu year in and year out. I will emphasize three components of an effective national flu fighting strategy that will ensure a stable flu vaccine supply and develop systems to ensure maximum coverage of target populations:

1) The federal government must take responsibility for ensuring a safe and adequate supply of flu vaccine every year

We see states and municipalities individually scrambling to secure their own additional supplies of vaccine from Canadian and European sources because of our obligation to take care of our citizens, and advocating with FDA to approve the sources. This is not an effective approach to vaccine supply.

Only the federal government has the ability to assure adequate and safe influenza vaccine supply each year. The current supply crisis is not the only one we have experienced in recent years. However, this is the most significant. The federal government should take whatever steps are necessary to ensure a stable supply in future years.

Relying simply on market forces does not work when it comes to the flu vaccine. In order to ensure manufacture of adequate volumes of vaccine, the federal government may have to offer some type of financial guarantee to manufacturers, or contract directly with suppliers, even if it means that in some years our supply exceeds the actual demand for vaccine.

Developing the capability to produce vaccine throughout the year and encouraging additional manufacturers to enter the market are two initiatives to address this issue. Also, NIH research to investigate new technologies to produce flu vaccine in more expeditious and efficient ways are necessary. Finally, recent news that intradermal injection of inactivated flu vaccine could produce an immune response in selected populations using fractional doses is both a supply and cost issue and this option should be pursued.

2) The federal government must help create an adult immunization program

A robust adult immunization program is necessary because approximately 90% of the annual 36,000 influenza-related deaths that occur in the U.S. are among those aged 65 and older. Due to influenza's profound impact on older adult health, ACIP broadened the recommendations for flu vaccination in 2002 to include adults aged 50-64 years in addition to adults 65 years and older.

This season, adults recommended to receive inactivated influenza vaccine include those with chronic medical conditions or weakened immune systems, those aged 65 and older or those in contact with high priority groups, such as most health care workers or caregivers to children aged less than six months.

One objective of Healthy People 2010 is to achieve 90% coverage of non-institutionalized adults aged 65 years and older for both influenza and pneumococcal vaccinations. However, the CDC reported recently that perhaps only 50-60% of those eligible for influenza vaccination in this population receive it in a given season. There is no specific federal/CDC funding available to the states or the private sector for adult vaccination programs; all immunization grants are intended to serve childhood vaccination programs before serving adults, and the grants have been insufficient to meet both childhood and adult needs.

Funding for adult immunization programs in the United States would not only assist achieving the national 2010 health objective, but decrease morbidity and mortality from influenza and pneumonia in the U.S. population. It would also reduce health care costs because morbidity and mortality would be reduced.

3) The federal government must maintain and enhance the infrastructure necessary for an optimal emergency response

In addition to the supply problems, the infrastructure necessary for an optimal emergency response requires several elements related to the distribution of vaccine.

We must better address issues of both communication and the ability to re-direct allocation. A decentralized ordering and distribution system requires strong provisions for communication regarding location of existing supply and the ability to redirect allocation. The CDC's Secure Data Network has worked well in disseminating vital information these last couple of weeks and has made vaccine re-allocation dur-

ing phase II far less burdensome than in phase I. We recommend that it be used regularly throughout the flu season to communicate flu vaccine allocation patterns to public health officials.

We have depended on Michigan's emergency preparedness network during the vaccine shortage. Both the State and local health jurisdictions have used the emergency preparedness contact system (the Health Alert Network) to send and receive information from providers and other health care colleagues. This system was built after 9/11 to address cases of bioterrorism, but the vaccine crisis demonstrates the importance of this infrastructure to an adequate and timely response to a wide variety of public health events. Continued and enhanced federal support for Michigan and other states' emergency preparedness is absolutely vital.

Likewise, Michigan's public health order has served our citizens well by restricting the use of flu vaccine to those individuals in the CDC's priority groups. We advocate that the Department of Health and Human Services have similar authority to potentially restrict the use and to manage the allocation of flu vaccine during severe shortages.

Thank you for this opportunity to speak with you today. I believe addressing these critical issues should be made a priority by Congress in order to protect our communities and avoid a potential large-scale flu outbreak. I would be pleased to answer any questions you may have.

Mr. WALDEN. Thank you.

Again, just a reminder to the other panelists of the 5-minute rule, if you could.

Ms. Heinrich, thank you for being here today. We look forward to your comments.

STATEMENT OF JANET HEINRICH

Ms. HEINRICH. Mr. Chairman and members of the subcommittees, I am pleased to be here today to discuss issues regarding the annual production and distribution of flu vaccine and efforts to target high-risk populations when there are shortages.

Each year, influenza viruses are associated with deaths and hospitalizations, especially for persons age 65 and over. The best way to prevent influenza is to be vaccinated each year. But in the past several years, this country has experienced periods when the demand for flu vaccine exceeded the supply.

Ensuring an adequate and timely supply of vaccine is difficult under the best of circumstances and has become more so with only a few manufacturers. As we are seeing this year, problems at one manufacturer can significantly upset the fall delivery of vaccine and cause fluctuations in who has ready access to the vaccine.

Those who ordered from the manufacturer experiencing problems did not have any vaccine even for high-risk patients, while other providers who ordered the vaccine from the manufacturer without the problems could hold clinics in early October that were available to anyone who wanted a vaccination.

Matching the supply and demand is also a challenge. For example, in work we did in 2000-2001, we saw a substantial proportion of flu vaccine distributed much later than usual due to manufacturing problems, causing temporary shortages, but then was followed by decreased demand as more vaccine became available later in the year.

Last year's shortages of vaccine have been attributed to an earlier than expected and more severe flu season and to higher than normal demand, likely resulting from the media coverage of pediatric deaths associated with influenza. So far this year, clearly, demand is outpacing the available supply.

Our work has also found continuing obstacles to delivering flu vaccine to high-risk individuals in a time of short supply, as we have just heard. During the fall 2000 vaccine shortage, for example, many physicians reported that they felt they did not receive priority for vaccine delivery, even though about two-thirds of seniors generally get their flu vaccinations in medical offices.

For the current season, we have heard that CDC has revised its recommendations for vaccination to include only the estimated 85 million people in high-risk groups as well as about 13 million people in other priority groups, such as health care providers. Although HHS has limited authority to control distribution, it is working with the remaining major manufacturers as well as the State and local health departments to assess needs, prioritize customers and make plans to redirect the remaining vaccine.

While CDC can recommend and encourage providers to immunize high-risk patients first, it does not have direct control over the distribution and cannot ensure that its priorities will be implemented.

As these actions play out, more time is needed to gauge the success of the CDC's efforts to mitigate the current flu vaccine shortage and direct the vaccine to high-risk individuals.

In conclusion, ensuring an adequate and timely supply of vaccine to protect high-risk individuals from influenza and flu-related complications continues to be a challenge. The limited number of manufacturers and the problems experienced in recent years illustrate the fragility of the vaccine production process.

The abrupt loss of nearly half of the Nation's vaccine supply has further highlighted the potential inequities that can result from the current vaccine distribution system. Despite efforts by CDC and others, there remains no system to ensure that persons at high risk from complications receive the vaccine first when vaccine is in short supply.

Mr. Chairman, that concludes my statement. I am happy to answer any questions.

[The prepared statement of Janet Heinrich follows:]

PREPARED STATEMENT OF JANET HEINRICH, DIRECTOR, HEALTHY CARE—PUBLIC ISSUES, U.S. GOVERNMENT ACCOUNTABILITY OFFICE

Messrs. Chairmen and Members of the Subcommittees: Thank you for the opportunity to be here today as you discuss the nation's response to problems with the supply and distribution of influenza vaccine. This year's loss of roughly half of the country's supply of flu vaccine highlighted what has become a growing problem—the fragility of the vaccine production and distribution system. We have been monitoring this issue for a number of years, and we are starting new work for the House Committee on Government Reform to analyze this year's situation in greater detail. My testimony today focuses on (1) the challenges in ensuring adequate supply to meet demand for vaccine and (2) the mechanisms in place to target high-risk populations when, as happened this year, a vaccine shortage occurs.

My remarks are based on reports and testimony we have issued since May 2001 [1] as well as work conducted to update key information. Our prior work on flu vaccine included analysis of information provided by and interviews with Department of Health and Human Services (HHS) officials, vaccine manufacturers, medical distributors and their trade associations, companies that provide flu vaccinations at retail outlets and work sites, physician and other professional associations, and other purchasers. We also surveyed physician group practices and interviewed health de-

[1] See "Related GAO Products," at the end of this testimony, for a list of our earlier work related to flu vaccine.

partment officials in all 50 states about their experiences in the 2000-2001 flu season. In September and November 2004 we updated this work with analysis of information provided by Centers for Disease Control and Prevention (CDC) officials, one major manufacturer, and other sources. We obtained information on (1) the available doses and demand for the 2002-2003 and 2003-2004 flu seasons, (2) the status of this year's flu vaccine, and (3) CDC activities, including actions taken following the announcement that one major manufacturer could not supply any vaccine for the U.S. market this year. We conducted all of our work in accordance with generally accepted government auditing standards.

In summary, the current situation demonstrates the challenges of ensuring an adequate and timely flu vaccine supply. Only three manufacturers produce flu vaccine for the U.S. market, and the potential for future manufacturing problems such as those experienced both this year and to a lesser degree in previous years is still present. When shortages occur, their effect can be exacerbated by the existing distribution system. Under this system, health providers and vaccine distributors generally order a particular manufacturer's vaccine and have limited recourse, even for meeting the needs of high-risk persons, if that manufacturer's production is adversely affected. By contrast, providers who purchased vaccine from a different manufacturer might receive more of their order and be able to vaccinate their high-risk patients.

The current situation also reflects another concern: the nation lacks a systematic approach for ensuring that seniors and others at high risk for flu-related complications receive flu vaccine when it is in short supply. Once this year's shortage became apparent, CDC took a number of steps to influence distribution patterns to help providers get some vaccine for their high-risk patients. These steps are still playing themselves out, and it will take more time to assess how well they will work. Problems have not been totally averted, however, as there have been media reports of long lines to obtain limited doses of vaccine and of high-risk individuals unable to find a flu vaccination in a timely fashion.

BACKGROUND

Influenza is associated with an average of more than 200,000 hospitalizations and 36,000 deaths each year in the United States. Most people who get the flu recover completely in 1 to 2 weeks, but some develop serious and life-threatening medical complications, such as pneumonia. People who are aged 65 and older, people of any age with chronic medical conditions, children younger than 2 years, and pregnant women are more likely to get severe complications from influenza than other people.[2]

For the 2004-2005 flu season, CDC initially recommended in May 2004 that about 185 million Americans—about 85 million in high-risk groups and over 100 million in other target groups—receive the vaccine, which is the primary method for preventing influenza. Groups at high-risk for flu-related complications included people aged 65 years or older; residents of nursing homes and other chronic-care facilities; people with chronic conditions such as asthma and diabetes; children and adolescents aged 6 months to 18 years who are receiving long-term aspirin therapy; pregnant women; and children aged 6 to 23 months. Other target groups identified in the May 2004 recommendations included persons aged 50 to 64 years and people who can transmit influenza to those at high-risk, such as health care workers, employees of nursing homes, chronic-care facilities, and assisted living facilities, and household contacts of and those who provide home care to high-risk individuals.[3] Not everyone in these high-risk and target groups, however, receives a vaccination each year. For example, based on the 2002 National Health Interview Survey and other sources, CDC estimates that only about 44 percent of individuals at high-risk and about 20 percent of individuals in the other target groups were vaccinated.

It takes about 2 weeks after vaccination for antibodies to develop in the body and provide protection against influenza virus infection. CDC recommends October through November as the best time to get vaccinated because the flu season often starts in late November to December and peaks between late December and early March. However, if influenza activity peaks late, vaccination in December or later can still be beneficial.

---

[2] Influenza and pneumonia rank as the fifth leading cause of death among persons aged 65 and older. Persons aged 65 and older are involved in more than 1 of 2 hospitalizations and 9 of 10 deaths related to influenza.

[3] See HHS, Centers for Disease Control and Prevention, "Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP)," *Morbidity and Mortality Weekly Report,* vol. 53 (2004). CDC also recommended a vaccination for anyone who wanted one.

Producing sufficient quantities of influenza vaccine is a complex process that involves growing viruses in millions of fertilized chicken eggs. This process, which requires several steps, generally takes at least 6 to 8 months from January through August each year, so vaccine manufacturers must predict demand and decide on the number of doses to produce well before the onset of the flu season. Each year's vaccine is made up of three different strains of influenza viruses, and, typically, each year one or two of the strains is changed to better protect against the strains that are likely to be circulating during the coming flu season. The Food and Drug Administration (FDA) and its advisory committee decide which strains to include based on CDC surveillance data, and FDA also licenses and regulates the manufacturers that produce the vaccine for distribution in the United States.

In a typical year, manufacturers make flu vaccine available before the optimal fall season for administering flu vaccine. For the 2003-2004 flu season, two manufacturers—one with production facilities in the United States and one with production facilities in the United Kingdom—produced about 95 percent of the vaccine for the United States. A third U.S. manufacturer produces a flu vaccine that is given by nasal spray and is only approved for healthy persons aged 5 through 49 years. This nasal spray vaccine is not recommended for individuals at high risk for flu-related complications. According to CDC, this manufacturer produced about 4 million doses of the nasal spray vaccine for the 2003-2004 season.

Flu vaccine production and distribution are largely private-sector responsibilities. Like other pharmaceutical products, flu vaccine is sold to thousands of purchasers by manufacturers, numerous medical supply distributors, and other resellers such as pharmacies. These purchasers provide flu vaccinations at physicians' offices, public health clinics, nursing homes, and at nonmedical locations such as workplaces and various retail outlets. Millions of individuals receive flu vaccinations through mass immunization campaigns in these nonmedical settings, where organizations such as visiting nurse agencies under contract administer the vaccine.[4] In a typical year, most influenza vaccine distribution and administration are accomplished within the private sector, with relatively small amounts of vaccine purchased and distributed by CDC or by state and local health departments.

For the 2004-2005 season, CDC had estimated that about 100 million doses of flu vaccine would be available for distribution through this network. On August 26, 2004, one major manufacturer announced a small quantity of its flu vaccine did not meet sterility specifications and that distribution of its vaccine would be delayed until after further tests were completed. On October 5, 2004, this manufacturer announced that the regulatory body in the United Kingdom, the Medicines and Healthcare Products Regulatory Agency (MHRA), had temporarily suspended the company's license to manufacture flu vaccine in its facility in Liverpool, England. The manufacturer stated that this action prevented the company from releasing any vaccine for the 2004-2005 flu season—effectively reducing the anticipated U.S. supply by nearly half. This sudden disruption of the supply set off the chain of events the nation has experienced in the past 6 weeks, and has focused national attention on the flu vaccine supply and distribution system.

