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[Senate Hearing 110-]
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AGRICULTURE, RURAL DEVELOPMENT, FOOD AND DRUG ADMINISTRATION AND
RELATED AGENCIES APPROPRIATIONS FOR FISCAL YEAR 2009

TUESDAY, APRIL 15, 2008

U.S. Senate,
Subcommittee of the Committee on Appropriations,
Washington, DC.

The subcommittee met at 10 a.m., in room SD-192, Dirksen
Senate Office Building, Hon. Herb Kohl (chairman) presiding.
Present: Senators Kohl, Dorgan, Reed, and Bennett.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

STATEMENT OF ANDREW C. VON ESCHENBACH, M.D.,
COMMISSIONER

ACCOMPANIED BY:

JOHN DYER, DEPUTY COMMISSIONER AND CHIEF OPERATING OFFICER,
FOOD AND DRUG ADMINISTRATION
RICHARD TURMAN, DEPUTY ASSISTANT SECRETARY FOR BUDGET,
DEPARTMENT OF HEALTH AND HUMAN SERVICES

OPENING STATEMENT OF SENATOR HERB KOHL

Senator Kohl. Good morning to one and all. Today we welcome
Dr. von Eschenbach, the FDA Commissioner; Mr. John Dyer, the
Deputy Commissioner for Operations; and Mr. Richard Turman, the
Deputy Assistant Secretary for Budget at HHS. We thank you for
appearing this morning to discuss the FDA's budget for 2009.

American consumers spend 20 cents of every dollar on
products that are regulated by the FDA. Food, medicine, medical
devices, vaccines, the blood supply, cosmetics, and veterinary
products all fall within FDA jurisdiction. FDA has a
responsibility to make sure that all of these are safe and
effective.

As you appreciate better than anyone else, it is, indeed, a
daunting task that grows more complex every year.
Unfortunately, your budget request does not keep pace with
these huge responsibilities.

For fiscal year 2009, the administration proposed an
increase of \$54 million, or just over 3 percent. It recommends
modest increases for food safety and medical products. While
that is a welcome contrast compared to cuts proposed for HHS
and USDA, I find it hard to believe that this recommendation
will achieve anywhere near the goals that FDA has set.

The budget purports to hire over 200 additional FDA
inspectors, as well as staff, but in reality, you do not
request enough money to pay for the staff that you have now.
Specifically, the budget clearly states that FDA needs \$60
million more than last year simply to maintain current staffing
levels, but you only request \$54 million new dollars.

What this really suggests to me is that any additional
money you claim to be for new food and medical safety
activities will really be used to maintain current staff. There
is no new money for food safety, medical products safety, as
well as anything else.

FDA recently published a food protection plan and import
safety action plan. Both documents outline important steps
needed to keep our food supply safe, and those steps will cost
money. Serious work also needs to take place to ensure that the
drugs, which FDA approves are indeed safe, and we need
assurances that necessary follow-up will happen. We have all
heard that 80 percent of the raw ingredients going into our
medicines come from overseas. It would take FDA 13 years to
inspect each of these plants just once.

I know that you are aware of these issues and many more,
and I believe you want to move in the right direction. But I
also feel obliged to address your recent complaint that
Congress has failed to give FDA the money it needs. That
complaint seems a little specious to me. Congress gave FDA \$90
million more than you sought for the current year, and we
provided \$17 million more than you sought in fiscal year 2007.
So I take issue with that complaint and we look forward to your
comments and explanations.

We have developed a good working relationship over the past
several years, and I am sure that will continue this year.
Although we seem to be far apart on how we would interpret this
budget right now, we want to work with you to make sure that
your agency, one that affects every single American every day,
has the necessary funding to be effective, as we both think it
should be.

We will now turn to Senator Bennett for his opening
statement, and following that, we look forward to hearing from
you, Senator Bennett.

STATEMENT OF SENATOR ROBERT F. BENNETT

Senator Bennett. Thank you very much, Mr. Chairman. You
have covered many of the points that I wanted to highlight as
well.

The FDA's regulatory authority is vast. It encompasses 80
percent of the food we eat, all animal and human drugs and
medical devices, along with some other products, and 20 percent
of all consumer expenditures go for some product that is
regulated by the FDA. That is \$1.5 trillion worth of
expenditures. So this is a very important agency.

And, Dr. von Eschenbach, I want to take this occasion--this
will be your last appearance in defense of the budget--to thank
you for the stewardship you have provided at this agency.

We more often hear about problems connected with the agency
than we do about the success in making the United States food
and drug supply the safest in the world, as I believe that it
is.

But there have been problems and I expect we will hear
about some of them, the widely reported recall of heparin
because of contaminated ingredients that came from the supplier
in China, the recall of peanut butter tainted by salmonella,
followed by a massive pet food recall, also having to do with
contaminated ingredients from China. As we look at those
problems, we sometimes, as I say, lose sight of the fact that
overall we do have the safest food and drug supply in the
world.

But I agree with the chairman that we need to pay attention
to the amount of money that is required here and that the
budget that has been submitted to us by the administration
appears to me to be inadequate to meet those challenges. I have
sat on your side of the table. I know the kinds of fights that
go on in an executive agency between what you feel is your best
judgment and what OMB feels is its best judgment and the very
difficult position you get put in when you are sent up here to
defend OMB's number when in your heart you might prefer a
higher one. You need not comment on that. I will not put you in
that box. But I have seen that kind of thing happen before. And
I feel, with the chairman, it may be our responsibility to fix
OMB's mistake here. I think you probably have more friends here
than you might have at other places in town.

It is not just money, however. You need leadership. You
need good people. You need to be able to attract the right
people and hold onto the right people. Those are some of the
things we will be talking about.

Senator Kohl. Thank you, Senator Bennett.
Senator Dorgan, do you have a statement?
Senator Dorgan. No, thank you.
Senator Kohl. We will now ask Dr. von Eschenbach for your
statement.

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In 2008, the subcommittee appropriated increases for drug safety, critical path generic drug review, drug advertising review, and pandemic preparedness programs at FDA. Thanks to the commitment of this subcommittee, specifically Senator Bennett, we will commence 50 important critical path activities across all medical product programs. This is our effort to transform the design, development, testing, and use of medical products.

PRODUCT SAFETY

We continue to address our need for product safety and development, including our ability to provide increased staff and oversight for targeted increases in blood and blood products, human tissue safety, criminal drug investigations, and device import safety, as well as animal drug grants under the Minor Use and Minor Species Animal Health Act.

PREPARED STATEMENT

This \$2.4 million contains essential resources on that trajectory to continue to build the FDA of the 21st century that will protect and promote the health and safety of the American public. And we are deeply grateful for your commitment to that continuous, ongoing effort to recreate and redefine and modernize the FDA.

Thank you, Mr. Chairman. I look forward to your questions.
[The statement follows:]

Prepared Statement of Andrew C. von Eschenbach

Introduction

Chairman Kohl and members of the subcommittee I am pleased to present the President's fiscal year 2009 budget request for the Food and Drug Administration (FDA). I am joined by Mr. John Dyer, FDA's Deputy Commissioner and Chief Operating Officer, and Mr. Richard Turman, Deputy Assistant Secretary for Budget at the Department of Health and Human Services.

At the outset, I want to lay out the trajectory reflected in FDA's budgets during my tenure. When I first sat before you on behalf of the FDA 2 years ago, I presented a budget that recognized the need for additional resources so that FDA can accomplish its mission. Just as important, FDA also recognized the need to establish plans that define how to use our resources wisely.

For the past 2 years, we requested additional resources to meet important public health challenges. We also developed detailed plans that communicate how we will deploy our resources to overcome the challenges that we face. However, you also expect performance while we are developing plans for the future, and we have delivered.

Recent FDA Achievements

Thanks to funding appropriated by this subcommittee, FDA is achieving important public health milestones, and we thank you for your support. Since I appeared before you last year, FDA worked with Congress on the FDA Amendments Act (FDAAA) to extend key user fee programs including the Prescription Drug User Fee Act (PDUFA) and the Medical Device User Fee Act (MDUFA), to reauthorize the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act. During the past year FDA also:

- published comprehensive plans for food defense, food safety, and import safety
- negotiated and signed food and medical product safety agreements with China
- expanded FDA's capacity to detect radiological contamination of food by 150 percent
- launched a national initiative to strengthen State food safety programs
- issued a current good manufacturing practices rule for dietary supplements
- approved a second-generation smallpox vaccine to enhance U.S. preparedness
- approved the first U.S. vaccine for humans against H5N1, the avian influenza virus
- approved the sixth seasonal influenza vaccine, allowing manufacturers to produce a record number of flu vaccine doses
- approved a decellulitized heart valve, a new drug-eluting stent, and the first artificial cervical (neck) disk
- approved new treatments for hypertension, Crohn's disease, cancer, HIV, diabetes, Parkinson's, Fibromyalgia, leukemia, and blood clotting disorders, including 22 new molecular entities and 18 orphan products
- tentatively approved the 64th anti-retroviral product under the President's Emergency Plan for AIDS Relief (PEPFAR)
- issued more than 680 generic drug approvals or tentative approvals during fiscal year 2007--a 30 percent increase from the previous year
- approved new tests for blood typing and to detect malaria, West Nile Virus, certain breast cancers, respiratory viruses, and other infections
- identified Critical Path opportunities for generic drugs and conducted Critical Path workshops on cancer clinical trials and developing anti-cancer agents
- proposed new standards and a new UVA rating for sunscreen products
- released a report on science and regulatory issues associated with nanotechnology
- conducted enforcement actions to protect consumers against unapproved drugs and devices and from unsafe dietary supplements
- identified 25 drugs products that must submit safety plans under Title 9 of FDAAA.

These are important public health accomplishments, and they demonstrate FDA's performance while we also prepare for the future. My FDA colleagues and I recognize that we have important work to do in all FDA program areas. We also have challenges that cut across all FDA programs, such as expanding FDA's reach beyond our borders, modernizing our Information Technology, and working with the General Services Administration to complete our new campus at White Oak.

FDA's 2009 Budget Request

The President's fiscal year 2009 budget request for FDA builds on the fiscal year 2008 appropriation by proposing a 5.7 percent increase. FDA will focus its increased resources on protecting America's food supply and improving the safety of human and animal drugs, medical devices, and biologics--including vaccines, blood products, and human tissues.

This increase will provide FDA with a budget of \$2.4 billion, which consists of \$1.8 billion in discretionary budget authority and \$0.7 billion in user fees. FDA user fee programs provide supplemental resources that not only allow FDA to review manufacturers' product applications but also ensure that Americans have access to safe and effective medical products.

As I mentioned, Congress reauthorized user fee programs for prescription drugs and medical devices last year in FDAAA. This year, the successful program to support animal drug review, the Animal Drug User Fee Act (ADUFA), expires on September 30, 2008. We have engaged with stakeholders to develop proposals to extend this program for an additional 5 years. FDA published a draft proposal for ADUFA II in the Federal Register and conducted a public meeting with stakeholders on March 11, 2008.

Finally, our budget includes \$48 million for four proposed user fees related to reviewing generic drugs, reviewing generic animal drugs, reinspecting facilities, and issuing export certificates for food and animal feed.

FDA Food Protection Plan Investments

On November 6, 2007, the administration issued the Import Safety Action Plan (ISAP), a comprehensive, strategic roadmap to strengthen import safety. In conjunction with this release, FDA released its Food Protection Plan (FPP), a comprehensive initiative to protect America's food supply.

The FPP is a risk-based, production-to-consumption strategy to assure the safety of domestic and imported food. FDA's plan relies on three core elements--prevention, intervention, and response--and calls

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for ten new legal authorities. The plan is designed to identify potential food defense and food safety threats and to counteract those threats before they harm consumers.

FDA has begun implementing the FPP and ISAP with the resources that the subcommittee appropriated in fiscal year 2008. In fiscal year 2009, FDA requests an additional \$42 million to protect the food supply and to continue to implement our plan. These funds will allow FDA to advance important food defense and food safety priorities. Fiscal year 2009 prevention activities include performing essential food research, determining the threats of intentional and unintentional contamination to the food supply, and expanding food protection activities beyond our borders. Our intervention activities include conducting more risk-based inspections and surveillance and deploying new food defense and food safety screening tools. Fiscal year 2009 response activities include establishing more rapid response teams, strengthening emergency response, and improving our ability to conduct food tracebacks.

To achieve these objectives and safeguard American consumers, FDA will also improve IT systems that support our research, risk assessment, inspection, and surveillance. Finally, FDA's fiscal year 2009 food protection initiative includes \$12 million for the cost of living pay increase for FDA food safety and food defense programs. These funds allow FDA to retain its professional workforce that conduct food safety and food defense activities. Overall, our food protection investments for fiscal year 2009 support an additional 94 full-time equivalent (FTE) staff, including 68 FTE to conduct domestic and foreign inspections through FDA's field operations in the Office of Regulatory Affairs.

Investments for Safe and Effective Medical Products

For fiscal year 2008, Congress appropriated increases for drug safety, Critical Path, generic drug review, drug advertising review, and pandemic preparedness programs at FDA. With these increases, FDA will strengthen medical product development, safety, and review activities that the subcommittee identified as fiscal year 2008 priorities. I assure you that FDA will be a good steward of the funds you provide and that we will search for effective solutions to the public health challenges involving medical products.

For fiscal year 2009, FDA is proposing a \$17 million initiative for medical product safety and development, including funds for the cost of living pay increase. FDA is also proposing targeted increases for our medical product programs.

With the fiscal year 2009 increase, FDA's Biologics Program will strengthen its ability to prevent, detect, and respond to emerging safety threats in blood and blood products. FDA will also improve tissue safety by expanding our program to educate industry about tissue processing and tissue safety technologies.

In the Human Drugs Program, FDA will improve import safety by conducting additional investigations of criminal drug activity. The volume of drugs imported into the United States will likely increase by 12 percent during fiscal year 2009, and the additional import volume creates a need for criminal investigators to support drug import surveillance.

In the Device and Radiological Health Program, FDA will strengthen import safety by improving the ability of the ORA field operations to work on import issues with Customs and Border Protection and other agencies. Finally, in the Animal Drugs and Feed Program, FDA will provide targeted grants to stimulate the development of new animal drugs under the Minor Use and Minor Species Animal Health Act of 2004.

Implementing FDAAA

In the fall of 2007, Congress enacted legislation reauthorizing prescription drug and medical device user fees, the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act. This legislation also grants new authorities to ensure the safety of the food supply and the safety and effectiveness of medical products--drugs, devices, and biologics. As I mentioned previously, FDAAA also reauthorized user fees for prescription drug and medical device review. Implementing FDAAA is a formidable challenge. The legislation is complex, with eleven titles containing more than 125 new requirements.

To cope with the breadth of this act, FDA launched a detailed implementation plan. And, in the spirit of transparency, the details of our progress to implement FDAAA appear on our website. Within FDA, we established working groups to confirm the scope of our FDAAA responsibilities and identify the actions and timetables necessary to conduct our new work. As you might expect, we are giving our first attention to FDAAA provisions that have the greatest implications for public health.

The new law is barely 6 months old, but our accomplishments are already tangible. As of today, FDA published 20 Federal Register notices related to FDAAA. We are methodically working through the new law, giving priority to new standards that will have the greatest public health impact. Achieving all of the goals and objectives of this landmark legislation will require a sustained effort from many individuals inside and outside of FDA for years to come.

The Scope of FDA Challenges

FDA will face many challenges in the 21st century. Thanks to the talented professionals who serve the American public at FDA, we are addressing many daunting challenges within all areas of our mission. We must modernize our workforce, our work plans, and the infrastructure that supports our mission to assure that we remain the gold standard for food and drug regulation.

In this era of change, FDA has developed strategic plans to respond to high-profile challenges in priority areas. During the past 2 years, we presented comprehensive plans to Congress and the American public on food and import safety, and responded to the Institute of Medicine Report on drug safety.

My colleagues and I at FDA are committed to our mission and committed to the changes necessary to protect America's public health. Thanks to your support, the FDA of the future--the near future--will better protect the public from the threats that we experience today. At the same time, FDA will better promote the discovery, development, and delivery of lifesaving products that improve the quality of our lives.

Conclusion

The fiscal year 2009 request of \$2.4 billion contains essential resources to protect and promote the health and safety of the American public. The funds that we request will allow FDA to strengthen the safety of the food supply, to assess, review, and approve new products, and to better predict--earlier and more accurately--the safety and effectiveness of drugs, biologics, and medical devices.

With the fiscal year 2009 resources, FDA will work to ensure that Americans enjoy the benefits of personalized medicine, a safe and wholesome food supply, and the promise of a better, healthier future. Meeting these challenges is only possible with your leadership and with the support that you consistently demonstrate for the mission of the Food and Drug Administration.

Senator Kohl. Thank you, Dr. von Eschenbach.

Dr. von Eschenbach, how do you reconcile your statement about Congress not providing you with enough funding when, in fact, over the past 2 years, this committee has provided you with over \$100 million more than you asked for?

INCREASED PRODUCTS AND RESPONSIBILITIES

Dr. von Eschenbach. Mr. Chairman, with great credit to you and to other Members of Congress, you have more recently been very, very generous in your support of the FDA. I think what we are both faced with is the realization that over the past 2 decades the FDA has been immersed in this rapidly and radically changing world that has increased the scale and scope of the portfolio of products and responsibilities facing the FDA, as well as increasing complexity in the nature of those products and the nature of their production and their consumption. And I think it is in the context of that rapidly and radically changing world that over the past 2 decades the resources required have not kept pace with the needs.

But I certainly commend you and other Members of Congress for your recent attention to our need to perhaps accelerate our

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ability to create that trajectory so that we can, in fact, bring the FDA up to the level of that we currently anticipate will be needed for this modern world.

SCIENCE BOARD

Senator Kohl. Dr. von Eschenbach, we would be remiss if we did not discuss the FDA Science Board's recommendation for your budget. Their report states--and I quote--"FDA's resource shortfalls have resulted in a plethora of inadequacies that threaten our society including, but not limited to, inadequate inspections of manufacturers, a dearth of scientists who understand emerging new science and technologies, inability to speed the development of new therapies, an import system that is badly broken, a food supply that grows riskier every year, and an information infrastructure that was identified as a source of risk in every FDA center and function." This is a board full of experienced and knowledgeable people that was established at your request.

So let us start with the overall number. Your budget requests a \$54 million increase this year, but the Science Board recommends \$375 million. Is your budget adequate? How do you respond to the Science Board's recommendations?

Dr. von Eschenbach. Mr. Chairman, I was very gratified by the report by the Science Board, which I had convened in order to have an external, objective assessment of FDA's scientific infrastructure. I think what the report has pointed out is the need for change within FDA. We have attempted to address those changes based on a strategic plan for implementation of the needed changes over a period of time.

The resources that are required will continuously need to be increased. I think the board reflects the fact that if we wish to accelerate the time line for that modernization effort and the implementation of many of the changes that are necessary to align the FDA with the modern rapidly and radically changing world around us, that level of support would be required.

ADDITIONAL \$375 MILLION

Senator Kohl. Could the FDA absorb an additional \$375 million in 1 year?

Dr. von Eschenbach. No, sir. I do not believe it could absorb that in 1 single year. I do believe, however, that we have now put in place the trajectory that I indicated before in which we have plans which define time lines, outcomes, and deliverables so that there is the rational investment of those additional resources and the ability to demonstrate a return on that investment to the American people.

I believe we could absorb significant increases in our budget and we are prepared to address how they would be applied if they were to be available. And we are doing that in the context of recognizing that our budget is one part of a larger portfolio of responsibilities to the American people that is reflected by both the President and the Congress.

NECESSARY RESOURCES

Senator Kohl. Is the FDA underfunded, hugely underfunded, grossly underfunded? What would you tell the American people?

