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# THE FOOD AND DRUG ADMINISTRATION'S CRITICAL MISSION AND CHALLENGES FOR THE FUTURE

## HEARING

BEFORE THE

## COMMITTEE ON OVERSIGHT AND GOVERNMENT REFORM

## HOUSE OF REPRESENTATIVES

ONE HUNDRED TENTH CONGRESS

FIRST SESSION

MAY 1, 2007

## Serial No. 110–24

Printed for the use of the Committee on Oversight and Government Reform

Available via the World Wide Web: http://www.gpoaccess.gov/congress/index.html
http://www.house.gov/reform

U.S. GOVERNMENT PRINTING OFFICE

38–161 PDF WASHINGTON : 2007

For sale by the Superintendent of Documents, U.S. Government Printing Office
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# THE FOOD AND DRUG ADMINISTRATION'S CRITICAL MISSION AND CHALLENGES FOR THE FUTURE

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**TUESDAY, MAY 1, 2007**

HOUSE OF REPRESENTATIVES,
COMMITTEE ON OVERSIGHT AND GOVERNMENT REFORM,
*Washington, DC.*

The committee met, pursuant to notice, at 1:15 p.m., in room 2154, Rayburn House Office Building, Hon. Henry A. Waxman (chairman of the committee) presiding.

Present: Representatives Waxman, Cummings, Kucinich, Tierney, Higgins, Braley, McCollum, Cooper, Hodes, Murphy, Sarbanes, Davis of Virginia, Platts, Cannon, Duncan, Issa, Marchant, Foxx, and Bilbray.

Staff present: Phil Schiliro, chief of staff; Karen Nelson, health policy director; Andy Schneider, chief health counsel; Sarah Despres, senior health counsel; Ann Witt, health counsel; Robin Appleberry, counsel; Steve Cha, professional staff member; Earley Green, chief clerk; Teresa Coufal, deputy clerk; Rachel Sher, counsel; Kerry Gutknecht, Will Ragland, and Miriam Edelman, staff assistants; David Marin, minority staff director; Larry Halloran, minority deputy staff director; Jennifer Safavian, minority chief counsel for oversight and investigations; Keith Ausbrook, minority general counsel; Ellen Brown, minority legislative director and senior policy counsel; Howie Denis and Susie Schulte, minority senior professional staff members; Brian McNicoll, minority communications director; and Benjamin Chance, minority clerk.

Chairman WAXMAN. The meeting of the committee will come to order.

Before I make any specific comments on today's hearing on FDA, I want to say a few words about an important initiative this committee is undertaking.

One of the most important debates in modern politics is the role of government. Some believe in the smallest government possible and live by the old joke that the scariest words imaginable are "I'm from the Federal Government and I have come to help."

I and others have a fundamentally different view. I think government can be a tremendous instrument for good, and I have seen it help Americans in countless ways. The Social Security system transformed this country. Landmark health and environmental laws have improved the quality of life for millions of Americans. Regulatory and consumer agencies have made financial stability, basic safety precautions a part of our everyday life.

In this regard, FDA has had a remarkable record of achievements. It has been and by and large remains an agency with highly qualified and dedicated staff doing a big job under difficult circumstances. It is our job to ensure that it has the resources to continue to perform with competence.

We have reason to be concerned, to examine the strengths and weaknesses of this agency in the light of ever-increasing demands and to ensure that it remains strong. Because we know from other areas that without proper support or without deliberate strengthening of the agency and support for the agency's leadership, or without making sure there is not unwarranted outside interference, things can change. We need only look at FEMA. FEMA once was one of the most prominent and well-respected agencies of Government, but something has gone very wrong in recent years.

We saw government at its worst during the Hurricane Katrina disaster. FEMA completely failed American citizens. We saw it break down again at Walter Reed Hospital in the deplorable conditions provided to our bravest Americans. And we have seen profound problems from government's handling in the Iraq war, where there was flawed basic intelligence to failure to supply our troops with the right armor and equipment.

In all of these cases, we know that incompetent government can have deadly consequences, so one of the most important responsibilities for our committee is to understand what has gone wrong, how did some of the best Government agencies become so weak, and we need to work together in a bipartisan way to get Government back on track.

I know colleagues on both sides of the aisle share my view on this. We don't want Government programs to be ineffective; we want them to be models of excellence. So over the next year our committee is going to hold a series of hearings on making government effective again by looking at the performance of a number of different agencies.

We start today with FDA. By the end of these hearings, we will have a better idea of the impact of budget cuts and cronyism on current problems. I expect we will have legislative solutions that would ensure taxpayers get the Government they deserve.

Today we start this effort. We are in the fortunate position of looking first at an agency that has not been decimated by the pressures placed upon it or the lack of resources made available to it, but there have been a number of public health crises, from the belated withdrawal of Vioxx to deadly bacteria in spinach to contaminated pet food. These have revealed alarming cracks in the foundation of FDA's ability to protect the American public.

The warning signs are clear. FDA is an agency in crisis. We need to act now and to learn from the vast experience of those who have managed the agency through the years.

Today we are fortunate to have an unprecedented assembly of experts, including three former FDA Commissioners and the current Commissioner, Dr. Andrew von Eschenbach, in addition to former Commissioners whose schedules did not allow them to be here in person. We will submit written testimony.

I especially want to thank the Commissioner for accommodating the committee's request that he testify on the same panel as the

other witnesses. I recognize it is the administration's policy for Governmental officials to testify on panels without non-governmental witnesses, and today's arrangement is not intended to nullify that policy. Since this hearing presents a highly unusual circumstance, gathering the former and current head of a single agency, we appreciate the Commissioner's departure from the general agency practice today. Thank you very much.

FDA oversees thousands of products so routine that we don't even notice them: oatmeal, aspirin, even microwaves and cell phones. FDA also oversees products for the times in our life that are anything but routine, days we need emergency surgery, chemotherapy, or a blood transfusion.

FDA's mission is vast and daunting, but not impossible. The agency's history is full of success stories, whether it was protecting consumers from rotten meat in the early 1900's, saving lives by refusing to let thalidomide on the market in the 1950's, or speeding aged drugs to patients in the 1990's. But, as I have said, recent years have brought signs of trouble at the FDA, and at this hearing we hope to learn the causes of these problems, and we will look at four major areas of concern.

The first and most critical issue facing FDA is simple—resources. The agency, in my opinion, is vastly under-funded, relying on an already shrinking budget to tackle a rapidly expanding list of responsibilities. In fact, FDA's entire budget for fiscal year 2007 is less than the budget for Montgomery County Maryland's schools, the whole system, for this year.

A second major concern is scientific integrity at the agency. In recent years, key decisions at FDA have been made under the cloud of real or perceived political interference, undermining FDA's most basic foundation.

A third are of concern is enforcement. Investigations by our staff and other analysts have found that across the agency, from postmarket drug trials to drug advertising to the handling of fresh produce, FDA's enforcement activity has declined. Strong enforcement is a critical component of FDA's work, and I am concerned to see how it has atrophied in recent years.

Finally, we must look closely at FDA's legal authorities to examine whether its governing provisions are outdated or inadequate. One prominent example is in the area of food regulation, where our standards are literally a century old.

On the topic of food safety, I want to acknowledge that this morning the FDA announced that it will create a new position for food protection at the agency. This idea of a food safety czar seems like a reasonable idea, and I support FDA in taking steps to increase the priority of food safety at the agency.

I hope that as the agency begins to undertake long-term strategic thinking, I think the need remains for an immediate response to the current crisis, and hope that today's announcement will be followed by concrete and effective action.

For all its challenges, FDA remains one of our Nation's greatest assets. I called this hearing because I believe in this agency and I want to see it work. As the primary oversight committee of the House, it is the committee's responsibility to identify and begin to

address the urgent challenges facing the FDA, and we will see in other hearings other agencies, as well.

I hope that this series of hearings will lead to real solutions for FDA and for Government, restoring the full capacity and preparing this agency and others to serve its critical mission many years into the future.

I thank our witnesses for being here today. I look forward to their testimony.

Before we call on them and recognize them, I want to have the ranking member of our committee, Mr. Davis, have time to make an opening statement.

Mr. DAVIS OF VIRGINIA. Thank you, Mr. Waxman. I know how important these issues have been to you over the years, and you really hit it on the head: it is about governance. Some on my side just think we ought to have very little government. Let's starve it, let's not give it the funding. There are others who think the more government the better, that we can accomplish more. But we don't focus enough on the governance issues, and that is getting it right and making it efficient.

I want to thank you for holding today's hearing to consider the critical mission of the FDA and the many challenges the agency faces, keeping pace with rapidly evolving science and an increasingly global marketplace.

The FDA's basic mission is to promote and protect public health by approving and monitoring the marketing of safe and effective products. The agency is also responsible for providing current science-based information to the public on key health issues.

In recent years the FDA has stumbled through some high-profile mis-steps. The withdrawal of the pain killer Vioxx caused many to ask if drugs were being approved too fast and monitored too little after reaching the marketplace. The shortage of vaccine for the 2004–2005 flu season raised questions about how best to regulate and stimulate production of biopharmaceutical products. The FDA role in food safety arose again when e-coli contamination was found in fresh spinach this year, and most recently with the nationwide recall of Peter Pan peanut butter.

Most Americans believe that once something gets FDA approval it carries the Federal Government's equivalent of the Good Housekeeping Seal of Approval. It can be used without worry or risk. We need to be sure that confidence is not misplaced or grounded only on the legend of an infallible FDA or the myth of risk-free products. We should indulge neither legend nor myth when entrusting critical questions of safety, efficacy, and risk to Federal decisionmakers, but we should do everything possible to ensure the FDA has the statutory tools, the talent, and the resources necessary to operate effectively, efficiently, and transparently.

I don't want you to have any cause to doubt that, even if they sometimes get it wrong. The FDA is guided only by the best science available and acts solely in the interest of the American consumer.

At stake in the FDA getting it right is the health and safety of the American people and the viability of a huge and growing sector of our economy. Industries regulated by the FDA generate hundreds of millions of dollars in sales revenue, support important research, and create high-value jobs. Continued loss of confidence in

the FDA takes us down a path we simply cannot afford either financially or in terms of public health.

The FDA has to stand out as a trusted, unbiased, vigilant watchdog over the Nation's food and drug supply. Nevertheless, recent high-profile recalls and contaminations heighten concerns about the capability and credibility of the Federal agency charged to ensure the safety and effectiveness of so many medicines, foods, cosmetics, and other products millions of Americans use every day.

So we ask: how can we strengthen the security and safety of foods that now travel around our country and across the world with unprecedented speed? How can FDA work with regulated industries to better ensure the safety of approved drugs and medical devices? What can be done to improve product manufacturing and handling practices? How can post-marketing surveillance of approved products be strengthened, and who will pay for it? And do current adverse event reporting systems capture the reliable and timely data FDA needs to inform sound regulatory decisions?

This committee has looked at some of these questions before. Mr. Chairman, I convened similar oversight hearings on drug safety and post-marketing surveillance issues surrounding withdrawal of Vioxx from the market. We also investigated FDA oversight of reprocessed single use medical devices. Hearings were held on efforts to address the growing problems of illegal pharmacy Web sites. We have closely monitored food safety and dietary supplement issues. Our investigation into the flu vaccine shortage resulted in more-frequent FDA inspections of vaccine manufacturing facilities.

With regard to these major issues, it can't be said we didn't do some oversight. I am happy Chairman Waxman had chosen to keep the focus on these important issues. He believes fervently in the need for a strong, independent, effective FDA and has worked over many years to sustain and strengthen the agency's capabilities.

Given that bipartisan consensus, I look forward to a thoughtful discussion today on the future of the FDA and how to address the many complex challenges faced by the critical Federal agency.

We are fortunate to have before us such a distinguished panel of witnesses. All have held the top leadership post at the FDA and share invaluable experience running one of the Nation's most important public health and consumer protection agencies. We look forward to their testimony, their insights, and their perspectives.

[The prepared statement of Hon. Tom Davis follows:]

**Statement of Rep. Tom Davis**
**Ranking Republican Member**
**Committee on Oversight and Government Reform**
***"FDA's Critical Mission and Challenges for the Future"***
**May 1, 2007**

Thank you Mr. Chairman for holding today's hearing to consider the critical mission of the Food and Drug Administration (FDA) and the many challenges the agency faces keeping pace with rapidly evolving science and an increasingly global marketplace. This is a very important subject worthy of this Committee's continued attention.

The FDA's basic mission is to promote and protect public health by approving and monitoring the marketing of safe and effective products. The agency is also responsible for providing current, science-based information to the public on key health issues. But in recent years, the FDA has stumbled through some high-profile missteps. The withdrawal of the painkiller Vioxx caused many to ask if drugs were being approved too fast and monitored too little after reaching the marketplace. The shortage of vaccine for the 2004-2005 flu season raised questions about how best to regulate and stimulate production of biopharmaceutical products. And, the FDA role in food safety arose again when E-coli contamination was found in fresh spinach last year, and most recently with the nation-wide recall of Peter Pan peanut butter.

Most Americans believe that once something gets FDA approval, it carries the federal government equivalent of the Good Housekeeping Seal of Approval, and can be used without worry or risk. We need to be sure that confidence is not misplaced, or grounded only on the legend of an infallible FDA or the myth of risk free products. We should indulge neither legend nor myth when entrusting critical questions of safety, efficacy and risk to federal decision makers. But we should do everything possible to ensure the FDA has the statutory tools, the talent and the resources necessary to operate effectively, efficiently and transparently. No one should have any cause to doubt that, even if they sometimes get it wrong, the FDA is guided only by the best science available and acts solely in the interest of the American consumer.

At stake in the FDA getting it right: the health and safety of the American people and the viability of a huge and growing sector of our economy. Industries regulated by the FDA generate hundreds of billions of dollars in sales revenue, support important research and create high-value jobs. Continued loss of confidence in the FDA takes us down a path we simply cannot afford, either financially or in terms of public health. The FDA has to stand as the trusted, unbiased, vigilant watchdog over the nation's food and drug supply.

Nevertheless, recent high-profile recalls and contaminations heightened concerns about the capability and credibility of the federal agency charged to assure the safety and effectiveness of so many medicines, foods, cosmetics and other products millions of Americans use every day. So we ask: How can we strengthen the security and safety of foods that now travel around our country and across the world with unprecedented speed? How can FDA work with regulated industries to better ensure the safety of approved drugs and medical devices? What can be done to improve product manufacturing and handling practices? How can post-marketing surveillance of approved products be strengthened, and who will pay for it? And do current adverse event reporting systems capture the reliable and timely data FDA needs to inform sound regulatory decisions?

This Committee has looked at some of these questions before. As Chairman, I convened similar oversight hearings on drug safety and post-marketing surveillance issues surrounding the withdrawal of Vioxx from the market. We also investigated FDA oversight of reprocessed single-use medical devices. Hearings were held on efforts to address the growing problem of illegal pharmacy websites. And, we have closely monitored food safety and dietary supplement issues. Our investigation into the flu vaccine shortage resulted in more frequent on-site FDA inspections of vaccine manufacturing facilities. With regard to this range of issues, it can't be said Republicans did no oversight for six years.

So I am happy Chairman Waxman chose to keep our focus on these important questions. He believes fervently in the need for a strong, independent and effective FDA, and has worked over many years to sustain and strengthen the agency's capabilities. Given that bipartisan consensus, I look forward to a thoughtful discussion today on the future of the FDA and how to address the many and complex challenges faced by that critical federal agency.

We are very fortunate to have before us such a distinguished panel of witnesses. All have held the top leadership post at the FDA and share invaluable experience running one of the nation's most important public health and consumer protection agencies. I look forward to their testimony, their insights and their perspectives.

Chairman WAXMAN. Thank you very much, Mr. Davis.

We do have a very distinguished panel before us. We have our first witness, Dr. Donald Kennedy. He was the FDA Commissioner appointed by Secretary Joseph Califano in April 1977 and served until 1979. During his tenure, the agency dealt with the repercussions of the attempt to ban saccharin, attempted to overhaul the drug provisions of the Food, Drug, and Cosmetic Act in the proposed Drug Regulation Reform Act of 1978. He is an internationally recognized neurophysiologist who headed both the FDA and Stanford University, and at the present time serves as the editor in chief of Science.

We are pleased to have you with us.

Our next witness will be Dr. Frank Young, who was the FDA Commissioner sworn in by Secretary of Health and Human Services Margaret Heckler in August 1984 and served until December 1989. During his tenure, he initiated the user fee process and approved the first drug to combat AIDS and instituted a fast track approval system for AIDS drugs. He was also appointed by President Reagan and confirmed by the Senate as the U.S. member of the Executive Committee of the World Health Organization. He is currently the chairman and CEO of the Cosmos Alliance, a partner in Essex Woodlands Health Ventures, and serves on the Board of Directors of five companies.

We are pleased to have you, Dr. Young.

Our third witness will be Dr. David Kessler, the FDA Commissioner appointed by President George H.W. Bush in 1990 and reappointed by President Clinton, serving until 1997. During his tenure he acted to speed approval of new drugs, placed high priority on getting promising therapies for serious and life-threatening diseases to patients as quickly as possible. He introduced a number of new programs, including: nutrition labeling for food, user fees for drugs and biologics, preventive controls to improve food safety, and the MEDWatch program. He served as the Dean of the Yale University School of Medicine, and is currently the Dean of the School of Medicine and the Vice Chancellor for Medical Affairs at the University of California, San Francisco.

Dr. Kessler, we are pleased to have you.

And the final witness will be Dr. Andrew von Eschenbach, who was sworn in as the 20th Commissioner on December 13, 2006. At the time of his appointment he was the Director of the National Cancer Institute. Dr. von Eschenbach is a nationally recognized urologic surgeon and oncologist.

We are pleased to have you, as well.

It is the practice of this committee for all witnesses to have them sworn in, and so I do ask you to please rise and raise your right hands.

[Witnesses sworn.]

Chairman WAXMAN. The record will reflect that each of the witnesses answered in the affirmative.

Now we would like to call on the witnesses. Our first witness is Dr. Kennedy.

**STATEMENTS OF DONALD KENNEDY, PH.D., FORMER COMMISSIONER, 1977 THROUGH 1979, FOOD AND DRUG ADMINISTRATION; FRANK YOUNG, M.D., PH.D., FORMER COMMISSIONER, 1984 THROUGH 1989, FOOD AND DRUG ADMINISTRATION; DAVID KESSLER, M.D., J.D., FORMER COMMISSIONER, 1990 THROUGH 1997, FOOD AND DRUG ADMINISTRATION; AND ANDREW C. VON ESCHENBACH, M.D., COMMISSIONER, FOOD AND DRUG ADMINISTRATION**

**STATEMENT OF DONALD KENNEDY**

Mr. KENNEDY. Mr. Chairman, thanks very much. It is a pleasure to appear before the committee. I want to thank you especially for organizing this splendid reunion.