CHALLENGES EXIST IN ENSURING AN ADEQUATE AND TIMELY FLU VACCINE SUPPLY

Ensuring an adequate and timely supply of vaccine is a difficult task. It has become even more difficult because there are few manufacturers. As we are witnessing this year, problems at one or more manufacturers can significantly upset the traditional fall delivery of influenza vaccine. These problems, in turn, can create variability in who has ready access to the vaccine.

Matching flu vaccine supply and demand is a challenge because the available supply and demand for vaccine can vary from month to month and year to year, as the following examples illustrate.

• In 2000-2001, when a substantial proportion of flu vaccine was distributed much later than usual due to manufacturing difficulties, temporary shortages during the prime period for vaccinations were followed by decreased demand as additional vaccine became available later in the year. Despite efforts by CDC and others to encourage people to seek flu vaccinations later in the season, providers still reported a drop in demand in December. The light flu season in 2000-2001, which had relatively low influenza mortality, probably also contributed to the lack of interest. As a result of the waning demand that year, manufacturers and distributors re-

[4] Data collected by states through the CDC Behavioral Risk Factor Surveillance System during 2002 indicate that among persons aged 18 years or older reporting receipt of flu vaccine, about two-thirds reported getting their last flu vaccination at a health care facility, such as a doctor's office, health center, or health department, while about one-third reported getting vaccinated at a workplace, community center, store, or other location.

ported having more vaccine than they could sell. In addition, some physicians' offices, employee health clinics, and other organizations that administered flu vaccinations reported having unused doses in December and later.

• For the 2002-2003 flu season, according to CDC officials, vaccine manufacturers produced about 95 million doses of vaccine, of which about 83 million doses were used and about 12 million doses went unused.

• For the 2003-2004 flu season, shortages of vaccine were attributed to an earlier than expected and more severe flu season and to higher than normal demand, likely resulting from media coverage of pediatric deaths associated with influenza. According to CDC officials, this increased demand occurred in a year in which manufacturers had produced about the same number of doses used in the previous season—about 87 million doses total—and that supply was not adequate to meet the demand.

If production problems delay or disrupt the availability of vaccine in a given year, the timing for an individual provider to obtain flu vaccine may depend on which manufacturer's vaccine it ordered. This happened in the 2000-2001 season, and there are reports of similar problems this season after one manufacturer that had previously stated it expected to supply 46 million to 48 million doses announced that it would not deliver any flu vaccine to the U.S. market. Those who ordered from this manufacturer did not receive their expected vaccine—a different situation than those who ordered from the other manufacturer, which reported sending its vaccine on schedule beginning in August and September. As a result, one provider could have held vaccination clinics in early October that would be available to anyone who wanted a flu vaccination, while another provider may not yet have had any vaccine for its high-risk patients.

Shortages of flu vaccine can result in temporary spikes in the price of vaccine. When vaccine supply is limited relative to public demand for flu vaccinations, distributors and others who have supplies of the vaccine have the ability—and the economic incentive—to sell their supplies to the highest bidders rather than filling the lower priced orders they had already received. When there was a delay causing a temporary shortage of vaccine in 2000, those who purchased vaccine that fall—because their earlier orders had been canceled, reduced, or delayed, or because they simply ordered later—found they paid much higher prices. For example, one physician's practice ordered flu vaccine from a supplier in April 2000 at $2.87 per dose. When none of that vaccine had arrived by November 1, the practice placed three smaller orders in November with a different supplier at the escalating prices of $8.80, $10.80, and $12.80 per dose. On December 1, the practice ordered more vaccine from a third supplier at $10.80 per dose. The four more expensive orders were delivered immediately, before any vaccine had been received from the original April order.

With the severely reduced vaccine supply this year, opportunities exist for vendors who have vaccine to significantly inflate the price of available supplies. CDC is collecting information on allegations of such price increases and is providing information to respective state attorneys general. To date, CDC officials report receiving and forwarding over 100 reports of alleged price gouging that they received from 33 states.

Following the 2000-2001 flu season, HHS undertook several initiatives to address supply and demand of flu vaccine and to protect high-risk individuals from flu-related complications when vaccine is in short supply. Actions taken include the following:

- Extending the optimal period for getting a flu vaccination until the end of November, to encourage more people to get vaccinations later in the season.
- Expanding the target population to include children aged 6 through 23 months.
- Including the flu vaccine in the Vaccines for Children (VFC) stockpile to help improve flu vaccine supply. For the 2004-2005 flu season, CDC had originally contracted for a stockpile of approximately 4.5 million doses of flu vaccine through its VFC authority—of which 2 million doses were ordered from the manufacturer whose license was temporarily suspended and therefore will not be available. CDC officials said the remaining 2.5 million doses intended for the stockpile will be apportioned as they become available.
- Taking steps to identify additional sources of influenza vaccine from foreign manufacturers that, once approved for safe use, could help increase the flu vaccine supply in the United States.

CHALLENGES PERSIST IN TARGETING FLU VACCINE TO HIGH-RISK INDIVIDUALS

Our work has also found continuing obstacles to delivering flu vaccine to high-risk individuals in a time of short supply. During the fall 2000 vaccine shortage,

for example, targeting limited doses to high-risk individuals was problematic because all types of providers served at least some high-risk individuals. Some physicians and public health officials were upset when their local grocery stores were offering flu vaccinations to everyone when they, the health care providers, were unable to obtain vaccine for their high-risk patients. Many physicians reported that they felt they did not receive priority for vaccine delivery, even though about two-thirds of seniors—one of the largest high-risk groups—generally get their flu vaccinations in medical offices.

For the 2004-2005 flu season, despite early indications that one manufacturer was having production difficulties, CDC published guidance in September 2004 stating that it did not envision any need for tiered vaccination recommendations or prioritization of vaccine for those at higher risk of flu-related complications. Following the suspension of one manufacturer's license and the announcement it would not supply any vaccine to the U.S. market this season, CDC revised its recommendations and took steps to mitigate the vaccine shortage.

Although HHS has limited authority to control flu vaccine distribution,[5] upon learning that nearly half of the nation's expected flu vaccine supply was in jeopardy, it took steps to help direct the available vaccine to help providers get some vaccine for their high-risk patients. In particular, CDC officials have worked with the remaining major manufacturer, as well as state and local health departments, to assess needs, prioritize customers, and make plans to distribute the remaining vaccine.

CDC also convened its Advisory Committee on Immunization Practices (ACIP) to reassess and revise the recommended vaccination priorities for the flu season.[6] The revised priority groups for the 2004-2005 flu vaccine include the estimated 85 million people in high-risk groups, but they do not include many of the other target groups. In addition to high-risk individuals, the revised priority groups include an estimated 7 million health care workers and an estimated 6 million household contacts of children aged 6 months or younger, for a total population of about 98 million in the revised priority groups.

While CDC can recommend and encourage providers to immunize high-risk patients first, it does not have direct control over the distribution of vaccine (other than the generally small amount that is distributed through public health departments); thus, CDC cannot ensure that its priorities will be implemented. As these actions play out, more time is needed to gauge the success of CDC's efforts to mitigate the current flu vaccine shortage.

Despite the efforts by CDC and others, many high-risk individuals appear to be experiencing problems getting a flu vaccination. Media across the country are reporting that some seniors are waiting hours for flu vaccinations and others are so frustrated they are traveling to Canada or Mexico to get vaccinated. There are other media reports of anxious seniors unable to get vaccinated in a timely fashion. How many high-risk individuals ultimately get vaccinated against influenza this season remains to be seen. We are beginning new work to analyze this year's vaccine shortage and the federal response.

CONCLUDING OBSERVATIONS

Ensuring an adequate and timely supply of vaccine to protect high-risk individuals from influenza and flu-related complications remains a challenge. The limited number of manufacturers and the manufacturing problems experienced in recent years illustrate the fragility of vaccine production. The abrupt loss of nearly half of the nation's vaccine supply has further highlighted the potential inequities that can result from the current vaccine distribution system. Under this system, some providers can be left with little immediate recourse for meeting the needs of those most at risk. CDC is responding by working with the remaining major flu vaccine manufacturer and states and local public health agencies to better target high-risk populations. Nonetheless, with this flu season, there are reports of long lines, people crossing international boundaries to obtain their flu vaccinations, and anxious seniors unable to obtain a vaccination on a timely basis. Whatever the outcome of this

[5] Under the Federal Food Drug and Cosmetic Act, FDA ensures compliance with good manufacturing practice and has limited authority to regulate the resale of prescription drugs, including influenza vaccine, that have been purchased by health care entities such as public or private hospitals. This authority would not extend to resale of the vaccine for emergency medical reasons. The term health care entity does not include wholesale distributors. CDC has a role in encouraging appropriate public health actions.

[6] See HHS, Centers for Disease Control and Prevention, "Interim Influenza Vaccination Recommendations, 2004-2005 Influenza Season," *Morbidity and Mortality Weekly Report,* vol. 53 (2004).

flu season, ensuring that vaccine can be made available as expeditiously as possible to those who need it most in times of shortage remains a challenge.

AGENCY COMMENTS

We shared the facts contained in this statement with CDC officials. They informed us they had no comments.

This concludes my statement. I would be happy to answer any questions the Chairmen or other Members of the Subcommittees may have.

RELATED GAO PRODUCTS

Infectious Disease Preparedness: Federal Challenges in Responding to Influenza Outbreaks. GAO-04-1100T, Washington, D.C.: September 28, 2004.

SARS Outbreak: Improvements to Public Health Capacity Are Needed for Responding to Bioterrorism and Emerging Infectious Diseases. GAO-03-769T, Washington, D.C.: May 7, 2003.

Infectious Disease Outbreaks: Bioterrorism Preparedness Efforts Have Improved Public Health Response Capacity, but Gaps Remain, GAO-03-654T, Washington, D.C.: April 9, 2003.

Flu Vaccine: Supply Problems Heighten Need to Ensure Access for High Risk People. GAO-01-624T, Washington, D.C.: May 15, 2001.

Mr. WALDEN. I appreciate your comments, and your full statement, obviously, is in the record as well.

Let me go now to Mr. Rosenbloom. Thank you for being here today, and we look forward to your comments.

STATEMENT OF ALAN ROSENBLOOM

Mr. ROSENBLOOM. Thank you, Mr. Chairman, both to yourself and to all the members of the committee, for the opportunity to join you.

As you know, my name is Alan Rosenbloom. I serve as President and Chief Executive Officer of the Pennsylvania Health Care Association and the Center for Assisted Living Management. We are part of a larger national federation, the American Health Care Association and the National Center for Assisted Living Management. Together, we represent roughly 10,000 long-term care provider organizations who provide care and treatment to about 1.5 million elderly and disabled residents of the United States, all of whom by definition are in high-risk categories for receipt of flu vaccine.

We also employ about 1 million direct-care workers, all of whom by definition are in high-risk categories for receipt of flu vaccines.

Before beginning my substantive testimony, I also want to share greetings from AHCA's new CEO, Hal Daub, who is a former colleague of yours here in the House.

I applaud the opportunity that you have given us to offer perspectives from long-term care providers. As I mentioned, the long-term care facility probably provides a unique nexus of high-risk populations, those over 65, those who reside in long-term care facilities, those between the ages of 2 and 64 who suffer from chronic conditions and direct health care workers. In that environment, as you can well imagine, flu spreads like wildfire, and the risk of dying from flu is quite high.

I also appreciate the fact that I am appearing here from Pennsylvania where our Department of Health announced last week that we will be 1 million doses short in flu vaccines for our at-risk population.

In the spirit of the title of this hearing, which is Protect and Strengthen, I would like to offer some views on what has worked well with respect to the partnership between CDC, the State government and the long-term care provider community and then,

with respect to the latter, strengthening, some suggestions for improving how we work together in the future.

It is noteworthy that there has been strong collaboration among CDC, CMS, which is, of course, the primary payer for a large chunk of long-term care services in this country, and representatives of the long-term care provider community.

CDC recognized the special circumstances that long-term care provider situations present. They have collaborated very closely with the American Health Care Association and the National Center on Assisted Living to gather information to assess the situation on the ground in these facilities to get a handle on what the needs are, what the available resources are, what the gap is and how we might be able to close it.

CDC shared extensive information on prevention, infection-control practices, prophylactic use of antiviral medications, treatment use with antiviral medications and the like, and we have had substantial support from the Centers for Medicare and Medicaid Services in this effort as well.

For example, CDC, CNF, Aventis, Pasteur and AHCA collaborated on a survey to assess the circumstances on the ground in long-term care facilities so that the Federal Government and State health departments could plan effectively and act quickly.

Having said that, there are some lessons learned that we would like to offer for ways in which this process can be improved, hopefully starting as soon as possible and certainly as we look out into future years.

No. 1, clearer communication between Federal and State governments would be helpful. For example, Pennsylvania's health department right now is conducting yet another survey of long-term care providers in the Commonwealth for reasons that remain obscure given the work that has already been done at the Federal level.

Second, clearer guidance on the scope of what other long-term care settings, beyond nursing homes, would be very helpful as well, depending on how a State chooses to define those other settings: Are they assisted living? Are they home care? Are they personal care? Are they congregate living? Are they something else? The possibility exists that subsets of individuals who clearly should be within at-risk groups could be lost in the shuffle.

In Pennsylvania, for example, we call assisted living personal care, and it is licensed by our Department of Public Welfare, not our Department of Health. As a consequence, when the Department of Health is, if you will, protecting institutional residents, they tend to look much more strongly at those entities they license, hospitals, nursing homes and the like, and so there is a risk that personal care homes in Pennsylvania and their residents, all of whom by definition are at-risk, could be lost in the shuffle.

Third, we urge the CDC to rethink its decision not to provide guidance on what to do when there are partial doses allocated, when there is not enough of a dosage to make effective decisions about who you do and who you don't give medications to.

In a nursing home, for example, do you choose your residents or your direct care workers? If you have to choose between residents, why choose one resident over another? Particularly in a climate

where the liability risk to long-term care providers is growing, where there are more and more negligence suits for the decisions that are made in long-term care settings, it is particularly important, not only for the care and services that people receive but also to provide appropriate insulation from liability, that more guidance be made available.

Finally, we recommend that the Center for Medicare and Medicaid Services establish a consistent payment standard for vaccines and for antiviral medications that can be used if there are no vaccines available. Right now, Medicare pays for most vaccines, Medicaid might or might not pay for most vaccines, depending on how the State Medicaid program works.

Right now, Medicare generally does not pay for antiviral medications. However, the Medicaid program in a given State might or might not, depending on the choices that an individual State makes.