Dr. von Eschenbach. I believe that from the perspective of our recognition of the changes that are occurring in the world around us, the need for the FDA to significantly change its strategies as to how it is addressing those changes, be they the incredible opportunities that are emanating from the discoveries in science and technology with new products such as will occur with regard to our ability to recognize the fruits of nanotechnology and regenerative medicine, all the way through to the recognition of the threats that are now emanating from globalization and the fact of our need to secure integrity of supply chain of these medical products from production to consumption, be it food or medical products, all of this is requiring a change within the Food and Drug Administration that is both strategic and a change that is also resource-dependent.

So the answer is I believe that we have been eminently successful up to this point in time. We are the world's gold standard, but if we wish to continue that record of excellence, we must change as the world around us is changing and we must change from the perspective that as our portfolio is expanding, so are the need for our resources to meet those expectations in that portfolio.

Senator Kohl. So in order to meet those expectations I think what you have said--I believe what you said--is that in order to discharge those responsibilities to the American people, the FDA is underfunded. Hugely underfunded, grossly underfunded. One could debate that, but underfunded.

Dr. von Eschenbach. I believe that we need additional resources. I am presenting a budget today that asks for additional resources. I have asked for more additional resources. I believe we could and would apply any additional resources wisely and effectively, given the fact that, as I indicated in my opening statement, it is not simply a matter of asking for more. It has rather been our responsibility to define how we would spend more, spend it wisely and strategically, and be able to then assure a return on that investment by enhancing the American people's access to safer and more effective medical products and food.

Senator Kohl. Thank you.

Senator Bennett.

FUNDING ABSORPTION

Senator Bennett. I would like to continue the line of questioning that the chairman has started down. You said you could not absorb \$375 million in a single year. I think that is probably right. How much could you absorb? This is not asking you to break with OMB. This is just a theoretical question that you can answer in a scholarly kind of way. How much could you absorb?

Dr. von Eschenbach. I believe that what we have attempted to do, Senator Bennett, in our planning process, both in our food protection plan, as well as in our strategic plan, and participating even in the larger agenda, like our import safety working group, our drug safety initiatives, across the context of food and medical products, enhancing safety, as well as rebuilding and recreating the infrastructure at FDA, we have laid out a series of initiatives, a series of opportunities. If additional funding was available, depending upon the level of funding, we would apply it to that portfolio of opportunities which we have outlined in these plans. We would do that initially around those opportunities having to do with assuring safety of food and of medical products.

BEYOND OUR BORDERS

So, for example, we have embarked upon initiatives now recognizing that FDA must go beyond our borders. And establishing an FDA presence in geographic regions around the world is a new initiative to which we could apply new dollars and accelerate our ability to implement the establishment and support of those offices, which would enable us to, one, work with our partners in other parts of the world to build capacity, to assure quality being built into the production of food and medical products, as well as being able to enhance the completion of White Oak and our data center.

FUNDING ABSORPTION

Senator Bennett. I am sure you would go through this

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orderly process. I am looking for a number. If we were to, in our wisdom, decide that OMB was wrong and we needed to add an extra \$100 million to the amount that you have taken, just to pull a number completely out of the air, could you handle that? You said \$375 million you could not handle. You said you could handle more than \$54 million. I am looking for something ball park in between as to, yes, we could comfortably absorb and handle an extra \$50 million, an extra \$100 million. You get beyond that, we are looking at future years.

It is an unfair question, but it is not because if we are moved to help you, we want to move in an area that is prudent rather than extravagant.

Dr. von Eschenbach. First of all, I would certainly welcome an opportunity to present a scenario and portfolio of options given additional possible investment. Certainly just as you say, today I do believe we could absorb the \$100 million that you referred to and do that quite rapidly and quite effectively. As we would get closer and closer to the larger number that you presented, I think it would require greater stewardship to be certain that we could implement those dollars as rapidly and as effectively as we need to.

CRITICAL PATH

Senator Bennett. I appreciate your emphasis on safety, and I agree with that.

But as you know, I am very much concerned about the critical path activities. You came to the University of Utah and testified at a hearing there, and we all got excited about the opportunities that are there. We provided \$7.5 million in 2008, and \$2.5 million was made available for competitive critical path research grants. Is that one area where you are expecting, even with what you have asked us for, to make additional resources, or is that an area that would benefit tremendously if we were to go above the number you have suggested?

Dr. von Eschenbach. Well, again, I think critical path is an excellent example of how we have tried to create this trajectory. We have, within critical path, 50 areas of opportunity for investment. They are a different grain size. As dollars are available to us, we can strategically apply them to those initiatives but do that in a way that is addressing the modernization of our drug development and medical product development process and also do it in a way that demonstrates a return on investment.

WARFARIN

Let me give you one quick example of how we have utilized some of the resources you have already applied. In taking on our ability to look at the drug warfarin and use pharmacogenomic testing in order to be able to appropriately define the right dose for the right patient, that is now a part of FDA's labeling of that particular drug. That enabled us to begin to reduce the complications of either under-dosing patients experiencing clots or overdosing and having them unnecessarily bleed. And by getting that right dose based on our understanding of pharmacogenomics, that is projected to result in the savings of \$1 billion per year for our health care system by the elimination of emergency room visits for the complications of an inappropriately dosed level of warfarin.

So I see this as a strategic business plan as well as a strategic opportunity to transform the science, and with additional dollars, we would expand our investment in a variety of those initiatives across the critical path.

INFORMATION TECHNOLOGY

Senator Bennett. And I see it as a business plan too. Unfortunately, in the way we structure Federal budgets, unlike businesses that I ran or businesses that the chairman ran before we came here, we still find things so that we do not recognize that there would be a billion dollar benefit, but it is in somebody else's budget. So we do not get credit for it as we think about it here.

Let us talk about IT. You are spending roughly what--10 percent of your budget--on IT right now, and the results are less than satisfactory. Talk to us about what has to be done to bring your IT capability up to where it needs to be.

Dr. von Eschenbach. When I arrived at FDA, the two most critical areas I believe to address was our workforce development and our information technology infrastructure because we are, in fact, an information management business. With regard to the information technology, we are spending, according to benchmarks, about \$200 million a year on IT. But the problem that we encountered was it was being spent on woefully inadequate equipment to kind of attempt to maintain it at huge cost, and we did not have the modern information systems running on that equipment.

So we have been engaged in a transformation of our entire IT infrastructure, moving to modern servers and equipment, increasing their efficiency from what has been around 30 percent to a 70 percent target, consolidating them so that we have shared activities across those servers, as well as implementing the Bioinformatics Board to redefine the programs that need to be operationalized on that IT infrastructure to create integration across the agency and information sharing, especially from our field to our centers. That is now an investment of about \$247 million a year.

WHITE OAK AND INFORMATION TECHNOLOGY

White Oak construction includes plans for our implementation and build-out of a data center at White Oak which will help us to continue our efforts to put FDA on a complete electronic infrastructure and move us away from paper.

As we had more dollars to invest, we could accelerate the implementation of that IT strategic plan.

Senator Bennett. So that brings us back to White Oak. What is your time line, and is the construction of White Oak, which is not just bricks and mortar, as you have just indicated, it is also massive increases in efficiency as you get the kind of data center that you are looking to from your IT investment there, proceeding more slowly because we are not putting enough money into it? Would it be completed more rapidly if we gave you more money? And what is your time line for getting it done?

GSA

Dr. von Eschenbach. Well, we obviously are dependent upon the appropriations that the General Services Administration, GSA, receives, and they are responsible for the bricks and mortar and maintaining that development on its time line for full completion by 2012. If those dollars were to fall off and construction slowed, that would create serious problems for us in terms of our transition into that consolidated facility from what are currently leased and widely dispersed facilities.

More importantly, as you point out, are opportunities lost with regard to consolidation. We see White Oak as our opportunity to integrate our science more effectively by virtue of having modern state-of-the-art laboratories that are working in an interdependent fashion.

Senator Bennett. Would you see savings if White Oak were finished in 2010? And could it be if more money went to GSA?

Dr. von Eschenbach. I have not done a cost analysis in terms of savings by virtue of acceleration. I certainly can tell you that there are huge losses--we would sink a lot of cost if that time line was slowed down. So how much would we gain back?

Senator Bennett. Yes.

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DATA CENTER

Dr. von Eschenbach. I certainly know by completion of such things like our data center would have a significant impact across the entire FDA operation, not just the White Oak campus. Senator Bennett. We need to do everything we can to get that finished in as logical a time as we can. Thank you very much. Thank you, Mr. Chairman. Senator Kohl. Thank you, Senator Bennett. Senator Dorgan.

HEPARIN--FOREIGN INSPECTIONS

Senator Dorgan. Mr. Chairman, thank you very much. Dr. von Eschenbach, thank you. I want to ask about the issue of inspections of foreign properties, especially about the issue of heparin, if I might. Heparin is a blood thinner-- we are well familiar with it--commonly used by dialysis patients, recently pulled from the market after it was linked to some 62 deaths. Baxter Health Care, which markets heparin in the United States, indicated the allergic reactions appeared to be caused by a contaminant that was added in place of the active ingredient in heparin somewhere in the manufacturing process, they suspect, mostly in China. They have purchased the active ingredient for heparin from a company called SPL, which is based in Wisconsin, and they purchased pig intestines from Chinese pig farms and processed the intestines in China and Wisconsin.

I am going to show you some charts. The Wall Street Journal did something about this. It published a series of photos of the Yvan Intestine and Casing factory which processes pig intestines used to make heparin. Now, I am not tracing this heparin to this place because none of us can know that or do that. But this shows the types of unsanitary conditions in which production maybe taking place. We will go down the list of these photographs. This is a place that is processing what is an active ingredient in heparin. This is processing pig intestines.

My understanding is that the FDA inspected 1,222 plants in the United States in a year and conducted only 17 inspections of plants in China. Further, when we met with Baxter, we asked Baxter had the FDA ever inspected the plant in China that is using pig intestines to create the active ingredient in heparin. Baxter said that the FDA had scheduled an inspection but actually ended up inspecting the wrong factory.

So 62 people are dead. We hear about the danger of re-importing FDA-approved prescription drugs from Canada, which is beyond me, by the way. They do that routinely in Europe under something called parallel trading where they move FDA-approved drugs from country to country. But even though we hear about the danger of that, including from the FDA I might add, it appears to be the active ingredient in heparin, which may well have caused some 60-some deaths, is coming from areas in China where there have been no inspection.

So tell me about that, 17 inspections in China, 1,100 inspections in the United States.

GLOBAL SUPPLY CHAIN

Dr. von Eschenbach. Senator, your question is very perceptive in that I think the heparin experience points out to us many of the principles that we have been discussing this morning. Let me try to succinctly address what is a very complex issue.

We are engaged in now a global supply chain, and FDA, rather than it being a gatekeeper, is now invested in a strategy of being engaged in the total life cycle of products from production to consumption. That then requires us to look at that comprehensively and look at it from the point of view of prevention of problems, building quality in at the outset, intervention when there is a suspicion or concern, and response when there is evidence of an adverse event. So all parts of that equation must be emphasized and enhanced, our ability to respond rapidly and efficiently, as well as our ability to intervene but, most importantly, to begin to emphasize the front end, building quality in at the outset.

Senator Dorgan. But, Dr. von Eschenbach---

Dr. von Eschenbach. Inspections are important, and I completely concur with our need to enhance our foreign inspections.

But this issue points out the fact that that inspection would not have detected the contamination of heparin because the contaminant is not detectable by our routine testing methods. And it was apparently, we suspect, done by virtue of economic fraud and, therefore, we had to devise new testing methods which now are being used around the entire world by our other agencies to address the problem.

ACTIVE INGREDIENTS

Senator Dorgan. A fair point.

But, Dr. von Eschenbach, these plants have not been inspected. My assumption is even if you could detect the active ingredient and the problems there, you would not allow this plant to process pig intestines and send an active ingredient in the U.S. drug supply. And my understanding is that 40 percent of the active ingredients in the U.S. drug supply come from China and India, and I just described what we have here. Seventeen inspections in all of China in 1 year, 1,200 inspections in this country.

Now, Senator Bennett asked you the question about the resources needed. Is FDA only doing 17 inspections because they do not have the resources?

BEYOND OUR BORDERS

Dr. von Eschenbach. FDA inspects all the factories or all sites of production for new active pharmaceutical ingredients for which an application is being submitted. It is the reinspections where we need to begin to expand our capacity. We are doing that in terms of, one, our initiative, FDA Beyond our Borders. We are in the process of working with the Chinese Government and we have signed memorandums of agreement to work directly with the regulatory agency. We are anticipating opening five FDA offices around the world. China will be our first with offices in Beijing, Guangzhou, which is the source of major food production, and in Shanghai where we have the port. We will work directly through that process to enhance inspections but, more importantly, to work to build, with our Chinese counterparts, systems that will assure quality in the production of these products long before they actually come into our supply chain.

FOREIGN INSPECTIONS

Senator Dorgan. This comes from the Congressional Quarterly. It says the Food and Drug Administration wanted to inspect 3,249 factories overseas and it was able to inspect 212 in all countries. You were able to inspect 6.5 percent of that which you wanted to inspect.

Again, my point is if 40 percent of the active ingredients for prescription drugs comes from China and India and we have such a small amount of inspection going on and you say and everyone says we are in a global economy. Well, it does not look like we are in a global inspection system. Obviously, those patients who have died as a result of the heparin situation paid the price for that.

CANADIAN DRUGS

But I want to make one final point that is related to this.

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We are not inspecting these foreign sources of the elements of prescription drugs, but here are two pill bottles of Lipitor. As you know, the FDA itself has been helpful to the pharmaceutical industry in recent years in saying, well, if U.S. consumers were allowed to reimport FDA-approved drugs from a Canadian drugstore where they are sold at fraction of the price, these two bottles--one is the U.S. bottle; the other is Canada--both made in the same place, put in the same size bottle, a couple different changes in the label. The only difference here--the same pill, same bottle, same company, FDA-approved--is the U.S. consumer gets to pay twice the price. And yet, the FDA says, in assistance to the administration and the pharmaceutical industry, there is a problem with allowing the reimportation of a FDA-approved drug from Canada even while this occurs, such a miserable level of inspections internationally.

Now, I am not laying this all at your feet, Dr. von Eschenbach because you have not been there all that long. But I do think it relates to the questions asked by the chairman and the ranking member about resources and what are we deciding to do to protect the health of the American people with respect to these issues.

Dr. von Eschenbach. Senator, I think it is both resources and a completely different way of doing business. First of all, with regard to the process, we need to work more effectively and collaboratively with other regulatory agencies in other countries, but also with regard to the developers and suppliers of these drugs. They have an integral and important part to play in this as well.

TRACK AND TRACE

We are embarking upon this in a more comprehensive way than just simply increasing the number of inspections, which we will do, but we will do that in a risk-based model. We will do that in a very tiered fashion so that electronically we are able to be aware of all of the things in a track and trace and then define where we need to target those specific inspections where we believe there is the greatest potential for risk.

ACTIVE INGREDIENTS

Senator Dorgan. Now, last year I added report language to an appropriations bill that directs the FDA to tell us where are drugs made and where do the active ingredients come from. We have not yet received that. Is that on its way from the FDA to the Congress?

Dr. von Eschenbach. We are in the process of--again, as we talked about earlier, our need for revamping and rebuilding of our information technology infrastructure to be able to create a system where we have product identification and we can actually track and determine all things that are coming---

UNITED STATES VERSUS CANADA

Senator Dorgan. But is the report on its way to Congress on where active ingredients come from? That is a requirement.

I have taken more time than I think I am allowed. One final question if I might.

This issue of United States versus Canada. Canada has an almost identical chain of control of prescription drugs, as we do. Most everyone understands and agrees with that. Europe has had a parallel trading program for 20 years. If you are in Spain and want to buy a prescription drug from Germany, no problem. If you are in Italy and want to buy it from France, no problem. Why is it that the FDA seems to think Europe can do something that we cannot do?

Dr. von Eschenbach. First of all, Senator, the report is in progress and I cannot tell you exactly when it will be delivered to Congress. But it is in process and it is being prepared for delivery.

Let me separate this into two issues. One issue is how do we address the integrity of the supply chain of the development of that product. The second is how do we address the issue of the introduction of counterfeits into the supply chain with regard to reimportation. They are two completely different problems and require two completely different approaches because---

Senator Dorgan. Europe has done that for two decades.

Dr. von Eschenbach. I just returned from---

Senator Dorgan. If they can do it, we can do it.

COUNTERFEITS

Dr. von Eschenbach. I have just returned from some interactions with counterparts in which some of the transshipments through countries are detecting a significant degree of counterfeit being introduced into that process. We are addressing both of these, Senator, because they are both of critical importance to assuring the product that Americans use, when they take those drugs home and give them to their children or to themselves, that they are, in fact, getting the right product.

Senator Dorgan. Mr. Chairman, you have been generous.

Dr. von Eschenbach. Would you be worried if a member of your family were taking a prescription drug that was FDA-approved and purchased in a Canadian drugstore?

Dr. von Eschenbach. If I purchased it in a Canadian drugstore and---

Senator Dorgan. A registered pharmacy in Canada. FDA-approved, registered pharmacy in Canada. Would you be worried about the efficacy of that drug?

Dr. von Eschenbach. It would depend on the drug, but no, I would not. But that is different than me having that imported into the United States through a website.

Senator Dorgan. That was not the question. You said no because, I assume, that the drugs for your family you would purchase in a registered Canadian pharmacy you feel has the same chain of command, almost identical to the United States. Is that---

Dr. von Eschenbach. I have a high degree of respect for the Canadian system with regard to their own regulation of drugs. Yes, sir.

Senator Dorgan. Thank you, Dr. von Eschenbach.

Senator Kohl. Senator Reed.

INDOOR TANNING DEVICES

Senator Reed. Thank you, Mr. Chairman. Thank you, Commissioner.

By September 27, 2008, the FDA must submit a report to Congress on its labeling requirements for indoor tanning devices. What is your understanding of the science of the risk of tanning devices and what progress has FDA made on reviewing these labeling requirements that you are required to promulgate?

Dr. von Eschenbach. We have been actively involved in preparing that report to Congress, Senator. It really looks at the issue of warning labels, as you have requested. Personally as a melanoma survivor, I obviously have great interest and concern about this even though I am not directly involved in the specifics of this issue. But we are addressing this and addressing this as a public health need.

Senator Reed. Your last statement presumes that existing scientific evidence suggests this is a public health problem.

Dr. von Eschenbach. The concern is certainly--the concern is always with regard to potential problems for over-exposure or over-use.

Senator Reed. Some individuals and groups are suggesting that indoor tanning devices are actually palliative, not dangerous at all. For this reason, we are very eager for

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scientific evidence of their effects. Can you be more specific as to your progress? I presume if you are working towards this labeling, that there is some scientific predicate to labeling. Otherwise, you would come back to us and say the labeling is unnecessary.

Dr. von Eschenbach. Well, the labeling needs to address the risks, as well as the benefits that may be associated with the use of this particular kind of device and the appropriate use of the device. And I believe that the Center for Devices and Radiologic Health is addressing this, both from the scientific perspective as well as from a consumer's understanding and appreciation of health messages associated with these products, and we will be presenting that report to Congress before September.

SUNSCREENS

Senator Reed. Thank you very much, Commissioner.

In a related matter, the FDA is in the process of finalizing its proposed rule on sunscreen products. Can you give us an estimate of when it will be completed? It has been pending for a while now.

Dr. von Eschenbach. Yes, sir. It was a matter of addressing the issue of adding the UVA component to the UVB standards with regard to the rule so that we now have two test methods for UVA and the inclusion of the appropriate warning statements. That proposed rule is in process, and I cannot give you an exact date of when it will be presented, but it is an issue that is being actively worked on for finalization.

Senator Reed. Can you give an estimate? Within this quarter or next quarter?