You asked me to provide some information that might be helpful to the committee in examining its responsibilities for oversight of the Food and Drug Administration as it faces new challenges. I am going to touch briefly on some of those before turning to an analysis of other factors.

Among the current problems, as you have noted, are food safety, difficult questions surrounding the safety of already marketed drugs, preparations for pandemic influenza, and an old problem that owes much to the unavailability of a sound adverse reaction reporting system, problems in monitoring the safety of already marketed drugs.

These problems naturally arise within the orbit of FDA's own statutory and regulatory authority, but there are some problems that seem to have arisen from the outside. Let me just mention those briefly.

For only a fraction of the past 6 years has FDA had at its head a Commissioner confirmed by the Senate. I think we all know that the FDA could function pretty well for short periods without a leader. It has a competent, highly graded, technical Civil Service staff. But FDA enjoys frequent external challenges that must be met by leadership that is fully authorized and credible and in place, and too often it has not had that kind of leadership. I am glad it does now.

A second problem is that FDA has for some time been chronically under-funded and under-staffed. If you compare the 2003 budget with the current one for 2007, it is a disheartening story. To conserve its purchasing power from 1 year to the next, FDA would require an increase of about 5.8 percent in that-year dollars, and at that rate of increase FDA's 2007 budget would have been about $1.924 billion and, in fact, its actual appropriation was $1.558, a shortage amounting to an under-budgeting of 20 percent below what was needed.

I think my fellow ex-Commissioners would agree that an appropriated budget of $2 billion in fiscal year 2008 would be needed to restore FDA's capabilities to the level at which it functioned in 2003.

FDA is, furthermore, a payroll-intensive agency, and I am sure it is no mystery to members of this committee that it has the same problems that a small business has, and that is with the rising share that benefits programs, especially health benefits programs, take of the budget.

So, as a consequence, FDA not only has less money in 2007 than it had in 2003; surprisingly, it has a disproportionately lower number of FTEs. So it is a truly difficult situation for the agency.

It might be asked whether an increase in user fees couldn't substitute for appropriated funds. I don't think so, for two reasons.

First, some citizens, on hearing that the drug industry contributes significantly to FDA's work, may wonder whether that opens the door to subtle influence. I am convinced that it does not, but the perception may be more general than we hope.

Far more important is that FDA's user fees are restricted to activities related to the new drug approval process. They are, thus, not equivalent to appropriated funds, which must cover the full spectrum of FDA activities. The user fees permit the hiring of more drug reviewers, but don't pay the external cost that any additional FTE undoubtedly brings to the rest of the organization. So when the drug approval process succeeds, food suffers.

I want to echo a point made by the recent study of the Institute of Medicine of the National Academies. It makes a point that there is a large disparity between the resources available for the new drug review and approval processes at FDA and those available for the monitoring of drug safety.

The IOM report makes some useful recommendations concerning the capacity of FDA to undertake risk assessment and risk management with respect to already marketed drugs, which I will mention a little bit more later.

I hope the Congress will examine with special care those recommendations about the public availability of the results of clinical trials actions. In agreement with several major medical journals, IOM urges that the industry sponsors be required to register at clinicaltrials.gov all of the clinical trials that they are about to conduct through phase four.

The key here is that full information about the conduct of these trials and the problems that may arise with them should be made available to the public. Are they? FDA has invested significant labor in making those records available at its Web site. This appears to be an appropriate response to section 5.1 of the IOM report, but to call it publicly available in any real sense is not right.

With the help of the director of clinicaltrials.gov, I got walked through that Web site to find records of the trials for Ketek, a drug about which important safety issues have arisen. One can get to the right pages, but although the trials are listed there, there is no information about the institutions, the investigators, or the problems that might have arisen in the course of those trials. One can get to the right pages, but you can't learn very much from them.

Even the list is impossible to find unless one knows what one is looking for, and the studies cannot be linked to from clinicaltrials.gov.

I think that, with some support for information technology, the navigability of this site could be improved to validate FDA's promise that this vital information is publicly available.

I want to make two more very quick points related to that topic.

First, the IOM report asks Congress to give FDA authorities that it could apply to require conditions for distribution of already mar-

keted drugs. These would include the capacity to make FDA-initiated changes in drug labels, a moratorium on direct consumer advertising if that were deemed necessary, or various other conditions.

As with other needs, this is going to require appropriated funds and not user fees.

I also want to make a quick mention of another serious risk that FDA confronts now in the drug area, namely antibiotic resistance. That problem is bad both on the supply side and the demand side. The demand side doctors and patients are not conforming to the most risk-averse kind of behavior, and need some encouragement, as do hospitals. More important, perhaps, on the supply side there is a good case for a kind of orphan drug protection for new antibiotics where already-existent antibiotics have shown serious resistance problems and may need replacement.

Mr. Chairman, FDA had to explain repeatedly to the Congress back in my day that it was difficult to pursue a comprehensive program for evaluating the safety of already marketed products. The reason is that in order to calculate an adverse reaction rate you need to know the numerator, the number of observed problems, and the denominator, the number of prescriptions that are out there. You can't find the rate without both.

FDA's numerator depends on a largely voluntary reporting system involving doctors and firms. The denominator has to be constructed, for example, through a prescription system in which an extra copy recording only the drug's identity and the dosage is made centrally available for data storage.

That, unfortunately, is not available, and the ironic result of the Vioxx study done by FDA is that it had to be done at Kaiser Permanente, the only health care organization, HMO, that had enough patients and a good enough record keeping system so that you could get both the numerator and the denominator. That is a problem that really needs fixing.

I will conclude with just a couple of other quick summary notes.

This is an important agency, as you know. It accounts for about 25 cents out of every consumer dollar spent in this country. If we expect to have our spinach uncontaminated, our pet food safe, Congress needs to provide FDA with the resources and the authorities it needs, especially on that broken food side, of which I know you will hear more from Dr. Kessler.

I hope your staff and your colleagues on the committee will continue your diligence about pursuing FDA resource needs.

Unfortunately, to hear the bad news you have to rely occasionally on old-timers like me, because budget authorities at HHS and OMB prohibit present officials in the agency from speaking out publicly as enthusiastically as they would like about the need for more funding.

I used to squirm about this in my day, but it is a fact of life. I know this is no news to you, but I hope that the American public, which expects a lot from the FDA, knows that when its officials express satisfaction with their budget allocations, they have their fingers crossed underneath the witness table.

Thank you very much, Mr. Chairman.

[The prepared statement of Mr. Kennedy follows:]

Statement of Donald Kennedy, Ph.D., former Commissioner, FDA; President, emeritus, Stanford University and Editor-in-Chief, Science

Mr. Chairman:

It is a pleasure to appear before the Committee on Oversight and Government Reform, and to make your acquaintance once again. You have asked that I provide information that might be helpful in examining the critical mission of the Food and Drug Administration as it faces new challenges. If I may, I'd like to begin by citing a few of those contemporary challenges, and then move to a consideration of FDA's needs to guarantee the future quality of its work. Among the current problems are food safety, as evidenced by recent recalls owing to bacterial contamination; preparations for pandemic influenza; difficult questions surrounding the safety of already marketed drugs – an old problem that owes much to the unavailability of a sound adverse-reaction reporting system in this country -- and problems in maintaining inspection and analytic capabilities to deal with a wider range of problems and production sites.

These problems, of course, all lie within the orbit of FDA's statutory and regulatory responsibility. Others, however, lie outside the agency itself. For example, in only a fraction of the past 6 years has FDA had at its head a Commissioner confirmed by the Senate. I think we all knew that FDA could function well for short periods without a leader; it has competent, highly graded technical civil service staff. But FDA enjoys frequent external challenges that must be met by leadership that is fully authorized, credible, and in place.

A second problem is that FDA has for some time been chronically under-funded and under staffed. A comparison of FDA's budget comparing 2003 with the current fiscal year tells a disheartening story. To conserve its purchasing power from one year to

the next – that is, to enable the agency to buy the same bundle of goods and services at next year's costs – would require an increase of about 5.8% in that-year dollars, and at that rate of increase FDA's 2007 budget would have been $1,924, 000, 000 (1 billion 924 thousand) but its actual appropriation was only $1,558,000,000 (1 billion 558 thousand) – nearly 20% below what it needed to be. I think my fellow ex-Commissioners would agree that an appropriated budget of 2 billion in FY'08 would be needed to restore FDA's capabilities to the level at which FDA functioned in FY'03. FDA is, furthermore, a payroll-intensive agency. I hope it has not escaped the Congress that FDA – like other medium-sized businesses – has suffered chronically because health and other benefits costs for its employees have risen much faster than salaries. As a consequence, FDA not only has less money in '07 than it had in '03; surprisingly, it has experienced a disproportionate reduction in its number of employees!

It might be asked whether increases in user fees could not substitute for appropriated funds. I think not, and for twos reasons. First, some citizens on hearing that the drug industry contributes significantly to FDA's work, may wonder whether that opens the door to subtle influences. I am personally confident that PDUFA and the agency have that under control, but the perception may be more general than we hope. Far more important is that FDA's user fees are restricted to activities related to the new drug approval process. They are thus not equivalent to appropriated funds, which must cover the full spectrum of FDA activities; the user fees permit the hiring of more drug reviewers but don't pay the external costs they bring to agency management. With respect to present needs, the recent report from the Institute of Medicine of the National Academies makes a useful point: there is a large disparity between the resources

available for the new drug review and approval process at FDA, and those available for the monitoring of drug safety. The IOM report makes a number of useful recommendations concerning the capacity of FDA to undertake risk assessment and risk management with respect to already-marketed drugs, of which more later. I hope the Congress will examine with special care the IOM recommendations about the public availability of the results of clinical trials. In agreement with several major medical journals, IOM urges that industry sponsors be required to register at clinicaltrials.gov all Phase two through Phase four clinical trials. The key here is that full information about the conduct of trials and the problems that may arise with them must be made available to the public. FDA has invested significant labor in making such records available at its website, http://www.accessdata.fda.gov/scripts/cder/drugsatfda.

This appears to be an appropriate response to section 5.1, of the IOM Report, but to call them publicly available in any real sense is silly. With the help of the Director of clinicaltrials.gov, I was walked through this website to find records of the trials for Ketek, a drug about which important safety issues have arisen. One can get to the right pages, but although the trials are listed there is no information about the institutions, the investigators, or problems. Even the list is impossible to find unless one knows what one is looking for, and the studies cannot be linked to from clinicaltrials.gov. With some more support for information technology, the navigability of this site could be improved to validate FDA's promise that this vital information is really publicly available.

One other point on this topic: the IOM report asks Congress to give FDA authorities that it could apply to require conditions for distribution of already marketed drugs. These would include the capacity to make FDA-initiated changes in drug labels, a

moratorium on direct consumer advertising, and various other conditions. As with other needs, this will require appropriated funds and not user fees.

You may remember, Mr. Chairman, that FDA had to explain repeatedly to the Congress, back in the late 1970s, that it was very difficult for the agency to pursue a comprehensive program for evaluating the safety of already-marketed products. The reason is that in order to calculate an adverse reaction rate, you need to know the numerator – the number of observed problems – and the denominator – the number of prescriptions that are out there. FDA's numerator depends upon a largely voluntary reporting system involving doctors and firms; the denominator might be constructed, for example, through a prescription system in which an extra copy recording only the drug's identity and the dosage is made centrally available for data storage. That, unfortunately, is not available. The ironic result, in the case of the Vioxx problem, is that FDA had to make use of the nation's largest health maintenance organization, Kaiser Permanente, which had a record of Vioxx prescriptions and an extensive medical records database. With enough patient numbers and a frequently prescribed drug, a careful assessment of the risks associated with Vioxx could be made.

Let me summarize a few of these thoughts. Public confidence in the Food and Drug Administration is a vital asset for an agency that regulates about 25 cents out of every consumer dollar spent in the United States. If we expect our pet foods to be safe and our spinach uncontaminated, Congress needs to provide FDA with the resources and the authorities it needs. Americans won't tolerate, nor should they be asked to tolerate, an undermined sense of confidence in the safety of products they need every day. The additional resources FDA requires to fulfill its responsibility are pretty moderate by

federal budget standards, but the need for that help is really desperate. Congress provided a system for industry to subsidize the drug and device approval program through user fees – but the rest of the FDA is broken, and urgently needs repair.

So I hope you and your staff will continue your diligence about pursuing FDA resource needs. But to hear the bad news, you may have to rely occasionally on old-timers like me, because budget authorities at HHS and OMB specifically prohibit present officials in the agency from speaking out publicly about the need for more funding. I used to squirm about this in my day but it's a fact of life. Of course I know this is no news to you. But I hope that the American public, which expects a lot from the FDA, will know that when its officials express satisfaction with their budget allocations, they have their fingers crossed underneath the witness table.

I have enjoyed being here, and it is a real pleasure to speak out with enthusiasm and even some love on behalf of an agency I continue to care about very much.

Chairman WAXMAN. Thank you, Dr. Kennedy.
Dr. Young.

**STATEMENT OF FRANK YOUNG**

Dr. YOUNG. Mr. Chairman, it is a pleasure to be with you again and to have the opportunity with uncrossed fingers to talk about the agency.

I would like to mention a few things based on my experience of 12 years in Government, part in the FDA, part in the Office of the Assistant Secretary, and also part as a citizen, as a pastor, a person that works in industry as well as with consumers, and focus on the point that this is the single most important consumer agency in the world.

We are the gold standard. Much of the world follows the FDA. At least in our time, when the FDA sneezed, the world got pneumonia. It is an agency that is watched and has been looked at for guidance.

Yet, unfortunately, this agency is suffering, and it is suffering significantly. It is suffering from neglect of short-term Commissioners, it is suffering from a workload that greatly outstrips its resources, it is suffering from accelerating technological challenges without the ability to recruit the people that are necessary for those new fields. It needs to be at the forefront of science. We are in the world now of genomics, proteomics, variety of nanotechnologies, a program where we are looking at cellular therapy, cellular regeneration, as well as the classical issues of the drug safety, food safety, veterinary safety, cosmetics.

The new challenges cannot be addressed without a steady stream of recruitment of personnel at the forefront of their science fields, and importantly an opportunity for their continual education, continued training, and I would definitely submit research.

As you know and this committee knows, the research at the Center for Biologics Evaluation and Research has been eviscerated. There is very little research at the Center for Drug Evaluation and Research. Yes, we do have coordination with NIH, but it is, in my opinion, important to have a research program available within FDA, itself.

Similarly, there are problems with the research programs in the Center for Foods.

I would submit that the agency requires much more than a bandage. In fact, as important as additional resources are, they are not the sole solution. I would like to point out some of these other points that are necessary for you to make a diagnosis of what is safe for the professionals and those outside the agency that rely on it, and what is effective to restore this agency to its previous strong state.

I would like to start exactly where Dr. Kennedy did. The turnover in the short-term Commissioners in recent years has been scandalous. It is very difficult for the agency to have a directed focus if it has a revolving door syndrome at the agency. The career professionals are outstanding, but without guidance and direction of where the agency should be going and, yes, protection at congressional hearings and other events, it is difficult for the agency to function.

I would also submit and would recommend that you look at the recruitment process at FDA for Commissioners. Dr. Kennedy an I were recruited by search committees. We were able to be appointed by the secretarial process. Dr. Kessler had a lightning swift hearing for confirmation. I guess he said it was about 8 days. There have been months and months of prolonged foot dragging of getting Commissioners confirmed. I wonder whether it would not even be better to return to the pre-confirmation status. I would ask you to look at that.

I would also suggest that you consider a 6-year term for the Commissioner. There needs to be stability, and for an individual to know that this is his mandate or her mandate for a period of time and our professional leader of the agency.

When I was in the agency I converted to a professional status in the Commission Corps and stayed in Government for the rest of my professional life in medicine. I think that concept of being recruited to come to Government for service is very important. It is a lot easier for lawyers to come in and out of Government, harder for professionals in health science to come in, but I would urge that we make that possible.

The next thing that I would like to urge your Members to look at is really the strength of the scientific base. In addition to the topics that I mentioned earlier is the need to allow professionals to have training and time to pursue their own studies. When I was running a large lab I had about 33 people with me when I was at the University of Rochester. I stumbled onto the fact that I would get much more productivity out of a post-doc or a graduate student if I asked them to work 80 percent on my effort and 20 percent on their own. Some of the best leads came from their time, not my imaginations.

I think it is important that the professional staff of the agency have time for professional renewal and, when appropriate, research in the very areas that they are regulating.

In my watch we recruited Cathy Zoom from NIH at the very time when interferon was being looked at for evaluation. She was skilled and actually did research on that. It was one of the fastest approvals of new biologics because she could weigh the safety, the effectiveness, and was familiar with it. That familiarity I think is key in the scientific personnel.

I also would recommend that there be a comprehensive review of the drug and biologic evaluation process. The last one occurred over 20 years ago. There have been many excellent initiatives that have been added, but they have sort of been added like onion rings around the surface of the small nub, and each administration adds a larger and larger number of onion rings, and for those on the outside looking, whether it is clinical trial research and results, food safety, or the persons trying to submit proposals for evaluation to FDA, it becomes a morass of conflicting, overlapping, difficult-to-understand regulations.

I would urge that all of this, in this time when there is a review of FDA, be looked at and possibly seen as a way to go forward and revise this sort of a program.

I think unequivocally a comprehensive drug safety program is essential.

I would also like to take this opportunity to look just briefly at the budget distortions that PDUFA made. I had the privilege, as you mentioned, of initiating that. my good friend, David Kessler, continued it. Neither of us ever thought that the distortions that have occurred would occur here, where the one portion of the budget stays high and the other goes down. Very, very difficult to manage the agency. And drug safety has been left behind.

I would urge that if at all possible that there be a program to have an appropriated budget for that. It is what I favor. However, if it is not possible, we cannot delay in some sort of a program where a data base is built with a small charge, maybe a nickel a script, so that we can have a Kaiser-like system over the entire drug safety review. In that way FDA could point out what reviews need to be done and, if necessary, folks in the private sector could undertake those analyses. But to let this go one more congressional session without strongly addressing drug safety would be a charade and an abuse of the American public that relies on safe and effective medicines.

I would also urge that we bring a screeching halt to unfunded mandates. During the time that I was Commissioner there were 22 of them. We scrambled around. We, as a Coordinating Council, met to try to see where we could shift resources, but it was very hard. You know and I know very well of the act that bears your name, the Hatch-Waxman Act. I had the privilege of trying to implement that. It was under-funded. We had a terrible time trying to bring those standards in.

You are now looking at follow-on biologics. I would urge strongly that the greatest caution be taken in devising the law, implementing the new regulations, and providing both the resources for evaluation but also enforcement. We had great problems in the early days of enforcement with the Hatch-Waxman Act. I think that needs to be looked at.