According to CDC recommendations, however, if you are in a world where you have to administer antivirals prophylactically, you should be giving them to every resident and every direct care worker for up to 3 weeks as a time. If the resources are not made available to pay for those pharmaceuticals, then the preventive use of antivirals will suffer and the epidemic could spread on a building-by-building basis.

In summary, we think that a lot has gone right; we think a lot could go better. And we urge the committee and the CDC and other branches of the Federal Government to look at those recommendations seriously.

I appreciate the opportunity to be here and would be happy to answer questions at an appropriate time.

[The prepared statement of Alan Rosenbloom follows:]

PREPARED STATEMENT OF ALAN ROSENBLOOM ON BEHALF OF THE AMERICAN HEALTH CARE ASSOCIATION

Good morning Chairman Barton, Chairmen Bilirakis and Greenwood, Ranking Members Brown and Deutsch, and members of the subcommittees. I appreciate the opportunity to be here with you today to discuss current efforts to deliver the flu vaccine to the nation's frail, elderly, and disabled citizens living in nursing facilities, assisted living residences, and intermediate care facilities for individuals with mental retardation and developmental disabilities, and to begin to lay the foundation for next year's anti-flu preparations.

My name is Alan Rosenbloom, and I am President and Chief Executive Officer of the Pennsylvania Health Care Association and the Center for Assisted Living Management—the largest organization of for- and not-for-profit long term care and assisted living facilities in Pennsylvania, and an affiliate of the American Health Care Association and the National Center for Assisted Living—organizations representing nearly 10,000 providers of long term care services, who serve more than 1.5 million elderly and disabled people annually and employ more than 1 million caregivers.

I am here on behalf of the American Health Care Association and the National Center for Assisted Living and their new President and CEO Hal Daub. Today I would like to describe for you the efforts the long term care community, in collaboration with the Centers for Disease Control and Prevention, the Centers for Medicare & Medicaid Services, and Aventis Pasteur has made to ensure patient and resident protection against the flu this season, as well as the lessons we have learned that will make next year's preparation more efficient and effective.

But before I do that, let me first explain why it is so important that the flu vaccine be available to the residents we serve. Long term care patients can be at risk of death should they contract influenza. The stakes are that high. In the nursing home setting, the average patient is 85 years old and is dependent on others for roughly four activities of daily living, including bathing, dressing, and toileting.

The typical assisted living resident, who also is 85 or older, needs help with three or more activities of daily living, and that number continues to increase as the government shifts more high-acuity individuals away from skilled nursing care and toward assisted living settings.

Our members also care for many of the 106,000 clients with mental retardation and developmental disabilities living in congregate settings, many of who suffer from chronic health conditions, such as cerebral palsy and respiratory illnesses.

Clearly, the population we care for is at high-risk for contracting the flu, and the dangers associated with a diagnosis are greater than those for the average American.

That's why the American Health Care Association and the National Center for Assisted Living member organizations took swift and decisive action upon learning that there would not be enough flu vaccine this season to protect our patients and residents.

That is also why we were glad that CDC and CMS paid special attention to the long term care population early on in the process. Almost immediately, the Centers for Disease Control and Prevention collaborated with the American Health Care Association and the National Center for Assisted Living on an initial survey to learn how facilities were faring during the flu shortage. From that survey, they learned how widely and seriously LTC facilities were impacted by the problems at Chiron. The CDC quickly and appropriately identified "residents of nursing homes and long term care facilities' as a priority group. Recognizing that an epidemic in any of our settings would be devastating, CDC rightly maintained a broad definition for long term care facilities so that assisted living residences and facilities for people with mental retardation and developmental disabilities were included.

The CDC was further cautionary by listing as a priority group "health-care workers involved in direct patient care." We absolutely must keep healthy those who care for our very vulnerable population, and the CDC recognized this.

Additionally, CDC maintained early and consistent communication with our national association and used us as a resource for establishing the extent of the vaccine need in our member facilities. The CDC also provided us with a wealth of information in lieu of the vaccine, including infection control techniques, signage that could easily be reproduced and placed in facilities, and recommendations on the use of influenza anti-viral medications specific to this flu season.

The Centers for Medicare & Medicaid Services was equally supportive, and the agency's clear interest in moving vaccines to our facilities expedited the process in some states and helped allay our fears. CMS was particularly helpful in our communication efforts.

The best example of the successful collaboration between our association, CDC, CMS, and Aventis Pasteur was the coordination and dissemination of a more in-depth second survey to which more than 13,000 long term care facilities nationwide responded, identifying their vaccine needs. We worked together to quickly design a survey that would efficiently and effectively meet Aventis and CDCs' need to not only learn which facilities had none or limited vaccine, but also that recreated the chain of distribution. Results from this survey provided facility level data on the number of beds and direct care staff, among other things, that helped identify vaccine needs. The survey was posted on the AHCA web site, and CMS helped get the word out to facilities. The distribution of this critical survey was the centerpiece of an unprecedented collaboration.

Allow me to clarify the process of getting vaccines from the maker to the facility. The vast majority of vaccines distributed by Aventis Pasteur go directly to end users; however, this is not the case for long term care facilities. For the most part, our members rely on long term care pharmacies for all their pharmaceutical needs because these pharmacies best meet our unique needs—special carts, special packaging of medications, and emergency deliveries, to name a few. These long term care pharmacies, in turn, order from their supplier, which may be a wholesaler or a group purchaser or the manufacturer. The wholesaler or group purchaser would then order from the manufacturer, and in most cases this year, the manufacturer was Chiron. And it's worth noting that providers, like others involved in the distribution of flu vaccine, bear liability risk.

Despite the government's rapid response and the good intentions and efforts of all those involved with getting the vaccine into facilities, there were several areas of the vaccine shortage efforts that could have been handled differently and should be noted as we look toward next year's flu season.

AHCA/NCAL Recommends that the CDC Tighten Its Communications to State Health Departments

We observed a significant disconnect between the state health departments and the CDC relating to the dissemination and use of the results of the survey that we all worked so hard to collect. It took the CDC two full weeks to get the survey results to the state health departments, and because the CDC decided to turn over the vaccine to the states for distribution, the states needed that information desperately. Our national association interceded in several states to get the survey results from CDC to the appropriate state contact. In the future, the CDC must liaison better with the state health agencies.

AHCA/NCAL Recommends that the CDC Offer More Guidance to State Health Departments and to Providers

The CDC also should provide more guidance to the states than was offered this flu season. Without CDC's guidance, states are not required to give precedence to the congregate care elderly and disabled over adults aged 65 and older.

While we agree that in many circumstances decisions should be state-based, the overwhelming evidence of the particular risk to persons in congregate settings should lead the CDC to establish national policy. The refusal to sub-prioritize was and continues to be an impediment.

Furthermore, guidance on best practices from CDC to the states would help prevent delays in getting vaccines into providers' hands. While some states like Mississippi and Virginia were very efficient, others such as my own home state of Pennsylvania were not.

We also requested guidance from the CDC on how best to handle partial orders. For facilities that received or will receive less than their full order, there are questions about who should be vaccinated first while awaiting the complete order. Do you immunize the workers on the theory that they have more contact with the outside world, or do you immunize the patient/resident on the theory that they are more fragile? And which residents should be vaccinated first? Do you make decisions based on proximity, or should you look at elements such as age or illness? These are the issues that we are grappling with right now and guidance from the CDC would be most helpful.

The CDC also should offer guidance regarding the state distribution of vaccine to the congregate long term care population, where influenza spreads like wildfire. State health departments ought to be advised to treat residents in assisted living settings and in intermediate care facilities for persons with mental retardation similarly to the skilled nursing population per the CDC priority grouping, and the CDC must ensure that it's inclusion of all long term care settings in the priority group is replicated at the state level.

CMS Should Design Reimbursement System for Influenza Anti-Viral Medications and Prophylaxis

The issue of who will pay for influenza anti-viral medication and prophylaxis must also be addressed, especially since CDC recommended the use of the drugs in the absence of vaccine. CMS should begin work now on a way to reimburse for influenza anti-viral medication or other medication that is used to prevent epidemics when there is a health emergency.

Thank you for the opportunity to join you today. I commend the CDC and CMS for fine work, and our profession stands ready to collaborate further with the centers to fulfill our mission of quality long term care.

Mr. FERGUSON [presiding]. Thank you very much. We appreciate your suggestions. That is what we are after today.

Mr. Paradiso, I hope I produced your name correctly or close.

STATEMENT OF PETER R. PARADISO

Mr. PARADISO. Very close. Good afternoon, Mr. Chairman and members. My name is Peter Paradiso, and I am the Vice President for New Business and Scientific Affairs at Wyeth.

Wyeth has been in the business of researching and manufacturing vaccines and biologicals for over 100 years, and I have been part of that effort for the past 20 years. We are proud of the contributions our products have made to public health.

As important as these products are to society, the vaccine enterprise has become increasingly difficult. The shortage of flu vaccine is but a symptom of a larger problem. To address flu vaccine supply and the limited number of manufacturers, we need to understand the reasons there are so few manufacturers of vaccines of any type.

Some of the unattractive facets of the vaccine business are not inherent but are the result of government policies, some justifiable and others more questionable, that have an impact on the development and the subsequent supply of vaccines. These barriers can hinder existing vaccine companies and act as disincentives for new participants. These derive in part from a mindset intolerant of even theoretical risk, and therefore often skew the risk benefit ratio to the point where the benefit is forgotten.

One of the biggest changes that has occurred in the vaccine industry in the time that I have been working in this field is the change in the regulatory and compliance environment. In our company, almost all of the new hires in vaccine research over the past several years are involved in FDA compliance-related issues. Manufacturing facilities that are licensed for new products are outdated within 2 years and require significant and seemingly continuous large investments. Using our new Prevnar vaccine as an example, this product is manufactured at two facilities that were licensed in 2000. More than $300 million of capital has been invested in the existing Prevnar facilities in the last 3 years; that is since the product was licensed in 2000. Due to the diligence of the FDA and the efforts of manufacturers, the safety record of the vaccine manufacturing supply is exemplary. So it is hard sometimes to understand why we need still higher standards.

In the case of Wyeth influenza vaccine flu shield, continued investment was not sustainable. The fact is that our influenza vaccine business had lost money 4 of its last 5 years, and significantly more investment in manufacturing was required. We had 8 million unsold doses of the vaccine at the end of 2002. We announced that we would exit the injectable flu business in November 2002.

While Wyeth no longer makes an influenza vaccine, we are still in the vaccine business, and I would like to address some of the marketplace challenges in pediatric vaccines. Roughly 60 percent of the U.S. Market is one customer, the Federal Government. This customer has the legal power to control prices. The government-fixed price for tetanus vaccine is so low that no company has bid to provide the vaccine to the government for many years. While it is an obligation of government to be a prudent purchaser, it is also an obligation of government to protect the public health. By overemphasizing the former, one risks jeopardizing the latter.

Another poorly understood risk of the vaccine business is liability. Vaccines are given to virtually every young child in this country, and therefore, the likelihood that any child affliction would occur in temporal proximity to an immunization is high just because of the frequency with which immunizations are given. Vaccines have been accused of causing epilepsy, multiple sclerosis, attention deficit disorder, cancer, autoimmune disease, learning disabilities, Gulf War Syndrome and even the AIDS epidemic. Today's allegations linking vaccines with autism are but the latest in a long

history of accusations, none of which has been proven to have scientific validity.

In 1986, Congress created the Vaccine Injury Compensation Program administered by the Department of Health and Human Services. Although that statute has been helpful, it needs to be reformed to reflect today's reality. There is a widespread perception that this program completely shields companies from liability, but that is not the case. Today, companies that produce childhood vaccines have been served with over 350 lawsuits, some of them massive class actions. These suits allege that vaccines cause autism.

In May 2004, the Institute of Medicine issued a report concluding that there is sufficient scientific evidence to reject a causal relationship between autism and vaccines. Despite this, we estimate that the companies involved in this litigation have spent more than $200 million collectively in outside legal costs, and the first case has not yet come to trial.

These and other issues confront companies as they decide whether to enter the vaccine business. There are constructive steps that Congress can take. For example, the Administration has a proposal that would remove the price cap on childhood vaccines and allow CDC to develop a stockpile of pediatric vaccines to utilize in the event of shortages. H.R. 3758 would provide tax incentives for upgrading or building a new vaccine facility and also offers a method of purchasing unsold doses of flu vaccine at the end of the season. These would be positive steps.

The FDA has announced a project which they call GMPs for the 21st century. I would urge the FDA to make review of vaccines' GMP the top priority. And finally, the liability burden facing company needs to be addressed. Various attempts to do so were commenced during this Congress, and a new start needs to be made in the next Congress.

I am excited about the scientific possibilities for the future of vaccines, but recent events serve as a reminder of the fragility of this enterprise. Thank you for this opportunity.

[The prepared statement of Peter R. Paradiso, follows:]

PREPARED STATEMENT OF PETER R. PARADISO, VICE PRESIDENT, NEW BUSINESS AND SCIENTIFIC AFFAIRS, WYETH

INTRODUCTION

Good Morning Mr. Chairman and members of the committee. My name is Peter Paradiso and I am the Vice President for New Business and Scientific Affairs at Wyeth. Wyeth has been in the business of researching and manufacturing vaccines and biological products for over 100 years and I have been part of that effort for the past 20 years. We are proud of the contributions we have made to public health throughout this time including our contribution to the eradication of smallpox worldwide not only through the supply of vaccine but also the technology for a bifurcated needle delivery device critical to the mass immunization programs. For nearly 20 years we were also the sole U.S. producer of oral polio vaccine, which conquered polio disease in the U.S. with the last case of indigenous disease occurring in 1979.

Most recently we introduced the first conjugate vaccine to prevent meningitis and other invasive infections of childhood caused by the pneumococcal bacteria, an organism that not only causes serious diseases, but also was developing antibiotic resistance at an alarming rate. In the 4 years that this vaccine, named Prevnar, has been on the market in the U.S., childhood pneumococcal disease has declined by over 80 percent. Furthermore, studies have shown that invasive disease caused by pneumococcus in adults has also decreased significantly due to fewer ill children spreading disease to adults. In total this means that not only have serious diseases and death declined but the need to use antibiotics has decreased as well which should serve

to stem the rising tide of antibiotic resistance. While I speak of Wyeth vaccines in particular, vaccines made by our competitors can boast of the same type of dramatic results in decreasing or in some cases eliminating the former scourges of childhood diseases. The record shows that vaccines have had one of, if not the greatest impact of any public health intervention over the last century.