Dr. von Eschenbach. I would be reluctant to give you an estimate and then not be able to assure that, Senator. But I will assure you that this is not something that is being ignored. It is being given appropriate attention and the expectation is to finish this.

GENERIC DRUGS

Senator Reed. Thank you.

We all recognize that generic drugs play an important role in the health care system today. I have been told that there are about 1,400-1,500 generic drug applications currently pending, with 570 or so pending over 180 days. Do you need increased funding for these generic reviews? Do you need something to expedite their approval?

Dr. von Eschenbach. We are both blessed and challenged by the success that we have achieved with regard to bringing generic drugs to the American people. This year we received 880 applications--in 2007, rather. And we have approved 682, which was a 33 percent increase in 2007 over 2006. So the track record is extraordinary, but because the funnel has increased so significantly, that has continued to create the backlog issue.

NEW STAFF

Now, we have approached that on a variety of fronts. One is, as you indicated, applying additional resources. So we have hired approximately 40 new staff to address generic drug review. We are also beginning to attempt to try to prioritize the review process to get the first generics and also beginning to address things like process improvement, as well as enhancement of our infrastructure, specifically IT, work with the people who are creating these drug applications to get better quality into the applications so that they go through the regulatory process in a lot more efficient way. And I think the net effect of all of that would be to continue to enhance our productivity and reduce the backlog.

Senator Reed. Thank you, Mr. Chairman.

ADDITIONAL STAFF

Senator Kohl. Thank you, Senator Reed.

Dr. von Eschenbach, going back to a comment I made in my opening statement, you say that your budget provides funding for increased activities for food safety and medical product safety and that you will hire several hundred additional staff this year. But the budget request is not enough to even pay for the staff that you now have. So how do you equate your intentions with respect to additional staff when you do not have money to even pay for the staff that you now have?

Dr. von Eschenbach. Well, we are on the trajectory to increased staff. We do, in fact, have to absorb additional costs associated with that staff over and above what we currently have available to us in the budget. So it is perhaps slowing it down a little bit, but the trajectory is still very positive and we are still increasing the number of staff that we have. It is just we will not do it at the rate that we had anticipated because of needing to absorb the cost of living of \$34 million that you indicated.

So the simple answer to your question, Senator, is we have to make accommodations in the pace with which we will bring those people on board in order to stay within our budget framework, but it will not be a negative. It will not be a deficit. It will be just not as rapid an accrual of those numbers as we had anticipated. We will just have to push it off a little bit.

Senator Kohl. I appreciate that, but what I think I and others are taking from what you are saying is that the lack of the necessary funding will, in fact, have a severe impact on your ability to do the things that you are saying you want to do.

Dr. von Eschenbach. There are a very large number of important initiatives that we have identified that are part of what I consider to be the essential modernization of the FDA. Depending upon available resources, we would be able to implement many of those initiatives in as an effective way as possible. So I do agree with you from the perspective that there is much to be done and we are prepared to do it, and with support, we would implement those programs in a strategic way but also with great stewardship, recognizing how precious these resources are and how many other needs there are across the entire Federal Government.

CHINA OFFICE

Senator Kohl. Dr. von Eschenbach, can you provide us with a status update of the office that you are trying to open in China? How many FDA employees do you anticipate working there, and what do you intend their focus to be?

Dr. von Eschenbach. We anticipate a total of 13 individuals that will be making up our China office. Eight of those will be full-time FDA employees. Five of them will be locally employed staff. That will be give us great opportunity with regard to our ability to integrate effectively locally.

OTHER FOREIGN OFFICES

We also look forward to offices in India, the Middle East, Latin America, and Europe. And I have been engaged in conversations with governments and counterparts, as has Secretary Leavitt, in all of those areas. It is a balance between their willingness to welcome us and accept us at the government level. We have not yet secured that welcome from China officially, but we certainly have great interest and enthusiasm on the part of the ministers and government officials in China with whom we have discussed this. So I anticipate that it will occur.

We really look forward to the China office being fully implemented within this fiscal year, and we are laying the

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groundwork and would like very much to begin to develop the other sites as rapidly as possible.

POST-MARKET SAFETY

Senator Kohl. Dr. von Eschenbach, you noted in your statement several new medical devices that FDA approved last year. Post-market safety of medical devices obviously is an important issue for patients. But the number of staff in the FDA devices program is, in fact, decreasing this year. So can you comment on how you plan to continue improving these important devices, as well as ensuring their safety after they have been approved with the very minimal funding increases and, in fact, while at the same time losing staff?

Dr. von Eschenbach. We are doing a number of things, Senator, one of which, as I had indicated earlier, is this ability to create much greater integration and interdependence across programs. For example, in this regard, I believe we could effectively enhance the performance in post-market surveillance, whether it is drugs or devices, by virtue of our information technology infrastructure and our ability to do much more effective post-market surveillance. We look forward to being able to streamline and enhance the very effective programs that are already underway in the Center for Devices and Radiologic Health with regard to working with the industry in post-market surveillance.

So I think it is a combination of building the trajectory, as I have indicated before, finding ways to leverage currently ongoing resources or programs like IT, and continue to make strategic investments, especially as user fees contribute to this opportunity. And we expect our user fee program to increase. In 2009, there will be \$52.5 million in this particular area. So we do look forward to growth, but it is going to come in different ways.

Senator Kohl. Senator Bennett.

CLOSING REMARKS

Senator Bennett. Thank you very much, Mr. Chairman. I think all of the issues I have on my list have been covered either by you or Senator Dorgan or in my previous questions.

So let me again thank Dr. von Eschenbach and his team for their willingness to serve in what must occasionally be a somewhat contentious atmosphere, and I wish them well.

Senator Kohl. I want to associate myself with Senator Bennett's statements. I think it has been a good hearing. I think we have brought out very clearly, number one, the huge and expanding responsibilities the FDA has and, number two, the lack of satisfactory funding to carry out your responsibilities. Clearly, there is a very important job that we need to work together to achieve.

In fact, it is clear to us that you cannot carry out the responsibilities you have in a way that I believe would satisfy you without the necessary and adequate funding. I think there are plenty of professional people on your staff, most importantly yourself, who can and would get the job done with adequate funding, but without the funding, it is pretty hard to do the job that you need to do.

If you want to respond to that statement, that would be fine. You could make a comment or two and then we will close the hearing.

Dr. von Eschenbach. I would just close, Mr. Chairman, with echoing what I know is both your sentiments and Senator Bennett's sentiments. This country and this agency is truly blessed by the people of the Food and Drug Administration. I have the privilege every day to witness their sacrifice, their commitment, and their unbelievable performance, given the nature of the challenges that they are burdened with every single day. If we were to talk about resources, it is resources that are not about programs. It is resources about people. And the Food and Drug Administration's most precious asset, this Nation's most precious asset, are these incredible individuals.

We need more of them. We need more of them with new and different skill sets that are going to be aligned with the challenges of the 21st century, new science that is emerging, new technologies that are emerging, new complexity in the production and consumption of products. One needs only to go and walk through a supermarket and realize that with the exception of meat and chicken, every other thing in that supermarket is their responsibility to assure to the American people the quality of those products.

Every dollar that you choose to invest in, I believe, my responsibility to use to nurture and support that workforce. We need a fellowship program that will be able to create the intellectual capital of tomorrow. We need career development for the people that are already there. We are going to hire over 700 new people, which I believe is a wise use of the resources that you will make available to us.

But if I was to leave you with one final word, it would be I do not believe that there is any greater investment the American people could make than to invest in the people who make up the Food and Drug Administration.

ADDITIONAL COMMITTEE QUESTIONS

Senator Kohl. Thank you very much. That is a fine statement. You made a fine appearance here this morning. We thank you, as well as Mr. Dyer and Mr. Turman for being here. And at this time we will close the hearing.

[The following questions were not asked at the hearing, but were submitted to the Department for response subsequent to the hearing:]

Questions Submitted by Senator Herb Kohl

FDA SCIENCE BOARD RECOMMENDATIONS

Question. If additional funding was provided to FDA this year above your request level, what are the top 3 most pressing needs you would address?

Answer. On November 6, 2007, the administration released its Action Plan for Import Safety. The Action Plan for Import Safety recognizes FDA's central role in ensuring the safety of America's food supply and the safety and effectiveness of medical products, regardless of where the food and medical products are produced.

Implementing the Action Plan for Import Safety is a top FDA objective, and FDA has three priorities to achieve that objective: FDA Beyond Our Borders, building a modern IT infrastructure, and risk-based science.

Beyond Our Borders is a core element of the Action Plan for Import Safety. Beyond Our Borders includes establishing offices in China, India, and other locations. The FDA Beyond Our Borders initiative also relies on greater collaboration with foreign regulators, the use of third parties to provide information about the compliance of regulated industry with FDA standards, and greater FDA direction to regulated industry to ensure that their global activities meet FDA standards.

FDA foreign inspection and import exams are also an essential part of the Beyond Our Borders Initiative. In addition to providing greater deterrence, FDA will better target inspections to firms and products that pose the greatest risk to consumers.

Consistent with recommendations in the Action Plan for Import Safety, FDA must modernize its IT systems. Improving FDA's IT will help the agency target inspections to foreign firms whose products pose the greatest risk. IT improvements will allow FDA to better predict the firms and products that pose the highest risk imports.

Under the Action Plan for Import Safety, FDA must also strengthen its capacity to conduct the science that supports risk-based inspections. FDA risk-based science is essential to assure that imports are safe, and to assure that FDA scientists stay ahead of those who accidentally or intentionally defeat FDA oversight of imports. The Action Plan for Import Safety requires a strong FDA program of risk-

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based science and laboratory support so that FDA can ensure the safety of imports for patients and consumers.

Question. Please provide a professional judgment budget, regardless of constraints faced by FDA due to DHS or OMB, on additional funding needed by the Agency that could reasonably be expended, in fiscal year 2009.

Answer. The following document is an assessment of immediate resource needs based on a professional judgment analysis, without regard to the competing priorities that FDA, the President, and the President's consider as budget submissions to the Congress are developed. As the response indicates, the amounts identified are in addition to amounts appropriated to FDA in fiscal year 2008.

[The information is attached.]

FDA FISCAL YEAR 2009 PROFESSIONAL JUDGMENT ESTIMATE		
[Dollars in millions]		
	Fiscal year 2009	FTE
Food Protection.....	\$125	259
Safer Drugs, Devices, and Biologics.....	100	160
Modernizing FDA Science and Workforce....	50	71
Total.....	275	490

The amounts identified in this document support three strategic investment areas--protecting our food supply, assuring safer drugs, devices, and biologics, and modernizing the essential infrastructure of FDA's science and workforce. The amounts are in addition to amounts appropriated to FDA in fiscal year 2008. Investing in these three strategic areas will permit FDA to rapidly achieve important public health goals that cut across strategic components of the Agency.

This document responds to the request for the FDA's professional judgment concerning resource needs. The document was developed without regard to the competing priorities that the President and his advisors must consider as budget submissions to the Congress are developed.

FDA FISCAL YEAR 2009 BUDGET AMENDMENT: FOOD PROTECTION PLAN (+\$125 MILLION)			
Core Elements and Strategic Activities	FPP Output	Amount	FTE
Prevention:			
1.1 Promote Increased Corporate Responsibility to Prevent Foodborne Illnesses: FDA will ensure the safety of imports by increasing FDA's presence beyond our borders and building capacity with foreign partners.	Increase FDA presence beyond our borders, including increased training for food safety best practices abroad. Offices in four additional countries with 7/8 FDA FTE and 4/5 foreign nationals per country/region. Yields FDA presence in five countries or regions of the world.	\$16,000,000	24
	Increase technical assistance on food standards in at least 3 of the countries accounting for the major share of imports.	5,000,000	2
	Develop systems and tools for an international information exchange database related to inspections and quality.	5,000,000	3
1.2 Identify Food Vulnerabilities and Assess Risks: FDA will conduct risk-based prevention to better protect America's food supply. FDA will better understand food safety and food defense risks and use this understanding to define the optimum preventive controls to establish.	Increase capacity to collect & interpret data for risk-based prevention for products of greatest concern.	5,000,000	10
	Research and develop risk-based prevention strategies based on scientific data and protocols.	7,000,000	20
1.3 Expand Understanding and Use of Effective Mitigation Measures: FDA will develop and validate rapid detection tools to quickly detect and mitigate a potential problem.	Develop and validate rapid detection technologies and assays (see 2.3 for deploying technologies and assays): For high risk foods, commence work to develop two new priority tools and to validate two test methods for toxic chemicals or microbes developed by industry.	5,000,000	10
Sub-Total.....		43,000,000	69
Intervention:			
2.1 Inspections and Sampling Based on Risk: FDA will apply risk analysis to set priorities for food inspections and interventions.	20,000 more import food exams at the port of entry \1\ (\$300 each). 800 more foreign food production and/or processing facility inspections and support for foreign inspections \1\ (uc=\$16.7K).	6,000,000	36
	800 more domestic food safety inspections \1\ (uc=\$8k).	13,500,000	50
2.2 Enhance Risk-Based Surveillance of Imported Foods at the Border: FDA will design and build risk-based algorithms to conduct inspections and detect food risks. Understanding the risks defines the number and types of inspections and tests needed to ensure that preventive controls are working.	Integrate and assimilate risk-based information into data systems.	6,500,000	33
2.3 Better Detect Food System Signals that Indicate Contamination: FDA will deploy rapid detection technologies and assays and build laboratory infrastructure for faster testing. FDA will deploy state-of-the-art technology to improve the integration of incoming signals and achieve faster mitigation and response.	Improve signal detection of intentional and unintentional chemical and microbial contamination. Deploy 1-2 rapid detection assays to test high risk foods. Acquire advanced technology and deploy such equipment to FDA field and conduct technology transfer to industry. Build high throughput rapid detection technology into laboratory infrastructure.	10,000,000	15
		5,000,000	5
		5,000,000	5
		11,000,000	10
Sub-Total.....		57,000,000	154
Response:			
3.1 Improve Immediate Answer. FDA will enable real-time communication of lab results. FDA will develop protocols to facilitate tracebacks of foodborne illnesses. FDA will rapidly detect and respond to foodborne outbreaks.	Develop and implement a system for traceback from product consumption back to the source of production using, for example, electronic pedigrees and industry applied technologies of bar coding and radio frequency identification. Enhance interoperable information technology networking system between FDA and Federal, State, and local testing labs.	10,000,000	20
		10,000,000	6
3.2 Improve Risk Communications to the Public, Industry, and Other Stakeholders: FDA will enhance risk communication through aggressive, targeted food safety campaigns that disseminate clear and effective messages with regular updates through a variety of media to all target audiences.	Create a health hazards alert communication system using multiple media outlets to quickly inform a broad cross section of the public.	5,000,000	10
Sub-Total.....		25,000,000	36

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GRAND TOTAL, Food Protection Plan.	125,000,000	259
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\1\ FDA will hire and train additional field inspectors throughout fiscal year 2009. As a result, by fiscal year 2010, the proposed investment will allow FDA to increase its inspection and surveillance capacity by the number of inspections identified in this FPP output

FDA FISCAL YEAR 2009 BUDGET AMENDMENT: ENSURING SAFE AND EFFECTIVE MEDICAL PRODUCTS (+\$100 MILLION)			
Strategic Activity	Output	Amount	FTE
Safer Drugs, Devices, and Biologics:			
1.1 Science to Improve Medical Product Safety and Development: Use new science and analysis to improve the safety of medical products. In some cases, new science creates opportunities to leverage advances from one product area to promote safety in a different area.	Establish a unique device identification system to track devices, facilitate recalls, and support inventory management during disasters and terrorism response. Implement FDAAA safety requirements related to pediatric drugs and devices, postmarket study commitments, clinical trials, active drug surveillance, labeling and safe use of drugs.	\$7,500,000 14,000,000	17 10
Sub-Total.....		21,500,000	27
1.2 Data Analysis Tools to Identify Safety Issues: Develop and implement quantitative decision-making tools to assess the safety and effectiveness of drugs, biologics, and devices throughout their lifecycle.	Build Regulated Product Information Data Warehouse that will enable intelligence sharing with other regulatory agencies. Data access and analysis for active safety surveillance with development of scientific methods of data mining for signals of adverse events.	15,000,000 15,000,000 6
Sub-Total.....		30,000,000	6
1.3 Risk-Based Inspection and Compliance: Strengthen field operations to better protect public health. The sheer volume of products, manufacturing plants, distributors, and importers demands a more robust inspection force with better capacity to reach the community that FDA regulates.	250 more foreign medical product facility inspections \1\ (uc=\$45,000). Increase FDA's presence beyond our borders to five countries or regions of the world. 250 more domestic medical product inspections (uc=17.7K). Improve lab infrastructure and tools for rapid analysis of product/ingredient content. Increase import exams (10,000) and sampling/laboratory analysis (300). IT systems to achieve an integrated inventory database. Improve risk communications to public and industry.	11,200,000 10,800,000 4,400,000 7,500,000 6,600,000 3,000,000 5,000,000	50 18 14 5 35 5
Sub-Total.....		48,500,000	127
GRAND TOTAL, Medical Product Safety and Effectiveness.		100,000,000	160

\1\ FDA will hire and train additional field inspectors throughout fiscal year 2009. As a result, by fiscal year 2010, the proposed investment will allow FDA to increase its inspection and surveillance capacity by the number of inspections identified in this output

FDA FISCAL YEAR 2009 BUDGET AMENDMENT: MODERNIZING FDA SCIENCE AND WORKFORCE (+50 MILLION)			
Strategic Activity	Output	Amount	FTE
Modernizing FDA Science and Workforce:			
1.1 Science Leadership and Coordination: FDA will enhance science programs across the agency, especially in emerging areas such as nanotechnology and tissue engineering. FDA will establish mechanisms to access the best scientific knowledge and expertise to modernize its regulatory science. FDA will strengthen its capacity to support emerging areas of science and manufacturing that are essential to regulating FDA products.	Strengthen programs of emerging science in Centers and at the National Center for Toxicological Research and enhance integration. Strengthen capacity to support nanotechnology, cell and gene therapies, robotics, genomics and proteomics, Critical Path initiatives, and advanced manufacturing technologies.	\$5,000,000 27,000,000	15 40
Sub-Total.....		32,000,000	55
1.2 Investments to Support Science-Based Regulation: FDA will upgrade its science capacity by providing more training and professional development support for FDA science staff. FDA will create an Agency-wide 2-year Science Fellows Program intended to include up to 2,000 trainees to develop a new cadre of emerging leaders in regulatory science. FDA will upgrade facilities that do not adequately support FDA's current or future mission.	Expand science training and professional development for career employees. Launch Science Fellows Program and initiate recruitment of first 500 fellows. Improve facilities outside of the Washington region to support FDA's mission and enable these facilities to accept new food and medical product technologies.	4,000,000 4,000,000 10,000,000	8 8
Sub-Total.....		18,000,000	16
GRAND TOTAL, Modernizing FDA Science and Workforce.		50,000,000	71

PAY COSTS

Question. If you plan to ``absorb'' the pay costs that you haven't actually paid for in the budget, what will you cut to do it?

Answer. The fiscal year 2009 President's Budget for FDA includes an increase of \$25 million for the cost-of-living increase for FDA employees. The cost-of-living increase allows FDA to retain the professional workforce that performs FDA's public health mission. FDA will cover its fiscal year 2009 cost increases through a combination of strategies, reducing operating costs, and adjusting its hiring plan.

OVERSEAS STAFFING

Question. I understand that FDA has also expressed interest in opening other overseas offices to deal with the large and continually growing number of imported products--including one in India. Again, however, I don't see this reflected in the budget. Is this something you are considering? If so, where, and what would the cost be?

Answer. FDA has agreements in place and we are making final arrangements for offices in China. FDA is also planning to establish additional offices in India, and is exploring the possibility of opening offices in three additional regions. The President's fiscal year 2009 budget provides \$3.1 million to establish the office in China. We have not developed specific estimates for additional offices by location because developing these estimates requires significant discussions with the host countries and the Department of State. The cost to establish additional foreign offices will depend on the office location, the activities that FDA staff will perform at the location, and the number of staff that FDA assigns to the location.