The inspectional staff in FDA is under-funded, under-manned, and overwhelmed. I remember at one hearing at OMB I brought in a dead chicken. We left it out deliberately for about 24 hours, put it on Barry Clendenin's desk. It was at room temperature, also. And then we brought a pacemaker. I said the Department of Agriculture has over 12,000 inspectors. They watch those chickens go by. We have heart-implanted devices, pacemakers, valves, and there are 1,400 FDA inspectors. I can smell a dead chicken that is rotten; I can't smell anything on a pacemaker or an artificial valve. We need the proper inspections.

When the new initiative comes like follow-on generics, biologics, if it does, my goodness, we can't steal from anything else to leave the protection for us under-manned.

I would also urge that we have an equal playing ground and playing field for imports versus domestic products. Inspecting at about 3 to 5 percent, getting caught is a cost of doing business. We really need to have high-quality foods, drugs, devices, biologics coming into the United States in a good system to make sure that they play on that equal field.

Finally—and maybe I shouldn't say finally—I think having the appropriates in agriculture is sort of a historical accident and silly. It would be as silly as having the Congress' Health and Labor Com-

mittee oversee the Defense budget. We have now moved to a different era where we have a need for having those committees that appropriate health and labor budgets oversee the budget of FDA. This is a major problem. I think that Congress can have and should have the will to deal with that.

There is one other little piece of suggestion that I could humbly make, or maybe not so humbly. Possibly it would be considered to reduce the overlapping authorities that oversee FDA. I think there were about nine different committees that I testified in the over 100 testimonies that I gave, and it was very difficult to go to this committee, this committee, and this committee. If we could have a coordination in oversight as you are doing today and focusing on the agency from a comprehensive standpoint, I think it would be very, very helpful.

[The prepared statement of Dr. Young follows:]

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STATEMENT BY

# FRANK E. YOUNG, M.D., Ph.D.

**FORMER COMMISSIONER**
**FOOD AND DRUG ADMINISTRATION**
**1984-1989**

BEFORE THE

COMMITTEE ON OVERSIGHT AND GOVERNMENT REFORM

UNITED STATES HOUSE OF REPRESENTATIVES

MAY 1, 2007

**Introduction:**

Thank you, Chairman Waxman and Mr. Davis, for the opportunity to testify before you today. My name is Frank E. Young, M.D., Ph.D. I served as Commissioner of the FDA from July 7, 1984 to December 12, 1989 and remained in the Department of Health and Human Services serving as Deputy Assistant Secretary for Health, Science and Environment (1989-1993) and as Director of the Office of Emergency Preparedness and the National Disaster Medical System with concurrent responsibility for Emergency Support Function (ESF 8) under FEMA's Emergency Response Plan from 1993-1996 and representative of DHHS on the Council of Deputies of the National Security Council (1993-1996). My testimony is based on 12 years of government service. I appreciate the opportunity to discuss the future of FDA, an agency that is vital to the well being of our citizens.

FDA has long enjoyed a reputation as one of the most important, trustworthy, and effective regulatory agencies in the United States. Indeed, FDA is heralded as the gold standard among public health regulatory bodies around the world. Regrettably, the agency's reputation is suffering as FDA's recent performance has been compromised by: neglect due to short term Commissioners; a work load that greatly outstrips its resources; accelerating technological challenges coupled with insufficient resources to remain at the forefront of the science it regulates; a crush of imported goods with an insufficient number of enforcement personnel; and an ever increasing degree of political influence in what should be a scientifically based agency. FDA is wounded! The agency requires more than a bandage of additional resources as important as they are! It needs, in fact the public should demand, a careful diagnosis and appropriate therapy that is both safe for the many outstanding professionals in the agency and those in the global community that depend on it and effective in restoring it to its previous healthy state. Only a robust FDA can assure the safety and effectiveness of new drugs and biologics, the safety and utility of new devices, the proper registration of cosmetics, ensure the safety of our food supply and prepare for the impact of the genomic revolution on new foods. Recently, the animal health of our pets has been threatened by contamination of the pet food that our consumers bought in good conscience. This flaw illustrates of particular importance is the effective regulation of imported products, as we exist in an ever growing global economy. Our public needs a uniform safety standard for imported and domestic products. Sufficient resources are required for both FDA inspectors and FDA regional labs that support them.

I congratulate the committee for holding this hearing aimed at remedying the current debilitated state of the agency. Here are a number of observations to facilitate your diagnosis. These will be followed by some recommendations for treatment.

**1. Leadership** FDA has had substantial periods of time under the leadership of acting commissioners and short term commissioners. The agency is partially paralyzed by this revolving door syndrome. Strong and sustained stable leadership is required to gain the trust of the agency and the nation. Accordingly, it is recommended that the commissioner be appointed for a 6 year term and subject to removal only for malfeasance or non professional behavior.

**2. Commissioner Recruitment:** All commissioners after my tenure have been Senate confirmed. The past practice of suggesting candidates to the Secretary through a search committee composed of health professionals familiar with the functions of the agency has been abandoned. It is recommended that the process be less political and that the Commissioner have expertise in some of the areas regulated by FDA. More independence from both Administration and Congressional political agendas is required to ensure that the public health needs that are critical to the well-being of the nation are met based on science. For example, Secretary Heckler recruited me to address the biotechnology revolution. My background was in rDNA and, before joining FDA, I had attended the Asilomar meeting and was a charter member of the NIH Recombinant DNA Committee (RAC). I was charged by the Secretary, among other things, to develop an action plan to renew the agency and to focus on the regulations for the safe development of rDNA drugs, biologics and diagnostic reagents. During my tenure the number of approved products in the field increased from 4 to over 10,000 and the national and international guidelines for the safe use of these products were developed and implemented by staff within the FDA.

Now, as noted in a speech by former Commissioner McClellan [1] at Harvard, the field of genomics is likely to impact foods in a similar fashion to the eighties when the influence of rDNA on biologics, drugs and diagnostics introduced new regulatory scientific and safety considerations. As this field progresses, and the line between foods and drugs becomes blurred, there will be a need for careful regulatory delineation. These advances in technology require that both the Commissioner and the staff of FDA be scientifically competent. Thus, an environment to scientific inquiry as well as resources is essential. Sound regulation in new and expanding fields is built on a foundation of sound science.

**3. Scientific Expertise:** There has been a major erosion of the scientific expertise within the FDA. Research in the Center for Biologic Evaluation and Research has been eviscerated through the recent reorganization and is almost non-existent in the Center for Drug Evaluation and Research. To maintain the expertise necessary for expeditious but highly competent decisions on new breakthrough products, and to have the proper knowledge to evaluate potential safety problems in foods, biologics, drugs and animal biologics and drugs as well as the knowledge to evaluate new devices, it is essential to have a well trained scientific staff that is given the time to not only maintain scientific expertise but to pursue career development in their chosen field of science. It is also necessary for these scientists to be able to express their opinions freely but to appreciate that when a decision arrived at through careful scientific investigation and consensus is reached, that Agency policy will be implemented. Therefore, recruitment and retention

[1] On July 1, 2003 former Commissioner McClellan noted "it's quite possible that, within the next decade or two, genomics will not only provide many valuable insights into the development of highly effective, individualized medical treatments; it may also give us the knowledge we need to understand which foods may be particularly risky or beneficial for particular persons, so that we can make specific, individualized adjustments in our diets to prevent some serious diseases. There is a small but growing field called "nutrigenomics" that is seeking to combine the increasing insights from genomics to our understanding of how dietary choices affect our health."

of outstanding scientists must be redressed through staff expansion and provision of time for professional development including, as appropriate, laboratory research. This applies not only to drugs and biologics but to all aspects of foods as well. The genomic and proteomic revolution as well as regenerative cellular therapies and devices that will reduce the burden of disease require a highly skilled staff in order to reach sound regulatory decisions.

**4. Evaluation process:** There is a substantial problem in the biologic and drug evaluation process. The certainty and predictability of the process needs to be improved. There have been layers upon layers of Congressional mandates and Administration-led regulations that have grown like onion rings with each new administration. Not only should the cost of medicines be reduced through competitive processes (such as the generic drug initiative) but the cost of development needs to be reassessed through a comprehensive overhaul of the product review process, including the phase 4 process. An unpredictable regulatory process complicated by high staff turnover inevitably leads to a greater cost of the development of new therapies and stifles innovation of new drugs and biologics. I already detect a shift in the market place of investments to favor devices over drugs and an emphasis on later stage investments to reduce the uncertainty in return on investment. The erosion of innovation and entrepreneurial leadership in the United States needs to be stopped through a compressive review of the process for product review. The last comprehensive of the drug evaluation occurred during my tenure over 20 years ago (the IND and NDA re-writes). Furthermore, although I suggested the implementation of user fees while I was Commissioner and Senator Hatch introduced the first User fee bill, the implementation of user fees has resulted in a substantial reduction in other areas of the agency's budget. It is important to remember that the user fees were initiated out of desperation. It is proposed that Congress carefully weigh the proportion of funds allotted to user fees and appropriated funds.

**5. Safety of Drugs and Biologics:** The evaluation of safety of drugs and biologics has been reduced by the strict provisions of the user fee legislation (Prescription Drug User Fee Act; PDUFA) and reductions of the core sections of the agency budget. While I strongly favor appropriate levels of funding of FDA's budget to develop a well financed and properly staffed office for drug and biologic safety within FDA, current financial constraints within FDA due to budgetary imbalances between appropriated and PDUFA funds led to a compromise of the drug safety program and precluded a comprehensive analysis of drug safety. The history of the FDA demonstrates that major legislation follows crises within the FDA regulated products. The initial revision in 1938 was due to the use of ethylene glycol as a solvent for Elixir Sulfanilamide resulting in the death of 107 people and the Kefauver-Harris Drug Act of 1962, which required that new drugs must be shown to be both safe and effective followed the thalidomide crisis. Rather than waiting for each new crisis, such as the current problem stemming from the Vioxx recall, there must there be a comprehensive analysis of drug safety. For example, it is difficult to obtain a comprehensive analysis of safety of new drugs due to infrequent events based on the study a few thousand patients in phase 3. Yet, it is inappropriate to study tens of thousands of patients during the NDA studies, as it would unnecessarily prolong the evaluation process. It must be emphasized that all new drugs and biologics present a

risk-benefit equation as no new chemical or biological drug is absolutely safe. Therefore, comprehensive safety analysis should be performed through active post-market surveillance. Ideally these studies can be financed by appropriated funds. I favor this approach. If Congress deems that such monies are not available within the appropriation budget, there may be another mechanism of ensuring drug and biologic safety through privatization of the process but under FDA oversight. For example, a fee of $0.05 per script could be collected and pooled to be used to evaluate the safety of marketed drugs and biologics. FDA would have the responsibility of selecting the products for review annually, based on a risk-benefit assessment following the NDA approval and establishing the review process, but the analysis could be undertaken by the appropriate private sector organization. While I personally strongly favor an appropriated process and a staffing of the effort within FDA, as it spreads the burden more equitably and retains complete oversight functions within the FDA, the need for a comprehensive safety program is of sufficient magnitude that we must, as a nation, find a solution.

**6. Appropriations and Oversight:** Examination of the appropriations process reveals a major anomaly. The Agency charged with the protection of the drug and biologic supply of our citizens, the security of the blood supply and the tissue and cellular products and the complex devices that are implanted in our body like pacemakers and artificial joints is funded through the Agriculture Committee. It is essential that we have a sound national agricultural appropriations process, but I submit that funding a medically based regulatory agency through a committee that primarily funds agriculture is as silly as funding the defense budget through a Labor and Health Committee. Congress can readily abolish this anomaly if it has the will! I strongly recommend that Congress undertake this politically courageous action. At the same time Congress should, in my opinion, re-examine the overlapping committee structure that has oversight of FDA functions and consolidate them into fewer committees.

**7. Inter-agency coordination:** The public health inter-agency coordination is effete and ineffectual. In the 1990's the role of the office of the Assistant Secretary of Health in coordinating public health policy was markedly reduced. Instead of bi-weekly meetings of the public health agency heads led by a medically qualified Assistant Secretary who could coordinate the solution of pressing public health problems and develop interactive budgets, the coordination is now greatly diminished and primarily occurs at the more political secretarial level. This results in less harmonized and less expeditious development of public health policies. I recommend that the responsibility for ensuring coordination of the public health agencies be re-examined.

**8. Inspection:** The FDA's inspection personnel and regional laboratories are inadequate to ensure that the same high standard in quality applies to both domestic and imported products sold to the American public. In my opinion, there are substantial inequities between the regulation of domestic industry and the foreign industries.. Because the level of inspections of imported products is so low, it is better for the importers to have

goods seized as the cost of doing business, rather than to comply with FDA standards. A comprehensive needs analysis for ensuring a level playing field needs to be undertaken.

**9. Unfunded Mandates:** New Congressionally mandated programs are frequently mandated without resources for adequate implementation—instead, they need to be adequately resourced. While I was Commissioner there were mandates for 22 new activities without accompanying appropriations. If the program cannot be funded, the agency should not receive the additional responsibility. Congress is currently considering generic versions of biological drugs (called follow-on biologics). The establishment of such a major new program requires care and adequate resources For example, I can attest to the difficulty the agency faced in the initial implementation of the Hatch Waxman Act for the expeditious evaluation of generic drug products. Because the financial rewards for industry were so great, there were major problems in the development of procedures within FDA, inadequate resources available for crafting the regulations, and difficulties in the implementation of the initial ANDA review processes. Similarly, there were substantial budgetary needs for adequate enforcement of procedures for approval of products developed by industry during the initial implementation of the act. The agency was in uncharted waters. Nevertheless, with time and agency experience, this legislation was successful although some questions about bioequivalency and safety persist. Now, almost 50% of the prescriptions are for generic drugs. Great care will be required to craft the legislation and regulations for follow-on biologics if they are deemed appropriate. Particular attention will be needed to ensure that the agency has sufficient qualified scientific personnel and the required resources to ensure safe and effective follow on biologics. These compounds are proteins with more complex structures and substituents. The task establishment of similarity is very difficult.

**Conclusion:** Based on my career of 12 years in DHHS serving as Commissioner of FDA, Deputy Assistant Secretary of Health, Science and Environment and Director of the Office of Emergency Preparedness, I can attest to the dedication and expertise of most of the employees within what used to be an integrated Public Health Service. We need to give these professionals the tools, continuing education and a constant stream of new professionals which are the life blood of the FDA. Before the posturing of election politics gets into full swing, it is time to lay the foundation of a revitalized FDA in a bipartisan fashion. I am pleased to see this committee address such a task.

I hope these observations and recommendations will assist you as you focus on the revitalization of FDA, an agency that is so essential to the protection and enhancement of health in our nation. I strongly recommend that you carefully evaluate the budgetary proposals of the FDA Alliance and the Coalition for a Stronger FDA that recommended resources to support these initiatives.

Thank you for your attention. I shall be pleased to respond to your questions.

Chairman WAXMAN. Thank you very much, Dr. Young. Those are very helpful and specific ideas. I appreciate them.

Dr. YOUNG. Thank you, Mr. Chairman.

Chairman WAXMAN. We are going to review them very carefully. Dr. Kessler.

**STATEMENT OF DAVID KESSLER**

Dr. KESSLER. Mr. Chairman and members of the committee, thank you for the opportunity to participate in today's hearing. Most importantly, Mr. Chairman, thank you for your belief and support for the mission of the FDA.

The opportunity and challenges this Congress has before it now to equip the Food and Drug Administration to meet the public health challenges of the 21st century are as pivotal as those the Congress faced in 1938 and 1962 when it gave the agency the fundamental responsibility of insuring drug safety and efficacy.

We are seeing a confluence of factors—chronic under-funding, a lack of enforcement authority, severely outdated scientific and regulatory frameworks that are creating a lack of confidence in the FDA and its many dedicated and talented people.

At the same time, there are considerable challenges the agency must be able to address if it is to remain the world standard for public health protection. This includes globalization of markets, particularly in food and drugs, and the imminent and profound shift toward a new era in medicine in which treatments are geared toward individuals rather than mass markets.

I want to focus, Mr. Chairman, if I may, on food safety. My written remarks address many of the issues that my colleagues have already talked about, but let me focus my oral remarks, if I may, on food safety.

Simply put, our food safety system in this country is broken. We have no structure for preventing food-borne illnesses in this country. The reality is that there is currently little mandate, little leadership, little resources, nor scientific research base for prevention—and I underline the word prevention—of food safety problems.

The fact is there is no one in the executive branch with the clout and authority who focuses, whose job it is to prevent food-borne illnesses.

FDA can react to outbreaks, but the emphasis needs to be on preventing outbreaks before they happen. Over the past 20 years, there has been robust debate about FDA's role in drug approval and safety. The focus on drugs also has been reflected in agency funding and management attention, and legislation currently under consideration will continue to strengthen our drug safety system. Now it is time, indeed overdue, to address the same attention and concern to the agency's food safety mission.

In 1938, when the statute was written, people were not thinking about food safety in terms of global markets and worldwide supply and distribution networks. Spending weeks or months tracing bad cases of food-borne illnesses to their origin, although important, is too much like chasing the horse after it has left the barn, and too often with devastating results in illness and death.

Congress and the administration should act urgently to strengthen FDA by meeting its resource needs and by unifying and elevat-

ing food safety leadership within FDA and the Department of Health and Human Services.

Food safety cannot compete with drug or device safety for resources and leadership. Food safety cannot be delegated to second-tier management within the agency. The fact is that food safety has been a second-tier priority within the FDA.

In addition, the current structure in the agency for food safety is fragmented. Responsibilities for food are spread across the Center for Food Safety and Applied Nutrition, the Center for Veterinary Medicine, and the Office of Regulatory Affairs. There must be clear recognition within HHS that food safety is an essential part of protecting the public health, and it cannot be housed in the Department of Agriculture, because the Secretary of Agriculture does not speak for public health.

We need a Commissioner of Foods at FDA who is responsible and accountable for all that FDA does on food safety at headquarters and the field who reports directly to the Secretary.

Our focus today needs to be on prevention, not just reaction, if we are to have any hope of averting future failures in the food safety system.

FDA must have the scientific capability to do the research and to develop the right processes and controls. Producers and suppliers must be required to take steps to protect their link in the food chain, and the agency must have the authority to hold producers and suppliers accountable for the failure to establish the necessary protections and standards.

Mr. Chairman, I appreciate your longstanding interest in these issues and your willingness to devote your time and energy and that of the committee to finding the solution to the challenges confronting this very, very important agency. I offer to you whatever help I can to you as you work toward strengthening the ability of the FDA and the Federal Government to continue to protect the health of the American people.

Thank you very much.

[The prepared statement of Dr. Kessler follows:]

**Testimony of Dr. David Kessler**

**before the**

**U.S. House of Representatives**

**Committee on Oversight and Government Reform**

**"FDA's Critical Mission and Challenges for the Future"**

**Tuesday, May 1, 2007**

Mr. Chairman and members of the Committee, thank you for the opportunity to participate in today's hearing. I am Dr. David Kessler, Dean of the School of Medicine at the University of California, San Francisco.