As important as these products are to society, it has become increasingly difficult to justify remaining in the vaccine business. While the primary focus of this hearing is on influenza vaccine, the shortage of flu vaccine and flu vaccine manufacturers is but a symptom of a larger problem. There are only four companies left that make vaccines routinely used in childhood. Many vaccines are now made by only one company. And while it did not grab the public's attention to the extent of the flu vaccine shortage, during the early part of this decade most children's vaccines experienced dramatic shortages as well. To address flu vaccine supply and the limited number of manufacturers, one must look at the small number of manufacturers overall, and understand the reasons that the current situation exists.

In February 2002, the National Vaccine Advisory Committee (NVAC), under the auspices of the National Vaccine Program Office (NVPO), reviewed the issues associated with the shortages in vaccine supplies. The conclusions of this detailed assessment highlighted numerous efforts that could impact vaccine supply in a positive way. These strategies included, among others, expansion of vaccine stockpiles, increased support for regulatory agencies, maintenance and strengthening of liability protections, financial incentives to manufacturers, streamlining the regulatory process without compromising safety or efficacy, and a campaign to emphasize the benefits of vaccination. I will highlight several of these issues in my comments but all of them are important and thoughtful approaches to the vaccine supply issue.

Every company must weigh the benefits versus the risks in each business opportunity when deciding where to place its resources. Some unappealing factors are inherent to vaccines and not to other types of drugs. As an example, most vaccines are used by children in a particular age group and for a defined and limited number of doses. This is in contrast, for example, to drugs for hypertension, which are taken by a significant portion of adults across multiple birth cohorts and are taken multiple times a day perhaps for the lifespan of the individual. Also as a society we are generally willing to pay more for products that treat diseases than for products that prevent them. One very telling figure that illustrates these points is that the total worldwide market for vaccines made by all manufacturers around the globe is estimated to be around $8 billion. There are single drugs on the market that rival the size of the global vaccine market.

Another inherent feature is that many drug products that are successful in the market find themselves with an ever-expanding market as new medical applications are found. With vaccines, the more effective a product is, the more likely it is to become obsolete. The smallpox and oral polio vaccines are both examples of highly effective products that worked themselves out of a market by eliminating disease.

I will address issues that relate to the changing environment in the vaccine field. These include changes in research and development, manufacturing, regulation, liability and the overall marketplace dynamics. In addition, I will touch on some potential areas where this Congress can have a positive impact on securing vaccine supply.

VACCINE RESEARCH AND DEVELOPMENT

Some of the unattractive facets of the vaccine business are not inherent but are the result of government policies, some justifiable and others more questionable, that have an impact on the development process and can result in barriers that hinder existing vaccine research companies and serve as disincentives to new participants. These derive, in part, from a mindset intolerant of even theoretical risk and therefore often skew the risk/benefit ratio to the point where the benefit is forgotten. This mindset persists despite the fact that the vigilance of FDA and the efforts of manufacturers have produced an exemplary safety record.

Clinical trials for vaccines are much larger in scope than for drugs, which one would expect since these are products that are given to largely healthy individuals. The clinical trials for our Prevnar vaccine included over 40,000 children. Press reports about a vaccine to prevent childhood diarrhea under development at other companies have indicated that more than 60,000 children are in each trial. By contrast, drug trials typically involve 3000-5000 people. Importantly, however, vaccine development has become much more complex and costly over the last ten years. This ranges from increasingly stringent requirements for producing test vaccines to be used in clinical trials, to larger and more complex clinical programs. In fact, over the last five years in our company, the majority of the new hires in vaccines R&D

are working in compliance, quality assurance or regulatory affairs rather than doing actual vaccine research. This has significantly increased our costs and lengthened our timelines.

MANUFACTURING

The complexity of manufacturing a vaccine is much higher than for small molecule drugs (e.g., pills) in part because of the use of living organisms as opposed to a more predictable chemical process and in part because of the subsequent complexity of the quality control and compliance processes. It takes approximately five years to build and validate a vaccines manufacturing facility. As a result, it is necessary to commit to building facilities at the same time that pivotal clinical trials are starting and while their outcome is uncertain.

However, the investments in manufacturing do not end with licensure. Using Prevnar as an example, this product is manufactured in two facilities that were licensed in 2000 after inspections by reviewers from the Centers for Biologics Evaluation and Review (CBER). Since then, to improve compliance and increase production capacity, we have made significant changes in these facilities and in our manufacturing and quality processes. Over $300M of capital has been invested in existing Prevnar facilities since 2000 and operating expenses have nearly doubled in the past three years. Over 2,000 people are involved in the manufacture of Prevnar and an additional 500 people are employed to insure that we are compliant with all of the regulatory requirements. It takes, on average, 50 weeks to produce and release a batch of product. It is, in part, this timeline that makes rapid response to shortages very difficult.

Once licensed, it is possible to rationalize this level of investment for a new product like Prevnar for which we are the sole global supplier. It is much more difficult to justify the ongoing investment for older products with prices reflective of the environment decades ago. This need to make significant investments in facilities to meet ever more stringent cGMP (good manufacturing practices) requirements becomes a critical factor in deciding whether to continue to keep a product on the market. In the case of Wyeth's DTaP and influenza vaccines, this continued investment could not be justified.

THE VACCINE MARKETPLACE

Once on the market, pediatric vaccines, which constitute the bulk of vaccine products, must deal with the fact that roughly 60 percent of the U.S. market is one customer, the federal government. Having one customer with that degree of dominance in the market is daunting enough but when that customer has the legal power behind it to control prices, the market becomes much less attractive. Further, some states have ignored definitions in federal law and have taken steps that would make the percentage of the government market even greater. To date the Department of Health & Human Services (HHS) has not undertaken any activity to uphold federal law and inhibit that expansion.

When the Vaccines for Children program passed the Congress as part of OBRA 1993, it created price controls on the vaccines that were on the market at that time. This situation has become so egregious that the price for tetanus vaccine is so low that no company has bid to provide it to the government for many years. Merck's MMR vaccine is listed on the government schedule at around $16.25 while the market catalog price is $38.05. Haemophilus influenzae type b vaccines are capped at $7.65/dose but are over $21.78/dose in the private market. The CDC is the largest purchaser among the government agencies, and has the leverage of a price controlled federal supply schedule, designed primarily for use by the VA and DOD, to use in driving prices downward. While it is an obligation of government to be a prudent purchaser, it is also an obligation of government to protect the public health. By over-emphasizing the former, one risks jeopardizing the latter.

LIABILITY

One poorly understood risk of being in the vaccine business is liability. Since vaccines are so stringently regulated, both before and after marketing, and have such an outstanding record of safety, it might seem baffling why liability should be so problematic. The root of the problem lies in the fact that vaccines are given to virtually every young child in this country and as every parent knows, many diseases and afflictions manifest themselves in young children. The likelihood that any of these conditions would occur in temporal proximity to an immunization is high just because of the frequency with which shots are given.

Further, since nearly every child receives vaccines, any affliction without a known cause could be blamed on immunizations the child has received. Since the advent

of the Internet, numerous unsubstantiated theories about vaccines have abounded. Over the course of the past 15 years, vaccines have been accused of causing epilepsy, multiple sclerosis, autism, attention deficit disorder, cancer, autoimmune disorders, learning disabilities, and Gulf War Syndrome. Vaccines have even been accused of being the cause of the AIDS epidemic. Today's allegations linking vaccines to autism are but the latest in a long history of accusations, none of which have been proven to have scientific validity.

While there were many more manufacturers making children's vaccines in the 1970's, that number has dwindled now to just four. The decrease has several causes but clearly the mostly precipitous decline occurred in the early 1980's as manufacturers left the market due to an explosion of lawsuits alleging damage from DTP vaccine. This explosion of litigation scared liability insurers away from vaccines and companies were left with no insurance coverage. The situation became so perilous that there was only one company left making this vaccine, which prevents diphtheria, tetanus, and whooping cough, and public health officials had to take the step of not immunizing two year olds against these diseases because of vaccine shortages. The one remaining company was forced to raise its price to cover the cost of litigation and at the height of the problem fully 75 percent of the cost of DTP vaccine was directly attributable to the cost of litigation.

Congress intervened in 1986 and created the Vaccine Injury Compensation Program (VICP) administered by the Department of Health & Human Services to cover vaccines routinely recommended for use in children. This program was created to ease recovery for alleged vaccine-related injuries while protecting manufacturers from the costs and uncertainties of litigation that could potentially jeopardize the Nation's vaccine supply. There is a widespread perception that this program shields companies from liability but that is not the case. The law requires that anyone alleging an injury from a vaccine must first file a claim in the compensation program. However, whatever the decision from the program as to whether or not the injury was actually caused by a vaccine, the claimant has a right to leave the compensation program and proceed against the vaccine manufacturer in civil court. Furthermore, if a claim has been pending for more than 240 days and no decision has yet been rendered, a claimant can opt out of the program and proceed against the vaccine manufacturer in civil court.

The VICP determines the validity of claims based on the preponderance of the scientific evidence. A petitioner who has sustained an injury on the table of compensable events during the specified time period is presumed to have a vaccine related injury and is compensated by the VICP without having to actually demonstrate causation or fault. If a petitioner brings a claim for an injury that is not listed on the table, then the petitioner must show by the preponderance of the scientific evidence that the injury was caused by vaccine, but unlike civil court, the claimant does not have to demonstrate that the vaccine was defective. Since the inception of the program in 1986, the Institute of Medicine has done periodic reviews of scientific studies and has reached various conclusions related to causation which have in turn aided the VICP in determining causation.

Today, companies that make children's vaccines are facing a liability situation that dwarfs that of the 1980's when manufacturers were driven from the market. Each company has been served with over 350 lawsuits, some of them massive class actions, alleging injuries arising from the vaccine preservative thimerosal. There are also 4200 related pending petitions in the VICP, which are proceeding together as part of the Omnibus Autism Proceeding. These petitions, which may one day turn into lawsuits directed at manufacturers, allege that autism may be caused by MMR vaccination or the preservative thimerosal, formerly found in other childhood vaccines, or by some combination of the two.

In May 2004, the Institute of Medicine issued a report concluding that there is sufficient scientific evidence to reject a causal relationship between autism and vaccines. Although to date, not one of the 350 or so lawsuits has proceeded to trial, we estimate that the companies involved in this litigation have spent more than $200 million collectively in outside legal costs. Actual trials seeking damages for injuries are scheduled to commence early next year, at which point the legal costs will increase exponentially. Further, executives and scientists from the companies will spend countless hours in depositions and at trial. While there is overwhelming scientific evidence refuting any alleged link between vaccines and autism, no company would want the dynamics of a jury contemplating a disabled child versus a faceless corporation.

RECENT CHANGES IN THE WYETH VACCINE BUSINESS

All of the factors laid out above serve as the context in which our decision was made to leave various vaccine businesses including flu vaccine, and the routinely used DTaP vaccine for children. Regarding influenza, Wyeth had produced this vaccine in Marietta, PA, for nearly 20 years. A new manufacturing facility was built in the 1990s and licensed in 1998. We announced in November 2002 that the 2002-2003 would be our last season in the business. Our influenza vaccine business had lost money in four of its previous five years due largely to doses left unsold at the end of each season. Compounding that situation was the fact that in 2000, two years after licensure of the new manufacturing facility, the FDA informed us that extensive changes would need to be made at the site to remain in compliance with evolving standards. Wyeth reached an agreement with the FDA to enter into a consent decree focusing on the company's compliance with current Good Manufacturing Practices (cGMP). One of the sites involved was our flu manufacturing facility in Marietta, PA. When this significant compliance action was taken, FDA publicly acknowledged that there had been no safety risk to patients with any products that had been made at that site. During the interval from 2000 to when we close the doors at the facility at the end of this year, we will have invested over $100 million in capital improvements for that facility alone. We could not justify further investment. If we had opted to persist in the flu vaccine business, many more millions of dollars in investment would have been required and our manufacturing costs would have continued to escalate.

Faced with this financial prospect and coupled with the fact that we had eight million unsold doses of vaccine at the end of 2002, the only rational decision was to leave this flu vaccine business and focus our resources on the new intranasal vaccine, FluMist, that we were developing in collaboration with MedImmune Company. FluMist was licensed in 2003 but unfortunately not for any of the high-risk groups for whom flu vaccine is recommended. As a result, millions of doses of FluMist went unused in 2003 even in the face of a severe early epidemic and vaccine shortages.

Our decision to leave the DTaP business had some common factors with the flu situation. The facility in Pearl River, NY where DTaP was produced was also subject to the consent decree we agreed to in 2000. We had known for several years that our DTaP had a limited lifespan in the market. Pediatricians and public health officials were understandably interested in combining some of the children's vaccines into one shot to reduce the number of injections given to babies. We had undertaken clinical trials to combine our *Hemophilus influenzae type b* (Hib) vaccine with DTaP, but our trials showed, as did the trials of other manufacturers, that combining these products resulted in a diminished immune response to the Hib component. Other potential vaccines that could be combined with DTaP were Hepatitis B and inactivated polio vaccines. Since we did not make either of those but our competitors did, we realized that our DTaP would not be a viable product much longer. In July 1999, the U.S. Public Health Service asked manufacturers to move away from using the thimerosal preservative in their vaccines. The U.S. Public Health Service and the American Academy of Pediatrics felt that removal of this preservative would be a means of maintaining parental confidence in vaccines while both organizations acknowledged that there was no scientific evidence to suggest any danger from the product. Our vaccine would have required a new manufacturing process, clinical trials, and re-licensure. These development requirements, coupled with the significant facility investments and the short projected lifespan of the product all contributed to our exit from this market.

POTENTIAL SOLUTIONS

These are examples of the types of decisions facing vaccine companies in terms of justifying remaining in this business relative to other investment opportunities. As mentioned, some of relatively unattractive components of the vaccine business are inherent. Others, however, can and should be addressed.

The Administration has proposed some changes to the Vaccines for Children program which have been incorporated into a Senate bill but no corresponding bill has yet been introduced in the House. The bill would remove the price caps on children's vaccines. It would also implement a technical change needed by the CDC in order to develop a stockpile of pediatric vaccines to utilize in the event of shortages. And it would transfer a category of needy children from an appropriated CDC account to an entitlement program which would not only benefit these children and the state public health departments that serve them but would also help manufacturers of new vaccines to know that government funds would be available to pay for the roughly 60% of the market controlled by the government.

Another worthwhile approach is proposed in H.R. 3758, which would provide tax incentives for upgrading or building a new vaccine facility. This tax credit would diminish the cost differential between drug and vaccine facilities and would be very helpful, particularly if constructed so that the tax credits could be carried forward. H.R. 3758 also offers a method of purchasing unsold doses of flu vaccine at the end of the season.