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FOOD PROTECTION PLAN

Question. Last year, we provided you with a \$56 million increase for food safety, and attached some very specific directives, including hiring additional inspectors, forming rapid response teams, and contracting with the National Academy of Sciences on a food safety study. You talked in your statement about what you have planned for 2009--can you provide us with specifics on how the money we've already given you has been spent?

Answer. With the funding provided in the January 1, 2008 increase, FDA has undertaken additional food safety activities. These funds were used to support planning and the initial stages of implementation of several Food Protection Plan initiatives. These initiatives include the FDA hiring surge, the Food Protection Plan, and the Import Safety Action Plan.

FDA was granted direct hire authority in April 2008 and will hire 161 new FTEs to work in food safety. The Office of Regulatory Affairs--ORA--completed a 3-year plan to increase State inspections and will hire an additional 77 new FTEs with the fiscal year 2008 appropriation and an additional 53 new FTE with the funds from the Consolidated Appropriations Act, 2008, which will be available on July 1, 2008 to conduct food field exams, inspections, and sample collections. These investigators will conduct critical activities such as import food field exams and assist senior investigators in performing high risk food inspections.

The Center for Food Safety and Applied Nutrition, known as CFSAN, hired one new FTE with the fiscal year 2008 appropriation and will hire an additional 28 new FTEs with the funds from the Consolidated Appropriations Act, 2008, which will be available on July 1, 2008 to assist with food safety work aimed at developing guidance to minimize microbial food safety hazards, developing best practices for preventive controls that rapidly determine the source of food contamination, developing risk ranking models for imported and domestic foods, providing technical assistance to foreign countries on Good Agricultural Practices, and continuing research to improve surveillance, sampling and traceback activities and other tools to rapidly detect and minimize the public health impact of foodborne pathogens, toxins, and other contaminants that threatens the U.S. food supply.

In addition, CFSAN is working with the Western Center for Food Safety at the University of California Davis to focus on the interface between food protection and the agricultural production of commodities. FDA has met with the National Academy of Sciences and discussed a statement of work for a comprehensive study of the gaps in public health protection provided by the United States' food safety system. In addition, FDA issued a Request for Applications for forming rapid response teams. Also, the Office of Crisis Management will hire two new FTEs with the fiscal year 2008 appropriation to assist FDA in quickly responding to food safety threats.

Question. You said as part of your statement that during the past year that FDA has expanded its capacity to detect radiological contamination of food by 150 percent. We discussed at length last year the importance of being able to identify contaminants in the food supply as quickly as possible and provided money for those activities--can you further discuss your achievements in that regard?

Answer. In fiscal year 2007, FDA, through the Food Emergency Response Network, also known as FERN, awarded cooperative agreement grants to three additional State FERN radiological laboratories. These three labs increased the number of FDA's FERN cooperative agreement radiological laboratories to five. This is the basis of the statistic that FDA expanded its capacity to detect radiological contamination of food by 150 percent.

These five labs are geographically distributed and uniformly equipped with the latest detection equipment for responding to radiological contamination in foods. The cooperative agreements also provide funds to purchase reagents, supplies, and personnel. The model used for the development of these laboratories follows that of the FERN chemistry cooperative agreement labs. State FERN chemistry labs are fully equipped and trained to run FDA's FERN chemistry methods that are used to screen large numbers of samples. FDA used the FERN chemistry cooperative agreement labs very successfully to identify melamine contamination. FERN labs screened large numbers of plant protein samples in a short time frame.

The radiological labs participate in Federal and State surveillance sampling programs to monitor the food supply, and are involved in developing and validating contamination detection methods. Using FERN rapid screening methods, the labs also serve to dramatically increase the surge capacity of the laboratory network to respond to terrorist attack or a national emergency involving the food supply. The increased capacity to rapidly test large numbers of samples of foods that may be radiologically contaminated allows FDA's FERN laboratories to respond quickly to food safety events to protect public health and mitigate disruption of the distribution of important foods.

FIELD EXAMS/SAMPLES

Question. The budget States that FDA plans to perform additional 20,000 import field exams for food this year, but at the same time, the percent of import lines physically examined is going to decrease from the 2007 level. I know the number of import lines is growing rapidly, but this is a perfect example of your budget not keeping up with your mission. What does a "field exam" actually entail, and why is the percentage of imports physically examined actually decreasing?

Answer. As displayed in the fiscal year 2009 Congressional Justification (CJ), import physical exams are the total of import field exams and import laboratory sample analyses. A field exam is a visual examination of food to determine whether it complies with FDA requirements. The field exam involves actual physical examination of the food for admissibility factors such as storage or in transit damage, inadequate refrigeration, rodent or insect activity, lead in dinnerware, odor, and compliance with labeling requirement. A field exam cannot be used to test for microbiological or chemical contamination. As a result, FDA also conducts import sampling and analysis to test for such contamination.

In fiscal year 2009, FDA plans to perform an additional 20,000 import food field exams and an additional 75 food import lab sample analyses. In addition, FDA electronically screens all FDA-regulated products offered for import into the United States for a variety of risk factors. FDA electronically screens 100 percent of human food and animal feed prior notice submissions which are required for all food and feed imports.

In fiscal year 2007, the percent of import lines examined was 1.28 percent. For fiscal year 2008, FDA estimates that it will examine 1.13 percent of import lines. For fiscal year 2009, the estimate rises to 1.26 percent. Between fiscal year 2007 and fiscal year 2009, FDA is experiencing a decline in the percent of import lines physically examined at the same time that the number of import field exams is increasing due to the rapidly rising volume of food imports.

FDA will continue to focus resources on products that pose the highest potential risks to the United States. The benefit of physical exams comes from the quality and targeting of review activities, not from the volume of imports analyzed. The quality of import screening is a better measure of FDA's import strategy than simply focusing on the number of items physically examined.

THIRD PARTY CERTIFICATIONS

Question. The Food Protection Plan mentions in several places FDA's interest in expanding third-party certifications for domestic and international inspections and examinations. How would these work, and why is it cheaper than having FDA employees actually do the work?

Answer. The universe of domestic and foreign food establishments subject to FDA inspection is immense and is expected to see continued rapid growth. Third party certification programs, when correctly designed and implemented, allow FDA to accredit independent third parties, or to recognize entities that accredit third parties. FDA plans to use information gathered from third party inspections to evaluate compliance with FDA requirements and to allocate inspection resources more effectively. This would allow FDA to gather more information about manufacturers, especially foreign manufacturers, in a much more resource efficient way. Using third party certification

GENERIC DRUGS

Answer. The increased resources recently provided by Congress have enabled FDA to hire more scientific review staff and achieve a 33 percent increase in the number of approvals and tentative approvals--from a total of 510 in fiscal year 2006 to 682 in fiscal year 2007.

A key performance measure of our generic application review process is the total number of ANDA actions, which include "approvals," "tentative approvals," "not approvable," and "approvable" actions. Under the fiscal year 2009 President's budget, we expect to be able to increase the number of total ANDA actions to 1900, an increase of 7 percent over fiscal year 2008 and fiscal year 2007.

MEDICAL PRODUCT SAFETY

Answer. FDA plans to use the funding increase for the Medical Product Safety and Development Initiative to support priority activities in the Biologics, Human Drugs, Device and Radiological Health, and Animal Drugs and Feed Programs.

In the Biologics Program, the resources in this initiative will also allow FDA to strengthen medical and microbiologic review and acquire greater epidemiologic expertise to conduct adverse event analysis and safety investigations. FDA will also improve tissue safety by conducting workshops to educate industry about tissue processing and tissue safety technologies.

In the Animal Drugs and Feed Program, the resources in this initiative will allow FDA to provide grants to stimulate development of new animal drugs under the Minor Use and Minor Species Animal Health Act of 2004.

Question. In your statement, you note that the volume of drugs imported into the United States will likely increase by 12 percent during fiscal year 2009, but your budget for the Human Drugs Program--not including user fees--is only increasing by 1.3 percent. If you add in user fees, the increase is 8.5 percent. And this money is mostly for approving drugs, not monitoring them. How will you keep up?

MERCURY TESTING

Why did FDA alert consumers to mercury poisoning risks in fish and at the same time reduce the number of tests for mercury and other metals in imported fish?

Because NHANES data identify the extent to which Americans are exposed to methylmercury, FDA's sampling program is primarily designed to learn the range of methylmercury concentrations in commercial fish species, including the highest and lowest concentrations and the mean concentration. We can then compare new results against these known values. In recent years, all our samples have been within the known ranges.

FOOD PROTECTION PLAN

Answer. On February 7, 2008, FSIS officials wrote to officials at FDA and stated, "FSIS personnel may be available to help provide coverage as an effective governmental presence in the riskiest FDA plants." In a February 21, 2008 letter, FSIS officials clarified, "this statement was not meant to suggest the FSIS employees would definitely be available to do this work. In point of fact, we have no

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reason to believe at this time, that any of the initiatives that we are undertaking will result in employees being available to provide inspection at FDA plants." In light of the clarification that FSIS provided, FDA did not respond to the letter in writing. Instead, FDA is conducting regular monthly meetings with FSIS on how to best leverage resources and work cooperatively to ensure a safe food supply for all Americans.

ESTRIOL

Question. On January 9, 2008, FDA announced that it was banning the use of estriol in compounded estrogens prescribed for decades by doctors for the treatment of menopause symptoms in women. Please provide the committee with documentation of specific adverse events from the use of estriol during the past three decades, as well as details of specific scientific and medical research supporting the FDA's decision to ban estriol.

Answer. FDA has not banned estriol. Our January 9, 2008 action was aimed at false and misleading claims of certain compounding pharmacies that offer estriol products without a valid investigational new drug application, also known as an IND. Except in rare instances, compounding pharmacies do not report adverse events to FDA. However, the absence of evidence of a risk does not demonstrate the absence of the risk. One of the reasons we are encouraging IND submissions for estriol products is so that we will receive any adverse event information for these products.

Question. How many women are potentially affected by the FDA decision to ban estriol? What does the FDA estimate it will cost these women to return to their doctors and get a prescription for an alternative treatment?

Answer. FDA does not know how many women are potentially affected by FDA's decision to require health care practitioners to obtain INDs for compound estriol products. This is due, in part, to the fact that FDA has imperfect information about both the number of compounding pharmacies and the scope of pharmacy compounding operations. In general, there is no requirement for pharmacies to register or list with FDA.

We do not have information about the costs that women incur in connection with compounded or approved estrogen therapies. However, because healthcare providers can continue to treat patients under an FDA-sanctioned IND, FDA does not believe there is a need for women to return to their health care providers for alternative new prescriptions and treatments when they are receiving estrogen therapy under an FDA-sanctioned IND.

Question. I understand that the FDA action on estriol will not restrict access to this medication as a doctor can continue to prescribe estriol if he or she files an investigational new drug application (IND). FDA has further indicated that it is developing a simplified or streamlined IND for doctors. Can you give the committee specific information on this issue, including detailed information on the proposed simplified process, including if the development of this simplified process would be subject to notice and comment rulemaking?

Answer. Your understanding is correct. No drug containing estriol has been approved by FDA, and the safety and effectiveness of estriol is unknown. Therefore, physicians may not prescribe estriol, and pharmacies may not compound drugs under a physician's prescription that contain estriol, unless they have an FDA-sanctioned IND application.

An IND is an application submitted by a physician who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. A physician might submit an IND to propose studying an unapproved drug, or for an approved product to study use in a new indication or in a new patient population.

Regulations describing the IND requirements can be found at 21 CFR 312, and detailed instructions for IND applications can be found on the FDA website. FDA also provides pre-IND consultations and assistance in developing applications.

An IND must generally contain information in three broad areas: Animal Pharmacology and Toxicology Studies, Manufacturing Information, and Clinical Protocol and Investigator Information. In the clinical protocol section, the Investigator must also give a commitment to obtain informed consent from the research subjects, obtain review of the study by an institutional review board and agree to adhere to the IND regulations.

We would like to clarify that there is no official streamlined or simplified IND process; however, we use our discretion in determining how much and what type of information is appropriate for an application. For example, in the case of estriol, preclinical animal toxicology and pharmacology data might not be necessary because the product has already been used in humans. INDs can cover research involving several patients, so that a physician need not submit separate INDs for individual patients. These types of decisions in evaluating IND applications would not be made through the rule-making process.

Question. If the FDA's assertion is correct, and an IND process can be developed that is simple and that will not discourage physicians from writing prescriptions containing estriol, can you estimate how many doctors would submit the simplified IND? Since the FDA is required to review every application for an IND, can you also estimate the cost and time required for the FDA to review these submissions, and the effect this would have on the agency's ability to process other INDs?

Answer. As FDA does not know how many women are potentially affected by FDA's decision, we cannot estimate how many doctors would submit an IND. Without knowing how many INDs the FDA will receive we cannot estimate the total cost and time required for the FDA to review these submissions, nor how it would affect FDA's ability to process other INDs.

Question. INDs require well-controlled, randomized clinical studies including a placebo or control arm. Is the FDA suggesting that some women would receive a placebo without their knowledge?

Answer. INDs do not require that well-controlled, randomized clinical studies be conducted. One of the objectives of the IND requirement is to help assure the safety and rights of subjects. There are various ways for conducting clinical trials, and not all methods require use of placebo controls. FDA is not suggesting that a woman would receive a placebo, and certainly not without informed consent which would inform her of that possibility.

REPORTS

Question. Please provide monthly updates on the status of all outstanding reports requested as part of the report accompanying Public Law 110-161.

Answer. I will be happy to provide a status report of all outstanding reports.

[The information follows:]

REPORT	STATUS
BSE.....	Transmitted to Congress 5.20.08
Diacetyl.....	Transmitted to Congress 3.25.08
Folic.....	Transmitted to Congress 5.20.08
Food Safety Quarterly (1st Q).....	In Clearance Process
Food Safety Quarterly (2nd Q).....	HHS Awaiting FDA Draft
Foreign Drugs (Interim).....	In Clearance Process
Foreign Drugs (Final).....	In Clearance Process
Front Label Symbols.....	In Clearance Process
GAO Recommendations.....	In Clearance Process
Ketek.....	In Clearance Process
Mammography TQM Recommendations.....	In Clearance Process
Med Guide.....	Not due until Dec 08
Methamphetamine.....	Transmitted to Congress 4.22.08
Microbial Resistance.....	Transmitted to Congress 1.2.08
National Research Initiative.....	In Clearance Process
OTG Recommendations.....	In Clearance Process

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Post Marketing Studies.....	In Clearance Process
Removing Food Safety from GAO High Risk List.	In Clearance Process
Women's Health (Quarter 1).....	Transmitted to Congress 4.14.08
Women's Health (Quarter 2).....	HHS Awaiting FDA Draft

POST-MARKET SURVEILLANCE OF SILICONE BREAST IMPLANTS

Question. When the FDA approved the use of silicone breast implants in 2006, I understand that it included a requirement that all women who receive these implants must participate in a post-approval study to ensure that these implants were safe. However, I understand that participation in these studies is now discretionary. What is the status of the post-market safety studies of silicone breast implants, and what authority does FDA have to require that manufacturers conduct the studies?

Answer. When the FDA approved the use of silicone breast implants in 2006, FDA required Mentor Corporation and Inamed Corporation, which is now named Allergan, to conduct post approval studies, also known as PAS, to answer particular questions. FDA allowed the companies the opportunity to develop different study designs and other protocol elements to meet this requirement. The goals were to design studies that would minimize bias in the study results and in which the subject enrollment goals could be achieved. The participation could be voluntary or mandatory. The companies proposed the specific study designs to answer those questions and submitted them for FDA approval. Allergan proposed, and FDA approved, a study with voluntary participation. Mentor originally proposed, and FDA approved, a study where participation was mandatory in order for women to obtain the Mentor product.

In April 2007 FDA approved Mentor's request to amend the MemoryGel™ Large Post-Approval Study protocol to allow for voluntary instead of mandatory participation of study subjects to address concerns regarding enrollment.

The status of Allergan's and Mentor's postmarket studies of silicone breast implants and conditions is summarized in a table that I would be happy to provide for the record.

[The information follows:]

STATUS OF ALLERGAN'S AND MENTOR CORPORATION'S SILICONE GEL-FILLED BREAST IMPLANT POSTMARKET STUDIES AND CONDITIONS

Approval Condition	Allergan	Mentor
Core Post-Approval Study.....	Reporting status: On time \2\ Study Status: On time \3\.	Reporting status: On time 2 Study Status: On time \3\
Large Post-Approval Study.....	Reporting status: On time \1\ Study Status: On time \1\ Overdue \3\ (12-month patient enrollment target was not met).	Reporting status: On time \1\ Study Status: On time \3\
Device Failure Studies.....	Reporting status: On time \2\ Study Status: On time \3\.	Reporting status: On time \2\ Study Status: On time \3\
Focus Group Study.....	Reporting status: On time \2\ Study Status: On time \3\.	Reporting status: On time \2\ Study Status: On time \3\
Informed Decision Process.....	Reporting status: On time \2\ Study Status: On time \3\.	Reporting status: On time \2\ Study Status: On time \3\
Adjunct Study.....	Reporting status: On time \2\ Study Status: On time \3\.	Reporting status: On time \2\ Study Status: On time \3\

- \1 Reporting status for Larger Post-Approval Study is "On time" if 15-month report was received by the February 16, 2008 due date.
\2 Reporting status is "on time" if 12-month report for a post-approval study other than the Larger Post-Approval Study was received by November 17, 2007 due date.
\3 Study progress status for a post-approval study condition is "On time" if patient enrollment and follow-up targets have been met and "Overdue" if the interim enrollment target was not met.

FDA may require that manufacturers conduct studies under 21 CFR section 814.82 or 21 CFR Part 822.

MDUFMA

Question. As you know, the President's budget calls for increased funding for the medical device user fee program, and the Congress has provided inflationary increases to fully fund the program in the past. How the agency is doing in regards to meeting the performance goals associated with the user fee program with the funding it has gotten to date?

Answer. FDA continues to succeed in improving the process for the review of medical device applications and meeting the performance goals first established under the Medical Device User Fee and Modernization Act of 2002, known as MDUFMA. Title II of the Food and Drug Administration Amendments Act of 2007 continued MDUFMA performance goals.

MDUFMA requires close collaboration with stakeholders and increased communication with applicants. FDA is working to clarify its regulatory requirements and make its decisions more transparent through new guidance, educational materials, and meetings. We continually seek to enhance the efficiency and flexibility of our review processes. These efforts help applicants improve the quality of their submissions, and help FDA provide timelier, better-focused reviews. Our ultimate objective is to make important new medical devices available to patients and healthcare providers earlier, while continuing to ensure the quality, safety, and effectiveness of those devices.

I would be happy to provide for the record a table that summarizes FDA's performance on the goals established for the fiscal year 2003-fiscal year 2007 receipt cohorts, showing results achieved through March 31, 2008. The goals applicable to the fiscal year 2008 receipt cohort have been in place for only 6 months, so it is too early for statistical measures to provide useful insights into our progress towards achieving those goals. FDA has, however, taken action to ensure that we are well positioned to achieve the goals for fiscal year 2008-fiscal year 2012. FDA is developing and implementing a new interactive review process that will contribute to better communication with applicants and more rapid resolution of review questions.