The opportunity and challenge this Congress has before it now, to equip the Food and Drug Administration (FDA) to meet the public health challenges of the 21st century, are as pivotal as those that Congress faced in 1938 and 1962 when it gave the Agency the fundamental responsibility of ensuring drug safety and efficacy.

I know of no other regulatory Agency that touches the lives of so many people so directly. The safety and efficacy of our drug products, vaccines, blood supply and medical devices, and the safety of our food should be at the top of our nation's priorities. I am concerned that this is not the case.

We are seeing a confluence of factors - chronic under-funding, a lack of enforcement authority, severely outdated scientific and regulatory frameworks - that are creating a lack of confidence in the Agency. At the same time, there are considerable challenges the Agency must be able to address if it is to remain the world's standard for public health protection. These challenges include the globalization of markets, particularly in food and drugs, and the imminent and profound shift toward a new era in medicine in which treatments are geared to individuals rather than mass markets.

As just one symptom of the Agency's condition, there has been a dramatic drop in the number of FDA enforcement actions. The number of inspections went down in recent years, and the number of warning letters issued by the agency dropped dramatically since 2000. It is difficult, if not impossible, to believe that this is driven by industry reform and true absence of violations. In fact, the number of recalls during this period increased significantly, suggesting that there are more serious problems, not fewer.

This would be a grim assessment but for the fact that the history of the Agency is such that it is precisely in times of crisis that the great leaps forward have been made. But this is not to make light of the task that Congress and the Agency face.

While there are important questions about the adequacy of the FDA's authorities and the need for sustained leadership, perhaps the most fundamental issue is ensuring that the Agency has the resources necessary to effectively meet its obligation to protect the public health. That means the resources to reclaim its scientific leadership in the fields it regulates, to implement enforcement programs that have a reasonable prospect of assuring compliance with essential public health protections, to expand the scope of its reach to encompass the global marketplace, and to earn and retain the confidence of the American people that the

food they eat is safe and the drugs and medical devices they use are safe and effective, and available to patients as quickly as possible.

There is a paradox here that needs to be addressed. We have funded the Agency responsible for the safety of products that comprise a quarter of all consumer spending at a level wholly inadequate by any measure - and then asked it to do even more with less. In just the past several years, the FDA has had to contend with a 16-fold increase in reports of adverse drug events, a doubling of direct to consumer television advertisements, a 65% increase in food imports, and an increased role in battling bioterrorism - all with a budget that has essentially been flatlined.

While Congress has attempted to provide resources for burgeoning public health needs on other fronts, support for the FDA has faltered in comparison. In 1986, FDA's budget was comparable to 97% of the budget for the Centers for Disease Control and Prevention (CDC) and 8% of the National Institutes of Health's (NIH) budget. By last year, it had dropped to 28% of the CDC's budget and 5% of NIH's. Significantly, while the NIH's budget to fund the research that leads to discoveries that ultimately fill the FDA's drug pipeline has doubled over the last five years, FDA's budget has not grown.

We can debate the merits of the model of industry paying fees to supplement the Agency's budget for drug approvals. But the truth is, at least as it relates to funding, the reality has never matched the program's design. The Prescription Drug User Fee Act (PDUFA) was never intended to be the predominant source of funding for drug approvals. It was intended to serve as a commitment from both drug manufacturers and the federal government to adequately fund the Agency. The drug industry lived up to its part of the bargain, but I submit that the federal government has not. In that sense, PDUFA has failed, and it has had the unintended consequence of shifting resources away from post-market drug safety and other important public health protection functions.

However, we also need to remember that PDUFA did succeed in helping to shorten review times. I saw how it gave hope to patients with cancer, HIV/AIDS and other illnesses for whom a significant reduction in review time was a matter of life and death.

Against a backdrop of essentially level appropriations and rising responsibilities, the need to meet PDUFA funding requirements has exacerbated the funding shortfalls not only in drug safety, but also in other Agency functions, with food safety being a glaring example. The minor increases in funding for food safety that FDA has received in recent years have been eclipsed by rising costs and additional responsibilities.

The FDA regulates 80% of the nation's food supply and products that involve more than 50,000 different manufacturers, processors and warehouses, yet it receives only 24% of the

federal food safety budget, the majority of which is directed to the US Department of Agriculture, which is not a public health agency. As a consequence, FDA has an insufficient number of inspectors to handle the workload and must increasingly rely on the industry to police itself. During my last year as Commissioner, there were around 3 million FDA-regulated products imported. This year, there will be about 20 million imports. Yet there has been no increase in staff for inspections.

Moreover, FDA scientists are ill-resourced to do the research necessary to turn scientific findings about foodborne illness into practical guidance that food companies can implement to make our food supply safer. This lack of scientific leadership does not make the headlines, but there is no question that one of the greatest losses from lack of resources is the Agency's ability to serve as a leading voice on sound scientific decision-making.

The erosion of funding has struck hard at the Agency's ability to support its proud tradition of groundbreaking research in regulatory science. While in the past, the Agency led the way in developing new scientific paradigms for approving biologics and assessing food contaminants - to the benefit of both industry and consumers - resources for FDA to lend its intellectual firepower to addressing key regulatory questions are increasingly scarce. Historically, other nations in Europe, the Far East and worldwide have looked to the FDA for its scientific leadership and as a model for public health protection, I am concerned that the Agency is losing its leadership role.

While lack of money is a significant obstacle, the FDA is also severely hampered by archaic authorities, outdated science and outmoded regulatory paradigms. As the public has come to learn, the FDA has virtually no authority to compel drug manufacturers to continue to study the safety of products after approval, require timely changes to drug labels, ensure that direct-to-consumer advertising serves a public health interest, or require that the results of clinical trials be shared with the patients who make them possible. Where it does have the authority to act, it is forced to work within the century-old regulatory concept of determining a product to be "adulterated" or "misbranded" - two terms that made sense in the days when snake-oil salesmen hawked their tonics on the street but have little relevance to today's mass-marketing. And, when it does determine that a product is adulterated or misbranded, it is constrained by inflexible enforcement tools that too often leave the Agency with the untenable option of doing nothing or pulling a drug from the market that may still hold some benefit for certain patients. Once a drug has been approved, the FDA is virtually powerless and cannot compel a manufacturer to change the drug's label, even if there is new, important information about the drug that physicians or patients need.

In particular, the FDA's authority to protect children's health lags even further behind. We have made great strides in the past decade with bipartisan legislation that created a "carrot and stick" approach to prompting the testing of drugs for children. This approach has been extraordinarily successful, yielding hundreds of pediatric studies and over 170 new or

improved labels for children. Yet, we're still denying children the same protections we demand as adults. While adults have had the right to safe medicines since 1938 and to effective medicines since 1962, the idea of permanently granting children those same assurances is still under debate in 2007.

When it comes to protecting consumers from unsafe food products, the problems are even more dramatic. Currently, FDA has no mandate for leadership on prevention of food safety problems, no funding to do important research to find ways to prevent food-borne illness, and no tools to hold companies accountable for implementing food safety measures and taking quick action when a problem is discovered. The fact is that the federal government has more authority to halt the distribution of dangerous toys than it has over unsafe food products. Because the process is entirely voluntary, FDA has no ability to verify that the manufacturer has in fact removed an unsafe product from the marketplace promptly and thoroughly. And, in contrast to the federal government's authority over recalls of toys, cars or medical devices, FDA has no ability to impose fines on a company that is slow to act.

The ultimate consequence of our failure to provide the Agency with sufficient resources and authority is that FDA's regulatory presence is diminished, to the detriment of the public health. Without the real potential for the Agency to act against unsafe drugs or contaminated foods, the likelihood of compliance diminishes. Without a strong agency, incidents like those recently covered in the Washington Post on food safety are inevitable. According to the Post, FDA inspectors had concerns about salmonella in a Georgia peanut butter factory in 2005. But because they relied on voluntary compliance, there was no follow-up action when company officials refused to provide requested food safety documentation. That factory was linked to more than 400 cases of food-borne illness in 44 states.

Over the past 20 years, there has been robust debate about the FDA's role in drug approval and safety. This focus on drugs also has been reflected in Agency funding and management attention. Now, it is time, indeed overdue, to address the same attention and concern to the Agency's food safety mission. In 1938 when the statute was written, people were not thinking about food safety in terms of global markets and worldwide supply and distribution networks. Spending weeks or months tracing back cases of food borne illness to their origin, although important, is too much like chasing the horse after it has left the barn - and too often with devastating results in illness and death.

Our focus today needs to be on prevention, not just reaction, if we are to have any hope of averting a future failure in the food safety system. FDA must have the scientific capability to do the research to develop the right processes and controls, producers and suppliers must be required to take steps to protect their link in the food chain, and the Agency must have the authority to hold producers and suppliers accountable for the failure to establish the necessary protections.

I believe we also need to look very seriously at the structure and leadership of the food safety system. Under the current structure, no FDA commissioner can be a strong leader on blood safety, vaccines, drugs and medical devices and also on food safety all at the same time. The American public should not have to choose between safe food and safe drugs, but when those two missions compete for the same scarce resources and leadership attention, that choice is being made for them. Shortchanging food safety to advance or address other aspects of the Agency's mission is dangerously shortsighted, and it has seriously compromised the effectiveness of the Agency's food safety program.

Congress and the Administration should act urgently to strengthen FDA by meeting its resources needs and by unifying and elevating food safety leadership within FDA and the Department of Health and Human Services (HHS). Food safety must not compete with drug or device safety for resources and leadership. Food safety can't be delegated to second-tier management within the agency, and the fact is that food is a second-tier priority within the FDA. In addition, the current structure is fragmented in FDA. Responsibilities for food are spread across the Center for Food Safety and Applied Nutrition, the Center for Veterinary Medicine, and the Office of Regulatory Affairs. There must be a clear recognition within HHS that food safety is an essential part of protecting the public health. And it cannot be housed in the Department of Agriculture, because the Secretary of Agriculture does not speak for public health. We need a commissioner of foods at FDA who is responsible and accountable for all that FDA does on food safety, in headquarters and the field, and who reports directly to the Secretary.

A first step toward correcting these problems must be for Congress and the Administration to commit to a substantial increase in funding for the Agency. To bring the FDA's framework for drug regulation up to date, legislation proposed by the Chairman and by Senators Kennedy and Enzi are strong steps in the right direction. In my view, individualized plans for managing drug risk, backed by increased and more flexible enforcement authority, are a sensible solution and should be enacted.

When it comes to the mission to protect the public health, FDA must lead. There should be, in my view, no reasonable debate on that question. It is our responsibility - Congress, the Administration, and the public - to give the Agency what it needs to do that.

Mr. Chairman, I appreciate your long-standing interest in these issues and your willingness to devote your time and energy to finding a solution to the challenges confronting the Agency. I offer to you whatever help I can provide as you work toward strengthening the ability of the FDA and the federal government to continue to protect the public health.

Chairman WAXMAN. Thanks very much, Dr. Kessler.
Dr. von Eschenbach.

**STATEMENT OF ANDREW C. VON ESCHENBACH**

Dr. VON ESCHENBACH. Thank you, Mr. Chairman, Ranking Member Davis, and members of the committee, I am pleased to join you this afternoon for what I know will be a productive discussion of the future of the Food and Drug Administration.

I have been at the helm of the FDA as a fully confirmed Commissioner for approximately 5 months, obviously a period of time that pales in comparison to the combined experience of the three former Commissioners that I am proud to have surround me on this panel.

Although my tenure at FDA has been brief, I am no stranger to the radical changes, the radical changes in science and technology that over recent years have transformed the health care environment in which the FDA must achieve its mission of protecting and promoting the public health.

Whether caring for cancer patients or conducting research or heading the National Cancer Institute, I have witnessed discoveries at the molecular level that are transforming medicine, health care, and are impacting our regulatory environment across the full continuum of food and drugs, biologics, devices, and other consumer products.

Now, from my current vantage point as Commissioner of the FDA, I have the privilege of being able to create and implement a strategic plan that will enable the agency to remain the world's leader and gold standard, a record my predecessors can be justifiably proud of. Our focus, therefore, today and our theme is not simply to address repairing the FDA of the old, but, most importantly, to build the FDA of the future in the context of the radical changes that are occurring in the world around us.

I am committed to leading an FDA that, in addition to responding in a visionary and strategical manner to these challenges, will also be effectively and efficiently managed. It must and will be a regulatory agency that is always science based but also science led, and engaged in the full life cycle of the products that we must regulate, whether they are foods, drugs, devices, or commodities.

Americans still want the assurance and the security of knowing that life-sustaining and life-enhancing products will be rapidly available to them to promote their well-being, but at the same time they also want to know that the latest scientific and technological advances are being brought to bear in the prevention and detection of adverse outcomes that could impact their health.

To meet these expectations in this radically different and new environment will require a modern FDA that, as my colleagues have indicated, is adequately resourced to fully implement its regulatory authorities and new scientific tools.

Since arriving at the FDA, we have worked with the FDA staff and leadership to develop a plan for increased resources, and I am grateful to the Congress for its support in fiscal year 2007 and look forward to the increased resources that are proposed in the President's budget for fiscal year 2008, which will account for an additional $77 million more than 2007.

We are well into formulating a continuation of this trajectory of increases as we formulate our strategic budget proposals for fiscal year 2009. I will look forward to continuing to work with all Members of Congress during this appropriations process.

To address the increases in funding, we are also supplementing the taxpayer dollars with increases that are also being proposed as you address reauthorization of the Prescription Drug User Fee Act and the Medical Device User Fee Modernization Act, as well as consideration of additional fees for out ability to continue to manage the increasing demands posed by regulation of generic drugs.

Congress is also interested in FDA's legal authorities and whether they need to be altered or increased, and we will continue to contribute to those discussions, as well. However, I believe it is important to not only address how additional essential resources we could use effectively to be able to enhance the authorities that we currently already have. Efficient and effective measures such as guidances and rulemaking can be powerfully important tools when they have the resources to be fully utilized, as opposed to unfunded mandates and statutes that are ultimately doomed to failure.

FDA now has permanent, confirmed leadership and organizational changes are occurring that can lead us to greater efficiency and effectiveness. I pledge that we will continue this effort as we continue to look at the FDA's responsibilities and opportunities and challenges of the future.

Some organizational changes have already occurred that address many of the concerns my colleagues have raised. For example, the appointment of Dr. Janet Woodcock specifically as Deputy Commissioner and FDA's Chief Medical Officer to oversee our scientific portfolio and to be able to lead its modernization and amplification, particularly benefiting from the current effort that is underway by our Scientific Advisory Board to totally reassess the scientific portfolio of the FDA to find greater opportunities for integration, efficiency, and also the ability to find strategic areas in which we can enhance that scientific effort.

She is also responsible for addressing many of the issues with regard to career development of our current staff and, most importantly, is taking on a very aggressive effort to create an FDA-credentialed training and fellowship program that we expect over the next 3 to 5 years will bring approximately 2,000 fellows into the agency.

More recently, I named John Guyer, a seasoned executive with executive government experience, as Deputy Commissioner and Chief Operating Officer. He will bring streamlined management processes to our planning and budgeting for the future.

We are also strengthening the agency's infrastructure. A new Chief Information Officer is now in place with the mandate of modernizing FDA's information systems so that we will be equipped and prepared to fully integrate into the rapid changes that are occurring in the health care environment where we will, in fact, have access to data bases that are being developed and health care infrastructures such as the one that Dr. Kennedy alluded to, and therefore be able to provide a rapid, seamless, efficient way of being able to data mine and learn and understand about the utilization of these devices, drugs, biologics, and products in the real world.

We will continue much of the effort of modernization, even including the opportunities for new facilities that are becoming available to us as we build out our consolidation of much of FDA at our new White Oak campus, and we expect that to pay dividends in the synergies and productivity and efficiency of the organization.

Mr. Chairman, we at the FDA concur with you that we must focus on the future and address the increasingly emerging challenges, but also the unbelievably exciting opportunities that this new world of science and technology is providing for us, and, most importantly, is hoping and offering to the American people and the world for greater solutions to their problems.

I am honored to be leading this proud agency whose mission today, tomorrow, and as always as in the past will be to promote and protect the public health. I would be pleased to continue this dialog with you and my colleagues as we explore that new future.

Thank you, sir.

[The prepared statement of Mr. von Eschenbach follows:]

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

**STATEMENT BY**

**ANDREW C. VON ESCHENBACH, M.D.**
**COMMISSIONER, FOOD AND DRUGS**

**FOOD AND DRUG ADMINISTRATION**

**BEFORE THE**

**COMMITTEE ON OVERSIGHT**

**AND**

**GOVERNMENT REFORM**

**UNITED STATES HOUSE OF REPRESENTATIVES**

**May 1, 2007**

RELEASE ONLY UPON DELIVERY

**INTRODUCTION**

Mr. Chairman and Members of the Committee, I am Andrew von Eschenbach, M.D., Commissioner of Food and Drugs and head of the United States Food and Drug Administration (FDA or the Agency). I am pleased to be here today to talk about the importance of the work that FDA performs every day to protect and promote the public health. I also want to share my vision for the future of FDA and how we are planning to address the new challenges of the 21st Century the Agency is facing.

FDA is responsible for ensuring the safety and high quality of more than a trillion dollars worth of products that are critical for the survival and well-being of all Americans -- products that include some 80 percent of the United States food supply, all human health care products, electronic products that emit radiation, animal drugs and feed, and cosmetics.

For over 100 years, FDA has been recognized and praised as the gold standard of regulation throughout the world. Being given the opportunity to lead the Agency at this time, it is my responsibility to continue the excellent work of my predecessors and ensure that the Agency is equipped to handle the challenges of today and the future. The world is experiencing a rapid expansion of scientific knowledge and globalization that will have dramatic impacts on the industries and products that we regulate. The Agency must be equipped with the expertise and infrastructure to meet emerging challenges, such as: foodborne disease outbreaks, intentional or unintentional; evaluation of complex drugs

and biologics brought about by emerging progress in molecular biology; the potential for pandemic flu; and medical devices bioengineered, miniaturized, and increasingly autonomous in evaluating and modulating our state of health. Even cosmetic safety is becoming more complex through incorporation of the products of rapidly expanding technology, such as nanoparticles.

## FDA's COMMITMENT TO PROTECTING PUBLIC HEALTH

### FDA's Commitment to Food Safety

FDA is committed to ensuring that America's food supply continues to be among the safest in the world. But we face challenges. For example, consumption of produce, particularly "ready-to-eat" products, has increased dramatically during the past decade. This is a positive development from a nutrition perspective, but a new dynamic that challenges our food safety efforts. Americans usually consume these products in their raw state, harvested from the vine, stem, or soil and without processing to reduce or eliminate any pathogens that may be present. Consequently, the manner in which these products are grown, harvested, packed, processed, and distributed is crucial to ensuring that microbial contamination is minimized, and the risk of illness to consumers reduced. Even if a small percentage of a harvest is contaminated, severe and widespread illness can result.