The FDA has announced a project, which they call "GMPs for the 21st Century." Part of this endeavor is an examination of cGMP's (current good manufacturing practices) to determine if they are the correct approach. I would urge the FDA to make review of vaccine cGMP's a priority. The safety bar on vaccines must remain high but if FDA changes the requirements for cGMP it should only do so because of some demonstrable threat to the safety of the final product, not because it is possible to conduct a process differently. And finally, the liability burden facing companies needs to be addressed. An attempt to do so was undertaken last year and a new start needs to be made to ensure that manufacturers are not crippled from lawsuits born of unsubstantiated claims.

CONCLUSIONS

In closing I would like to say that as a research scientist, I am very excited about the future of vaccines. Over the past 20 years I have been privileged to be a part of the development of a number of childhood vaccines such as HibTITER, Meningitec and Prevnar that have had a dramatic impact on the health of children here and around the world. Advances in technology allow us to contemplate vaccines today that were beyond our dreams just a decade ago. At Wyeth, for example, we are working not only on vaccines for unconquered infectious diseases but also for conditions like Alzheimer's disease. Unfortunately while the scientific frontier is very exciting, the business barriers can be daunting. This is particularly true of companies contemplating entering this marketplace anew or maintaining an aging product portfolio. Thus even though we have been in the vaccines business for many years, we have discontinued several vaccine products in the past five years and have closed a vaccine research facility in Rochester, New York and a manufacturing facility in Marietta, PA. We remain committed to continuing our work in vaccine development because we recognize the incredible public health potential of these products and we hope that recent events will serve as a reminder of the fragility of this enterprise.

So I thank the committee for giving us the opportunity today to present our views and would urge you to continue to pursue ways to improve the business environment and stabilize the vaccine industry.

Mr. WALDEN [presiding]. Thank you for appearing. We appreciate your input.

Mr. Mlotek, thank you for being here. We look forward to your comments.

STATEMENT OF MARK E. MLOTEK

Mr. MLOTEK. Thank you, Mr. Chairman.

I would like to start with commending the panel on two important points. The first is highlighting the issue of flu vaccine shortage, obviously trying to find a solution quickly. It surely would be a tragedy that, now that the public is educated on the benefit of inoculation, that we do not have adequate supplies to meet that need.

Second is for allowing this, a different and perhaps more complete perspective of the distribution company to be heard. You are the first government body to really talk to the people who, in some respects, are closest to the issue from a business perspective. For example, some people might say, when the Chiron went out of market this year, that the issue was totally a distribution issue. We have heard that there is something like 86 million high-risk patients of which, in the normal year, 50 percent get inoculated. This year, there will be more than 50 million doses available—there will be close to 60 million doses available. In that respect, some people

may say the issue is one of distribution, not of supply. And that hasn't been addressed at all.

The distributor has a unique perspective in that, in that we are closest to the customer. At Henry Schein, we do business with over 30,000 flu vaccine customers. We do business with all three manufacturers in the market today: The primary distributor for Chiron; the exclusive distributor for MedImmune; and we do business with Aventis as well. And we have had extensive discussions with all potential entrants into the market to hear what their plans are and when they may come into market and what the issues are.

Some of the insight that we have had based on this experience is as follows: Like it or not, egg-based technology is here to stay. We see new technologies as coming to market in later years, but it is expensive to manufacture, produce and has not yet been shown to have higher efficacy.

The second issue is, distribution plays a key part of the flu vaccine business. Obviously, we communicate with customers constantly about CDC guidelines, about changes in supply, allocation schedules. We communicate with the manufacturing community. We communicate with government and participate in ACIP meetings.

On the logistics side, we receive in bulk the flu vaccine and have to repackage and redistribute in as small as one-vial containers to all remote parts of the country using sophisticated cold-chain expertise so that not one drop of the precious vaccine is lost. Over the last several years, our traditional spoilage rate is less than one-half of 1 percent. Most importantly, and this has not come out before, in the recent years, it is the distributor as much as the manufacturer who assumes risk in the flu supply chain-erupt equation.

Several years ago, we introduced a concept at Henry Schein of a take-or-pay contract with Powderject, that later became Chiron, and put our capital on the line saying, we would take all of the product manufactured on a no-return basis which then allowed Powderject to not worry about the then prevalent fear that there would be a glut and, at the end of the year, returns would wipe out all of the profitability. With that contract, Powderject was able to reinvest in its plant and expand capacity. This take-or-pay practice is now standard, so, again, it is the distributor as much as the manufacturer who stands in the greatest risk of oversupply.

The last key insight before I address some recommendations is that the doctor-patient relationship is critical in flu vaccine inoculation, because it is an essential part of case management. When there is a shortage of supply, who better than the doctor to determine among his or her patients who should get this critical treatment. Doctors make this sort of decision on an everyday basis. It is why, in the past several years, we have advocated giving a small amount of flu vaccine to as many doctors as possible and let them make the decision which of their patients should receive the inoculation. Instead, the plan this year and in the past is that States will receive doses to be administered by public health agencies, and the healthiest of the high-risk population, those who can stand in line for endless hours, will receive the shot while others, perhaps more needy but less able to meet this protocol, will not.

Based on these insights, a few key recommendations. First, fully fund the FDA and HHS, provide them with a mandate to do all that is possible to help the three existing manufacturers remain in the market and to move very quickly on an expedited basis to bring a new egg-based manufacturer that is operating today outside the U.S. To market in the U.S. There are people wanting to come to the U.S., and we have to fund the FDA to allow that process to move quickly.

Second, we need to fund a public-private initiative to increase the awareness of the benefits of flu vaccine. If we can raise demand, the profitability will be there, and more manufacturers will want to enter the market.

Third, we need to continue to increase reimbursement rates, again, so that the demand will be there and that, therefore, manufacturers will want to enter the market.

The fourth: In the short term, as we are increasing demand, we must provide a safety net for below-market purchases of unsold vials available to manufacturers and distributors alike—as I mentioned before, distributors assume risk in this equation—to make sure that the short-term oversupply until demand levels increase is balanced and that current players do not see their profits erode and leave the market, like Wyeth and Monarch did a few years ago.

Fifth, allow the distribution community a seat at the table in all emergency planning due to our unique perspective of understanding our customer needs and the manufacturing community in general.

I thank you for the opportunity to present today. I will be more than happy to answer any questions at the appropriate time.

[The prepared statement of Mark E. Mlotek follows:]

PREPARED STATEMENT OF MARK E. MLOTEK, HENRY SCHEIN, INC.

Mr. Chairman: Thank you for the opportunity to appear before your Committee this morning. You are hearing from a number of witnesses with unique roles in the flu vaccine market—from state public health representatives to nursing homes to vaccine manufacturers. We are very pleased to share with you the role of the distributor in the flu vaccine market. While I am Executive Vice President of Henry Schein, Inc. , the largest flu vaccine distributor in this country with more than 20 million doses sold in 2003, my comments have been discussed with the Health Industry Distributors Association, and I know that their views echo those of mine.

If you stop and reflect for a moment, you will recognize that on October 5 when Chiron announced that it would not be sending any vaccine to the US market, the challenge immediately became one of distribution. While the major focus in the government and media was one of increased supply, the real issue is how to get the small amount of available vaccine to the right place at the right time with the right cold chain expertise so that not one precious drop would be unused. We would suggest that in all emergency planning, that private sector healthcare distribution experts like Henry Schein and our industry associations can make a major contribution and should have a seat at the emergency planning table. This is true with respect to all emergency planning scenarios, not just flu, and includes pandemic planning or a bioterrorism threat.

From a public health perspective, we believe our greatest contribution would come from working more closely with the public health community to ensure that flu vaccine gets to where it is needed most. Just as the push packages in the Strategic National Stockpile ultimately must be delivered, broken down, and distributed to a designated site, flu vaccine must be received at one site, broken down into small lots and delivered with precise handling and shipping in a cold chain distribution process which calls for both heat and cold indicators as well as packing that ensures proper temperature control until the product can be received and used.

Let me give you a snapshot of the distributor's role. In a typical season, Henry Schein will distribute 25 percent or so of the nation's flu vaccine. In 2003, we shipped more than 20 million doses to over 20,000 customers. This season, before the Chiron issue, we had pre-book orders for over 30 million doses and we strongly believe that this amount was under-stated for this year. Many people were holding their orders for the "spot" market as all published communications by the CDC were that there would be an excess supply of flu vaccine this year, and people expected the pricing of flu vaccine to decrease as the year progressed.

Our typical customer is a physician practice that orders 10-20 vials per year. While we are capable of (and we do) ship large orders to hospitals, access companies, our expertise and core business is in marketing, distributing, and delivering small shipments for next day delivery with full cold-chain protection. We have been a reliable distributor of flu vaccine for our customers for the past 15 years. Customers look to us to manage the shortages that occur. If one manufacturer has an issue, our customers expect us to obtain supply from the other and service their needs.

With respect to the first issue addressed by the Committee—namely targeting high risk individuals, what have we been able to do to further the nation's interests in reaching this population? It is important to understand that each physician has high risk patients. In past shortages, it has always been our plan, which we have shared with the CDC and HHS, to get a small amount of flu vaccine to many practitioners and allow them to do what they do best—make the medical decision based on knowledge of their patients to allocate the flu vaccine and make sure it is given to those patients that need it most. We personally believe that this allocation makes more sense than relying on public health clinics for a few reasons. First, it is usually the healthy senior who can afford to stand on line for several hours to be able to receive a flu shot. Second, the doctor-patient relationship is quite important and needs to be furthered. According to the CDC, 70% of flu shots are administered in a doctor's office. Flu inoculation is one area of managing a patient's critical care. To exclude that as a separate medical treatment makes no sense.

Accordingly, we concluded that we would best serve the public health needs by distributing some amount of vaccine to all of our customers, rather than filling certain orders completely while leaving other customers with no supply.

Another service we provide is information. We have received tens of thousands of calls from doctors' offices, clamoring for information, including close to 40,000 calls the day after the Chiron announcement. Without good communication with companies such as ours which are closest to the customers, doctors have had to tell their patients that they have no certainty that any supply would be forthcoming. On voice mails and websites in doctors' offices across the country, messages like the following from a prominent Washington physician's office were posted:

"UNFORTUNATELY, DUE TO THE FLU VACCINE SHORTAGE THE CENTERS FOR DISEASE CONTROL IS CONTROLLING THE SUPPLY OF VACCINE IN THE UNITED STATES. WE WILL NOT BE RECEIVING ANY FLU VACCINES THIS YEAR. THANK YOU FOR YOUR UNDERSTANDING."

Doctors in private practice see themselves at the end of a depleted distribution chain. They perceived correctly that before October 5, millions of doses had already been distributed to large private employers and government agencies for employee clinics and to promotional "shoots" sponsored by retail outlets. If given the chance, distributors could have played a role after October 5 in redistributing some of that vaccine to where it was most needed.

Today, doctors perceive that the millions of doses remaining to be shipped have been earmarked for public health departments. Many, if not most, doctors are either unaware of that potential source or unwilling to tackle the red tape that they think would be involved in getting any of that vaccine.

In retrospect, we believe it would have been prudent for those responsible for allocation plans to give more attention to private sector distribution. While it is easy to be a Monday morning quarterback in the face of an enormous challenge, we note for the future that the distribution community could have helped with the allocation and reallocation planning. CDC focuses on the public health sector and on increasing supply, while manufacturers focus on large purchasers. Distributors focus on the entire market, including small purchases by doctors in private practice who typically vaccinate a large majority of all patients who receive flu shots.

To the second issue raised by the committee—how to strengthen the market, we do have some tangible suggestions and recommendations. For the 2005-2006 flu seasons, the US has a very short window of opportunity to encourage new production. We are not certain how many vaccine manufacturers will be producing flu vaccine, whether Chiron will be back in the market, and whether there will be new manufac-

turers who will have received timely FDA approval to bring vaccine into the country next year. It is extremely important that the FDA be able to move rapidly in examining other potential entrants and that the normal process of taking several years of review be expedited. If we are faced again with a limited supply, optimizing the distribution of that limited product will be critical. If we are fortunate and have an ample flu vaccine supply, we face a significant communications and public relations challenge in reversing course and telling those who were turned away this year to come back and get a flu shot—or to bring new patients in to get a flu shot. We would recommend that ample funding for a communications/public relations strategy be established.

Longer term, we face a real chicken and egg proposition in strengthening the flu vaccine market. The CDC's goal is to vaccinate 150 million people, a terrific public health objective in and of itself, but also a necessary objective for pandemic planning if we are to have adequate manufacturing capacity. If manufacturers had confidence that 150 million doses of flu vaccine would be sold in the US market, manufacturers would enter the market, competition would flourish, and we would not be faced with the issue of only having 2 or 3 manufacturers. Instead, only 80 million doses of flu vaccine have been sold consistently in the market over the past several years. If we could raise demand, we are confident that the supply would be forthcoming without any need for government support. The challenge, accordingly, is to develop a demand for 150 million doses in this market.

To get there, we must have a concerted and simultaneous attack on both supply and demand. We would recommend that the CDC, manufacturers and distributors undertake an aggressive joint public/private promotional program over the next several years calling for an increasing number of flu vaccine users. Universal flu inoculation should be the objective for 2008. The terrific public relations support that would be available to the CDC in the private sector will be key to meeting this goal.

CDC will correctly point out that they don't dare undertake a call for broader vaccination until they can count on adequate supply being available. During the first few build up years, government market support may be necessary. It is important that government support be provided in a fashion that does not eliminate market competition, probably by providing a safety net at the end of the flu season under which the government would purchase unsold doses at a pre-negotiated below-market price. It is also very important that this program be made available to the distribution network and not just the manufacturing community. In the flu market, the distributors take the risk of loss by purchasing a firm amount of vaccine with no return privileges. If this support is not available to the distributors and supply were to increase, the distribution network could be lost along with and the role it has played in the past in stimulating investment by the manufacturing community through committing to firm orders. We are confident that once a joint public/private effort results in the market developing to a level approaching demand for 150 million doses, competition will ensure the availability of ample supply.

Bottom line—distributors are an important part of the flu vaccine marketplace. Distributors physically deliver one-half of the flu vaccine to the market each year. Everybody has an interest, both for the remainder of this season and in future seasons, of working together to increase demand so that we build up our flu vaccine supply. It is important to get the distribution right before we confront a pandemic or a bioterrorist incident. We agree with the findings of the GAO, that distribution along with purchasing and administration are critical elements in the effective and efficient delivery of vaccines to high risk populations, in typical flu seasons as well as for pandemic preparedness. As you grapple with decisions about how best to stimulate supply, I would urge you to consider carefully the unique structure of the demand side, and the role that distributors play—especially the fact that distributors sign take or pay contracts with manufacturers, with no return privileges. If more supply comes in without concomitant demand, the distributor network will be lost. Accordingly, as support for manufacturing is considered, we need to factor in the distribution network as well. Henry Schein, and the entire distribution network, wants to serve our customers, but more importantly, we stand ready to do what we can do to help HHS, CDC and this committee, to respond to this or any public health crises.