[The information follows:]

QUARTERLY REPORT ON PROGRESS TOWARDS ACHIEVING MEDICAL DEVICE PERFORMANCE GOALS SUMMARY TABLES
[Actions through March 31, 2008--Data for FDA]

Activity		Performance Goals and Actual Performance to Date									
		Fiscal Year 2003		Fiscal Year 2004		Fiscal Year 2005		Fiscal Year 2006		Fiscal Year 2007	
		Review Time Goal									
		Goal	Actual Percent	Goal	Actual Percent	Goal	Actual Percent	Goal	Actual Percent	Goal	Actual Percent
PMAs, Panel-Track Supplements, Premarket Reports:											
FDA decision (approval, approvable, approvable pending GMP inspection, not approvable.		320 days.....	91.8	91.7	87.7	80	83.7	90	100		
FDA decision--Percent within 180 days.....		180 days.....	44.9	37.5	29.8	36.7	50	41.2			
Expedited PMAs:											
FDA decision (approval, approvable,		300 days.....	100	92.3	70	83.3	80	100	90		

FDA allocates medical device user fees and other medical device appropriations to best achieve FDA's public health objectives, device performance goals, and other expectations established under MDUFA, as amended. The Center for Devices and Radiological Safety (CDRS), the Center for Biologics Evaluation and Research (CBER) is based on the workload balance between the two centers. FDA estimates the percent of the device review workload performed by CDRH and CBER, and allocates MDUFA resources accordingly. Field resources are allocated among FDA district offices by the Office of Regulatory Administration. The Office of Regulatory Administration, CDRS, CBER, and ORA apportion their individual resource allocations to their offices, divisions, and branches.

As of April 15 2008, FDA has accredited 16 third-party organizations to conduct quality systems inspections of certain medical devices. FDA has also accredited 16 third-party organizations to conduct clinical trials inspections. In addition, 100 organizations have completed FDA's training requirements and FDA has cleared these individuals to conduct independent inspections. Through April 15, 2008, accredited organizations have conducted six inspections. Although few inspections have been completed, the new accreditation program under the Food and Drug Administration Amendments Act of 2007, also known as FDAAA, have the potential to eliminate certain obstacles to manufacturers' participation in FDA's programs for inspections by accredited third parties.

CDRH established the Medical Device Fellowship Program, also known as MDFFP, to increase the range and depth of collaborations between CDRH and the outside scientific community. The MDFFP offers short and long-term fellowship opportunities for individuals interested in learning about the regulatory process, sharing knowledge and experience with the regulatory process, and addressing the concerns medical device engineers, physicians with clinical or surgical experience, engineers in biomedical, mechanical, electrical and software areas, and individuals from many other scientific disciplines have participated in the fellowship program. Opportunities are available for students in many other areas as well. This collaboration improves FDA's review processes, postmarket surveillance, and research efforts. CDRH will continue its efforts to ensure patients and health care professionals have timely and continued access to safe and effective medical devices.

Answer. The agency makes extensive use of guidances to the extent possible. FDA's Good Guidance Practices have been in effect for more than 7 years. Under Good Guidance Practices, FDA centers make available draft and final guidance documents, for comment and use, covering a broad spectrum of topics. These guidances include technical guidances that address specific regulatory issues, such as the use of a particular chemical. FDA guidances also include non-technical guidances, called level 1 guidances that provide more complex scientific information or provide initial interpretations of statutory and regulatory requirements. During 2007, we published 95 Federal Register Notices alerting the public to the availability of draft and final guidances. While the recommendations in the guidances are not legally binding, these recommendations are important to agencies and companies thinking about the industry and the public. FDA believes that the guidances that we issue

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are very useful and that resources that FDA devotes to developing guidances are a worthwhile investment.

Questions Submitted by Senator Dianne Feinstein

FOOD SAFETY GAPS

Question. As you are well aware, gaps in our food safety system have been exposed and people have become sick and worse have died from contaminated products like spinach and peanut butter. Yet, the Food and Drug Administration has only asked for a slight increase in funding for fiscal year 2009. With the increase in food imports, and the changing structure of our food supply system in the United States, I am concerned that the Food and Drug Administration (FDA) is neither prepared nor taking steps to adapt to the changes to be effective in protecting our food supply.

Dr. von Eschenbach, can you tell me how many inspectors are currently employed at the Food and Drug Administration? What percentage is that of the total FDA workforce?

Answer. In fiscal year 2008, the Office of Regulatory Affairs, also known as ORA, currently estimates that it will have 1,218 investigators. Investigators represent approximately 12 percent of the total 9,975 FTE FDA workforce in fiscal year 2008.

In fiscal year 2009, ORA currently estimates that it will have 1,300 investigators. Investigators represent approximately 12 percent of the total 10,501 FTE FDA workforce in fiscal year 2009. It should be noted that the ORA hiring initiative is on-going in fiscal year 2008 and that ORA is still developing hiring plans based on the fiscal year 2009 requested increase. As a result, these figures are estimates and may change as hiring is completed.

Question. Can you tell me how many inspectors currently employed at the Food and Drug Administration are dedicated solely to food inspection?

Answer. In fiscal year 2008, ORA estimates 587 investigators will perform work in the Foods Program. Many field investigators are cross-trained and may perform work in multiple programs as work priorities change or emergencies arise. For fiscal year 2009, ORA currently estimates that approximately 650 investigators will perform work in the Foods program. It should be noted that the ORA hiring initiative is on-going in fiscal year 2008 and that ORA is still developing hiring plans based on the fiscal year 2009 requested increase. Consequently, these figures are estimates and may change as hiring is completed. Additional field staff in the foods program will support the fiscal year 2009 performance increases of 20,000 additional import food field exams and 50 additional foreign food inspections.

Question. Where are the FDA inspectors located? Please be specific. Answer. ORA field staff are dispersed throughout the United States. More than 85 percent of ORA's staff works in five Regional Offices, 20 District Offices, 13 Laboratories, and 168 Resident Posts and Border Stations. As a separate entity within ORA, Office of Criminal Investigations personnel are located throughout the field organization in 30 Field Offices, Resident Offices, and Domiciles, which are located throughout the U.S. FDA maintains offices and staff in Washington, D.C., the U.S. Virgin Islands, Puerto Rico, and in all States except Wyoming.

I would be happy to provide a table that highlights this information. The information provided in the following table specifically provides ORA's geographic distribution of facilities which includes the locations of FDA investigators nationwide.

[The information is attached.]

GEOGRAPHIC DISTRIBUTION OF FACILITIES				
Building Name	Center	City	State	OP DIV Subdivision
Resident Post--Mobile, AL...	ORA...	210--MOBILE.....	1--AL.....	SOUTHEAST (ATLANTA)
Resident Post--Montgomery, AL	ORA...	2130--MONTGOMERY.....	1--AL.....	SOUTHEAST (ATLANTA)
Resident Post--Birmingham, AL	ORA...	350--BIRMINGHAM.....	1--AL.....	SOUTHEAST (ATLANTA)
Resident Post--Anchorage, AK	ORA...	130--ANCHORAGE.....	2--AK.....	PACIFIC (OAKLAND)
Border Station--Nogales, AZ...	ORA...	330--NOGALES.....	4--AZ.....	SOUTHWEST (DALLAS)
Border Station--Nogales, AZ...	ORA...	330--NOGALES.....	4--AZ.....	SOUTHWEST (DALLAS)
Border Station--San Luis, AZ	ORA...	417--SAN LUIS.....	4--AZ.....	SOUTHWEST (DALLAS)
Border Station--San Luis, AZ	ORA...	417--SAN LUIS.....	4--AZ.....	SOUTHWEST (DALLAS)
Resident Post--Phoenix, AZ...	ORA...	490--TEMPE.....	4--AZ.....	SOUTHWEST (DALLAS)
Resident Post--Tucson, AZ...	ORA...	530--TUCSON.....	4--AZ.....	SOUTHWEST (DALLAS)
Resident Post--Little Rock, AR	ORA...	2320--LITTLE ROCK.....	5--AR.....	SOUTHWEST (DALLAS)
District Office W/Lab--San Francisco	ORA...	10--ALAMEDA.....	6--CA.....	PACIFIC (OAKLAND)
Border Station--Calexico, CA	ORA...	520--CALEXICO.....	6--CA.....	PACIFIC (OAKLAND)
Border Station--Calexico, CA	ORA...	520--CALEXICO.....	6--CA.....	PACIFIC (OAKLAND)
Resident Post--Fresno, CA...	ORA...	1370--FRESNO.....	6--CA.....	PACIFIC (OAKLAND)
Irvine Regional Laboratory--Security Gate House	ORA...	1713--IRVINE.....	6--CA.....	PACIFIC (OAKLAND)
Resident Post--San Pedro, CA	ORA...	1970--LONG BEACH/San Pedro..	6--CA.....	PACIFIC (OAKLAND)
Resident Post--Canoga Park, CA	ORA...	1970--CANOGA PARK.....	6--CA.....	PACIFIC (OAKLAND)
Resident Post--Nisco Pacific Warehouse--Compton, CA	ORA...	810--COMPTON.....	6--CA.....	PACIFIC (OAKLAND)
Resident Post--LAX (El Segundo)	ORA...	1980--LOS ANGELES.....	6--CA.....	PACIFIC (OAKLAND)
Regional Field Office--Pacific--Oakland	ORA...	2480--OAKLAND.....	6--CA.....	PACIFIC (OAKLAND)
Resident Post--Ontario, CA...	ORA...	2550--ONTARIO.....	6--CA.....	PACIFIC (OAKLAND)
Border Station--Otay Mesa, CA	ORA...	2610--OTAY.....	6--CA.....	PACIFIC (OAKLAND)
Resident Post--Sacramento, CA	ORA...	3150--SACRAMENTO.....	6--CA.....	PACIFIC (OAKLAND)
Resident Post--Otay Mesa, CA	ORA...	3260--SAN DIEGO.....	6--CA.....	PACIFIC (OAKLAND)
Resident Post--San Diego, CA	ORA...	3260--SAN DIEGO.....	6--CA.....	PACIFIC (OAKLAND)
Resident Post--San Jose, CA...	ORA...	3340--SAN JOSE.....	6--CA.....	PACIFIC (OAKLAND)
Resident Post--San Francisco Airport, CA	ORA...	3730--SAN FRANCISCO.....	6--CA.....	PACIFIC (OAKLAND)
Resident Post--Stockton, CA...	ORA...	3770--STOCKTON.....	6--CA.....	PACIFIC (OAKLAND)
Border Station--Tecate, CA...	ORA...	3835--TECATE.....	6--CA.....	PACIFIC (OAKLAND)
Resident Post--Carson, CA...	ORA...	602--CARSON.....	6--CA.....	PACIFIC (OAKLAND)
District Office W/Lab--Denver	ORA...	600--DENVER.....	8--CO.....	SOUTHWEST (DALLAS)
Resident Post--Bridgeport, CT	ORA...	80--BRIDGEPORT.....	9--CT.....	NORTHEAST (NEW YORK)
Resident Post--Hartford, CT...	ORA...	280--HARTFORD.....	9--CT.....	NORTHEAST (NEW YORK)
Resident Post--Wilmington, DE	ORA...	490--WILMINGTON.....	10--DE.....	CENTRAL (PHILADELPHIA)
Resident Post--Boca Raton, FL	ORA...	290--BOCA RATON.....	12--FL.....	SOUTHEAST (ATLANTA)
Resident Post--Fort Myers, FL	ORA...	1070--FORT MYERS.....	12--FL.....	SOUTHEAST (ATLANTA)
Resident Post--Jacksonville, FL	ORA...	1510--JACKSONVILLE.....	12--FL.....	SOUTHEAST (ATLANTA)
District Office--Florida.....	ORA...	1895--MAITLAND.....	12--FL.....	SOUTHEAST (ATLANTA)
Resident Post--Miami, FL--Import	ORA...	2010--MIAMI.....	12--FL.....	SOUTHEAST (ATLANTA)
Resident Post--Miami, FL--Domestic	ORA...	2010--MIAMI.....	12--FL.....	SOUTHEAST (ATLANTA)
Resident Post--Tallahassee, FL	ORA...	2940--TALLAHASSEE.....	12--FL.....	SOUTHEAST (ATLANTA)
Resident Post--Tampa, FL.....	ORA...	2950--TAMPA.....	12--FL.....	SOUTHEAST (ATLANTA)
District/Region--Atlanta.....	ORA...	280--ATLANTA.....	13--GA.....	SOUTHEAST (ATLANTA)
Resident Post--Savannah, GA...	ORA...	4910--SAVANNAH.....	13--GA.....	SOUTHEAST (ATLANTA)
Resident Post--Tifton, GA...	ORA...	5490--TIPTON.....	13--GA.....	SOUTHEAST (ATLANTA)
Resident Post--Honolulu, HI...	ORA...	2400--HONOLULU.....	15--HI.....	PACIFIC (OAKLAND)
Resident Post--Bridgeport, ID...	ORA...	160--BOISE.....	16--ID.....	PACIFIC (OAKLAND)
Border Station--Eastport, ID	ORA...	445--EASTPORT.....	16--ID.....	PACIFIC (OAKLAND)
Resident Post--Bensenville, IL	ORA...	740--BENSENVILLE.....	17--IL.....	CENTRAL (CHICAGO)
District Office--Chicago.....	ORA...	1670--CHICAGO.....	17--IL.....	CENTRAL (CHICAGO)
Regional Field Office--Central--Chicago	ORA...	1670--CHICAGO.....	17--IL.....	CENTRAL (CHICAGO)
Resident Post--Gurnee, IL...	ORA...	3670--GURNEE.....	17--IL.....	CENTRAL (CHICAGO)
Resident Post--Hinsdale, IL...	ORA...	3980--HINSDALE.....	17--IL.....	CENTRAL (CHICAGO)
Resident Post--Mount Vernon, IL	ORA...	5900--MT VERNON.....	17--IL.....	CENTRAL (CHICAGO)
Resident Post--Peoria, IL...	ORA...	6850--PEORIA.....	17--IL.....	CENTRAL (CHICAGO)
Resident Post--Springfield, IL	ORA...	8220--SPRINGFIELD.....	17--IL.....	CENTRAL (CHICAGO)
Resident Post--Evansville, IN	ORA...	1480--EVANSVILLE.....	18--IN.....	CENTRAL (CHICAGO)