FDA has addressed produce safety for a number of years. In response to the recent produce-related outbreaks, however, FDA is sharpening its focus in this area. To reduce the risk of foodborne illness at all points in the food chain, FDA has adopted a "farm-to-fork" approach

to food safety, an approach that systematically applies risk management principles at each step as food moves from growers and producers to consumers. For example, FDA has conducted foreign and domestic training and outreach on Good Agricultural Practices and has assisted industry in the development of several commodity specific guidances. In addition, FDA has issued a Produce Safety Action Plan and launched a Leafy Greens Safety Initiative in cooperation with the state of California, California growers and producers.

FDA is examining the recent outbreaks to determine what changes may be necessary to improve the safety of fresh and fresh-cut produce. We continue to work closely with states, produce growers, processors, and distributors to develop and implement programs at each point in the supply chain to prevent and minimize contamination from harmful micro-organisms. FDA recently issued draft final guidance to industry entitled "Guide to Minimize Microbial Food Safety Hazards of Fresh-cut Fruits and Vegetables" to enhance the safety of fresh-cut produce by minimizing the microbial food safety hazards. This guidance recommends that fresh-cut processors consider a state-of-the-art food safety program such as the Hazard Analysis and Critical Control Points (HACCP) system, designed to prevent, eliminate, or reduce to acceptable levels the microbial, chemical, and physical hazards associated with food production. Also, in response to the recent outbreaks, FDA held two public hearings to share information about recent outbreaks of foodborne illness associated with microbial contamination of fresh produce, and to solicit comments, data, and additional scientific information on this issue. We are soliciting input from all our stakeholders on ways to improve the safety of fresh produce.

In view of the recent recalls involving wheat gluten and rice protein concentrate in various pet food, FDA, in conjunction with state regulatory authorities, is testing for the presence of melamine in a variety of plant protein ingredients and finished products commonly found in the U.S. food and feed supply. FDA and state authorities also are raising awareness of food protection and defense measures by discussing the Federal government's new ALERT awareness initiative and the need for food manufacturers to ensure the safety of the ingredients they use as well as the packaging and processing supplies.

Reducing the risk of foodborne illness requires science-based methods capable of identifying both the sources of risk and effective control measures. For example, we are using molecular technology to identify foodborne illnesses and their causes by tracking the DNA fingerprints of the suspected contaminants. Regulations without science supporting the required interventions are a hollow promise, and ineffective at protecting consumers. We are collaborating with industry and state/local governments responsible for food safety. In addition, we are strategically deploying inspection resources toward the greatest risks to the food supply, including imported food.

**FDA's Commitment to Drug and Medical Product Safety**

New drugs, biologics, devices, and diagnostics present significant opportunities for improvements in health care. Ensuring the safety and effectiveness of medical products is a key focus of our commitment to protect and promote public health. FDA only approves new therapies if their benefits (lives saved, extended or enhanced) outweigh the risks they pose. Toward that end, FDA continually assesses its medical product safety programs. In

particular, over the past few years, FDA has reassessed its medical product safety programs due to rapid advances in science and technology resulting in increasing complexity of medical products, as well as the increased attention to safety-related issues by consumer advocates, health professionals, and academic researchers.

FDA has maintained its reputation for excellence over the past 100 years through its willingness to look internally to see what transformations are necessary to sustain this standard. For this reason, in 2005, the Agency asked the Institute of Medicine (IOM) to study the effectiveness of the U.S. drug safety system, with an emphasis on the post-marketing phase, and to assess what additional steps FDA could take to learn more about the side effects of drugs as they are actually used post-market.

On September 22, 2006, the IOM released its report entitled *The Future of Drug Safety — Promoting and Protecting the Health of the Public*. The report recognized the progress and reform already initiated by the Agency and made a number of recommendations for additional improvements. The Agency subsequently issued a report responding to the IOM recommendations. We are working diligently on initiatives for improving drug safety that we identified in our response and have already made significant progress on several projects. For example, in March we issued final guidance that describes FDA's current approach to communicating drug safety information, including emerging safety information, to the public. The guidance affirms the Agency's commitment to communicate important drug safety information in a timely manner, including in some situations when the Agency is still evaluating whether to take any regulatory action. FDA's drug safety communications are

available through the FDA website. In addition, we have issued guidance designed to make our Advisory Committee operations more consistent, transparent, and predictable.

The Agency's response to the IOM also details a series of initial steps to strengthen the drug safety system in three key areas: science, communications, and operations and management.

**1. Strengthening the Science**

First, I am committed to strengthening the science that supports our medical product safety system at every stage of the product life cycle, from pre-market testing and development through post-market surveillance and risk management. As part of the recent reorganization of the Office of the Commissioner, the Office of the Chief Medical Officer was created to provide oversight of scientific and planning related operations for the Agency. Led by Dr. Janet Woodcock, Chief Medical Officer, this Office shares responsibility and collaborates with the me in planning, organizing, directing, coordinating, controlling, and evaluating the Agency's scientific and medical regulatory activities in order to achieve the mission of FDA.

We will be focusing our resources on enhancing three areas of scientific activity: (1) benefit and risk analysis and risk management; (2) surveillance methods and tools; and (3) understanding adverse events. We propose that these activities be supported, in part, by Prescription Drug User Fee Act (PDUFA) IV funds.

Specifically, new scientific discoveries are generating a *science of safety* that will help prevent adverse events by improving the methods clinicians use to target specific drugs for use in patients for whom benefits are maximized relative to risks. This new science

combines an understanding of disease and its origins at the molecular level (including adverse events resulting from treatment) with new methods of signal detection, data mining, and analysis. This enables researchers to generate hypotheses about, and confirm the existence and cause of safety problems, as well as explore the unique genetic and biologic features of individuals that will determine how he or she responds to treatment. This *science of safety* encompasses the entire life cycle of a product, from pre-market animal and human safety testing to widespread clinical use beyond original indications. It should be applied to all medical products so that safety signals generated at any point in the process will robustly inform regulatory decision-making.

**2. Improving Communications**

Second, I am committed to improving communication and information flow among all stakeholders to further strengthen the drug safety system. This will require a comprehensive review and evaluation of our risk communication tools.

In agreement with the IOM's recommendation, we are working quickly to establish an FDA Risk Communication Advisory Committee to advise FDA on communication policies, practices, and strategies for all regulated products. Numerous administrative steps required by the Federal Advisory Committee Act have been completed, others are currently under review, and we are on target to announce a call for member nominations in the near future.

In addition, FDA proposed two new draft guidances for which it has sought public comment: "Draft Guidance for Industry, Advisory Committee Meetings - Preparation and Public

Availability of Information Given to Advisory Committee Members" (February 2007) and "Draft Guidance for the Public, FDA Advisory Committee Members, and FDA Staff on Procedures for Determining Conflict of Interest and Eligibility for Participation on FDA Advisory Committees" (March 2007). The Agency also has posted new information on its website to encourage applications for membership on FDA advisory committees as part of its ongoing efforts to recruit qualified experts with minimal conflicts of interest. Numerous nominations have already been received.

**3. Improving Operations and Management**

Finally, I am committed to improving operations and management to ensure implementation of the review, analysis, consultation, and communication processes needed to strengthen the U.S. drug safety system. Under my direction, the Center for Drug Evaluation and Research (CDER) has initiated a series of changes designed to effect true culture change that will strengthen the drug safety system. CDER has reinvigorated its senior management team and charged its members to lead the Center in an integrated manner. In addition, we have engaged external management consultants to work with CDER's senior managers to lay the foundation for an ambitious, comprehensive strategy for improving CDER/FDA's organizational culture. We are enlisting the help of external experts in organizational improvement to work with employees at all levels of the organization in implementing this transformation. Our goal is to provide CDER with the tools and expertise necessary to create a credible and sustainable environment of open and transparent communication, collaborative decision-making, and improved morale and staff retention.

For example, CDER has employed process improvement teams comprised of staff across organizations, including the Offices of Surveillance and Epidemiology (OSE) and New Drugs (OND), to recommend improvements in the drug safety program. Two significant recommendations, (1) to establish an Associate Director for Safety and a Safety Regulatory Project Manager in each OND review division, and (2) to conduct regular safety meetings between OSE and all of the OND review divisions, are now being implemented. We are committed to providing the management attention and support necessary to effect sustained culture change in our drug safety program.

**FDA's COMMITMENT TO PROMOTING PUBLIC HEALTH**

FDA is committed to promoting public health, as demonstrated by our dedication to making safe, effective, innovative and life-saving new medical products promptly available to patients. During my tenure as Commissioner, FDA has made major strides in implementing the Critical Path Initiative, a cooperative program that seeks to bring safe and effective medical products to patients faster by making their development more predictable and efficient. In the past year, we advanced this top-priority project through the following actions.

*Releasing the Critical Path Opportunities List:* FDA set forth 76 research projects, most of which are focused on the creation of smarter tools for early evaluation of candidate medical products suitable for further development. The Opportunities List, the central component of the Critical Path blueprint, invites scientists in academia, government agencies and industry to

cooperate in finding answers to unresolved issues in six broad topic areas: development of biomarkers; clinical trial designs; bioinformatics; manufacturing; public health needs; and pediatrics. By the end of 2006, almost one-half of the listed projects were in progress.

*Advancing Critical Path research:* FDA advanced research involving the two most important predictive instruments -- reliable biomarkers and focused clinical trials -- through the following actions:

- FDA released guidance on how to conduct very early clinical studies in people, and how to safely produce and test small amounts of experimental drugs;

- FDA, the National Cancer Institute of the National Institutes of Health, and the Centers for Medicare and Medicaid Services agreed to collaborate on improving the development of cancer therapies through biomarker development and evaluation.

- FDA and the Critical Path Institute announced the formation of the Predictive Safety Testing Consortium with five of America's largest pharmaceutical companies. FDA is assisting the Consortium in its prime function, sharing internally developed laboratory methods to predict the safety of new treatments before they are tested in humans.

*Spurring medical device development:* To help provide patients with new medical devices sooner, FDA launched an initiative to encourage early consultations between FDA and industry. The goals of the initiative are to promote scientific innovation in product development; focus device research on the latest science; modernize FDA's review processes;

and facilitate a least burdensome approach to clinical trials. As part of this effort, FDA issued draft guidance on the use of Bayesian statistical methods to design more efficient clinical trials by using safety and/or effectiveness data from previously developed medical devices.

**CONCLUSION**

FDA's mission is vital to the health and well-being of people, in our country and around the world. And, as you know, the Agency's most important resource is its employees. For this reason, I cannot overemphasize how important it is for the FDA to continue to have the ability to recruit and retain the best and the brightest personnel. A critical element of preserving this ability is for Congress to pass the user fee reauthorization bills without delay.

FDA and this Committee share the goal of a healthier, safer nation. I appreciate the valuable input I have received from Members of Congress and my predecessors, and I want to thank this Committee for focusing your attention on the important work being done at the Agency. I look forward to continuing to work productively together to address the challenges and opportunities of the future.

Once again, thank you for the invitation to testify before the Committee today. I am happy to respond to any questions.

Chairman WAXMAN. Thank you very much, Dr. von Eschenbach.

I will start the questioning. Each Member will get 5 minutes on the first round.

I think all of you have done a superb job in giving us a perspective at the FDA. The job of the FDA is varied. You deal with drugs, devices, food, different products, and there are different issues that come up. I think all of the suggestions are very worthwhile, and we want to take them under advisement.

I am going to pursue one area, and that is enforcement of the rules. It goes to the heart of FDA's mission. Without a strong enforcement arm, the standards set by the FDA are meaningless, and over the years experience has proved that a strong FDA enforcement leads to broader compliance with the law—we know when laws are enforced people are more likely to obey the law; greater consumer confidence, because the public knows that the law and the rules are being enforced; and improved public health, because that is what the rules are all about, to make sure that the public health is protected.

Dr. von Eschenbach, I want to ask you about, first of all, the field staff that is available to do the work of the inspections that are required. I understand that there are 3,460 full-time employees at FDA focusing on field inspection activities. Is that a correct number?

Dr. VON ESCHENBACH. Yes, sir. Without having the exact numbers before me, that is my recollection, as well.

Chairman WAXMAN. We have a poster on the side, if you would take a look at it. That poster indicates there was a sharp increase in field staff at FDA in 2003, and that was after the passage of the Bioterrorism Act, followed by a steep decline. I assume that, even though there has been a steep decline, there has not been a reduction in the FDA's responsibilities that would explain this decrease. Is that an accurate statement?

Dr. VON ESCHENBACH. That is correct, sir.

Chairman WAXMAN. I understand that FDA oversees over 200,000 food establishments in the United States. There are probably at least tens of thousands of other firms, including manufacturers of medical devices or biologics or drugs or animal feed, and that means the FDA field staff has to look at all those establishments, as well. Do you know, or maybe you want to provide for the record, how many establishments FDA oversees in each of these categories that I mentioned?

Dr. VON ESCHENBACH. I cannot give you a breakdown in terms of the categories. We will provide that for you as far as the record is concerned.

Chairman WAXMAN. Thank you. That would be helpful.

Let's assume that all of the field staff were just for food establishments. They are not, but let's just say that they were. In 2006, there were 1,962 field staff, most of whom are inspectors on food programs; is that a correct statement?

Dr. VON ESCHENBACH. Yes, sir.

Chairman WAXMAN. And, based on the total number of food establishments in 2006, 210,000, and 1,962 field staff, that translates to roughly one inspector for every 60 food establishments. I understand that in 2006 the total number of field personnel who visited

and evaluated all regulated facilities was 3,460. We know that there are far more regulated firms than food establishments, since there are also all of the firms involved in these medical devices, drugs, biologics, animal feed. But even if all of the field staff focused only on food, that would mean only one inspector for every 107 establishments. I want to know if you think that is a correct statement?

Dr. VON ESCHENBACH. I think your statistics are very well taken in that they point out exactly what the important challenge is going forward, and that is, with this large proliferation of sources from which these products come, what we must do is not simply look at the size of the work force, because it never would be equivalent to that number of that large a need, and so therefore the opportunities are how we strategically deploy that work force. That has been the strategy in terms of, No. 1, taking a risk management approach where recognizing among that large diversity there is a lot of heterogeneity in which some are considered to be of high risk, and therefore we focus our inspections on those particular firms, and that is based on product, the kind of product that they are producing and what level of risk comes from that, prior track record or source in which we know that there may be a concern.

So I think it is not only an issue of resources, but how those resources are applied strategically in a risk management basis that is an important way of going forward into the future.

Chairman WAXMAN. Do you look at the food side of the FDA responsibility as less risky than the drug or medical device side?

Dr. VON ESCHENBACH. No, sir, absolutely not.

Chairman WAXMAN. And do you devote more resources or less resources to food than you do in the other areas?

Dr. VON ESCHENBACH. I think the resources, as I indicated, are being applied strategically, and investigators or field investigators are applying scientific tools that can, in fact, be applicable under certain circumstances to food, and at other times they can even be applicable to medical devices. As we are seeing science and technology improve, what we are attempting to do is bring some of those tools out of the laboratory and into the hands of field inspectors at the point of inspection, and therefore that is an additional part of what you have seen in our proposal this year for our Office of Regulatory Affairs reorganization, which is a strategic way of enhancing inspections, the quality of the inspections, better tools for inspection, and focus strategic application of those inspectors to areas where we see concerns regarding risk.

Chairman WAXMAN. Thank you very much.

Mr. Davis.

Mr. DAVIS OF VIRGINIA. Over the past year we have seen a number of stories of food contamination, including the nationwide recall of fresh spinach due to e-coli, salmonella in peanut butter, and poisoned pet food. Several of you mentioned in your testimony that FDA is responsible for regulating 80 percent of the food supply, while the USDA receives 75 percent of Federal food safety budget. How is FDA's food safety program different from the USDA's?

Dr. VON ESCHENBACH. Mr. Davis, the Food and Drug Administration concentrates its oversight over food for products that have to

do with vegetables, produce, and seafood, and the USDA is addressing beef, poultry, and certain egg product derivatives.

What we do is work very closely with USDA in a collaborative, cooperative relationship, as well as work effectively with State agencies so that we are addressing that full continuum of our food portfolio.

Mr. DAVIS OF VIRGINIA. Is it efficient or is it very duplicative as they work together? I guess I ask, if FDA had the resources, what best practices and authorities would you want to borrow from USDA to create——

Dr. VON ESCHENBACH. Well, along with USDA what we are increasingly addressing is the realization of being engaged in the full life cycle of these products as they are changing radically with regard to how they are being produced and distributed.

The chairman has already made reference to the fact that, for example, we are seeing now going from farm to fork in a much more rapid way the use of fresh products that are eaten in the fresh state rather than cooked. These are creating new challenges with regard to our ability to assure safety, so USDA and FDA are both working to address those changes that are occurring in a collaborative way, and we are approaching it by building quality in by working with producers and, in our case, growers, as well as being able to utilize our inspections further on down the line in distribution.

Mr. DAVIS OF VIRGINIA. OK. Anybody else want to add anything to that? Dr. Kessler.

Dr. KESSLER. Congressman, there have been certain model programs in USDA, for example, the ground beef program, which I think could serve as best practices. Again, it is focused on preventing problems before they start.

I think the American people don't understand that if you go in and you order a pizza, that is regulated by FDA, but if you put pepperoni on it, it is U.S. Department of Agriculture. And in some ways that doesn't make sense, but, again, as I think the chairman indicated in his numbers——

Mr. DAVIS OF VIRGINIA. And if you have a beer with it, you get the Alcoholic Beverage Control on it.

Dr. KESSLER. I mean, do you want to be chasing the problem after it happens or do you want to have a system of preventive controls in place? That is what USDA, to its credit, did after the Jack-in-the-Box episode a number of years ago. I think we can learn lessons. But, again, the focus has to be on prevention standards, and that has not been at the core of our food safety system to date to the vast majority of products.

Mr. DAVIS OF VIRGINIA. OK. Dr. Young.

Dr. YOUNG. Thank you for that question. I think there is another problem that possibly emanates from where the appropriations come. There is a great imbalance in the amount of inspectional and enforcement authority in FDA versus Agriculture. As Dr. Kessler absolutely appropriately said, we need to focus on prevention, but with the numbers that are there it is very difficult to make that initiative work.

Mr. DAVIS OF VIRGINIA. OK. Let me go to how prepared is the FDA against the threat of terrorist attacks against food supply?

Have you given any thought to that? Are there specific actions and programs FDA has implemented over the past few years, and has FDA partnered with other Federal agencies and industry to protect against what we call agro-terrorism?