Mr. WALDEN. It has been helpful to have your perspective. Thank you.

Ms. Coelingh, your are welcome to testify now. We appreciate your being with us today. Thank you.

STATEMENT OF KATHLEEN COELINGH

Ms. COELINGH. Thank you. Good afternoon. My name is Dr. Kathleen Coelingh, and I am the senior director of regulatory and scientific affairs at MedImmune, a Maryland-based biotechnology company that manufactures the innovative intranasal influenza vaccine, FluMist. Approved by the FDA last year for healthy persons 5 to 49 years of age, FluMist is the first advancement in influenza prevention in 50 years.

We are at a critical juncture in defining what the influenza vaccine market will look like in the future and how U.S.-based vaccine manufacturers will meet the needs of this country going forward. What will be the incentives for companies to build the U.S.-based manufacturing facilities? How will our government drive vaccine acceptance, utilization, and demand, since it is demand that ultimately determines the supply of vaccine manufactured? And what will be the incentive for continued innovation?

MedImmune recommends that this committee support and encourage two key longer-term solutions in the realm of policy changes and incentives for innovation. The first recommendation is to move toward adoption of a universal recommendation for influenza vaccine for all Americans. The current recommendations, which are based on age groups and an ever-expanding list of underlying chronic medical conditions, are both complicated for the health care provider and confusing to the public. We believe that a universal recommendation will stabilize demand for vaccine and thereby lead to an increased vaccine supply and ultimately to substantially lowering the current mortality and morbidity rates.

As an interim step, MedImmune recommends required vaccination of school-aged children who have a very high influenza attack rate and spread influenza to their younger siblings, to their parents and to their grandparents. Thus, vaccination of school children would directly benefit not only the children themselves, but it may also have the potential to greatly reduce the impact of influenza in our communities. This concept of protecting an entire community by vaccinating the school-aged children has been demonstrated previously in Japan and also in studies in the U.S.

In conjunction with this interim step, money must be appropriated to expand the education of the public and the medical community about the seriousness of influenza every year and the value of influenza prevention every year.

The second solution that MedImmune recommends to ensure continued influenza vaccine supply is to provide tax incentives for scientific innovation and for construction of U.S.-based facilities. MedImmune is a primary innovator in the area of molecular techniques, which Dr. Fauci mentioned this morning, called reverse genetics. The use of reverse genetics is vital to producing seeds for the H5N1 pandemic vaccine. MedImmune owns multiple patents in this area and has granted free access to our reverse genetics intellectual property to government organizations and also to other companies who are developing pandemic influenza vaccines.

In addition, MedImmune is currently collaborating with the National Institutes of Health to produce intranasal pandemic influenza vaccines and to test those vaccines in clinical trials. MedImmune also has coexpertise in the innovative area of cell cul-

ture manufacturing. The main advantages, as we have heard today, are elimination of our dependence on eggs and a more consistent and rapid production of vaccine which will be critical in the event that the egg supply is decimated by the emergence of a pandemic virus.

The transition from egg-based to cell-based manufacturing will require considerable investment in the construction of new facilities and also clinical studies. Tax incentives to subsidize the cost of such innovations are necessary to guarantee a more stable vaccine supply on a yearly basis and also when the pandemic arises. The government also needs to incentivize manufacturers to build manufacturing facilities in the U.S. There is an increased risk that, with offshore manufacturing, companies will face political decisions that may prevent product from entering the United States, particularly in the event of a catastrophic pandemic. Tax incentives for U.S. based manufacturing facilities could encourage manufacturers to build more facilities in the U.S.

To address what MedImmune has done during the current vaccine shortage since October 5, we have worked with the appropriate authorities to first blend and fill our excess bulk material to produce an additional 2 million doses of FluMist, bringing our total production this year to 3 million doses. We have supplied the Department of Defense with up to 400,000 doses, the CDC with 125,000 doses, and we have supplied hospitals with over 60,000 free doses. Third, we have supplied the FDA with new storage data for FluMist, which they promptly reviewed and approved, allowing the additional 2 million doses to be stored in a household freezer without the requirement for a special freezer box. Finally, we have worked closely with ACIP and the CDC to clarify that FluMist is an option for all healthy people aged 5 to 9 to consider if they want to protect themselves against influenza this season.

Shifting gears a bit and looking forward to the next season, you must understand that the influenza manufacturing campaign for the 2005-2006 season is starting right now. We are already preparing the new vaccine seeds which we anticipate will be in next year's vaccine, and we are making decisions about how many doses of vaccine we will manufacture for next year, including how many eggs we are going to order. Thus, the amount of FluMist that will be available for next year will soon be finalized.

With some prompt additional regulatory cooperation, MedImmune has the capacity to produce between 8 to 10 million doses for next season. These regulatory actions include FDA approval allowing for production of larger lot sizes and product filtration, acceptance by FDA of our application to permanently eliminate the requirement for the FluMist freezer box, making shipping and storage infinitely easier for providers, and FDA acceptance of recently submitted data that supports the expansion of the FluMist indication to include the 30 million healthy Americans who are 50 to 64 years of age, a group that is not eligible for the injectable vaccine this season and may not be eligible again next year if the shortage should continue.

To summarize, MedImmune is clearly at a crossroads in determining not only how much FluMist will be available next season but also whether our investments and innovation will be recouped

in this market. Our level of production for next season depends on the occurrence of several immediate regulatory actions. But whether MedImmune expands its production and whether companies continue their efforts to develop influenza vaccine depends in large part upon the government's commitment to encouraging innovation and to driving demand. Requiring childhood flu vaccinations as an interim step toward a universal recommendation and legislating tax incentives for both scientific innovation and U.S. Based manufacturing will go a long way toward stabilizing and ensuring adequate supply of influenza vaccine in the near future. I thank you.

[The prepared statement of Kathleen Coelingh follows:]

PREPARED STATEMENT OF KATHLEEN COELINGH, SENIOR DIRECTOR OF REGULATORY AND SCIENTIFIC AFFAIRS, MEDIMMUNE, INC.

Good morning. My name is Dr. Kathleen Coelingh, and I am the Senior Director of Regulatory and Scientific Affairs at MedImmune, Inc., a Maryland-based biotechnology company that manufactures the innovative intranasal influenza vaccine, FluMist. Approved by the FDA last year for healthy persons 5 to 49 years of age, FluMist is the first advancement in influenza prevention in 50 years.

We are at a critical juncture in defining what the influenza vaccine market will look like in the future and how U.S. based vaccine manufacturers will meet the needs of this country going forward. What will be the incentives for companies to build U.S. based manufacturing facilities? How will our government drive vaccine acceptance, utilization, and demand—since it is demand that ultimately determines the supply of vaccine manufactured? And what will be the incentive for continued innovation?

MedImmune recommends that this committee support and encourage two key longer-term solutions in the realm of policy changes and incentives for innovation. The first recommendation is to move towards adoption of a universal recommendation for influenza vaccine for all Americans. The current recommendations, which are based on age groups and an ever-expanding list of underlying chronic medical conditions, are both complicated for the health care provider and confusing to the public. We believe that a universal recommendation will stabilize demand for vaccine, thereby leading to increased vaccine supply, and ultimately to substantially lowering the current morbidity and mortality rates.

As an interim step, MedImmune recommends required vaccination of school-aged children, who have a very high influenza attack rate and spread influenza to younger siblings, parents, grandparents, etc. Thus, vaccination of school children would directly benefit the children themselves and may also have the potential to greatly reduce the impact of influenza in our communities. This concept of protecting an entire community by vaccinating the school-aged children has been demonstrated in Japan and in studies in the U.S. In conjunction with this interim step, money must be appropriated to expand the education of the public and the medical community about the seriousness of influenza and the value of influenza prevention.

The second solution that MedImmune recommends to ensure continued influenza vaccine supply is to provide tax incentives for scientific innovation and for construction of U.S. based facilities. MedImmune is a primary innovator in the area of molecular techniques, termed "reverse genetics." The use of reverse genetics is vital to producing seeds for an H5N1 pandemic vaccine. MedImmune owns multiple patents in this area and has granted free access to its reverse genetics intellectual property to government organizations and to other companies developing pandemic influenza vaccines. MedImmune is currently collaborating with the National Institutes of Health to produce intranasal pandemic vaccines and to test them in clinical trials.

MedImmune also has core expertise in the innovative area of cell culture manufacturing. The main advantages of manufacturing using cell culture are elimination of dependence on egg supplies and more consistent and rapid production, which will be critical in the event that the egg supply is decimated by the emergence of a pandemic virus. The transition from egg-based to cell-based manufacturing will require considerable investment in the construction of new manufacturing facilities and clinical studies. Tax incentives to subsidize the cost of such innovations are necessary to guarantee a more stable vaccine supply on a yearly basis and when the pandemic arrives.

The government also needs to incentivize manufacturers to build manufacturing facilities in the U.S. There is an increased risk that with offshore manufacturing,

companies will face political decisions that may prevent product from entering the U.S.—particularly in the event of a catastrophic pandemic. Tax incentives for U.S.-based manufacturing facilities would encourage manufacturers to build more facilities in the U.S.

To address what MedImmune has done during the current vaccine shortage, since October 5th, we have worked diligently with the appropriate authorities to:

1) Blend and fill our excess bulk vaccine to produce an additional 2 million doses of FluMist, bringing total production this year to about 3 million doses;
2) Supply the Department of Defense with 400,000 doses, the CDC with 125,000 doses, and hospitals with over 40,000 free doses and more than 200,000 commercially purchased doses.
3) Supply the FDA with new storage data for FluMist, which they promptly reviewed and approved, allowing the additional 2 million doses of FluMist to be stored in a household freezer without the requirement for a special freezer box; and
4) Work closely with CDC and ACIP to clarify that FluMist is an option for *all* healthy people from 5 to 49 years of age to consider if they want to protect themselves against the flu this season.

Shifting gears a bit and looking ahead to next season, you must understand that the influenza vaccine manufacturing campaign for the 2005-2006 season is starting right now. We are already preparing the new vaccine seeds for strains anticipated to be in next year's vaccine and making decisions about how many doses of vaccine we will manufacture next year, including deciding how many eggs to order. Thus, the amount of FluMist that will be available for next year will soon be finalized.

With some prompt, additional regulatory cooperation, MedImmune has the capacity to produce between 8 and 10 million doses next season. These regulatory actions include:

1) FDA approval allowing for the production of larger lot sizes and product filtration;
2) Acceptance by the FDA of our application to permanently eliminate the requirement for FluMist storage in special freezer boxes, making shipping and storage infinitely easier for providers; and
3) FDA acceptance of recently submitted data that supports the expansion of the FluMist indication to include the 30 million Americans who are 50 to 64 years old, a group that is not eligible for the injectable flu shot this year, and may *not* be eligible again next year should we experience a continuing shortage.

To summarize, MedImmune is clearly at a crossroads in determining not only how much FluMist will be available next season, but also whether our investments in innovation will be recouped in this market. Our level of production for next season depends upon the occurrence of several immediate regulatory actions. But whether MedImmune expands its production and whether companies continue their efforts to develop influenza vaccines depends in large part upon the government's commitment to encouraging innovation and driving demand. Requiring childhood flu vaccinations as an interim step towards a universal recommendation and legislating tax incentives for both scientific innovation and U.S.-based manufacturing will go a long way towards stabilizing and ensuring an adequate supply of influenza vaccine in the near future.

Thank you.

Mr. WALDEN. Thank you, and all your colleagues on the panel here for your testimony today. I will start with the first round of questions. I appreciate your comments.

Doctor, you know, in the last, I don't know, 5 or 6 years, we have more than doubled the funding for NIH for medical research. Do you feel like NIH is a good partner and is doing what they need to do in this effort of developing new—assisting with basic research on the cell side, developing new vaccines and new ways to get about vaccines?

Ms. COELINGH. Yes, I do. NIH is—the thing the NIH does the best is research, and they have spent a lot of time and energy in not only developing new vaccines. FluMist is a great example of that. The other thing that NIH is very good at doing is they have good facilities, and MedImmune is cooperating with them in making pandemic vaccines.

Mr. WALDEN. Thank you.

Dr. Paradiso, Wyeth pulled out of the business of making injectable flu vaccine; you have testified to that. It doesn't seem like anybody has rushed in to fill the void here in the United States. And my concern is, what are we going to do come January 5? As you heard the FDA comment, they have to make a decision by January 5 on this plant where Chiron works and produces their vaccines. If that turns out not to be acceptable, what do people like us do here in the Congress to try and get flu vaccine next year but also in the years thereafter? You have alluded to the need for some tax incentives, some liability reform and all. But is that going to get it done?

Mr. PARADISO. You know, the influenza vaccine business is actually a little different than most vaccines. It is—as we have heard, the vaccine changes every year. It is a challenge that starts at the beginning of a year and needs to be completed by August. You need to be able to predict what the likely demand will be and try to match the demand. Our experience has been that, in fact, that was very hard to do. And as I indicated in my testimony, we throw away vaccine every year.

I think Mr. Deal said earlier a comment that is very telling: He didn't know that he wanted a flu vaccine until he couldn't get it. And so what happens is that, traditionally, Thanksgiving comes around, and we stop vaccinating, and it doesn't matter how much vaccine is available, and the result is that we end up all throwing away vaccine most years. And so, to my mind, stabilizing that demand and having some way that a company can be assured that, if they make excess vaccine, in the event that these kind of shortages occur, that there is some way for a sharing of that risk in order to encourage people to do that, either to get into the business or, even if you are in the business already, to make more than you can predictably sell.

Mr. WALDEN. I want to go back to Dr. Coelingh, because you said that FDA needed to make some regulatory changes for your company to be able to achieve an 8 to 10 million or 8 to 10 million doses of your product. How soon do you have to have those changes in order to be in a position to achieve that goal, that production goal by next year?

Ms. COELINGH. Well, as I mentioned in my presentation, we are at that time of year when the amount of doses—we have to decide the number of doses very shortly, and so we need a decision very shortly. If we don't know what our demand is going to be, we have to plan for another contingency. So there are a number of factors that we take into consideration, and some of these regulatory actions are absolutely required for us to go to that level.

Mr. WALDEN. Okay.

Ms. COELINGH. And they are required soon.

Mr. WALDEN. And soon is?

Ms. COELINGH. Soon, we are talking about weeks, not months.

Mr. WALDEN. That is what I needed to hear. All right.