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Resident Post--Indianapolis, IN.	ORA....	2210--INDIANAPOLIS.....	18--IN.....	CENTRAL (CHICAGO)
Resident Post--South Bend, IN	ORA....	4580--SOUTH BEND.....	18--IN.....	CENTRAL (CHICAGO)
Resident Post--Bates, IA	ORA....	3080--BATES.....	19--IA.....	SOUTHWEST (DALLAS)
Resident Post--Des Moines, IA	ORA....	2260--DES MOINES.....	19--IA.....	SOUTHWEST (DALLAS)
Resident Post--Sioux City, IA	ORA....	7850--SIOUX CITY.....	19--IA.....	SOUTHWEST (DALLAS)
District Office--Kansas City.	ORA....	3080--LENEXA.....	20--KS.....	SOUTHWEST (DALLAS)
Resident Post--Wichita, KS...	ORA....	5880--WICHITA.....	20--KS.....	SOUTHWEST (DALLAS)
Resident Post--Louisville, KY	ORA....	2090--LOUISVILLE.....	21--KY.....	CENTRAL (PHILADELPHIA)
Resident Post--Baton Rouge, LA	ORA....	150--BATON ROUGE.....	22--LA.....	SOUTHEAST (ATLANTA)
Resident Post--Lafayette, LA.	ORA....	1230--LAFAYETTE.....	22--LA.....	SOUTHEAST (ATLANTA)
Mandeville Square Shopping Center.	ORA....	1400--MANDEVILLE.....	22--LA.....	SOUTHEAST (ATLANTA)
Metairie Center.....	ORA....	1545--METAIRIE.....	22--LA.....	SOUTHEAST (ATLANTA)
Resident Post--Shreveport, LA	ORA....	2130--SHREVEPORT.....	22--LA.....	SOUTHEAST (ATLANTA)
Resident Post--Augusta, Me...	ORA....	160--AUGUSTA.....	23--ME.....	NORTHEAST (NEW YORK)
Border Station--Calais, ME...	ORA....	1250--CALAIS.....	23--ME.....	NORTHEAST (NEW YORK)
Border Station--Houlton, ME...	ORA....	3750--HOULTON.....	23--ME.....	NORTHEAST (NEW YORK)
Border Station--Houlton, ME...	ORA....	3750--HOULTON.....	23--ME.....	NORTHEAST (NEW YORK)
District Office--Baltimore...	ORA....	50--BALTIMORE.....	24--MD.....	CENTRAL (PHILADELPHIA)
Resident Post--Dundalk, MD--Import.	ORA....	50--BALTIMORE.....	24--MD.....	CENTRAL (PHILADELPHIA)
District Office--New England.	ORA....	1275--STONEHAM.....	25--MA.....	NORTHEAST (NEW YORK)
Resident Post--Worcester, MA	ORA....	1520--WORCESTER.....	25--MA.....	NORTHEAST (NEW YORK)
Resident Post--Boston, MA...	ORA....	120--BOSTON.....	25--MA.....	NORTHEAST (NEW YORK)
Detroit District Office--Office.	ORA....	1260--DETROIT.....	26--MI.....	CENTRAL (CHICAGO)
Border Station--Detroit, MI...	ORA....	1260--DETROIT.....	26--MI.....	CENTRAL (CHICAGO)
Resident Post--Grand Rapids, MI.	ORA....	2010--GRAND RAPIDS.....	26--MI.....	CENTRAL (CHICAGO)
Resident Post--Kalamazoo, MI.	ORA....	2520--KALAMAZOO.....	26--MI.....	CENTRAL (CHICAGO)
Border Station--Bluewater Bridge, MI.	ORA....	4060--PORT HURON.....	26--MI.....	CENTRAL (CHICAGO)
Border Station--Sault Ste Marie, MI.	ORA....	4480--SAULT STE MARIE.....	26--MI.....	CENTRAL (CHICAGO)
Resident Post--International Falls, MN.	ORA....	3480--INTERNATIONAL FALLS...	27--MN.....	CENTRAL (CHICAGO)
District Office--Minneapolis.	ORA....	4760--MINNEAPOLIS.....	27--MN.....	CENTRAL (CHICAGO)
Resident Post--Jackson, MS...	ORA....	1220--JACKSON.....	28--MS.....	SOUTHEAST (ATLANTA)
Resident Post--St Louis, MO...	ORA....	7080--ST LOUIS.....	29--MO.....	SOUTHWEST (DALLAS)
Resident Post--Springfield, MO	ORA....	7460--SPRINGFIELD.....	29--MO.....	SOUTHWEST (DALLAS)
Resident Post--Helena MT....	ORA....	590--HELENA.....	30--MT.....	PACIFIC (OAKLAND)
Border Station--Sweetgrass, MT.	ORA....	1125--SWEETGRASS.....	30--MT.....	PACIFIC (OAKLAND)
Resident Post--Omaha, NE....	ORA....	3620--OMAHA.....	31--NE.....	SOUTHWEST (DALLAS)
Resident Post--Las Vegas, NV.	ORA....	120--LAS VEGAS.....	32--NV.....	PACIFIC (OAKLAND)
Resident Post--Reno, NV.....	ORA....	170--RENO.....	32--NV.....	PACIFIC (OAKLAND)
Resident Post--Concord, NH...	ORA....	70--CONCORD.....	33--NH.....	NORTHEAST (NEW YORK)
Resident Post--Elizabeth, NJ.	ORA....	860--ELIZABETH.....	34--NJ.....	CENTRAL (PHILADELPHIA)
Resident Post--North Brunswick, NJ.	ORA....	2140--NORTH BRUNSWICK.....	34--NJ.....	CENTRAL (PHILADELPHIA)
District Office--New Jersey..	ORA....	2498--PARSIPPANY.....	34--NJ.....	CENTRAL (PHILADELPHIA)
Resident Post--Voorhees, NJ...	ORA....	3465--VOORHEES.....	34--NJ.....	CENTRAL (PHILADELPHIA)
Resident Post--Albuquerque, NM.	ORA....	30--ALBUQUERQUE.....	35--NM.....	SOUTHWEST (DALLAS)
Border Station--Columbus, NM.	ORA....	200--COLUMBUS.....	35--NM.....	SOUTHWEST (DALLAS)
Border Station--Santa Teresa, NM.	ORA....	735--SANTA TERESA.....	35--NM.....	SOUTHWEST (DALLAS)
Resident Post--Albany, NY....	ORA....	50--ALBANY.....	36--NY.....	NORTHEAST (NEW YORK)
Border Station--Alexandria Bay, NY.	ORA....	90--ALEXANDRIA BAY.....	36--NY.....	NORTHEAST (NEW YORK)
Resident Post--Binghamton, NY	ORA....	540--BINGHAMTON.....	36--NY.....	NORTHEAST (NEW YORK)
Import Office--Buffalo, NY...	ORA....	750--BUFFALO.....	36--NY.....	NORTHEAST (NEW YORK)
Resident Post--Long Island, NY.	ORA....	1050--CENTRAL ISLIP.....	36--NY.....	NORTHEAST (NEW YORK)
Border Station--Champlain, NY	ORA....	1080--CHAMPLAIN.....	36--NY.....	NORTHEAST (NEW YORK)
Resident Post--New Windsor, NY	ORA....	4130--NEW WINDSOR.....	36--NY.....	NORTHEAST (NEW YORK)
District/Region/Regional Lab--New York.	ORA....	4170--JAMAICA.....	36--NY.....	NORTHEAST (NEW YORK)
Border Station--Ogdensburg, NY.	ORA....	4420--OGDENSBURG.....	36--NY.....	NORTHEAST (NEW YORK)
Resident Post--Rochester, NY.	ORA....	5230--ROCHESTER.....	36--NY.....	NORTHEAST (NEW YORK)
Border Station--Hawes, NY...	ORA....	5275--ROOSEVELT TOWN.....	36--NY.....	NORTHEAST (NEW YORK)
Resident Post--Syracuse, NY...	ORA....	6010--SYRACUSE.....	36--NY.....	NORTHEAST (NEW YORK)
Resident Post--White Plains, NY.	ORA....	6670--WHITE PLAINS.....	36--NY.....	NORTHEAST (NEW YORK)
Border Station--Peace Bridge.	ORA....	750--BUFFALO.....	36--NY.....	NORTHEAST (NEW YORK)
Border Station--Lewiston Bridge.	ORA....	3220--LEWISTON.....	36--NY.....	NORTHEAST (NEW YORK)
Resident Post--Arden, NC....	ORA....	131--ARDEN.....	37--NC.....	SOUTHEAST (ATLANTA)
Resident Post--Charlotte, NC.	ORA....	870--CHARLOTTE.....	37--NC.....	SOUTHEAST (ATLANTA)
Resident Post--Greensboro, NC	ORA....	1940--GREENSBORO.....	37--NC.....	SOUTHEAST (ATLANTA)
Resident Post--Greenville, NC	ORA....	1950--GREENVILLE.....	37--NC.....	SOUTHEAST (ATLANTA)
Resident Post--Raleigh, NC...	ORA....	3750--RALEIGH.....	37--NC.....	SOUTHEAST (ATLANTA)
Resident Post--Wilmington, NC	ORA....	5060--WILMINGTON.....	37--NC.....	SOUTHEAST (ATLANTA)
Resident Post--Fargo, ND....	ORA....	1020--FARGO.....	38--ND.....	CENTRAL (CHICAGO)
Border Station--Pembina, ND	ORA....	2500--PEMBINA.....	38--ND.....	CENTRAL (CHICAGO)
Resident Post--Brunswick, OH.	ORA....	1085--BRUNSWICK.....	39--OH.....	CENTRAL (PHILADELPHIA)
District Office/Forensic Chemistry--Cincinnati.	ORA....	1610--CINCINNATI.....	39--OH.....	CENTRAL (PHILADELPHIA)
Resident Post--Columbus, OH...	ORA....	1800--COLUMBUS.....	39--OH.....	CENTRAL (PHILADELPHIA)
Resident Post--Toledo, OH...	ORA....	8120--TOLEDO.....	39--OH.....	CENTRAL (PHILADELPHIA)
Resident Post--Oklahoma City, OK.	ORA....	3550--OKLAHOMA CITY.....	40--OK.....	SOUTHWEST (DALLAS)
Resident Post--Tulsa, OK....	ORA....	4780--TULSA.....	40--OK.....	SOUTHWEST (DALLAS)
Resident Post--Beaverton, OR.	ORA....	180--BEAVERTON.....	41--OR.....	PACIFIC (OAKLAND)
Resident Post--Portland Airport, OR.	ORA....	1650--PORTLAND.....	41--OR.....	PACIFIC (OAKLAND)
Resident Post--Harrisburg, PA	ORA....	3500--HARRISBURG.....	42--PA.....	CENTRAL (PHILADELPHIA)
District Office/Region W/Lab--Philadelphia.	ORA....	6540--PHILADELPHIA.....	42--PA.....	CENTRAL (PHILADELPHIA)
Resident Post--Pittsburgh, PA	ORA....	6600--PITTSBURGH.....	42--PA.....	CENTRAL (PHILADELPHIA)
Resident Post--Scranton, PA...	ORA....	7460--SCRANTON.....	42--PA.....	CENTRAL (PHILADELPHIA)
Resident Post--Providence, RI	ORA....	57--EAST PROVIDENCE.....	44--RI.....	NORTHEAST (NEW YORK)
Resident Post--Charleston, SC	ORA....	410--CHARLESTON.....	45--SC.....	SOUTHEAST (ATLANTA)
Resident Post--Columbia, SC...	ORA....	320--COLUMBIA.....	45--SC.....	SOUTHEAST (ATLANTA)
Resident Post--Greenville, SC	ORA....	1040--GREENVILLE.....	45--SC.....	SOUTHEAST (ATLANTA)
Resident Post--Sioux Falls, SD.	ORA....	2450--SIOUX FALLS.....	46--SD.....	CENTRAL (CHICAGO)
Resident Post--Chattanooga, TN.	ORA....	400--CHATTANOOGA.....	47--TN.....	SOUTHEAST (ATLANTA)
Resident Post--Knoxville, TN.	ORA....	1300--KNOXVILLE.....	47--TN.....	SOUTHEAST (ATLANTA)
Resident Post--Memphis, TN...	ORA....	1620--MEMPHIS.....	47--TN.....	SOUTHEAST (ATLANTA)
District Office--Nashville...	ORA....	1760--NASHVILLE.....	47--TN.....	SOUTHEAST (ATLANTA)
Resident Post--Memphis, TN...	ORA....	1620--MEMPHIS.....	47--TN.....	SOUTHEAST (ATLANTA)
Resident Post--Austin, TX...	ORA....	330--AUSTIN.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--Brownsville, TX.	ORA....	940--BROWNSVILLE.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--Los Tomates/ Brownsville, TX.	ORA....	940--BROWNSVILLE.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--Los Tomates, TX.	ORA....	940--BROWNSVILLE.....	48--TX.....	SOUTHWEST (DALLAS)
District/Sw Imports--Dallas..	ORA....	1730--DALLAS.....	48--TX.....	SOUTHWEST (DALLAS)
Regional Office--Dallas, TX...	ORA....	1730--DALLAS.....	48--TX.....	SOUTHWEST (DALLAS)
Resident Post--DFW Airport, TX (Grapevine).	ORA....	1730--DALLAS.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--Del Rio, TX...	ORA....	1820--DEL RIO.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--Eagle Pass, TX.	ORA....	2030--EAGLE PASS.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--Bota, TX (El Paso).	ORA....	2190--EL PASO.....	48--TX.....	SOUTHWEST (DALLAS)
Resident Post--El Paso, TX...	ORA....	2190--EL PASO.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--El Paso, TX...	ORA....	2190--EL PASO.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--El Paso, TX...	ORA....	2190--EL PASO.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--Ysleta, TX...	ORA....	2190--EL PASO.....	48--TX.....	SOUTHWEST (DALLAS)
Resident Post--Fort Worth, TX	ORA....	2450--FORT WORTH.....	48--TX.....	SOUTHWEST (DALLAS)
Resident Post--Houston, TX...	ORA....	3280--HOUSTON.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--USPS Columbia Import Dock, Laredo, TX.	ORA....	3899--LAREDO.....	48--TX.....	SOUTHWEST (DALLAS)

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Border Station--USBS J&L Bldg. 2 Admin.	ORA....	3899--LAREDO.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--Laredo World Trade Bridge, TX.	ORA....	3899--LAREDO.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--Pharr, TX....	ORA....	5330--PHARR.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--Pharr, TX....	ORA....	5330--PHARR.....	48--TX.....	SOUTHWEST (DALLAS)
Border Station--Rio Grande City, TX.	ORA....	5780--RIO GRANDE CITY.....	48--TX.....	SOUTHWEST (DALLAS)
Resident Post--San Antonio, TX	ORA....	6090--SAN ANTONIO.....	48--TX.....	SOUTHWEST (DALLAS)
Resident Post--Salt Lake City, UT.	ORA....	1700--SALT LAKE CITY.....	49--UT.....	SOUTHWEST (DALLAS)
Border Station--Highgate Springs, VT.	ORA....	245--HIGHGATE SPRINGS.....	50--VT.....	NORTHEAST (NEW YORK)
Resident Post--Falls Church, VA.	ORA....	930--FALLS CHURCH.....	51--VA.....	CENTRAL (PHILADELPHIA)
Resident Post--Norfolk, VA--Import.	ORA....	1760--NORFOLK.....	51--VA.....	CENTRAL (PHILADELPHIA)
Resident Post--Norfolk, VA--Import.	ORA....	1760--NORFOLK.....	51--VA.....	CENTRAL (PHILADELPHIA)
Resident Post--Richmond, VA..	ORA....	2060--RICHMOND.....	51--VA.....	CENTRAL (PHILADELPHIA)
Resident Post--Roanoke VA....	ORA....	2100--ROANOKE.....	51--VA.....	CENTRAL (PHILADELPHIA)
Prior Notice Center.....	ORA....	2034--RESTON.....	51--VA.....	HEADQUARTERS
Border Station--Blaine, WA....	ORA....	150--BLAINE.....	53--WA.....	PACIFIC (OAKLAND)
District Office/Regional Lab--Seattle.	ORA....	170--BOTHELL.....	53--WA.....	PACIFIC (OAKLAND)
Resident Post--Oroville, WA..	ORA....	1610--OROVILLE.....	53--WA.....	PACIFIC (OAKLAND)
Resident Post--Seattle, WA....	ORA....	1960--SEATTLE.....	53--WA.....	PACIFIC (OAKLAND)
Resident Post--Spokane Valley, WA.	ORA....	2110--SPOKANE VALLEY.....	53--WA.....	PACIFIC (OAKLAND)
Resident Post--Tacoma, WA....	ORA....	2230--TACOMA.....	53--WA.....	PACIFIC (OAKLAND)
Resident Post--Morgantown, WV	ORA....	1840--MORGANTOWN.....	54--WV.....	CENTRAL (PHILADELPHIA)
Resident Post--Green Bay, WI..	ORA....	2000--GREEN BAY.....	55--WI.....	CENTRAL (CHICAGO)
Resident Post--Madison, WI....	ORA....	2780--MADISON.....	55--WI.....	CENTRAL (CHICAGO)
Resident Post--Wauwatosa, WI..	ORA....	5130--WAUWATOSA.....	55--WI.....	CENTRAL (CHICAGO)
Resident Post--Aguila, PR....	ORA....	2049--AGUILA.....	RQ--PR.....	SOUTHEAST (ATLANTA)
Resident Post--Ponce, PR....	ORA....	760--PONCE.....	RQ--PR.....	SOUTHEAST (ATLANTA)
San Juan--New Administration Building.	ORA....	930--SAN JUAN.....	RQ--PR.....	SOUTHEAST (ATLANTA)
Resident Post--St. Thomas, VI	ORA....	900--ST. THOMAS.....	VQ--VI.....	SOUTHEAST (ATLANTA)
Parklawn Building--Rockville, Maryland.	ORA....	5600--Rockville.....	MD.....	24--MD HEADQUARTERS

Question. Who inspects FDA regulated products if no FDA inspector is present at a port where products are being imported?

Answer. FDA has commissioned approximately 9,900 Customs and Border Protection, also known as CBP, employees to inspect food shipments that require prior notice data submission under the provisions of the Bioterrorism Act if FDA is not present to do so. However, regarding the admissibility of all FDA regulated commodities, much of FDA's work in screening and inspecting import shipments occurs at locations other than ports of entry.

Entry data for shipments of FDA-regulated products are transmitted electronically by CBP to FDA. FDA screens each entry line electronically against certain criteria for admissibility. Many of the shipments of FDA-regulated products are designated by the electronic screening system for admissibility review by FDA employees.

Entry reviewers often request additional documentation from the importers to determine if a product should be allowed entry or should be set up for examination. The reviewers allocate inspectional resources to best cover products that appear to pose the highest risk. The remaining products are allowed to proceed without examination.

With the exception of truck ports, most entry reviewers are located in district offices and resident posts, not at the port of entry. They may review entries for a dozen or more ports. The entry reviewers issue assignments to investigators requesting a field examination and/or sampling to be conducted on specific import entries.

If the shipment arrives when FDA is not present, unless specifically instructed to hold the shipment at the port for FDA's examination, CBP will issue a conditional release of the cargo and allow it to move to its destination. Such movement is done under bond and is permitted under Section 801(b) of the Food, Drug, and Cosmetic Act. If FDA decides to physically examine these goods, the work will be performed at the destination of the goods.

Question. If non-FDA inspectors are conducting inspections, what and how much training have they been given to inspect food?

Answer. By the phrase non-FDA inspectors, we assume that you are referring to inspections conducted by State personnel under contract with FDA. State personnel that conduct these inspections attend ORA sponsored inspection training courses with ORA personnel and receive the same training courses as ORA investigators. State personnel also receive on-the-job training by FDA. For example, State personnel join FDA investigators on FDA inspections as observers. To conduct inspections on behalf of FDA, State personnel attend the same training courses, participate in joint training inspections, and then perform an inspection in which they are audited by FDA. After State inspectors pass the initial field audit, they are re-audited over a 3-year cycle. In addition, State personnel have access to online training courses developed by ORA-University. These courses serve as classroom courses and continuing education.

FDA is also implementing the Manufactured Food Regulatory Program Standards under which the State will assess its program against a set of uniform standards. The uniform standards are the key elements of a State program, such as regulatory foundation, staff training, risk based inspections, quality assurance, foodborne illness/defense preparedness and rapid response, compliance and enforcement, education and outreach, resource management, and laboratory resources.

In addition to receiving FDA provided training, the State inspectors must also meet their individual State requirements to conduct food inspections.

Question. According to the Congressional Research Service, the FDA inspects only about 1 percent of all FDA regulated imports. Does this 1 percent include both paper and physical inspections? If not, how much of FDA regulated imports get physical inspections?

Answer. As displayed in the fiscal year 2009 Congressional Justification, or CJ, import physical exams are the total of import field exams and import laboratory sample analyses. A field examination is a visual examination of the product to determine whether the product complies with FDA requirements. It involves actual physical examination of the product for admissibility factors such as storage or in transit damage, inadequate refrigeration, rodent or insect activity, lead in dinnerware, odor and label compliance. A field exam cannot be used to test for microbiological or chemical contamination. As a result, FDA also conducts sampling and analysis to test for such contamination. Based on the fiscal year 2009 CJ, 0.82 percent of imports will be physically examined in fiscal year 2009.

In addition, FDA electronically screens all FDA-regulated products offered for import into the United States. FDA also electronically screens 100 percent of human food and animal feed import prior notice submissions and, as targeted, based on risk, performs intensive manual reviews on a subset of those prior notices.

FDA will continue to focus resources on products that pose the highest potential bioterrorism risks to the United States. The benefit of physical exams comes from the quality and targeting of review activities, not from the volume of imports analyzed. The quality of import screening is a better measure of FDA's import strategy than simply focusing on the items physically examined.

Prior Notice Security Reviews are only performed on human food and animal feed imported products and are performed as a requirement of the Bioterrorism Act which requires human food and animal feed importers to give FDA "prior notice" of their imported product being offered for entry into the U.S. Prior Notice Security Reviews are performed by Prior Notice Center reviewers using electronic databases, law enforcement data and other information sources to determine whether or not the shipment poses a significant security risk to the United States food supply. A significant difference between a field exam and the Prior Notice Security Review is that the Prior Notice Security Review is conducted on food and animal feed products "only" while a field exam is conducted on all FDA regulated products. Field exams are physical examinations of an imported product while Prior Notice

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Security Reviews use electronic data bases to assess security threats.

Question. What is the budget in FDA for food safety oversight and how is that broken down between the budget spent on domestic and imported food safety oversight and inspection?

Answer. Rather than trying to inspect all imports, FDA recommends targeted risk-based inspections to focus resources where they are most needed and will provide the greatest benefit to American consumers. ORA resources for food safety oversight in the fiscal year 2009

Congressional Justification include \$358.1 million in the Field Foods program and \$37 million in the Field Animal Drugs and Feeds program. These figures represent ORA's food protection resources for both human and animal food. In the Field Foods program, approximately 45 percent of these resources are allocated to domestic food safety oversight and inspection. The remaining 55 percent are allocated to import and foreign food safety oversight and inspection. In the Field Animal Drugs and Feeds program, approximately 78 percent of these resources are allocated to domestic food safety oversight and inspection. The remaining 22 percent of these resources are allocated to import and foreign food safety oversight and inspection.

Question. How many inspectors are needed to handle the volume of foods being imported? What would that cost?

Answer. The fiscal year 2009 Congressional Justification estimates that ORA will physically examine approximately 1.26 percent of food imports. The physical exam percentage is a combination of import field exams and import laboratory samples analyzed. In fiscal year 2009, ORA estimates allocating approximately 305 FTE and \$50 million to perform the import food field exams and collect food import samples for analyses. This estimate does not include laboratory resources to analyze the import samples. Also, this figure does not include resources to electronically review the imported products that are not physically examined, as well as resources for the Prior Notice Center. Finally, these numbers do not include Center or Agency overhead costs. Funding increases requested in the fiscal year 2009 CJ will allow ORA to perform an additional 20,000 import food field exams, as well as 50 additional foreign food inspections, and an additional 75 food import lab sample analyses.

Question. How many inspectors are needed by product line to handle the volume of all FDA regulated imports?

Answer. Rather than trying to inspect all imports, FDA recommends targeted risk-based inspections to focus resources where they are most needed and will provide the greatest benefit to American consumers. Because FDA recommends a targeted risk-based approach to inspections rather than inspecting 100 percent of FDA-regulated products, we have not estimated the cost of inspecting all imported foods. The fiscal year 2009 Congressional Justification (CJ) estimates that ORA will physically examine approximately 0.82 percent of all FDA-regulated imported products. This includes foods, cosmetics, human drugs, biologics, animal drugs and feeds, and medical device and radiological health imported products. The physical exam percentage is a combination of import field exams and import laboratory samples analyzed. In fiscal year 2009, ORA estimates allocating approximately 351 FTE and \$57.5 million to perform the import field exams and collect import samples for analyses across all field program areas. This estimate does not include laboratory resources to analyze the import samples. Also, this figure does not include resources to electronically review the imported products that are not physically examined, as well as resources for the Prior Notice Center. Finally, these numbers do not include Center or Agency overhead costs.

Question. What level of funding is needed to handle all the volume of FDA regulated imports?