Dr. VON ESCHENBACH. Yes, sir. We have approached the food issue from both the food safety perspective, which we have been discussing, and also from food defense, which takes a very specific view of where our vulnerabilities might be to intentional contamination, as opposed to unintentional. That has been done in collaboration with a variety of other Federal agencies. We have adapted models that have been developed in the Department of Defense, referred to as the Carver Shock Models, to begin to understand vulnerabilities that occur within our food chain and how they will need to be addressed from the point of view of protection against what would be considered a terrorist intentional effort to harm our food supply.

Chairman WAXMAN. Thank you very much, Mr. Davis.

Ms. McCollum.

Ms. MCCOLLUM. Thank you, Mr. Chair.

Thank you, gentlemen. This has been very, very interesting, especially in light of what has happened with the pet food issue in China and how imported foods aren't inspected. I am wondering if you could elaborate on that a little more and what you would recommend to Congress to do about this, because this is very disturbing. It was very open in China and for people who even scratched the surface on how there is little or no inspection and how they have had many, many failures in the past.

And then, Dr. Kennedy, if you could elaborate a little more on antibiotics resistance, especially with what we are seeing with HIV and tuberculosis and the extreme resistance to some of the antibiotics.

Dr. VON ESCHENBACH. Ms. McCollum, with regard to your important question, I want to echo a theme that Dr. Kessler has emphasized, and that is the issue of prevention. As I indicated to the chairman, whether it is food or drugs, the FDA has taken the approach of the full life cycle of that product, and we have been addressing the need to build quality in with regard to the production of food, so not only issuing good agricultural practices for growers within our own borders within the United States; we have been working with foreign countries, their governments as well as their producers, to begin to help assure quality of those products at those sites of production, because we have seen a continuous increase in the amount of food that is imported into this country each year. So we are attempting to provide those good agricultural practices, work with the governments, engage in inspections in terms of how these products are being produced, and create corrective measures at the very front end as a preventative strategy, and then apply the risk management to our borders.

Ms. MCCOLLUM. Doctor, I heard that all in the testimony. I think Dr. Young was going to say something.

When you go to a grocery store and you pick something up in the U.S. grocery store as a consumer, you already feel that you have the assurance, so telling me that you are going to try to provide assurances doesn't make me feel much better.

Dr. Young, you looked like you had something you wanted to contribute.

Dr. YOUNG. One of the major draw-backs, in my opinion, is an inability to adequately certify that the inspectional capability, their regulatory capability of the country of origin is similar to or equivalent to our country. This is a real problem, and I think you hit the nail on the head by focusing on the pet food concern.

If the standards are not comparable and they have a low level of inspection when these products come into the United States, then it truly is the canary in the cage, and it is not dealing with the front-end prevention. We need to be able to negotiate these international type regulatory treaties. We have some very good ones and good manufacturing practices in drugs. We have some others in regards to devices. The food area has not been focused on as well and, as you aptly pointed out, more and more is coming from different countries that may not have and, in fact, do not have the same standards of inspection that the United States does. This loophole needs to be closed.

Mr. KENNEDY. I think you asked a question about antibiotic resistance, Ms. McCollum?

Ms. MCCOLLUM. Yes.

Mr. KENNEDY. Thanks. With respect both to multiply resistant bacteria, staphylococcus, particularly, vancomycin resistance, there is dramatic growth even since 1985 in the proportion of hospitals that are reporting un-managed infections. As somebody once said to me, the good news is that your surgery went beautifully and everything is safe and it is wonderful. The bad news is you have an infection against which we have no treatment.

What can be done at the supply side end of that is to offer some real incentives to drug manufacturers to get back into that business, because it has dropped steadily over the past 10 to 15 years. One way of doing that would be if the Congress saw fit to engage with it in a statutory fashion by creating a specifically tailored orphan drug kind of exemption for an antibiotic that could replace an antibiotic that was already encountering substantial resistance in the target bacteria.

It would have to be so limited that you couldn't offer it carte blanche to anybody that developed a new antibiotic, but there ought to be some special intellectual property rewards for somebody who goes after an antibiotic that could replace one to which there is resistance.

Dr. YOUNG. Could I add one additional point to that question?

Chairman WAXMAN. Yes, Dr. Young.

Dr. YOUNG. One of the things that I have learned in my more recent activities in the industrial side of the marketplace is that the companies that are looking for a return on their investment, which is frequently the taxpayers' investment in insurance funds and others, gave what the agency is doing and what is likely to be difficult to get evaluation expeditiously and what is likely to be hard, so there is a marketplace that I must tell you is already shifting to devices from early startup biotech companies. So the very thing that Dr. Kennedy is talking about in areas that are judged to be risky, the private equity funds and the venture funds are decreasing. Part of that relates to what I try to point out as

the difficulty in understanding what these overlapping rules are and where the incentives are. That, again, is a topic that I strongly support what Dr. Kennedy said is extraordinarily critical in the field of antibiotics.

If you would like to I could tic off about ten other areas that we really need to look at that are high need and similarly are problems in regards to the regulatory structure.

Chairman WAXMAN. Thank you, Ms. McCollum.

Ms. Foxx.

Ms. FOXX. Thank you, Mr. Chairman.

I am going to give you back some of the statements that some of you all have made and then ask you if you could respond to them, and then ask a general question, I guess.

Have any of you or all of you made these same kinds of recommendations in the past? And are there reports, those of you who were formerly there, are there reports that we could get our hands on showing that you have made these same kind of recommendations for improvements at the FDA? If you would just answer me yes or no and then give us the dates on those reports or approximate dates and let our staff find them.

Dr. Young.

Dr. YOUNG. Yes. It is difficult to give you the reports because we don't take documents out of the Government.

Ms. FOXX. I understand, but do you have——

Dr. YOUNG. But yes, you could give the general period of what was focused on, yes.

Ms. FOXX. And could you do that today?

Dr. YOUNG. Yes.

Ms. FOXX. Not necessarily now, but if you could do it.

Dr. YOUNG. I would be happy to do it for the record.

Ms. FOXX. OK.

Dr. Kessler.

Dr. KESSLER. Yes, Congresswoman, I testified on food safety enforcement authority several times, and would be happy to provide you with those references.

Ms. FOXX.

And let me ask you, did you say then that the food safety system is broken?

Dr. KESSLER. I don't believe I did quite in as stark terms. I would have to go back and review my testimony and refresh my recollection. I believe I said the tools were significantly outmoded. In fact, we were dealing with tools that were enacted close to a century ago, and not for the current environment. But I think recent events have shown us that the problems continue to persist, and they really do require our attention.

Ms. FOXX. And Dr. Kennedy.

Mr. KENNEDY. My associates were kind enough to count while I was Commissioner, and I testified 47 times, and I do believe that at least six or seven of them dealt primarily with foods, and I think I could probably dig them up.

Ms. FOXX. OK.

Let me ask you a question. How much money do you all think it would take to guarantee a fail-safe program? You indicate that

is possible to have, so what would you predict it would cost to have a fail-safe food safety program in this country?

Dr. Kennedy, start with you, since you answered last.

Mr. KENNEDY. I think the candid answer has to be more money than you have.

Ms. FOXX. OK.

Mr. KENNEDY. I don't believe in perfect safety. We used to argue with Congressman Delaney that probably it wasn't a good idea to insist on complete safety. And so I think we could tailor a system that would be substantially improved and that it would reduce the risk level, but I think it would not reduce it to zero.

Ms. FOXX. Dr. Kessler.

Dr. KESSLER. I agree with Dr. Kennedy. There will be no fail-safe system. There will be no system that assures 100 percent safety. I think, as Dr. Kennedy taught me years ago, the real mission of FDA is to create the incentors for the purveyor of the product to produce as safe a product as possible. That is really what FDA is all about.

Ms. FOXX. Thank you.

Dr. Young, would you comment?

Dr. YOUNG. Again, there is no absolute safety. I believe that the budgets can be projected to reduce risk. I would be happy to provide information.

Ms. FOXX. OK. With your comments, though, you all indicate that throwing money at this issue would provide such a program, and that is why I wanted to ask you that, because it always is that if you will just put more money, more money, more money into agencies then we can get results, and I am always interested that if we have a responsible and accountable person, as I think Dr. Kessler said, who reports to the Secretary, then you can guarantee a safe program.

I don't think that in our bureaucracy we ever really have people lose their jobs because of lack of performance or that are really held responsible. What I would be curious in the particulars that you might have made before is did you set up an organization in such a way that people would be held responsible, because in the bureaucracy we don't do that, and I believe that unless we devise a system where people individually are held responsible at every step of the way for a certain level of performance, that no amount of money is going to create the kind of system you are talking about.

What I am interested in is you all, in the jobs you have, and the current person, are those the kinds of recommendations you are making, because, again, just putting money into it without standards, performance standards, we are not going to have it.

Last question I would ask you, and I guess would just ask for a yes or no, do you think it is possible we could have food inspection treaties with other countries? Would you make that as a recommendation?

Dr. YOUNG. If I could respond first, when I was Commissioner we had the opportunity in the biotechnology revolution and we made those treaties through OECD and through WHO, where I was a representative for the United States in both.

In regards to GNP, those initiatives were done at that time. Dr. Kessler and others continued them.

We have not had the same focus on imports as it relates to foods, and one of the problems that we have is we are bringing in products, and unless we have these treaties, unless we have an inspection that goes with them, I don't think it would work.

I also tried to say that the agency requires more than a bandage of additional resources, as important as they are, and I tried to focus on the need to address this incredibly bad swinging door that we have had at FDA. That has been a real difficulty, because there is not a continuity of leadership.

But in the last point I would say yes, there have been people that have lost their jobs. I will just give you two prominent ones, and I will go back in history rather than current, but the Assistant Secretary who oversaw the swine flu problem, that was Dr. Ted Kennedy, lost his job, and at that time the head of CDC lost his job. The Secretary had the cranberry bog problem. We have had others, and there are a lot of difficulties that people have had along the way.

The problem isn't accountability as much as it is the ability to build a system that is proactive in a culture to make a secure environment where people can make a decision without fear of political punishment. I am talking about regardless of whether it is Democratic administration or whether it is a Republican administration. Those issues can paralyze an agency. Without a Commissioner, it is even more striking.

Chairman WAXMAN. Thank you, Ms. Foxx.

Did any of the others of you want to comment on her question?

Dr. VON ESCHENBACH. Well, Mr. Chairman, if I can add, I both agree and disagree with Dr. Kessler. I disagree that our food system is broken, but I agree that we will never have a totally 100 percent fail-safe.

The approach for the FDA going forward is to be collaborative, cooperative with all the other parts of this equation in our food chain, to work with growers, to apply our protection at the borders, to work with USDA as we embrace models like the Hassop Model or the hazard analysis that he referred to, and to see this as a systems solution to a systems problem, with the FDA providing the leadership and the integrating force, but not see this as simply solved by just an inspections issue or just a trade treaty issue, but a real comprehensive approach that I think is really ultimately the best assurance to the American people that what they take home and feed to their children is, in fact, safe.

Chairman WAXMAN. Thank you very much.

Mr. Braley.

Mr. BRALEY. Thank you, Mr. Chairman. I would like to thank our panelists for appearing today.

Dr. Young, you made a comment, I think, a drug safety program is absolutely essential.

Dr. YOUNG. Yes.

Mr. BRALEY. What I would like to do is, for the panel, sort of review where we have come from in the last 8 years.

In 1999, the Institutes of Medicine, which most of you have referred to, issued this report, To Err is Human: Building a Safer

Health System, and at that time they projected that somewhere between 44,000 and 98,000 people die in hospitals every year due to preventable medical errors.

In March 2001 the IOM issued another report, Crossing the Quality Chasm: A New Health System for the 21st Century. Then, in 2003, the IOM issued Patient Safety: Achieving a New Standard for Care, which had recommendations not only for agencies of the Federal Government but also for Congress to make proactive steps to improve patient safety, especially in the area of medication errors. And then just this year the IOM released Preventing Medication Errors.

What I would like to know is whether we have actually made any tangible progress in reducing the 7,000 deaths per year identified in those earlier reports due to medication errors by adapting some of the technologies and recommendations, or do we still have as far to go as it sounds like we do in achieving real, tangible benefits in the area of patient safety from drug interactions?

Dr. YOUNG. I fundamentally think that we have a long way to go. When we do the pre-market evaluation, at most we are looking at 3,000 to 5,000 patients and we derive a basic assessment of safety. After that, we do not have a comprehensive system that looks at medicines, makes a judgment of which ones we should study that year, and then gets the denominator and the numerator. Unfortunately, the numbers that you cited are probably low. I think it is closer to 100,000 a year that have adverse medical responses.

Now, there are a couple of things that I should bring out. One is today's medicines are very complicated. I very fortunately had a bypass in 2000. I did not die, like my father did at his first and only coronary at 45 years of age. I take about five or six different cardiovascular medicines. I am very careful about those drug interactions. I read the fine print that comes out on these. But I have no way of saying is it right for me to take a particular generic model against what I am taking as the innovator brand, because I know the innovator brand works, and I don't have a large system that I can say yes, 500,000 people took this drug with a combination of this drug and there was no adverse effect.

We don't have these large numbers. We need that. That is why I said it is essential and a user fee may have to be done.

Mr. BRALEY. And let me add this comment, so the rest of the panel can also consider this. Two of the recommendations in the 2003 Patient Safety Report were improvement of computer detection rules using boolean search terms, and also data mining free tech searches for the exact same problems you are talking about. Yet, my perception from talking with public health officials is that, with the possible exception of some advancements made in our VA electronic medical management system, that, by and large, the general public is not that much safer from these type of recommendations being implemented in the real world than we were in 2003.

Can anyone comment?

Dr. KESSLER. Congressman, I think that there is a lot of science, and that is the good news, that will make our pharmaceuticals much safer.

One of the problems we have had over the last several years and the industry has had is this issue of the push for the blockbuster.

Blockbuster means you have a drug that sells to as many people, literally millions and millions of people. What we need, and we are finally getting the scientific base to figure out the right drug for the right person for the right indication at the right dose. That is what personalized medicine is all about.

If I sell a drug to 100 million people but only 1 million people are going to benefit, we have to change the system. And we are beginning to have the tools to understand who is going to benefit and understand that up front. That is going to take a lot of resources, and I think it is also going to require the FDA to lead in this area.

Mr. BRALEY. Let me just offer this observation about that comment. I mean, one of the problems that I hear repeatedly on how we reduce preventable patient errors is that it is not a people problem, it is a system problem. The system problems have been identified for a long time, and yet I am not hearing that we are making dramatic progress and institution-wide implementation of improvements to address the system failures, so that is the concern I am raising, and where are we going and what are the possible solutions that Congress plays in giving health care providers the resources they need to eliminate the system breakdowns.

Mr. KENNEDY. Can I try one, please?

Mr. BRALEY. Please.

Mr. KENNEDY. I think one thing that the Congress could do, and I think it will not be uncontroversial, is to make a requirement that there be an additional form on every prescription written in the United States that must go into a data base with no patient's name but with the dosage, and that provides the denominator base for looking at the number of adverse incidents and discovering what the rate is, because unless you have a rate you can't know.

Then the other thing Congress can do is to follow the IOM recommendation in its most recent report by providing authority for FDA to allow limited marketing under certain conditions. You can't do direct consumer advertising in this program drug. And the other one, there is a labeling requirement that we have to initiate.

I think that giving those additional authorities would solve some of the systems problems.

Thank you.

Dr. VON ESCHENBACH. Congressman, I agree that we have a long way to go, because the health care community has been slow to adopt electronic infrastructure in health care. But at the same time I think we are traveling that road much more rapidly today than we ever have in the past, and we are seeing the transition into health care technologies that have been developed in other areas like the banking industry, etc.

Now, FDA must participate in that transition to that new future, and part of what we are doing is now, as I indicated, immersing much more in post-market surveillance, and engaging and staying engaged in what happens to those drugs when they are used in the real world, as Dr. Young pointed out, where there are multiple drug interactions, working with the VA, working with the Center for Medicare and Medicaid services, working with some of the private health care delivery systems that are creating these electric medical record data bases, and using the kind of modern tools that

you alluded to for data mining, and benefiting from experience that has come from organizations such as Google, etc.

I think we are traveling that road much more rapidly today than we could have 5 or 10 years ago when we didn't have those technologies, and I anticipate FDA playing a very important role in this post-market surveillance opportunity to get to the point where we identify the early signals of potential problems and intervene, as we protect the lives of people who might otherwise be damaged.

Chairman WAXMAN. Thank you, Mr. Braley.

Mr. Cannon.

Mr. CANNON. Thank you, Mr. Chairman. I can't tell you gentlemen how honored I am to be here with you. I have followed your work when all of you were in office, and am particularly a big fan of Dr. von Eschenbach, who I have spent some time with. I have always thought that you had the hardest job on the face of the Earth. You have to guarantee people's safety when people do, among other things, stupid, human things.

Dr. von Eschenbach, do you know how many drugs were approved by FDA last year, new drugs?

Dr. VON ESCHENBACH. I think I would answer that for you for the record. My recollection is we had 12 new drug applications, four biologic license applications.

Mr. CANNON. That were approved?

Dr. VON ESCHENBACH. Yes, sir.

Mr. CANNON. I am going to lecture a little bit, but it will lead to a question, I assure you. But I would like to set the stage.

We have talked about several things that are very important. Ms. Foxx talked about food safety and whether or not we could have a perfect system. The answer is, of course, you couldn't have a perfect system, but we could have a system that is orders of magnitude better using the new technologies that are available and tracking data and using computers that are substantial, and maybe even lowering the cost using techniques like Google has pioneered.

Dr. Young talked about large numbers of drugs and how they interact, and also I guess Dr. Kennedy talked about a data base of all the drugs to see what those interactions are. The fact is these are things we can talk about today because we have—in fact, I think the gentleman from Iowa talked about a boolean search. I am going to go a step farther and talk about Bejan statistics, Bejan statistics being, of course, the finding correlations and conflicts data. This is a discussion we could have today. We couldn't have had it 5 years ago or even 3 years ago probably.

I want to set the stage by saying we are now in a different time and we are at a point where we are doing very few drugs, if I can characterize 12 that say—go ahead, Dr. von Eschenbach.

Dr. VON ESCHENBACH. May I please correct the record? I was giving you the priority approvals, and I apologize. The overall was 97 new drug applications and 4 biologics, so 101 total, of which what I gave you were priority accelerated approvals, so I apologize.

Mr. CANNON. But in the environment, even 100 is a relatively small number, given what several people, or I think Dr. Kessler referred to as personalized medicine.

This is a remarkably important issue, I think, to us as policymakers, and it is not partisan, as I think Dr. Young pointed out.