Ms. Olszewski, I am sure you had maybe a reaction to what Mr. Mlotek said about the distribution system, because Mr. Mlotek said that, if I understood correctly, the best distribution point when there is a limited supply is through a doctor's office so that they

can determine who best to give them to in terms of their patient load, who is most in need. And I am just curious, from a health clinic side, you obviously have some authority to make that decision as well and took that step. Does that same authority apply across other States, health departments? And is that an authority the CDC should have to mandate who gets it? Or do they even have that authority? If you would like to address that.

Ms. OLSZEWSKI. Every State does have some authority, but it depends on how their State public health laws are constructed. So all of us have slightly different imminent danger, public health emergency authorities to essentially limit how—or to handle any public health events. So all of us do have authority. And, as I indicated, several States—I know Oregon was one. Vermont was another. Michigan was a third. There are others who have done that. In my testimony, I did say that I thought the Federal Government in the form of the Department of Health and Human Services—it could be Centers for Disease Control—should have some authority as well on a national level.

Mr. WALDEN. You know, one of the things we hear though all too often is, don't trump our State's ability to make these decisions. Is that what you are asking for, is a Federal preemption over what you have the authority to do now and most States have the authority to do?

Ms. OLSZEWSKI. Well, as I said earlier, the issue with flu vaccine is—the supply issue is really a national issue. And when we get into supply shortages, there were States, for example, there were a few states that had no supply in their State on October 5 because they had put all their orders through Chiron. And so, in that situation, it does that State no good to have only State authority. And so I think there really is a role for the national level. I think we need to think carefully about what the respective roles of the Federal Government and the State government are. But that would be important.

Mr. WALDEN. Thank you. My time has expired.

I now recognize the ranking member at this point, Mr. Green.

Mr. GREEN. Thank you, Mr. Chairman.

One of the suggestions is that the government support a supply, a surplus vaccine buy-back program, and for the government to do it at the end of this season so manufacturers aren't stuck with it—they can't hold it for the next year, obviously, below market price. Can each member of the panel talk about that may be one of the solutions we are looking at to take away some of the fear that you will be stuck with overexcessive vaccine?

Mr. PARADISO. You know, I think that, in dealing with shortages in general of vaccines, one of the ideas that has come forward often is the idea of strategic inventories or stockpiles. For routinely administered vaccines, there is a different situation where you can build a stockpile and have some sort of rotation within that stockpile because you are giving the vaccine constantly over the years. For the flu vaccine, it is a little different situation, and so really, by the end of the year, if that vaccine is not used, you have to throw it away. And so if there is some way to share that risk, that is a positive step.

The better solution of course is to actually better meet the demand and the supply, and get better at actually making that connection, and, furthermore, appreciating the value of the vaccine and the importance of the vaccine. As I said before, the importance of this influenza vaccine is not appreciated until it is not available, and it is then that we try to rush to have these solutions and, people are willing to pay lots of money, as we heard earlier, and want to do anything they can to get a vaccine. And that is not the case year after year, and in fact, they don't get a vaccine.

Mr. GREEN. I agree. One of our members, I think, said they didn't know they really wanted one until they couldn't get one. But we have done a better job in the last few years of marketing this idea that you should have a flu vaccine, particularly if you are in the high-risk group. And so, you know, looking at ways, it would be great to be able to match the number of vaccines with the number of people who would be willing to get them.

Ms. Olszewski.

Ms. OLSZEWSKI. I think that is very important. And if we had some attention to an adult immunization program, we in the public health community could help stabilize that demand. I think that part of it is just a consistent message.

Unfortunately, we did make some progress last year, and we were making great progress this year in getting people to realize they needed a flu vaccine, and then we were hit with the shortage. So now we have given out an inconsistent message; you know, you want it and now you can can't have it. And I think if we had an adult immunization program where we could put some concerted effort into that marketing, into that education piece, then we could help stabilize demand.

Mr. MLOTEK. May I, sir?

Mr. GREEN. Yes.

Mr. MLOTEK. A few statements I just would like to clarify or perhaps even challenge. When Wyeth left the market, almost immediately the other two manufacturers issued press releases that they were going to increase production, and they ramped up production to amounts in excess of what Wyeth had produced. So this year—in previous years, the most that was ever produced was 80, 84 million doses. This year, the market was expecting to get 100 million doses, which was far more than the market had ever used before. In the past, the most that the market had ever bought was 80 million doses, and as a matter of fact, that amount had been stable for the last 3, 4, 5 years.

So with the increased communication that we have been doing, we have not been able to increase demand for the supply, and this year, the projection was there were going to be 10 to 20 million doses thrown away. And to incentivize people to come to market—and there are people who want to come to market as soon as next year if the FDA could be funded and do whatever they need to do to get them here. The idea that is needed is, there is going to be a short-term imbalance of demand versus supply until we can get the word out. And that is the need for short-term safety net until the free market economy can take over and work.

Mr. GREEN. And do you think some type of buy back and sharing the cost of the loss is something that could be on a short-term basis?

Mr. MLOTEK. I believe a short-term basis until supply and demand works, because, as soon as you increase demand, people will come in and be able to produce. The free market works.

Mr. GREEN. Let me ask another question, because I only have 28 seconds. But there is suggestion on tax incentives to spur investment and capability and facilities to do both sale and other emerging technologies, so maybe we won't have to have this shelf-life problem, that we could deal with it, whether it is grants or other incentives. Can somebody just address that to see the potential? Is that something that is really, that we could look at, or is it something that is still in the research stages?

Ms. COELINGH. Are you speaking of the cell cultures specifically?

Mr. GREEN. Cell cultures, or any way that we can produce it other than with the eggs technology.

Ms. COELINGH. All right. I think most of us in the business are quite enthusiastic about a move to cell culture, and there are a lot of reasons for that. Before we would make that move, of course, we have to show that we can get sufficient yields and that we can make vaccine consistently. But we have every reason to think that the consistency will be good and that we will have a little bit more flexibility in that we could maybe start off at a different time of year, or if we see a problem coming, that we could ramp up our production, whereas we couldn't do that sort of thing with eggs because of the long lead time.

And there are other advantages to working in cells, and that really relates specifically to a pandemic, because these avian strains are lethal for chickens. Okay? So we want to be ready, we want to have something other than eggs if at all possible that we can use.

The other thing I would like to add that I think gets lost in this conversation is that use of cell culture is not a new concept with vaccines. Most vaccines are made using cell culture. So it is not novel in that respect, it just has to be applied to influenza virus vaccines.

Mr. GREEN. Mr. Chairman, if you will indulge me.

Is there more interest now in doing the research so we could do the cell culture because of this year's example, either oversupply or this year's dramatic undersupply?

Ms. COELINGH. I think that it has gotten more on the front burner because of those two reasons, the pandemic and because of our current shortages, that we just realize that we would like to make some moves if at all possible to cell culture.

Mr. WALDEN. Doctor, do you want to go ahead and respond?

Mr. PARADISO. I would also just like to make a comment. I think we need to be sure to put the context of the flu vaccine into the context of the vaccine business in general, because a company generally—or most of the companies who are in the flu vaccine business are in the vaccine business generally. They have an infrastructure. This is the first vaccine for MedImmune, but they plan to make more vaccines in the future. You have to invest in, and there are so many issues within vaccines that need to be ad-

dressed. It is not just flu vaccine related issues. It is related to the amount of time it takes to develop a vaccine, the risks associated with that, the cost of facilities, the liability issues. And so the issues that influence vaccines, any one of them you could think of ways to overcome. But if you don't broadly address those issues to make it more attractive to manufacturers, manufacturers of even flu vaccine are going to wonder why they want to do that.

Mr. GREEN. And just briefly responding, I do an immunization day in August for our children, which is much more typically concerned with other than our annual flu shots. And I agree with you, and I would love and I think any member of the committee would like to have information on how we could do it on a statutory basis or even on a regulatory basis, encourage our agencies to do that. And if it takes statutes, then here at the authorizing committee, we don't give you money, we just can give you authority. But I would love to work with you on that.

Mr. WALDEN. Here is your checkbook, that is all you get. And I will go to my colleague from Illinois. I think this issue though of the pandemic is one that I hope we can get into here at some point because the briefing I have had in terms of what can happen coming out of Asia runs those birds right up the west coast of the United States and hits pretty close to home before you will have any vaccine in place.

And I would recognize the gentlewoman from Illinois.

Ms. SCHAKOWSKY. Thank you, Mr. Chairman.

It seems to me that the notion of all of this as a security issue, certainly a health security issue, and that has been referred to when we talk about pandemic, that is really what we are talking about. But it is really also, it seems to me, reflective of the potential of a national security issue as it relates to a bioshield and our ability to address that problem. And I was concerned when I read in the testimony of Dr. Crawford, he describes what we have as a fragile infrastructure, because of the fragile infrastructure and decision of manufacturers to leave the market. We have been talking a lot about the market.

Mr. Mlotek has said the market works. I think we have evidence I feel that the private market has not worked well for us. And Ms. Olszewski's statement that relying simply on market forces does not work when it comes to flu vaccine. So I want to talk a little bit about what I see as the necessity—and I heard you say that, Dr. Coelingh—that the importance of U.S. manufacturers for these vaccines, and I would agree.

But I want to go to Dr. Paradiso, where you said that in your testimony—I don't know if you said this in your—you talked about the tetanus vaccine, that the cost is so low that no company has bid to provide it to the government for many years, that Merck MMR vaccine is listed on the government's schedule at around $16.25 while the market catalog price is $38.05. Is Wyeth a profitable company?

Mr. PARADISO. Yes, it is.

Ms. SCHAKOWSKY. My understanding is that the 2003 profit margin was 19.56 percent; that in 2002, $44 billion in profits, an increase of 95 percent over 2001, the greatest rate of increase of any Fortune 500 company.

I am not against profits, but I am wondering, at what point do we say in a partnership with the providers of vaccines that we have an overriding public interest concern here that can't just simply be addressed in how big are the profits? And my question is, when we talk about, all right, Merck, the government's schedule at $16.25 while the market catalog price is $38.05. Does that mean that, at $16.25, or if there is something comparable with Wyeth, that you don't make any money, that you are actually losing money? Or is it just that there is not enough profit in making vaccine for U.S. companies to engage in that when they could be making so much more money doing something else?

Mr. PARADISO. Thank you. I think the issue for the prices that you are talking about are the results of the program when the Vaccines for Children program was put into place. And when that occurred, the vaccines that were available at that time were, the prices were fixed except for cost-of-living adjustments. That was over 10 years ago, and those rules are still in place.

And what is highlighted is an area that could be remedied, because most of the vaccines that were on that list to begin with are no longer used and have been superseded by new vaccines. So it is an area where I think that a change could be made that would be helpful. But when you talk about responsibility, and I think you talk about the vaccine enterprise, we have been committed for many years to make vaccines for children in particular; it has been our focus. We have provided vaccines that prevented serious diseases like meningitis, and in fact, our most recent vaccine, Prevnar, has had a dramatic impact on childhood invasive disease from pneumococcus, including meningitis, and that vaccine has been so effective in fact that parents and grandparents of those children are not getting diseases and pneumonia in particular.

And so from our perspective, vaccines are probably the most valuable product that we could actually put onto the market and have proven to be that over and over again. So I think, from the government perspective, getting back to those products you referenced, fair market value ought to pay for those products.

But when you talk about, for example, our flu vaccine, which is what we are talking about now, year after year, it was clear that the public didn't want that product from us and that there was ample product out in the marketplace that made it unnecessary for us to be in that business. And, in fact, since we were losing money every year and actually throwing doses away every year, and it was clear that the other manufacturers who were still available were able to supply the vaccine and did subsequent to our leaving the market, it was the decision that we made that was in fact responding to the marketplace at that time.

Obviously, what has happened this year has changed that paradigm and made us perhaps think about that differently. But I would suggest what it has made us think about is the actual value of influenza vaccination and whether we need to increase our perception of what the value of that is beyond when there is a crisis and on an ongoing basis.

Ms. SCHAKOWSKY. A universal—essentially a universal adult immunization program, Ms. Olszewski, you are suggesting, could sta-

bilize the market, that is, address some of these market concerns and could save a lot of lives in the United States.

Ms. OLSZEWSKI. Absolutely. It could save lives, it could save morbidity, mortality. It could also save health care costs, because obviously, those adults and children who suffer the complications of influenza, administering a flu shot is a lot cheaper than the hospitalization and the physician care that is required afterwards.

Ms. SCHAKOWSKY. And, Mr. Chairman, if you could just—I mean, what concerns me here is that the public health of the United States is at risk right now and that, while we absolutely need to look at the ways that the United States, that the government can assure a U.S. production of this kind of vaccine, I think we also can't simply say, if we don't get this market price and we don't make sufficient profits, that that is not going to be the only—that is not going to be the only concern that we need to address. We have to work in partnership to figure out exactly how we can address what I think is a—it could be a devastating crisis. Thank you.

Mr. WALDEN. Thank you.

The Chair now recognizes the chair of the full committee, Mr. Barton.

Chairman BARTON. I thank the chairman. I had to attend the Texas delegation lunch, and that is why I was absent. Excuse me, the Republican section of the Texas delegation lunch. I don't want Mr. Green to get chagrined there.

I have two questions, and they are general questions. And anyone who wants to can answer them, or all of you for that matter. No. 1, how confident are you folks that this won't repeat itself next year? And, two, if you think there is a possibility that we may have the same problem, what do we need to be doing, we the Congress, legislatively, to help change the system to minimize the potential for having these kind of problems that we are having this year?

Ms. HEINRICH. I will start out. I do think that we are at risk of having problems next year because we are not sure of what the flu vaccine supply is going to be. And it is absolutely critical that we identify the high-risk patient populations—and clearly, we have heard that the States are in the process of doing that—and that we identify the health care providers that are serving those high-risk groups, and that we find a way of quickly making sure that those providers are the ones that have the vaccine to give to the high-risk populations.

From a legislative perspective, other than some of the ideas that have already been put on the table here, giving CDC actual authority when there is a public health crisis at a time of shortage to actually have more direct authority for that distribution process, I am just not sure what more could be done in the short term. Because as we have heard, the manufacturers have to be planning now for the number of doses that they are going to be producing for next year.

Mr. MLOTEK. May I jump in with a quick comment? I agree that in terms of whether it is going to happen again for next year, it is a distinct possibility, and we will not know for a while. And, again, so what does it lead to is a little bit of a chicken-and-egg

situation. If they come back, there will be 100 million doses in the market. So at the same time——

Chairman BARTON. When you say they, Chiron?

Mr. MLOTEK. If they—Chiron comes back there will be over 100 million doses in the market, maybe 110 million doses. At the same time, the FDA should be going out and finding, with HHS, another potential manufacturer to enter the market. They are there, they just need to be inspected and gone through expedited approvals. They want to come to market. We have seen them. We have met with them. We know they want to come to market. The FDA needs to have the resources to be able to go out and inspect them and do expedited approval.