Answer. Rather than trying to inspect all imports, FDA recommends targeted risk-based inspections to focus resources where they are most needed and will provide the greatest benefit to American consumers. Because FDA recommends a targeted risk-based approach to inspections rather than inspecting 100 percent of FDA-regulated products, we have not estimated the cost of inspecting all FDA-regulated imports. The fiscal year 2009 Congressional Justification estimates that ORA will physically examine approximately 0.82 percent of all FDA-regulated imported products. This includes foods, cosmetics, human drugs, biologics, animal drugs and feeds, and medical device and radiological health imported products. The physical exam percentage is a combination of import field exams and import laboratory samples analyzed. In fiscal year 2009, ORA estimates allocating approximately 351 FTE and \$57.5 million to perform the import field exams and collect import samples for analyses across all field program areas. This estimate does not include laboratory resources to analyze the import samples. Also, this figure does not include resources to electronically review the imported products that are not physically examined, as well as resources for the Prior Notice Center. Finally, these numbers do not include Center or Agency overhead costs.

Funding increases requested for fiscal year 2009 in the Field Drugs Program will increase the Office of Criminal Investigations capacity to investigate criminal import violations. Funding increases requested in the Field Device Program will be directed towards the improvement of strategic information-sharing between FDA and regulatory partners, such as U.S. Customs and Border Protection. This activity directly supports intervention recommendations made by the Interagency Working Group on Import Safety in the Import Safety Action Plan.

Question. What level of funding is needed to handle all other FDA regulated activities outside of imports?

Answer. Rather than trying to inspect all imports, FDA recommends targeted risk-based inspections to focus resources where they are most needed and will provide the greatest benefit to American consumers. Because FDA recommends a targeted risk-based approach to inspections rather than inspecting 100 percent of FDA-regulated products, we have not estimated the cost of inspecting FDA-regulated products that are not imported. With the requested funding in the fiscal year 2009 Congressional Justification, the Office of Regulatory Affairs estimates that it will allocate \$200.7 million and 1,224 FTE for FDA domestic inspections in fiscal year 2009 and award \$15.7 million to the States for State contract inspections. These resources will allow ORA to inspect approximately 24 percent of the domestic inventory for which the Field has a recurring inspectional obligation. The domestic inventory estimate includes firms in all five field program areas: Foods, Human Drugs, Biologics, Animal Drugs and Feeds, and Devices and Radiological Health. The inventory estimate includes firm types such as manufacturers, repackers, relabelers, warehouses, blood banks, and bioresearch monitoring facilities. This estimate does not include mammography facilities because all mammography facilities are inspected annually using user fee funds. Finally, these funding estimates do not include Center or Agency overhead costs.

Question. Why does the OASIS database not accurately track volume or make it easily to ascertain the volume of goods coming from a given country?

Answer. There are three primary ways to measure the amounts of imported goods: declared value, quantity, as measured by weight, volume, or piece count, and count of entry lines. None of these measures is ideal. Importers are not required to provide FDA with either the value or the quantity of goods in an entry line, and often they do not. When quantity data are provided, entry filers sometimes make significant errors. Those errors can badly distort aggregate data. Entry lines can be counted precisely, but the value and quantity of the goods in any given line can vary enormously.

FDA uses the count of entry lines as the best available option. For the reasons given above, aggregation of data on declared value or quantity is not feasible.

Question. To protect the public from food borne illness from both domestic and imported products, what is the FDA doing to change the way it does business?

Answer. In November 2007, FDA released the Food Protection Plan, also known as the FPP, to address both food safety and food defense for domestic and imported products. The plan is integrated with the Administration's Import Safety Action Plan. The FPP is an integrated strategy that focuses on risks over a product's life cycle from production to consumption. The FPP targets resources to achieve maximum risk reduction and address both unintentional and deliberate contamination. The FPP relies on science and modern technology systems.

FDA was granted direct hire authority in April 2008 and will hire 161 new FTEs to work in food safety. The Office of Regulatory Affairs has completed a 3-yr plan to increase State inspections and will hire 77 new FTEs with the fiscal year 2008 appropriation and an additional

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53 new FTE with funds from the Consolidated Appropriations Act, 2008, which will be available on July 1, 2008 to conduct food field exams, inspections, and sample collections. The Center for Food Safety and Applied Nutrition will hire one new FTE with the fiscal year 2008 appropriation and will hire an additional 28 new FTEs with the funds from the Consolidated Appropriations Act, 2008, which will be available on July 1, 2008 to assist with food safety work aimed at protecting the Nation's imported and domestic food supply from both unintentional and deliberate contamination. The Office of Crisis Management will hire two new FTEs with the fiscal year 2008 appropriation to assist FDA in quickly responding to food safety threats. In addition, FDA is focusing on the interface between food protection and the agricultural production of commodities. FDA officials have also met with the National Academy of Science and discussed a statement of work for a comprehensive study of the gaps in public health protection provided by the United State's food safety system.

BREAST IMPLANTS

Question. The Food and Drug Administration approved silicone gel breast implants, manufactured by Mentor, in November 2006. This approval came with rigorous post approval conditions, including mandatory enrollment in longitudinal studies.

Following the approval of silicone gel breast implants manufactured by Allergan, the FDA made this enrollment in longitudinal studies optional.

What is the reason for this change? What specific data was presented to justify this change?

Answer. In November 2006, both Allergan and Mentor Corporation received FDA approval to market their silicone gel-filled breast implants in the United States, subject to requirements to conduct post approval studies, also known as PAS, to answer particular questions. FDA allowed the companies the opportunity to develop different study designs and other protocol elements to meet this requirement. The goals were to design studies that would minimize bias in the study results and in which the subject enrollment goals could be achieved. The participation could be voluntary or mandatory. The companies proposed the specific study designs to answer those questions and submitted them for FDA approval. Allergan proposed, and FDA approved, a study with voluntary participation, while Mentor originally proposed, and FDA approved, a study where participation was mandatory in order for women to obtain the Mentor product.

In April 2007 FDA approved Mentor's request to amend the MemoryGel™ Large Post-Approval Study protocol to allow for voluntary instead of mandatory participation of study subjects. Mentor's request reported that the company received many complaints from Institutional Review Boards--IRBs, hospitals, and other institutions, questioning the appropriateness of requiring patients to become subjects in a PAS in order to receive an approved device. Mentor indicated that mandatory PAS participation might not be consistent with standard PAS practice, and that several complainants indicated that in keeping with good clinical practice, patient participation should be voluntary. The concerns had also made it difficult for Mentor to obtain the IRB approval required to commence the study at a number of sites, slowing overall progress of the study.

Based on FDA's assessment of the supplement and principles of good study design, FDA approved the amendment to the MemoryGel™ Large Post-Approval Study protocol which changed the enrollment type from mandatory to voluntary and thus allows women access to this approved device without requiring participation in a research study. The change increases participation of women who meet the PAS inclusion criteria by eliminating barriers to IRB approval and patient enrollment.

The key points underlying FDA's decision are as follows. First, there is no scientific rationale for requiring mandatory subject participation. Mandatory and voluntary subject participation were acceptable alternative approaches to design the PAS. Second, participation in the post-approval study for Allergan's comparable silicone gel-filled breast implants is voluntary. Third, Mentor's request to allow voluntary participation of women who receive the MemoryGel™ implant is acceptable as an alternative study design and is justified to allow women access to this approved device without requiring participation in a research study and to potentially increase participation of women who meet the PAS inclusion criteria. Fourth, IRB participation and support is critical for the success of the Post-Approval Studies Program. In the silicone breast implant studies, the role of IRBs is even more important because the studies are long-term and involve tens of thousands of subjects.

Question. How many patients are currently enrolled in longitudinal studies of silicone gel breast implants made by Allergan and Mentor? What percentage of women who have received implants since the November 2006 approval are enrolled in these studies?

Answer. FDA believes this information about enrollment in ongoing studies is confidential commercial information protected from public disclosure by statute and regulation. It cannot be disclosed for the record absent permission from the companies. We apologize for any inconvenience this may cause. FDA does not have information regarding the percentage of women who have received implants since the November 2006 approval that are enrolled in these studies.

Question. What other changes have been made to the post approval study requirements?

Answer. In May 2007, FDA approved a protocol change for the Large Post-Approval Study, requested by Mentor, that allows the company to enroll Canadian patients who receive the MemoryGel silicone breast implant in addition to the U.S. study participants. The November 17, 2006, approval order states that Mentor will enroll in this study. Mentor requested this protocol change to meet Health Canada's post-approval conditions for the MemoryGel Silicone gel-filled Breast Implant. Mentor will use the FDA MemoryGel PAS protocol for the Canadian MemoryGel participants. The sponsor plans to perform the analysis twice, once on all study participants and a second time based only on U.S. study participants.

Question. Are Mentor and Allergan currently in full compliance with the post approval requirements?

Answer. The status of Allergan's and Mentor's postmarket studies of silicone breast implants and conditions is summarized in a table that I am pleased to provide for the record. Both Mentor Corporation and Allergan started enrolling patients in February 2007 as required by their respective approval orders and both firms have complied with the reporting requirements. The table below identifies the status of individual approval conditions that Allergan and Mentor must meet.

[The information follows:]

STATUS OF ALLERGAN'S AND MENTOR CORPORATION'S SILICONE GEL-FILLED BREAST IMPLANT POSTMARKET STUDIES AND CONDITIONS

Approval Condition			Allergan	Mentor
Core Post-Approval Study.....	Reporting status:	Reporting status:		
	On time \2\.	On time 2		
	Study Status: On time \3\.	Study Status: On time \3\		
Large Post-Approval Study.....	Reporting status:	Reporting status:		
	On time \1\.	On time \1\		
	Study Status: Overdue \3\ (12-month patient enrollment target was not met).	Study Status: On time \3\		
Device Failure Studies.....	Reporting status:	Reporting status:		
	On time \2\.	On time \2\		
	Study Status: On time \3\.	Study Status: On time \3\		
Focus Group Study.....	Reporting status:	Reporting status:		
	On time \2\.	On time \2\		
	Study Status: On time \3\.	Study Status: On time \3\		
Informed Decision Process.....	Reporting status:	Reporting status:		
	On time \2\.	On time \2\		
	Study Status: On time \3\.	Study Status: On time \3\		

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Adjunct Study..... Reporting status: Reporting status:
On time \2\ On time \2\
Study Status: On Study Status: On
time \3\ time \3\

\1 Reporting status for Larger Post-Approval Study is ``On time'' if 15-month report was received by the February 16, 2008 due date.
\2 Reporting status is ``on time'' if 12-month report for a post-approval study other than the Larger Post-Approval Study was received by November 17, 2007 due date.
\3 Study progress status for a post-approval study condition is ``On time'' if patient enrollment and follow-up targets have been met and ``Overdue'' if the interim enrollment target was not met.

Question. Based on the post approval data already reported by Mentor and Allergan, what findings has the FDA made regarding the safety of silicone gel breast implants?

Answer. FDA's review of the 12-month reports submitted by Allergan and Mentor for the six conditions of approval indicates that the results regarding the safety of the silicone gel breast implants presented in these reports are consistent with the data available at the time of approval. The studies are continuing to allow FDA to evaluate long-term device safety.

Question. Does the FDA have the necessary resources to enforce these post-approval requirements?

Answer. In 2005, CDRH transferred the responsibility for post-approval study oversight from the premarket staff of the Office of Device Evaluation and the Office of In Vitro Diagnostics to the postmarket staff of the Office of Surveillance and Biometrics, also known as OSB.

The fiscal year 2003-2005 cohort approval commitments for the silicone breast implants focuses on three areas: ensuring the timeliness of the study execution, ensuring that the FDA-approved protocols are properly implemented, and making sure that the studies are progressing well and provide meaningful results that can guide regulatory actions.

OSB has two project managers who are fully dedicated to overseeing manufacturer compliance with post-approval study commitments. They enable OSB to acknowledge receipt of study reports, monitor compliance with reporting requirements, and contact the manufacturer when the reports are not received as scheduled.

In 2006, OSB instituted an automated tracking system to monitor PAS study commitments. The project managers use this tracking system to make sure manufacturers send PAS study progress reports on time and that we review these reports in a timely manner.

Two OSB epidemiologists serve as the lead reviewers for post-approval commitments and review the study reports to make sure the studies are progressing well. A multi-disciplinary post market team of scientists is available as consultants to the epidemiologists.

The FDA Post-Approval Studies Website went live in April 2007. The site documents the status of PAS studies for the two implants. A user can search for information by the device name or manufacturer and view a description of the study, the reporting schedule, and status of the studies--such as whether the study is On Time or Overdue. The site is maintained by the project managers for Post-Approval Studies and updated once a month. I would be happy to provide the website address.

[The information follows:]
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma_pas.cfm.

Questions Submitted by Senator Robert F. Bennett

HEPARIN AND DRUG FACILITY INSPECTIONS

Question. Dr. von Eschenbach, the recent recall of the blood thinning drug Heparin has opened our eyes to some possible gaps in the agency's inspection processes. The recall has been particularly troubling because FDA has tied 62 deaths directly to the use of contaminated Heparin. The Chinese company that prepared the contaminated ingredient should have been inspected by FDA before product approval, but it was not. FDA stated that the agency thought the company had been inspected, but realized after the recall started that it had not received the required pre-approval inspection. The reason the company was not inspected is because the company's name is similar to another facility in China that had passed FDA inspection. FDA admits that the agency confused the names of the facilities on the drug application.

Can you help me understand how something like this could happen? I understand that manufacturers of active drug ingredients must be inspected prior to drug approval, how does FDA miss one?

Answer. Under section 505 of the Federal Food, Drug, and Cosmetic Act, prior to approval of a new drug application, abbreviated new drug application, or certain manufacturing supplements, FDA determines that the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the applicant's drug are adequate to preserve the drug's identity, strength, quality, and purity. Our policy has been, and continues to be that we approve drugs after verifying that this standard is met based upon a recent inspection of the manufacturing facility or facilities named in the application. If we have a recent, satisfactory inspection on record for a given facility named in the application, we generally will not conduct a new pre-approval inspection of that facility prior to approving the application. However, even if there is a recent inspection, we will inspect again if we determine that the circumstances warrant it.

In this situation, FDA learned in January 2008 that Baxter received FDA approval to use the active pharmaceutical ingredient (API) manufacturer, Changzhou SPL in Changzhou, China, although FDA did not conduct a pre-approval inspection of the plant. The plant subsequently shipped product to Baxter. As FDA has acknowledged, FDA's failure to inspect the plant was the result of human error. FDA staff entering data into a database confused the name of the Changzhou plant with another plant that had a similar name and had been previously inspected.

Question. What are you doing to make sure this doesn't happen again?

Answer. Process improvements in CDER are already underway that will prevent future data entry errors like this. These improvements include additional training for those who perform data entry on which inspection assignments hinge, hiring new staff dedicated to this data entry, and putting procedures in place that will provide FDA with the necessary data from drug manufacturers in a user-friendly way. In addition, efforts are underway to centralize all FDA's Information Technology, or IT, systems to meet the challenges of the FDA in the 21st century. Coupled with resource planning and development activities, FDA's Office of Information Management has undertaken detailed succession planning to ensure that the IT organization that FDA is building for the 21st century remains reliable in support of FDA's mission and is sufficiently flexible to accommodate the science and technology advances of the future.

Question. In media calls, the agency stated that the mix-up occurred because the company in question has a name similar to another Chinese company that had previously passed FDA inspection. From what I've heard, it appears that manufacturers of active drug ingredients are identified by name and not by some standardized system, for instance, numerically. Why? Do you think they should be identified using a standardized system?

Answer. A unique numerical identifier for each registered facility can be helpful for assuring FDA that the firm is the same entity of record in FDA databases, that the physical location of the facility is valid, and that the firm is still engaged in FDA-regulated business. Unique identifiers already in use at FDA, such as the Firm Establishment Indicator number, or FEI, could be used for these validation purposes. However, the FEI falls short of providing high-quality validation because it is not implemented with a rigorous validation protocol. For example, inter-agency computer applications can lead to the creation of new FEIs during importations when information is conflicting or missing. Having a unique identifier is useful only if the software and policy procedures use it for rigorous

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validation.

Although FDA has an ongoing effort to strengthen its own identity validation software, there are benefits of partnering with third party organizations that are in the business of uniquely identifying and collecting business information on companies. First, the commercial firms succeed by maintaining high-quality firm identifiers (including address) and business information. When a firm terminates business, the identifier is no longer valid. Second, the third party business databases offer rapid validation tools electronically. Finally, the third party databases provide business relationships not routinely visible to FDA that are often an aid during supply chain and other investigations.

FDA INTERNATIONAL OFFICES

Question. Currently, close to 15 percent of the food consumed in the United States is imported and the percentage is rising every year. In addition, the volume of prescription drugs imported into the United States is expected to increase by 12 percent during fiscal year 2009. It is clear that the global marketplace is having a significant impact on the products regulated by FDA. And, FDA currently does not have any staff located abroad.

In the fiscal year 2009 budget, FDA States that it will establish an office in China to better protect consumers from unsafe products. In addition, the fiscal year 2008 appropriations bill provided funding to increase domestic and import food inspectors, including international inspectors. I understand you've been working with the Chinese government to have employees stationed there.

What is the status of these discussions? When do you believe the first FDA employee will be stationed in China? And, how many employees do you expect will be stationed there?

Answer. The discussions with the Chinese Government concerning stationing FDA employees there are being handled by the U.S. Embassy. However, Secretary Leavitt and I have had discussions with their Chinese counterparts, who have signaled support. At this point, we are waiting for the Ministry of Foreign Affairs to endorse the proposal.

FDA has received approval from the Department of State to station eight employees in China. FDA expects that it will station the first FDA employee, the Country Director for the FDA Office, in Beijing by the end of calendar year 2008. FDA also plans to make additional hires for China offices during 2009.

Question. You have mentioned in public statements that China is not the only country FDA would like to place employees. In what other countries are you looking to locate employees, and have you begun negotiations with those countries?

Answer. FDA has agreements in place and we are making final arrangements for offices in China. FDA has conducted general discussions about FDA foreign offices with India and Jordan.

OVERALL FDA FUNDING

Question. Many people have said that FDA needs more money, including FDA's own Science Board. Specifically, the Science Board said that "FDA can no longer fulfill its mission without substantial and sustained additional appropriations." The Science Board suggested that an increase of \$375 million in fiscal year 2009 is necessary to help FDA fulfill its mission.

Dr. von Eschenbach, you appear to agree with the notion that FDA needs more money. In an interview with the Wall Street Journal earlier this year, you said "to do what [FDA] needs to do requires substantially more dollars than what has been invested in the FDA thus far." You also go on to state you wanted more out of the budget process this year than what finally ended up in the budget request.

While \$375 million in 1 year may be more than we can come up with, this subcommittee is determined to help FDA in any way it can. What do you think of the Science Board's assessment?

Answer. On December 3, 2007, the FDA Science Board accepted the report of its subcommittee entitled, "FDA Science and Mission at Risk." The subcommittee report reveals a number of areas that recommend increased investment. FDA takes this report seriously. The need to improve science at FDA is not in question. Nor is there any question that we must make a significant investment in improving the science.

FDA is keenly aware that we must develop comprehensive solutions to face an ever-changing scientific and technological landscape. We look forward to working with Congress and other stakeholders to strengthen the scientific base at FDA and ensure that in the next 100 years, FDA retains its reputation and preeminence as the gold standard through the use of cutting edge science and technology.

Question. Does FDA need more money than is requested in the President's budget?

Answer. FDA's fiscal year 2009 budget request of an additional \$50.7 million in budget authority and \$78.9 million in user fees for programs to protect America's food supply and for medical product safety and development reflects the competing priorities the President and the President's advisors must consider as budget submissions to the Congress are developed. In light of these competing priorities, FDA's fiscal year 2009 budget request is the amount designated to allow FDA to achieve its public health priorities.

Question. How much would you suggest is necessary in fiscal year 2009 to help FDA meet its demands and which program areas would benefit most from additional resources?

Answer. The following document is an assessment of immediate resource needs based on a professional judgment analysis, without regard to the competing priorities that the agency, the President, and the President's advisors must consider as budget submissions to the Congress are developed. As the response indicates, the amounts identified are in addition to amounts appropriated to FDA in fiscal year 2008.