These issues are very complex. I don't mean to simplify them. But we are in a complex environment with hugely more capable tools to deal with complexity, so Burt Rutan just got the X-prize for going into suborbital flight twice within a week. The next X-prize is for the company that can decode an individual's DNA for $1,000. I suspect most people in this room would get their DNA decoded if we get to the point where the price is that cheap. That means that we can actually really, truly personalize medicine and know why something that didn't work for Dr. Kennedy, didn't work for Dr. Young, and maybe if we had 100 people that used a similar combination of the medicines that Dr. Young is taking, why some of those people performed better with those drugs than other people.

That is where we need to get, and FDA as an organization has a difficulty getting there, it seems. That is the core of the question that I want to get to.

Let me just take it a little further. You have Merck out there that pled guilty recently to promoting an off-label use of a drug, and my understanding is I think GlaxoSmithKline is now being sued by a plaintiff whose spouse may not have died if they had made known an off-label use of one of their drugs that would have saved the spouse.

Is there not a way that we can take advantage of these massive changes, the vast decrease in the cost of millions of instructions per second on a computer and the vast decrease in the cost decoding DNA and the vastly reduced cost of tracking food products so that we could make orders of magnitude improvement in where we are going?

In fact, Dr. von Eschenbach, first let me just ask the other members of the panel, is it not possible to set up a system so that a doctor can suggest a protocol which may include a complicated set of drugs or an off-label use of a drug that becomes a standard and that the market then allows to become a standard and to be used, and that allows us to do what Dr. Kennedy was suggesting, which is track how drugs interact? Is it not possible to create a system where we know the toxicity of a drug and so an agency like the FDA could say that is a dangerous or it is not a dangerous protocol, and if it is not a dangerous protocol, allow us to track the data in a Bejan context and therefore make these orders of magnitude leaps forward, where we find out that there is actually a difference between Dr. Young's chemistry and my DNA, and therefore I can't take the same set of drugs, but maybe Mr. Issa can?

Let me go to Dr. von Eschenbach first. I would love to have all your comments on that.

Dr. VON ESCHENBACH. Thank you, Mr. Cannon. You have touched on a number of very important issues that are part of our critical path initiatives to address this entire spectrum of how we can begin to accelerate our ability to regulate these drugs, while both assuring their safety and their efficacy, so we built scientific tools in at the very front end, as Dr. Young has indicated, so we understand the patient from a genetic and molecular point of view, and the drug, and can understand both the impact as it relates to benefit and potential risk.

Then, at the same time, adapted trial designs, the kind of opportunities you are addressing in terms of looking at that drug and how it behaves in populations, can be also improved and be able to get information in real time to be able to adjust our subsequent protocols. And then, for finally, the ability to have the information tools that we were speaking of just a few minutes ago, to be able to monitor what is happening in utilization of those drugs in off-label use by physicians who are in practice adds the third piece of a full cycle from the very production to the very utilization of those drugs where we can continuously enhance our effectiveness, and yet assure minimum degree of risk.

Mr. CANNON. I see, Mr. Chairman, that my time has expired, but I would like to hear from the rest of the panel, but would the Chair indulge me by allowing me to make a very short refinement to the question?

You talked about trial design, and what I am suggesting is that in a world where people live and are complicated, if we create a system where we can track data, say through a protocol that is not created as a scientific design but actually tracks what people are doing, does that get us significantly beyond the rigid paradigm of FDA?

Dr. VON ESCHENBACH. As a clinical practice protocol for which, like with the CMS data base, we are getting the data as that is being done, and analyzing it would be a very important step.

Chairman WAXMAN. Yes, Dr. Young, did you want to respond?

Dr. YOUNG. I just wanted to make a quick response on one medicine, 5-fluorouracil, that is used very commonly in cancer treatment. Recently there has been a development of a test called single nucleotide polymorphism [SNIP]. It has been discovered that there are 22 SNIPs of different types, 3 of which can predict which individuals are likely to get severe neurological complications.

I have managed one patient who is a friend who was in a coma for 2 months after taking this medicine, because she had a genetic abnormality and could not metabolize the 5-fluorouracil. Now that is available. That is what we have been talking about with personalized medicine. But the incentives to switch the market and the incentives to be able to analyze this need to be built in.

It is going to be even more complicated when we look between the difference between foods and what foods are tolerated versus what aren't.

The Congress needs to address, the administration needs to address this whole development of science and give it adequate resources to make it really work an incentives to drive the marketplace.

Dr. KESSLER. Congressman.

Chairman WAXMAN. Dr. Kessler.

Dr. KESSLER. It is called the field of pharmacogenomics, and it is evolving, and you articulated it very well. Understand how profoundly it is going to change the pharmaceutical industry, because no longer are you going to be able to sell a drug just to thousands and thousands of patients. We are going to be able to target who is going to benefit, who is going to have the adverse reactions. That means in some ways smaller markets, and perhaps even higher-cost drugs, but it is going to have a major influence on our pharma-

ceutical industry, and I think some of the pains you see today that the industry is experiencing is being able to gear up for that change.

One of the most important things is how FDA can help lead in the policy formation with the Congress on this.

Chairman WAXMAN. Thank you very much.

Mr. CANNON. Can I just say in closing, Mr. Chairman, since I don't think Dr. Kennedy wanted to respond, particularly, that we have billions of doses taken annually around the world of medications, but if we can start tracking what is happening now, that is a vast improvement. That is orders of magnitude in reduction of the time and understanding it will be to get to that point of thinking.

Thank you, Mr. Chairman. I yield back.

Chairman WAXMAN. Thank you very much.

Mr. Cooper.

Mr. COOPER. Thank you, Mr. Chairman. I appreciate your sustained focus on these important issues.

I would also like to thank Dr. Kessler, in particular, for fighting the good fight against DTC ads. I am sorry you didn't win that battle, but you were pursuing the right cause.

You were talking a moment ago about pharmacogenomics. I would like to ask about pharmacoeconomics, compared to effectiveness. I hate to even bring this up before an agency that is so overworked and under-funded, but it seems to me that consumers need a reliable guide for value in the marketplace, especially when they are confronted with $5 billion worth of DTC ads on our broadcast television.

I have countless doctors come up to me complaining about these 30-second experts who, because they have seen a beautiful couple on TV, they didn't hear any of the warnings that were broadcast, but they want some of that, whatever it is. That seems to me to not promote the healing process.

What is the best way for us to pursue comparative effectiveness? Is FDA an appropriate agency? Should we do it in another way? I know folks like Gail Wolinsky have been talking about this, because safety and efficacy is one step of the process, but finding value for your money is another.

Dr. KESSLER. Congressman, I think what FDA is very good at is the science. I think that is something that I strongly believe, and my guess is my colleagues think that is what the FDA should focus on.

When it comes to two drugs and one has a riskier adverse event profile than the other, that is something that I think FDA should and does deal with.

I don't think today FDA has the tools nor necessarily you would want the FDA to go beyond safety. It is an important policy judgment for the Congress, but once you start allowing economic judgments to be made, not that they are not important, they are vitally important. What good is it if we get drugs out for people who work that we discover them and people can't afford them? So it is vitally important. The question really is: is FDA the right place for those decisions to be made?

Mr. COOPER. Dr. Young.

Dr. YOUNG. Thank you for that very thoughtful question. I would submit, as Dr. Kessler did, that this is not the place that it should be made. Once you start changing the scientific risk/benefit analysis and the safety profile and start doing the economics, I think you are compromising your standards. I also think, as a person who strongly opposed direct-to-consumer advertisement when it hit its head up on my watch, I think that is something that ought to be looked at and some guidelines be put into place, because you want the professional guidance primarily influencing what is helpful, safe, and effective for a patient, and not a wide manipulation of the market, particularly as we are going to more-personalized medicine. That makes it much more complicated.

Mr. COOPER. How about the more limited case of one chemical compound that is virtually identical to another, a so-called me-too drug? Is it appropriate for FDA to say it really has no therapeutic benefit or the number needed to treat is so small that it is really virtually identical?

Dr. YOUNG. I don't think you can say that yet. I will go back to my own personal example. I am on a number of medicines. I am very careful as to what I switch to, because I might have a polymorphism that this drug is slightly different and it doesn't work for me, as I tried to answer in the question of 5-FUDR. So I think that question is not quite right for exploitation at this time, as important as it is.

Mr. COOPER. On another topic, Dr. Kennedy brought up the important issue of hospital-borne infections. People want to know that the hospital is a safe place to go. It is my understanding that nosocomial infections have been, you know, about 15 percent per year, but if we were to have a sudden resurgence of antibiotic resistant bacteria, that could dramatically increase.

You mentioned giving a price or incentive for the discovery of a better antibiotic, but aren't there multiple issues here? First, many of our physicians have over-prescribed existing antibiotics. There are so many antibiotic soaps and feed for cattle and things like that have worn down our resistance. And then the simple issue of hand washing and facilities. Many of our health providers have not taken the time out to cleanse themselves properly between patients. So doesn't that all lead to this buildup of antibiotic resistance?

Mr. KENNEDY. Antibiotics are really a unique drug in the following sense: that when you prescribe one to a particular patient, the cost/benefit ratio is not limited to that patient because there are external costs that are spread to the rest of the population. I think educating doctors about that is terribly important.

I think that, besides encouraging the supply side to develop new antibiotics where there is clear evidence that they are needed, because there is a lot of resistance already, the other thing is to encourage—and I think probably CDC is the target here—as a routine hospital procedure, to do a diagnostic sample quickly on all new entering patients so that you will know if even the healthy ones are carrying a little bit of staphylococcus that can be detected to be antibiotic resistant, and they can be either housed separately or dealt with in a different way. That would knock down the likeli-

hood that future increases in antibiotic resistance are going to produce an increase in no-socomial infections.

Mr. COOPER. I see that my time is expired. If the good doctor could just answer the question, how much would that entry test cost per patient?

Mr. KENNEDY. I haven't costed it out so I can't give you a responsible economist answer. I am told that it is very inexpensive, but I don't want to be hung on that.

Chairman WAXMAN. Thank you, Mr. Cooper.

Mr. Duncan.

Mr. DUNCAN. Thank you, Mr. Chairman. I had other meetings, and I have just been here for about half an hour, so I apologize if this has been covered already, but I read in our briefing memo that food imports have quadrupled just since 1999, and they are now in the almost uncountable billions. And then there is a story in the Washington Post this morning that says about 99 percent of imported foods are simply acknowledged by computer and waved ashore, and it goes on to say "but processed ingredients are often nondescript, and in China, where a national passion for commerce has far out-paced the adoption of regulatory controls, marketers have repeatedly been caught adulterating such products, spiking pig feed with diet pill chemicals to make swine leaner, for example, and hiding sawdust in fish meal."

And we have heard reports in the last few days about Chinese products being involved in the pet food controversy and the product melamine that is used in plastic production. And then this morning, as I was driving in, I heard a news report saying that now it has been discovered that this Chinese melamine and perhaps other products have been placed in chicken feed on four huge farms in Indiana, and that it may be in as many as millions of chickens now.

What I am wondering about, I am wondering about the situation with China. Dr. von Eschenbach, when you find out that a country is doing crooked things, illegal, or what should be illegal or immoral type activities, have you given any instructions to increase the inspections or the testing of some of these food imports from China? Let's talk about China, specifically. Or do you intend to increase the inspections on Chinese imports?

Dr. VON ESCHENBACH. Congressman, with regard to your specific question, we do have now the opportunity for what is known as prior notice, so every shipment of food and products coming into this country, we have to be notified ahead of time about that food shipment. Any shipper or the source has to be registered with the FDA, so that gives us a data base from which we can begin to determine where we may see areas of risk and concern and areas where we have highly reliable and proven track records of confidence. We will focus on those areas.

So in the case of what you are alluding to specifically with regard to the pet food, obviously where there were two companies within China that embarked upon a practice that led to the adulteration of the melamine into material that would be subsequently used for pet food, we would clearly target those. Those companies are prohibited or blocked from bringing product into the country now. And we have even gone beyond that to look at the whole family of prod-

ucts having to do with vegetable protections, and we are retaining those and inspecting those.

So we have a both proactive as well as a responsive strategy to continue to focus on areas where we need to enhance protection.

Mr. DUNCAN. Well, I think that, based on what I have heard this morning and what I have read in this Post story, that it goes beyond pet food, and now it has gone into the animal feed and maybe into the human food supply. I can tell you that I think a lot of people are going to be concerned about this. I think the American people would appreciate a labeling program so they would know where some of this food was coming from, but we have been unable to do that in any effective way, so I suppose we can't do that, so we have to rely on the FDA and on your food safety programs.

But I think when we just get slapped in the face from the same country over and over and over again, that there needs to be some special attention paid to these imports, particularly from China. Apparently, that is where we are getting the largest volume of food imports by far anyway, so I think that the inspections and testing on these Chinese imports should be picked up substantially.

Thank you very much, Mr. Chairman.

Mr. ISSA. Will the gentleman yield?

Mr. DUNCAN. Sure.

Mr. ISSA. Following up on that, Dr. von Eschenbach, the FDA failed to prevent—and I am a California Member, like the chairman—the loss of $1 billion to the spinach industry, even though we had a registered user which was the single source for the e-coli from a single field. Do you want to answer not only Mr. Duncan's point, but also perhaps mine, on that point of what are you doing, even when you have registration, in order to make it quick and sure that we know what is good and what is not good?

Dr. VON ESCHENBACH. Yes, sir. And specifically with regard to the issue and difference having to do with spinach, as that process evolved, our first and foremost responsibility was to protect the public health, and at the outset, because of the fact that we are seeing significant changes in our distribution processes, where a product coming from one source gets rapidly disseminated into a variety of distribution pathways, as we were tracking that outbreak backward, before we even knew where the sole source was, we put out an advisory with regard to all spinach so that we would be assured that we were doing the utmost to protect the American people.

Once we began to define where that source was and that the rest of the supply was, in fact, free of any contamination, then it was important to identify the single source, and we have not done as good a job with regard to recovery as I think we need to with regard to our communications going forward, and that is one of the lessons learned and one of the areas where we are embarking upon opportunities for improvement so we can do exactly what you have requested, rapidly define the source, and not only take action against that but assure the American people that other options are safe and appropriate. We are working on that.

Chairman WAXMAN. It is your turn.

Mr. ISSA. I thought the time expired.

Chairman WAXMAN. It did.

Mr. ISSA. Oh, and you went right to my time?

Chairman WAXMAN. Yes.

Mr. ISSA. Thank you. I thank the chairman.

Chairman WAXMAN. I think Dr. Kessler wanted to respond.

Mr. ISSA. I guess I will followup quickly on that, then. I hear you, but I am disappointed that you couldn't say—and maybe you can say in a followup—if we had it to do over again, we would have told the American people with an abundance of caution we are concerned about all spinach, even though we have isolated so far the outbreaks to a single farm. That was never said on the front end, and it destroyed an industry.

Dr. VON ESCHENBACH. Well, let me be clear about what I tried to say. We had to make the announcement about our concern about spinach before we had the confidence and knowledge of what that single source was. That information did not come——

Mr. ISSA. Doctor, I appreciate that, but, unfortunately, it flies in the face of past experience. We have had ground beef e-coli in the past. Nobody said don't eat any ground beef. Nobody said ground beef is tainted. Even when we had multiple outbreaks, the assumption from day one was always it probably comes from one source, we have isolated no source or one source. You have a history of a lot of outbreaks of ground beef contamination. It is practically a seasonal occurrence. And you have never done it in a way that destroyed ground beef.

Certainly, some people got scared and they didn't listen that it was only 2-pound packs bearing the name of something-or-other, but the fact is you destroyed an industry by the ineptness of the response. I would hope that when you are answering a congressional inquiry that you say, "Look, not only did we have lessons learned, but this is how we would prevent this specifically in the future," not "We are trying to develop systems to prevent it." You didn't need to scare the bejezus out of everyone who ate anything green and uncooked, and yet that is what happened. The production not just of that but of lettuce and lots of other things went down.

Perhaps I am sensitive because I am a Californian, but the fact is it is an important lesson that has to be learned, because the next time, if it is ground beef and you treat it that way, we are going to have, what, all beef not eaten for a period of time?

Dr. VON ESCHENBACH. Well, your point is well taken, Congressman, but I want to emphasize the fact that, as we have been talking about today, we have seen radical and rapid changes occurring in both production and distribution and dissemination of our food supply, and when it is apparent to us that potential contamination could affect the entire product, we need to warn the American people of that. And as we progress with our investigation and get further-refined information, communicate that effectively to them, as well as part of the recovery.

Mr. ISSA. I appreciate that. I think we are going to agree to disagree and I will move on.

You know, the FDA has dramatically increased the number of medical guidebooks or leaflets that have to be given out, and yet my understanding is you have not allowed it to come into the 21st century where a pharmacist could take an online data base that is

more accurate than a printed leaflet, print it out directly, and hand it to the individual, rather than maintaining leaflets. Are you in the process, can we have an assurance that is going to happen in the near future?

Dr. VON ESCHENBACH. Yes, sir. We are in that process. The changes we made this year with regard to drug labels were specifically intended to move us more effectively into real-time updates in an electronic format of that drug label, with the expectation it ultimately could be distributed by pharmacists at the point of service.

Mr. ISSA. OK. And in closing, Dr. Young, I just want to thank you for your comments about the specifics of drugs and how very small differences in even conventional and certainly in follow-on biologics can make a difference and why we cannot simply substitute one for the other, even if they are dramatically similar.

I yield back and thank the chairman.

Chairman WAXMAN. Mr. Platts.

Mr. PLATTS. Thank you, Mr. Chairman.

Dr. YOUNG. Could I make a brief comment?

Mr. ISSA. I apologize. I didn't mean to cut anyone off.

Chairman WAXMAN. Yes, Dr. Young?

Dr. YOUNG. I wanted to point out one thing, and this is different than the question that you asked Dr. von Eschenbach about but related.

One of the problems, if you had a crisis—and I had a crisis of the Chilean grapes. We were able to take it off and bring it on in 18 days. But the thing that was key for me was the ability to have regional labs that are well equipped and are able to go in at that site and do the testing and narrow it down as fast as possible.

Once you do have a disaster, as Dr. von Eschenbach said, you have to throw everything at it, make the risk, but you try to bring it back on as fast as you can. But unless there are good laboratories in the region that are able to look at that and deal with it—and I would ask, Mr. Chairman, that you might want to take a look. I have no idea what the laboratory personnel is, but take that same 10 year period of time and look and see where we are in regional labs and the ability of the FDA labs to work and support the Commissioner's office.

Mr. ISSA. Thank you.

Dr. Kessler, do you want to respond?

Dr. KESSLER. Congressman, I think we have an obligation, the three of us, to push back a little here, if I may.

I am a Californian, and I will tell you I was very concerned about what happened to that industry. That industry clearly is over its head scientifically. It wants to do the right thing; it doesn't know what the right thing is to do. But we are going to have to stop saying—the hardest job, going to bed every night, being responsible, whether it is from China, whether that ship is coming in from South America and the water in that ballast that fresh produce is, you have set up the agency not to be able to do its job.