On the other hand, if they come to the market and Chiron is back, you have an oversupply. You have 140 million doses when the market has never used more than 70 to 80 million. So there has to be two tracks. The one is, get more people in, and the second is some sort of stability in the market in the short term while there is a supply demand imbalance while the CDC, the government, all of us, public, private together work to increase demand.

Chairman BARTON. I would assume that this is a question that I almost already know the answer. But you can't create—like we have the Strategic Petroleum Reserve, because you can store oil indefinitely. We couldn't create a strategic flu vaccine reserve where we built a reserve because the shelf life of the vaccine I guess is fairly short?

Mr. MLOTEK. And the strains change every year.

Ms. COELINGH. That is correct. I would like to add that, from my perspective, I think, every year, we are undervaccinating in the United States. And I can't help but have to go back to the fact that everyone is at risk. You know, we all are starting to forget that there is a high level of disease even amongst healthy children. We had 152 deaths among children last year from influenza, and many of those had no identified high-risk condition. So we can't take our eye off the ball. We can have short-term fixes. We can talk about strategic reserve. We can talk about buy-back programs. But in the long term, those may not be actually healthy for our industry, because if the government buys vaccine at below market prices and you don't get a fair return on your investment, that ultimately is not healthy for the industry overall. And so we need to make sure we have vaccine for next year, but remember that we have to talk about the long term as well. So that is where we come back to investing in the future, in the future vaccines.

Chairman BARTON. Do you all—and my time has expired. But do you all agree that this is part of a broader issue, that the way we do liability for immunizations and research, that it is not just flu vaccinations, it is the broader medical community and the way we address a lot of vaccinations and immunizations for various diseases that we need to take a look at that? Is that a fair statement?

Mr. PARADISO. I would like to comment that one of the reasons that Wyeth is one of the few remaining vaccine companies that are U.S.-based and working on vaccines, is because it is not an easy business to be in. So you are absolutely right. There are, as I said before, an accumulation of issues that are important to our vaccine enterprise. And they have been important for years, and we have

had these issues of shortages and childhood vaccines in the last several years. We have a shortage this year. We have had a lot of recommendations that I think are positive, and we talked about a lot of them today. And we need to move forward with them.

And I would just like to say one other thing. I talked about our pneumococcal vaccine for babies that has prevented an amazing amount of disease in the elderly and adults because they have stopped that spread. Well, it is the same thing as Dr. Coelingh was saying; with children, probably the best thing you can do to protect the elderly is actually to vaccinate their children and grandchildren. And so while we are focusing all our vaccine on the elderly this year, you have to remember that the 36,000 deaths that occur every year in the United States are occurring in the face of the fact that we are vaccinating 65 or 70 percent of those elderly. So they are not able to respond as well as we would like to begin with. So even if we were to raise that to 75 or 80 percent, there would still be a lot of morbidity in that age group, and that is because they are getting the disease from the people who are around them who could be protected from influenza more readily. And so if we expand that population of people vaccinated, we are more likely to protect the most at risk. If we expand that number and expand the suppliers to provide that number, we will be more prepared to deal with a pandemic if that occurs because we will have more sources of vaccine.

Chairman BARTON. My time has expired. I want to compliment you folks on showing up and being a part of our panel. And this is something that the oversight subcommittee and myself as full committee chairman, we are going to work cooperatively with the stakeholders and the Federal agencies not just in the short term but in the long term. And my understanding is that Congresswoman Eshoo and others offered to work with us on a bipartisan basis, that, if we need to implement a legislative package of reforms, we will try to expedite that. And I thank you all for your participation.

Mr. WALDEN. Thank you, Mr. Chairman.

I know Mr. Green wanted to make one final comment.

Mr. GREEN. Mr. Chairman, and, again, our chairman of the full committee. And I know there may be some liability issues, but this is just not liability. And so to pass liability protection for immunizations or for vaccines will not do the trick. There has to be a broad package. And I agree that—and of course the high risk are not typically the younger children or the grandchildren or the children of the elderly. So maybe we need to have a broader program like we do immunize every child by 2. Of course, I come from an area where we have low immunization rates for children, which is frustrating because it is marketed so much, and yet we still have problems. But, again, joining the chairman, both the subcommittees working together—I am not on Oversight and Investigations Subcommittee but on the Health Subcommittee, because it is part of the concerns about public health and the vaccines. And like him, I want to thank you for being here and appreciate what you do. Prevention is always so much better than the illness. So that is what we need to do on all vaccines.

Mr. WALDEN. I appreciate your comments. And as at least currently the vice chairman of the O&I, I concur with what the chairman said. And obviously, we need to get back at this issue of the pandemic as we work on the year-to-year chasing this flu bug and trying to stay ahead of it.

But in the information I have seen about what happens in the avian flu, if that ever converts over to where we get it, which could happen, you could see a pandemic where it is not 36,000; it could be 30 million. And we have got to figure out in terms of research how to accelerate and how to have what we need as an infrastructure to deal with that.

So we really appreciate your comments. Thank you for sticking with us today. Your testimony is very helpful as we work on this issue together.

And, with that, the committee record will remain open for a period of time for members to submit questions they may have had and for other comments. We do appreciate it and look forward to working with you. And, with that, the committee is adjourned.

[Whereupon, at 1:32 p.m., the subcommittees were adjourned.]

[The Department of Health and Human Services did not provide material requested for the record. The Department did not respond to questions for the record.]

[Additional material submitted for the record follows:]

PREPARED STATEMENT OF THE AMERICAN COLLEGE OF PHYSICIANS

The American College of Physicians (ACP)—representing 116,000 physicians and medical students—is the largest medical specialty society and the second largest medical organization in the United States. Internists provide care for more elderly and patients with chronic health conditions than any other medical specialty. As such, the College urges Congress and the Executive Branch to work together in a bipartisan fashion to address misdistribution and shortages of influenza vaccines. The current influenza vaccine shortage highlights many of the shortcomings of our existing system.

The development and use of vaccinations is one of the most successful and cost-effective public health initiatives in history. Vaccines reduce future medical costs and prevent the need for more expensive drugs. While high levels of immunization have been achieved in the U.S., especially among children, our current system of production and distribution cannot guarantee a stable supply of vaccines. This recurring problem brings into question whether the U.S. is prepared to manufacture and distribute vaccines in the case of an unexpected bioterrorist attack, let alone a potential outbreak of a number of routine diseases.

Going into this flu season, the public was assured that plenty of vaccine would be available to meet the nation's needs. The U.S. was expected to have 100 million doses of flu vaccine this year, up from 87 million last winter. Now, federal health officials expect to have only about 56 million doses of injectible vaccine and another one to two million doses of nasal flu vaccine spray.

ACP is gravely concerned about the impact these recurring shortages will have on the nation's health. Influenza, on average, results in 36,000 deaths and more than 200,000 hospitalizations each year in the U.S. While rates of infection are highest among children, rates of serious illness and death are highest among people over age 65 and people who have medical conditions, such as chronic diseases, that place them at increased risk for complications from influenza.— Persons aged 65 or older account for more than 9 of 10 deaths and 1 of 2 hospitalizations related to influenza. According to the Department of Veterans Affairs, the nation loses $1.3 billion each year due to causes related to the flu, including extended hospital stays and a lack of productivity from missed work and school days.

The current flu vaccine shortage points to several inadequacies in the U.S. vaccine production and distribution system. For one, the U.S. production system relies on too few providers. In 2002, children were endangered and the risk of a serious out-

break increased when five vaccines that prevent eight childhood diseases were in short supply, forcing more than 40 states to ration these vaccines to children entering school. At the time, only four manufacturers produced vaccines for American children, just two of which were American companies. This year, the unexpected suspension of Chiron Corporation's license to manufacture flu vaccine left the U.S. with a single supplier of injectible vaccine.

The unwillingness of manufacturers to enter or remain in the vaccine market has much to do with uncertain returns on investment and the lack of government interventions to avert such problems. There is little economic incentive to manufacture flu vaccines since flu strains are constantly changing, doses cannot be used from year-to year, and manufacturers must bear all of the cost of surplus vaccines. As a result, manufacturers tend to produce fewer doses so as not to risk creating a costly surplus. In 2002, manufacturers lost approximately $120 million through unused vaccines. As a result, 12 million fewer vaccines were produced in 2003 to avoid repeating such a loss.

Because manufacturing cannot begin until new virus strains are identified and grown, it is difficult to stockpile flu vaccine or plan ahead for future flu seasons. ACP appreciates that the Department of Health and Human Services (DHHS) has taken steps to ensure that once the virus is identified, resources are in place to ramp up production and produce enough vaccine to protect U.S. residents as quickly as possible. However, the vaccine industry still relies on outdated technology. In a report released in September 2004, the Government Accountability Office (GAO) noted that the current U.S. system relies on a 50-year old method that uses specially harvested chicken eggs to produce licensed influenza vaccines. Food and Drug Administration (FDA) officials and vaccine manufacturers have stated that this production process cannot be shortened to less than the current 6 to 8 months given the existing technology and safety standards.

Manufacturers are also reluctant to produce vaccine because of the threat of lawsuits over vaccine safety. In 1986, a no-fault compensation system called the Vaccine Injury Compensation Program (VICP) was created to lower the legal risk to vaccine manufacturers and providers who administer vaccines, and to ensure that injured patients are rapidly and appropriately compensated. Recently, the VICP has become overwhelmed with new claims—many of which have been found to lack merit. This has not only delayed consideration of legitimate claims, but caused the spill-over of costly lawsuits into our court system.

Despite the demonstrated effectiveness of vaccination in particular risk groups, our national distribution system also fails to ensure that high-risk patients will have access to vaccines first. Current distribution is based on the date the vaccine was ordered rather than who needs it most. If a manufacturer's production is disrupted, those providers who ordered vaccine from that manufacturer could experience shortages, while those who ordered vaccines from another manufacturer might not be affected at all. ACP is pleased that in response to the current shortage, the CDC is recommending prioritization of vaccine for those at higher risk. However, the agency currently has no authority to mandate that the vaccine go to priority patients or to track where it ends up.

ACP RECOMMENDATIONS

Access to an adequate supply of flu vaccine is especially critical for physicians of internal medicine, since many of our patients qualify as high-risk for complications from influenza, due to either chronic health conditions or age. During previous flu seasons, much of the limited flu vaccine supply went to non-professional distributors, such as drugstores and grocery stores, who distributed the vaccine on a first-come first-serve basis, regardless of risk.

ACP appreciates that the DHHS is taking positive steps to address the current problem and keep the public informed of measures to prevent and treat the flu. We are pleased that a task force has been created to ensure that the flu vaccine and treatment medication goes to those who need it most and without any price gouging. We are also pleased that it includes members of the public health community, physicians, law enforcement and prosecutors, trade associations and advocacy groups. ACP thanks the CDC and Aventis Pasteur for working to identify providers of high-priority populations, including primary care and specialty physicians. Finally, ACP appreciates that the American Jobs Creation Act of 2004 (P.L. 108-357), recently signed into law, takes a first step in the direction of adding the flu vaccine to the VICP. Adding the flu vaccine to the VICP would provide limited liability protections for flu manufacturers, while assuring victims compensation for injuries.

Despite these positive efforts, ACP is concerned that our nation lacks a permanent mechanism to ensure that vaccines reach internists and other primary care physicians who have been clearly identified as providers who care for high-risk patients. To improve our nation's vaccination efforts and ensure that patients most in need can continue to access vaccines, ACP makes the following recommendations for immediate action and offers additional steps for the future:

Recommendations for Immediate Action

- To ensure that patients most in need receive the vaccine, manufacturers of the influenza vaccine, non-professional distributors of the vaccine, and appropriate government agencies should ensure that limited supplies of the vaccine are made available to clinicians and other licensed health care providers who provide regular patient care to high-risk individuals.
  - —In taking steps to ensure that limited vaccine supplies reach providers who serve high-priority populations, the CDC should continue to recognize the role of physicians of internal medicine in treating a disproportionately large number of seniors and patients with multiple, chronic conditions—two patient categories that have historically been labeled by the CDC as high-risk. For many vulnerable patients, the physician's office is the best location to be immunized, especially for patients who are unable to stand in line at grocery and drugstores, and who require careful monitoring.
- Local public health departments should have an aggressive plan in place to distribute vaccine to local providers with the greatest need.
- States should thoroughly investigate reports of price gouging involving the flu vaccine and prosecute those found to be taking advantage of the vaccine shortage.
- To comply with emergency orders issued by state or local governments mandating vaccine be administered only to persons of high risk, physicians should have access to clearly communicated prioritization requirements, distribution plans, and other instructions. Physicians should not be penalized for failure to follow emergency orders that are not clear and timely and do not provide for due process to resolve situations outside the physician's control.

Additional Recommendations

- The CDC should be given the authority to organize the distribution of vaccines and implement a concentrated response system, particularly in emergency situations.
  - —Appropriate and adequate distribution plans should be formulated by the CDC prior to the start of a flu season. U.S. officials should not be scrambling for ways to modify the distribution system to make up for shortages as the flu season begins, as is the case this year.
  - —A vaccine clearinghouse should be established to facilitate donation of vaccine to individuals at high risk of infection.
  - —DHHS should be permitted to purchase vaccine from employers or wholesalers who are willing to sell it.
- Additional research and development to improve surveillance of strains and outbreaks and to improve current vaccine production methods should be encouraged.
  - —Research funding should be increased to help develop alternatives to egg-grown influenza vaccines.
- The federal government should be required to build and maintain a six-month stockpile of prioritized vaccines to prepare our nation for vaccine shortages.
- The federal government should offer incentives to encourage more manufacturers to research and produce vaccines, such as tax incentives for vaccine manufacturers to expand production capabilities and guarantees that the government would purchase unused supply.
- Funding available for state and local efforts should be expanded to boost immunization rates among adults and adolescents who are underserved or at high risk for vaccine-preventable diseases.
  - —Funding should be authorized under the Public Health Service immunization program for the distribution of influenza vaccine to qualifying health care providers, including internists.
- Increase education and outreach efforts for upcoming flu seasons.
- Revise provisions governing the Vaccine Injury Compensation Program (VICP) to ensure that unwarranted litigation does not further destabilize our vaccine supply.

- Vaccines manufactured abroad should only be used in the U.S. if the FDA has certified their safety.

For many years, unavailability of vaccine products has presented a challenge to physicians and patients. The federal government must have a system in place to assure an adequate and safe supply of lifesaving vaccines in the event of a disruption in the expected supply. It is also critical that an adequate and appropriate distribution system be in place to ensure that the most vulnerable patients have access to vaccines before all others.