We haven't changed the food safety laws in decades. We haven't given the agency basic scientific resources to do the science to help the industry to know how to prevent those problems, and we have

not established a preventive system of controls that help the farmers prevent those kind of devastating outbreaks.

This is not an FDA problem, alone; it is going to require the Congress and the industry, with the agency, to recognize that we can hold hearing after hearing on whether it is China or whether it is spinach or whether it is peanut butter, but we have a system that is in major need of reform.

Mr. ISSA. Thank you, Chairman.

Chairman WAXMAN. Mr. Platts.

Mr. PLATTS. Thank you, Mr. Chairman. I appreciate your holding this very important hearing, and your leadership on issues related to the Food and Drug Administration.

I want to raise an issue, and I hope I am not being repetitive, with managing several resolutions on the floor and other meetings and missing some of the testimony. It is an issue, Mr. Chairman, that you have been a leader on back in 1984 with legislation on generics, and I know recently raised with Senator Hatch on the issue of draft guidance on biologics and insulin and human growth hormone.

Dr. von Eschenbach, I wonder if you could give an update. I know my Governor, Governor Rendell, wrote to you about 2 months back, and I know a good number of Governors have either written you or spoken out on this issue about getting the draft guidance released to allow the process to go forward for generics on these specific biologics.

I was wondering if you could give us an update of where we stand, especially in light of—and correct me if I am wrong in my understanding, or at least the general timeframes—as early as a decade ago, that FDA committed to providing the guidance for these two specific biopharmaceuticals, and then in April 2002 it is my understanding they actually completed the science on the draft guidance regarding these two biologics. So if you could give us an update, I would appreciate it.

Dr. VON ESCHENBACH. I would be happy to pursue that and give you the update for that on the record with regard to what is occurring at this point. We have addressed this issue with regard to ongoing challenges, both with regard to generic, small molecules, as well as the need to begin to address the issue of generic biologics, or the follow-on proteins, and recognize this to be a portfolio in which there is tremendous diversity and complexity within that family of proteins, ranging from very simple ones like polypeptides to very complex molecules.

And so we take this as an approach in which science and scientific portfolio will lead us to be making these decisions. This is an area where Dr. Woodcock has really been working and focusing on developing our strategies for that scientific effort, and I would be happy to provide you the update on where we are with the guidance for the record.

Mr. PLATTS. If you can provide that to the committee for the record, and specifically I guess I would be interested in your response to Governor Rendell's correspondence of February 15th that is specific to insulin and human growth hormone, where we stand.

Dr. VON ESCHENBACH. Yes.

Mr. PLATTS. I know that there is a lot of focus. In fact, I think the chairman's letter was on that issue back earlier this past month in April.

Dr. VON ESCHENBACH. I appreciate your allowing me the opportunity with those two specific things to get the up to date information for you and respond to the record.

Mr. PLATTS. A followup on that, then, in a broader sense is the broad issue of your authority. Is it a belief that FDA, in the area of generic versions of biopharmaceuticals, that you do not have the current authority to move forward in this broad area? And if that is the case, have you looked at the legislation that is being considered to address that?

Dr. VON ESCHENBACH. Yes, sir, that is correct. In terms of biologics being included under the Public Health Service Act, we did not have a pathway within that particular act to deal with abbreviated applications. That is one of the issues that Congress is addressing.

With regard to regulatory authority, we are looking forward to continuing providing technical assistance with regard to that legislation, particularly from the point of view of addressing the unique differences between this family of products as opposed to what our previous experience has been with small molecules or generic drugs.

Mr. PLATTS. On insulin and human growth hormone, that is not an issue of authority, right?

Dr. VON ESCHENBACH. No, that was addressed independently of that.

Mr. PLATTS. Right. And so then the authority is going to these biologics in not addressing that?

Dr. VON ESCHENBACH. Correct. As you point out here, there are two statutes that govern our ability to deal with these compounds. Some of them come under the Food, Drug, and Cosmetic Act, and the biologics that we are now addressing come under the Public Health Service Act.

Mr. PLATTS. I do appreciate your following up with the committee and for all of us Members on that issue, because, you know, the important work of the chairman and Senator Hatch in 1984 and the access to pharmaceuticals is it is not just that we have them, but they are affordable, and so this is critically important.

I know back in Pennsylvania to our PACE program, our pharmaceutical contracted elderly program which truly makes a huge difference for so many seniors, in that one program this advancement, the estimate is, I think, over $100 million a year in savings. That means that many more seniors we can help.

So I hope that we will see progress on the guidance on the insulin and human growth hormone, as well as your agency working with this chamber and the Senate on legislation that broadens the authority for additional authority to your agency for generics on the biopharmaceuticals soon.

I certainly appreciate your leadership today and our previous Commissioners for your important work on behalf of your fellow citizens. I would be remiss if I didn't acknowledge the great dedication of you and your staff, present and past, at FDA.

Thank you, Mr. Chairman, for the time.

Chairman WAXMAN. Thank you very much, Mr. Platts.

Ms. Watson.

Ms. WATSON. Mr. Chairman, thank you so very much. I am so pleased that you are fulfilling the oversight function that this committee is authorized to do.

I have some concerns for the FDA, and I think a grievous oversight has come from in recent years is that the failure to stop the use of mercury in dental amalgams, and there have been studies done abroad that have shown empirical evidence that mercury is harmful to lactating women, harmful to children under 18, and probably harmful to humans. Mercury is always evaporating, regardless of how well it is sealed, because our teeth move around, they chip, they crack, and so on.

I am sorry that I was late. I have not heard your testimony, but I would like to hear from someone why the FDA has not taken on this issue and moved on it. We know that it is harmful internally, and why we would have any substance put in the mouth so it can go up to the T-zone, affect the meninges of the brain, and also go into the systems of women—so can someone respond why FDA hasn't taken action on mercury amalgam?

Dr. VON ESCHENBACH. Madam Congressman, we continue to be concerned about issues that you are alluding to and have continued to carefully monitor any scientific data and information that would impact upon a regulatory decision about the amalgams.

Ms. WATSON. Let me take my time back. I would be pleased to provide you with the scientific information. That is the response I got last year. You are dragging your feet on this issue. I wish you would speak to it. I am going to send that information to you ASAP, and I would hope that you would respond. It is not good enough to say we continue to look at it. We know the harm mercury can do. We had a mercury spill last year in Virginia. They closed down three high schools for 2 or 3 days until they cleaned the mercury up. WHO is removing mercury from thermometers. We removed mercurochrome off the market, and we still allow it to be used in those silver fillings in one's mouth. That ought to put a light on and you ought to move faster.

Dr. VON ESCHENBACH. I look forward to that information, Madam Congressman.

Ms. WATSON. Thank you, Mr. Chairman.

Chairman WAXMAN. Thank you, Ms. Watson.

Does any other Member have anything else pressing? I think our witnesses have been very generous with their time.

Let me thank you, because I think this has been a very helpful session to learn from past experiences, the present situation. I hope all of this will help you and help us figure out how to make FDA function even better. It is an agency that we all support, and I think you got a sense on both sides of the aisle that is the case. We want Government to work, and if there is any agency of Government that needs to work appropriately for the consumers of this country it is the Food and Drug Administration.

I think you have given us very specific and helpful suggestions and comments about different issues that you are dealing with at the FDA today and the other three have dealt with in the past.

Thank you so much.

Dr. VON ESCHENBACH. Thank you, Mr. Chairman.

Chairman WAXMAN. That concludes our hearing today. We stand adjourned.

[Whereupon, at 3:25 p.m., the committee was adjourned.]

[Additional information submitted for the hearing record follows:]

# Congress of the United States

Washington, DC 20515

May 11, 2007

The Honorable Andrew C. von Eschenbach, M.D.
Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane, Room 15-47
Rockville, MD 20857

Dear Dr. von Eschenbach:

Thank you for your participation in the Oversight and Government Reform Committee's May 1, 2007, hearing regarding the missions of, and challenges facing, the U.S. Food and Drug Administration (FDA). I regret that other commitments precluded me from being present for the questioning portion of the hearing. Accordingly, I would like to take this opportunity to pose some questions of great importance to me. I request that you provide complete, comprehensive information in response to the following inquiries:

1) You indicated in your oral testimony before the Committee that a number of "organizational changes" are occurring at the FDA that will allow for greater efficiency and efficacy, including the creation of an Office of the Chief Medical Officer. Please detail the following with respect to this office:

a) What is the relationship between the Office and the Center for Drug Evaluation and Research (CDER) and/or the Center for Biologics Evaluation and Research (CBER)?
b) How does the Office share in the FDA's drug safety-related regulatory responsibilities?
c) Who is the Chief Medical Officer's immediate supervisor?

2) What are the other "organizational changes" that are occurring?

3) In response to a question posed by Congressman Bruce Braley (D-IA), you stated that the FDA is "immersing much more in post-market surveillance" of drugs. What exactly is being done to accomplish this and why?

4) In your written testimony submitted to the Committee, you stated that the CDER has "initiated a series of changes designed to effect true culture change that will strengthen the drug safety system." What are these changes and what is the reasoning behind each change?

5) Therein, you also cited a need for improvement of the CDER/FDA's "organizational culture." What specifically needs to be improved? Moreover, what strategies are being employed in order to spur these improvements?

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6) Additionally, you indicated that inter-organizational "process improvement teams" have made recommendations for improvements in the CDER's drug safety program, including the creation of Associate Director for Safety and Safety Regulatory Project Manager positions in each Office of New Drugs and the establishment of regular OSE-OND "safety meetings." Please detail the following:

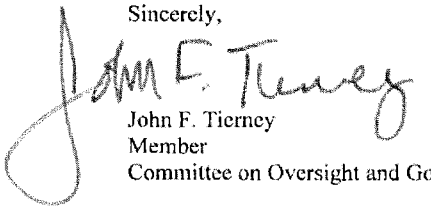
a) What are the duties, responsibilities, and authorities of each Associate Director for Safety and Safety Regulatory Project Manager?
b) Who is/are the immediate supervisor(s) of each Associate Director for Safety and Safety Regulatory Project Manager?
c) What is the relationship between each Associate Director for Safety and/or Safety Regulatory Project Manager and the staff of the Office of Surveillance and Epidemiology?
d) What is addressed in each OSE-OND "safety meeting"?
e) What are the other recommendations put forth by the "process improvement teams" to date?

7) Finally, on another topic, I am interested in learning more about the FDA's proposal to close the Office of Regulatory Affairs' Winchester Engineering and Analytical Center (WEAC) in Winchester, MA, and reportedly move its current operations to the Northeast Regional Lab in Jamaica, NY. Please detail the following with respect to this proposal:

a) What is the FDA's projected cost savings from closure of WEAC?
b) What is the projected cost of relocating WEAC's radiation detection capabilities and attendant training of personnel at the Northeast Regional Lab?
c) What entity/entities have performed the economic analysis pertaining to this proposal?
d) In a February 28, 2007, letter from you to certain Members of Congress, an "expiring lease" was cited as a reason for seeking closure of WEAC. However, my understanding is that WEAC's facilities are owned by the FDA. Please explain this discrepancy and why FDA is seeking closure of WEAC despite agency ownership of the facility.

Please provide this information by Friday, May 25, 2007. If have you have any questions concerning this request, please contact Stefanie Ackerman of my staff at (202) 225-8020.

Sincerely,



John F. Tierney
Member
Committee on Oversight and Government Reform

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COURTS, THE INTERNET & INTELLECTUAL PROPERTY
CONSTITUTION, CIVIL RIGHTS, & CIVIL LIBERTIES
REPUBLICAN POLICY COMMITTEE

May 8, 2007

Andrew C. von Eschenbach, M.D.
Commissioner
U.S. Food and Drug Administration
U.S. Department of Health and Human Services
5600 Fishers Lane, Room 15-47
Rockville, MD 20857

Dear Dr. von Eschenbach:

Thank you again for your participation in the May 1, 2007 hearing on the Food and Drug Administration. Your contribution was extremely valuable and I look forward to continuing the conversation on FDA's critical mission and challenges for the future.

I am writing to ask an additional question for the official hearing record. I am specifically interested in how the agency is implementing the Medication Guide program. These Medication Guides are special leaflets that manufacturers produce and pharmacists distribute to patients when they pick up their prescriptions. These Medication Guides focus on telling patients about the risks of using a medication. When the FDA finalized the regulation for the Medication Guide in 1999, it said that it only would add a few Medication Guides per year for drugs that had serious and significant side effects.

Over the past few years, FDA has added dozens of new Medication Guides not just a few drugs as they said they would, but for popular classes of drugs such as antidepressants, sleeping pills, ADHD drugs and pain killers. Right now about 240 different drug products have Medication Guides. I understand from my pharmacists that this has created a morass of paper MedGuides for pharmacists to distribute to patients with little evidence that patients read these leaflets.

Why is the agency not implementing the Medication Guide regulation consistent with how it said it would implement the regulation? Is there any evidence that all these new Medication Guides is making any difference in the safe use of medications?

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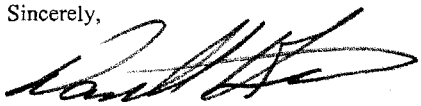
Additionally, I understand that some pharmacies have the capability of printing these Medication Guides electronically at the same time that they print the prescription label that goes on the prescription bottle. This would seem to increase the distribution of Medication Guides since pharmacists won't have to look for the pad with the Medication Guides. Instead, they can just provide the Medication Guide that is printed. Pharmacists asked the agency about two years ago to give them the authority to print these Medication Guides electronically when they print the prescription label, but the agency hasn't given them the authority to do that yet.

Can you tell me if the agency will allow pharmacists to print these Medication Guides electronically, and when is the agency going to make a decision on this request?

Thank you for your attention to these questions. I look forward to your response to include in the official hearing record. Please provide a response by no later than May 22, 2007. All responses should be sent to the attention of the Committee's Republican Clerk, Benjamin Chance, at B 350A Rayburn House Office Building. Should you have any questions regarding this request, please call Susie Schulte at (202) 225-5074.

Sincerely,



Darrell Issa
Member
Committee on Oversight and Government Reform

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

The Honorable Darrell E. Issa
House of Representatives
Washington, D.C. 20515-0549

JUN 11 2007

Dear Mr. Issa:

Thank you for your letter of May 8, 2007, in follow up to the May 1, 2007, "FDA's Critical Mission and Challenges for the Future" hearing regarding the implementation of the Medication Guide program. We appreciate the opportunity to respond for the official hearing record.

The Federal Food, Drug, and Cosmetic (FD&C) Act outlines the requirements for Medication Guides. In the last few years, we have redoubled our efforts to address drug safety issues and to communicate safety concerns about drug products in a clear and compelling way. As a result of those efforts, we have been issuing more Medication Guides.

In terms of implementation, under the regulation at Title 21, *Code of Federal Regulations* (CFR), section 208.24, *Distributing and Dispensing a Medication Guide*, manufacturers who ship drug products for which Medication Guides are required must ensure that sufficient guides are available for distribution to patients. They may do so by providing hard copy Medication Guides in numbers that allow distributors, packers, or authorized dispensers to provide the guides to all patients who receive the drug product. Alternatively, manufacturers may provide the means for distributors, packers, or authorized dispensers to produce and provide Medication Guides to these patients. Importantly, the regulation requires each authorized dispenser of a prescription drug for which a Medication Guide is required to provide the guide to the patient, or to the patient's agent when the product is dispensed, unless exempt from this requirement under 21 CFR §208.26.

The Food and Drug Administration (FDA) has taken steps to help pharmacists understand that they must provide Medication Guides when dispensing products requiring them. For example, FDA's website at *www.fda.gov/cder/offices/ods/medication_guides.htm* provides pharmacists with a list of drug products that require Medication Guides. Many pharmacists use software programs to alert them to dispense Medication Guides along with a medication.

We have heard concerns regarding both paper and electronic Medication Guides. Pharmacists report that they are inundated with paper to distribute to patients. Some pharmacists have advised FDA that manufacturers are not providing adequate quantities of

Medication Guides, and that they want Medication Guides in electronic format or to be able to transmit them to the patient electronically. In January of 2006, we wrote to all manufacturers of approved antidepressant products, reminding them that they must assure that sufficient Medication Guides are available for distribution, whether by providing adequate numbers of these guides in hard copy or by providing the means to receive and produce them electronically. In support of the latter option, FDA met several times in 2006 with pharmacists to discuss electronic distribution of Medication Guides. There is nothing that prevents pharmacists from using electronic means to reproduce Medication Guides for distribution. Using such means to access, print and distribute this information does not require FDA authority.

In response to concerns about Medication Guides, we are holding a public meeting on June 12-13, 2007, from 8:30 a.m. to 4:30 p.m., on the "Use of Medication Guides to Distribute Drug Risk Information to Patients" at the National Transportation and Safety Board Boardroom and Conference Center, 429 L'Enfant Plaza SW, Washington, D.C. The objective of the meeting is to discuss the purpose of Medication Guides generally, assess their effectiveness, discuss logistical hurdles to their distribution and dissemination as well as possible solutions, and issues related to electronic distribution of Medication Guides. We welcome input from you or your staff at this meeting. Please see our website for further information: *http://www.fda.gov/cder/meeting/medication_guides_200706.htm.*

It is not feasible for FDA to inspect pharmacies nationwide to determine if Medication Guides are being dispensed when they are required. In an effort to better understand the problem, whether it is a systemic issue or just related to specific products, we are seeking the help of the state pharmacy boards to ask pharmacists to report to FDA's MedWatch program when they do not receive Medication Guides in sufficient numbers, or the means to produce Medication Guides in sufficient numbers, to permit their requisite delivery to patients. We recently worked with the National Association of Boards of Pharmacy, which agreed to publish an article in its May 2007 newsletter asking state boards to let pharmacists know about MedWatch reporting for Medication Guide problems. Also, we are asking pharmacist and pharmacy organizations to reach out to their members to report problems that they encounter related to Medication Guides.

You asked whether there is any evidence that all these new Medication Guides are making any difference in the safe use of medications. FDA plans to use the public meeting, mentioned above, as an opportunity to hear from patients, pharmacies, and health professionals to help the Agency assess the effectiveness of Medication Guides in communicating the risks of certain drug and biological products to consumers.

The Agency is dedicated to making certain that all patients receiving drug products that require a Medication Guide receive one. We will continue to contact entities such as state regulatory authorities, national pharmacist trade associations, professional associations, and individual pharmacists to help ensure their collaboration and compliance in meeting the Medication Guide requirements. We hope that the upcoming public meeting will reveal the sources of the problems regarding distribution and dissemination and help identify corrective steps that can be taken to ensure that the Agency's Medication Guide program is successful.

Thank you for contacting FDA regarding this matter. If we can be of further assistance, please let us know.

Sincerely,

Stephen R. Mason
Acting Assistant Commissioner
for Legislation