[The information is attached.]

FDA FISCAL YEAR 2009 PROFESSIONAL JUDGMENT ESTIMATE [Dollars in millions]

	Fiscal year 2009	FTE
Food Protection.....	\$125	259
Safer Drugs, Devices, and Biologics.....	100	160
Modernizing FDA Science and Workforce...	50	71
Total.....	275	490

The amounts identified in this document support three strategic investment areas--protecting our food supply, assuring safer drugs, devices, and biologics, and modernizing the essential infrastructure of FDA's science and workforce. The amounts are in addition to amounts appropriated to FDA in fiscal year 2008. Investing in these three strategic areas will permit FDA to rapidly achieve important public health goals that cut across strategic components of the Agency.

This document responds to the request for the FDA's professional judgment concerning resource needs. The document was developed without regard to the competing priorities that the President and his advisors must consider as budget submissions to the Congress are developed.

FDA FISCAL YEAR 2009 BUDGET AMENDMENT: FOOD PROTECTION PLAN (+\$125 MILLION)

Core Elements and Strategic Activities	FPP Output	Amount	FTE
Prevention:			
1.1 Promote Increased Corporate Responsibility to Prevent Foodborne Illnesses: FDA will ensure the safety of imports by increasing FDA's presence beyond our borders and building capacity with foreign partners.	Increase FDA presence beyond our borders, including increased training for food safety best practices abroad. Offices in four additional countries with 7/8 FDA FTE and 4/5 foreign nationals per country/region. Yields FDA presence in five countries or regions of the world.	\$16,000,000	24
		5,000,000	2
		5,000,000	3

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	Increase technical assistance on food standards in at least 3 of the countries accounting for the major share of imports.		
	Develop systems and tools for an international information exchange database related to inspections and quality.		
1.2 Identify Food Vulnerabilities and Assess Risks: FDA will conduct risk-based prevention to better protect America's food supply. FDA will better understand food safety and food defense risks and use this understanding to define the optimum preventive controls to establish.	Increase capacity to collect & interpret data for risk-based prevention for products of greatest concern.	5,000,000	10
	Research and develop risk-based prevention strategies based on scientific data and protocols.	7,000,000	20
1.3 Expand Understanding and Use of Effective Mitigation Measures: FDA will develop and validate rapid detection tools to quickly detect and mitigate a potential problem.	Develop and validate rapid detection technologies and assays (see 2.3 for deploying technologies and assays); For high risk foods, commence work to develop two new priority tools and to validate two test methods for toxic chemicals or microbes developed by industry.	5,000,000	10
Sub-Total.....		43,000,000	69
Intervention:			
2.1 Inspections and Sampling Based on Risk: FDA will apply risk analysis to set priorities for food inspections and interventions.	20,000 more import food exams at the port of entry \1\ (\$300 each).	6,000,000	36
	800 more foreign food production and/or processing facility inspections and support for foreign inspections \1\ (uc=\$16.7K).	13,500,000	50
	800 more domestic food safety inspections \1\ (uc=\$8k).	6,500,000	33
2.2 Enhance Risk-Based Surveillance of Imported Foods at the Border: FDA will design and build risk-based algorithms to conduct inspections and detect food risks. Understanding the risks defines the number and types of inspections and tests needed to ensure that preventive controls are working.	Integrate and assimilate risk-based information into data systems.	10,000,000	15
2.3 Better Detect Food System Signals that Indicate Contamination: FDA will deploy rapid detection technologies and assays and build laboratory infrastructure for faster testing. FDA will deploy state-of-the-art technology to improve the integration of incoming signals and achieve faster mitigation and response.	Improve signal detection of intentional and unintentional chemical and microbial contamination.	5,000,000	5
	Deploy 1-2 rapid detection assays to test high risk foods. Acquire advanced technology and deploy such equipment to FDA field and conduct technology transfer to industry.	5,000,000	5
	Build high throughput rapid detection technology into laboratory infrastructure.	11,000,000	10
Sub-Total.....		57,000,000	154
Response:			
3.1 Improve Immediate Answer. FDA will enable real-time communication of lab results. FDA will develop protocols to facilitate tracebacks of foodborne illnesses. FDA will rapidly detect and respond foodborne outbreaks.	Develop and implement a system for traceback from product consumption back to the source of production using, for example, electronic pedigrees and industry applied technologies of bar coding and radio frequency identification.	10,000,000	20
	Enhance interoperable information technology networking system between FDA and Federal, State, and local testing labs.	10,000,000	6
3.2 Improve Risk Communications to the Public, Industry, and Other Stakeholders: FDA will enhance risk communication through aggressive, targeted food safety campaigns that disseminate clear and effective messages with regular updates through a variety of media to all target audiences.	Create a health hazards alert communication system using multiple media outlets to quickly inform a broad cross section of the public.	5,000,000	10
Sub-Total.....		25,000,000	36
GRAND TOTAL, Food Protection Plan.		125,000,000	259

\1\ FDA will hire and train additional field inspectors throughout fiscal year 2009. As a result, by fiscal year 2010, the proposed investment will allow FDA to increase its inspection and surveillance capacity by the number of inspections identified in this FPP output

FDA FISCAL YEAR 2009 BUDGET AMENDMENT: ENSURING SAFE AND EFFECTIVE MEDICAL PRODUCTS (+\$100 MILLION)			
Strategic Activity	Output	Amount	FTE
Safer Drugs, Devices, and Biologics:			
1.1 Science to Improve Medical Product Safety and Development: Use new science and analysis to improve the safety of medical products. In some cases, new science creates opportunities to leverage advances from one product area to promote safety in a different area.	Establish a unique device identification system to track devices, facilitate recalls, and support inventory management during disasters and terrorism response.	\$7,500,000	17
	Implement FDAAA safety requirements related to pediatric drugs and devices, postmarket study commitments, clinical trials, active drug surveillance, labeling and safe use of drugs.	14,000,000	10
Sub-Total.....		21,500,000	27
1.2 Data Analysis Tools to Identify Safety Issues: Develop and implement quantitative decision-making tools to assess the safety and effectiveness of drugs, biologics, and devices throughout their lifecycle.	Build Regulated Product Information Data Warehouse that will enable intelligence sharing with other regulatory agencies.	15,000,000	6
	Data access and analysis for active safety surveillance with development of scientific methods of data mining for signals of adverse events.	15,000,000	6
Sub-Total.....		30,000,000	6
1.3 Risk-Based Inspection and Compliance: Strengthen field operations to better protect public health. The sheer volume of products, manufacturing plants, distributors, and importers demands a more robust inspection force with better capacity to reach the community that FDA regulates.	250 more foreign medical product facility inspections \1\ (uc=\$45,000)	11,200,000	50
	Increase FDA's presence beyond our borders to five countries or regions of the world.	10,800,000	18
	250 more domestic medical product inspections (uc=\$17.7K).	4,400,000	14
	Improve lab infrastructure and tools for rapid analysis of product/ingredient content.	7,500,000	5
	Increase import exams (10,000) and sampling/laboratory analysis (300).	6,600,000	35
	IT systems to achieve an integrated inventory database.	3,000,000	5
	Improve risk communications to public and industry.	5,000,000	5

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Sub-Total.....	48,500,000	127
GRAND TOTAL, Medical Product Safety and Effectiveness.	100,000,000	160

\1\ FDA will hire and train additional field inspectors throughout fiscal year 2009. As a result, by fiscal year 2010, the proposed investment will allow FDA to increase its inspection and surveillance capacity by the number of inspections identified in this output

FDA FISCAL YEAR 2009 BUDGET AMENDMENT: MODERNIZING FDA SCIENCE AND WORKFORCE (+50 MILLION)			
Strategic Activity	Output	Amount	FTE
Modernizing FDA Science and Workforce:			
1.1 Science Leadership and Coordination: FDA will enhance science programs across the agency, especially in emerging areas such as nanotechnology and tissue engineering. FDA will establish mechanisms to access the best scientific knowledge and expertise to modernize its regulatory science. FDA will strengthen its capacity to support emerging areas of science and manufacturing that are essential to regulating FDA products.	Strengthen programs of emerging science in Centers and at the National Center for Toxicological Research and enhance integration. Strengthen capacity to support nanotechnology, cell and gene therapies, robotics, genomics and proteomics, Critical Path initiatives, and advanced manufacturing technologies.	\$5,000,000	15
		27,000,000	40
Sub-Total.....		32,000,000	55
1.2 Investments to Support Science-Based Regulation: FDA will upgrade its science capacity by providing more training and professional development support for FDA science staff. FDA will create an Agency-wide 2-year Science Fellows Program intended to include up to 2,000 trainees to develop a new cadre of emerging leaders in regulatory science. FDA will upgrade facilities that do not adequately support FDA's current or future mission.	Expand science training and professional development for career employees. Launch Science Fellows Program and initiate recruitment of first 500 fellows. Improve facilities outside of the Washington region to support FDA's mission and enable these facilities to accept new food and medical product technologies.	4,000,000	8
		10,000,000	8
Sub-Total.....		18,000,000	16
GRAND TOTAL, Modernizing FDA Science and Workforce.		50,000,000	71

PAY COSTS

Question. The budget request includes a net increase request of \$54 million in budget authority. The increase is supposed to fund pay costs and increases in food safety and medical product safety. However, the budget also states pay and benefits need for fiscal year 2009 is slightly more than \$59 million, approximately \$5 million more than the request.

It is apparent that maintaining current staff levels will consume your entire request amount in fiscal year 2009. Since this is the case, how will you accomplish the food safety and medical product safety activities promised in the budget? Will you be forced to cut back in other areas?

Answer. The fiscal year 2009 President's Budget provides staff for FDA to perform its public health mission and provide inspectors, medical and consumer safety officers, food safety technologists, medical product reviewers, postmarket safety experts, and other public health experts to safeguard the American public and implement the food and medical product safety activities outlined in the budget.

The President's fiscal year 2009 budget contains \$25 million to pay the cost of living increase for FDA employees. FDA will cover fiscal year 2009 cost increases through a combination of strategies, including reducing operating costs and the design of its hiring plan.

IT INVESTMENTS

Question. Dr. von Eschenbach, in a recent speech to the Food and Drug Law Institute you mentioned that FDA's information technology infrastructure is "adequately funded at \$200 million a year, but [it] remains antiquated, unreliable, and beset by high-cost maintenance." You said that FDA's IT infrastructure is essentially "a quilt of patched-together hardware and fragmented software packages."

In addition, one of the findings in the recent Science Board report was that "FDA lacks information technology capability and capacity to support monitoring of drug and food safety and is particularly challenged in the regulation of products based on new science." The Science Board goes on to recommend the development and execution of a comprehensive IT modernization plan.

FDA's budget for fiscal year 2008 is about \$2.2 billion. According to your numbers, the agency is spending about 10 percent of its budget on IT.

How is it possible that your IT systems are in such shambles if the agency is regularly spending about 10 percent of your budget on IT? Based on your statement, you appear to agree that \$200 million a year is "adequate".

Answer. We concur that FDA faces many challenges maintaining its current management information system while also upgrading its IT services to meet the challenges of the 21st century. However, FDA has made great strides since fiscal year 2004, and has accelerated its progress during fiscal year 2007 to centralize FDA-wide IT resources. FDA activities will result in strengthening FDA's base operations, eliminating duplicative systems, standardizing processes and procedures, and generally improving the efficiency of FDA IT systems.

Starting in 2004, the FDA Business Framework established and implemented the Bioinformatics Board, also known as the BIB. The BIB provides strategic direction, coordinates FDA business processes, and harmonizes information management initiatives. The BIB governance structure operates with five Business Review Boards to harmonize FDA business processes across strategic lines of business. The five Business Review Boards address Pre-Market Activity, Post-Market Safety, Product Quality and Compliance, Administrative Services, and Scientific Computing and Computational Science.

FDA progress coordinating the management of information systems matured in 2007 with the creation of the Chief Operating Officer position and the elevation of the Chief Information Officer. These actions signified the importance and criticality of Information Management at FDA. At the same time, the Business Review Board identified 5-year goals and strategic objectives for five FDA-wide Information Technology initiatives.

The first initiative is the Information and Computing Technologies for the 21st Century, which is designed to provide modernized servers and analysis mechanisms to meet Bioinformatics requirements.

The second initiative is updating MedWatch, which is a system created to provide a portal for adverse event reporting and consumer complaints.

The third initiative is the Harmonized Inventory Project, an exciting endeavor to clean up legacy data and provide one source of truth for registration and listing information.

The fourth initiative is the creation of a Common Electronic Document Room to facilitate data sharing across all of the FDA business lines.

Finally, the FDA Advanced Submission Tracking and Review System, upon completion, will move data across applications throughout the continuum of the product lifecycle, from pre-approval through consumption, creating a close loop system encompassing all FDA business

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lines.

In summary, these initiatives not only lay the foundation for integrating disparate existing systems across the FDA, but they also align with recently enacted legislation and action plans.

Continuing in 2008 and beyond, FDA will achieve business driven IT that is managed as an FDA IT investment portfolio. FDA will standardize approaches to developing systems to increase interoperability, minimize redundancy by centralizing IT and obtain economies of scale across FDA. FDA will deliver the systems and functionality to implement FDA Amendments Act, Import Safety Action Plan, and the Food Protection Plan.

These advances at FDA have raised Information Technology to a corporate level resource that is being directed, governed, and managed across FDA by the Bioinformatics Board and the CIO. This approach enables business driven IT support and services that allow FDA to achieve its mission of promoting and protecting public health.

Question. If you were to prioritize areas where IT investment could be made, what would those areas be and how much would you invest?

Answer. FDA's Business Review Board identified 5-year goals and strategic objectives for five FDA-wide Information Technology initiatives. The five initiatives are Information and Computing Technologies for the 21st Century, MedWatch, the Harmonized Inventory Project, a Common Electronic Document Room, and the FDA Advanced Submission Tracking and Review System. These are long-term IT projects and FDA is still evaluating the resource requirements to accomplish these IT priorities.

CRITICAL PATH ACTIVITIES

Question. Last year, you joined us in Utah for a subcommittee hearing on FDA's critical path initiative. During the hearing we discussed ways that FDA can work with universities and non-profit organizations to optimize drug dosing for certain patients, thus minimizing adverse events and helping people get the drug that is right for them. In the fiscal year 2008 appropriations bill, the Committee provided \$7.5 million for the critical path initiative, of which \$2.5 million was made available for competitive critical path research grants.

Could you update us on your progress in this area?

Answer. FDA has awarded more than \$3 million in grants and contracts so far this year to external organizations to support a variety of critical path activities, including efforts in support of personalized medicine.

For example, we renewed and extended our contract with the Critical Path Institute, C-Path. As you know, C-Path was co-founded by the University of Arizona and Stanford Research Institute, International, as a neutral ground for supporting collaborations on education and training in applied research and regulatory sciences. FDA and C-Path executed a memorandum of understanding that lays out the general parameters for these collaborations. One of these collaborations, the Predictive Safety Testing Consortium--PSTC--was announced in March 2006 to develop and qualify preclinical safety biomarkers. Although that effort will continue, significant progress already has been made. FDA and our European counterpart, the European Medicines Agency (EMA) currently are reviewing the validity of seven new tests, or biomarkers, to detect drug-induced kidney damage. The PSTC was able to bring together 190 international scientists to share scientific data and generate a novel simultaneous submission to both regulatory bodies.

We look forward to the possibility of further transatlantic cooperation for safer medical products. We hope for similar, continued advancements from our five working groups: Kidney Toxicity, Liver Toxicity, Blood Vessel Toxicity, Carcinogenicity, and Muscle Toxicity.

Question. Are there any particularly promising critical path projects that you would like the Committee to know about?

Answer. We would like to share four important projects with you today.

FDA is developing and implementing a single electronic portal for the receipt of all adverse event reports coming into the Agency--MedWatchPLUS. A 5-year contract was awarded to SRA International, Inc. in early 2008 for the integration of the MedWatchPlus portal and the FDA Adverse Event Reporting System, our new harmonized adverse events reporting system. This effort is critical for public health; it will greatly improve the quality and consistency of the adverse event reports that we receive. We are also working on a related effort with the National Institutes of Health to develop an electronic reporting questionnaire that will greatly reduce the burden on the healthcare community and the public when they report to us through the new portal.

FDA is working to explore the possibility of collaborating to create a national, integrated, electronic system for monitoring medical product postmarket safety. This Sentinel System would enable FDA to capitalize on the capabilities of multiple, existing data systems to augment the Agency's current postmarket monitoring capability.

C-Path is helping launch a large collaboration dedicated to advancing progress against major diseases, initially Alzheimer's and Parkinson's. The Coalition Against Major Diseases, CAMD, will enable FDA, industry, academic scientists, government agencies, and healthcare providers to share pooled data on the natural history of diseases. With these data we will generate a quantitative disease progression model that can be made available for all to use in designing clinical trials to more efficiently evaluate new therapies. This effort will be similar to our collective attack on HIV/AIDS.

Finally, the Clinical Trials Transformation Initiative, CTI, is a collaborative endeavor with Duke University and other academic and industrial Critical Path partners. The aim is to improve the efficiency and safety of clinical trials by incorporating new information technology and monitoring systems.

FOOD SAFETY RESEARCH

Question. In the fiscal year 2008 appropriations bill, the Committee provided \$3 million for food safety research under the National Research Initiative at USDA. We directed the Department of Agriculture and FDA to work together to develop food safety research priorities that benefit both USDA and FDA.

How is this effort progressing? Have you identified research priorities and started the process of awarding research grants?

Answer. The FDA and USDA's Cooperative State Research, Education, and Extension Service, also known as CSREES, have met on several occasions to discuss FDA's broad food safety research priorities in relation to how these priorities would benefit USDA. FDA's priorities from these discussions are incorporated in two of the current priorities that CSREES announced in their request for proposal, also known as an RFP. Fiscal year 2008 research priorities will address human enteric viruses or microbial toxins in the areas associated with seafood and in the areas of fresh fruits, nuts, and vegetables.

For fiscal year 2008, CSREES' Food Safety Program's review panel met April 22 through 24, 2008, to rank proposals received. One FDA scientist participated as a member of the review panel. Awards will be made based on normal CSREES extramural and contract procedures. FDA has had additional discussions with CSREES regarding establishing a more formal process for seeking FDA's input into the development of next year's RFPs, and FDA is currently moving forward with those arrangements.

Question. What are the food safety research priorities for FDA?

Answer. FDA's Food Protection Plan emphasizes the need to know the science underpinning how and where food becomes contaminated and the associated risks. The Food Protection Plan also highlights the use of science to determine optimal interventions to reduce the likelihood of contamination and harm. The Center for Food Safety and Applied Nutrition, known as CFSAN, the Center for Veterinary Medicine, known as CVM, and the National Center for Toxicological Research, known as NCTR, work collaboratively to advance research in the food safety arena.

The following information describes the CFSAN food safety research priorities. FDA periodically updates its research priorities to reflect the changing needs of food programs. CFSAN is currently updating its research priorities since the center successfully completed a cycle of research focused on food defense issues. The center is initiating research to support our Food Protection Plan. These priorities include addressing issues related to the prevention, intervention and response components of the Food Protection Plan. Priority regulatory activities that will require substantial research support are likely to include

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work in chemical and microbiological sampling and detection methods, interventions to prevent the contamination of produce and dairy products, assessing the safety of dietary supplements, research to support dietary guidelines, conducting of evidenced-based evaluation of health claims, and developing and disseminating guidance to stakeholders for food safety concerns. CFSAN will address these research needs through intramural and extramural research, Centers of Excellence partnership programs, and our established interactions with research agencies such as USDA's Cooperative State Research, Education, and Extension Service, USDA's Agricultural Research Service, and the National Institutes of Health.

The following information describes the CVM food safety research priorities. In the area of antimicrobial safety, CVM is developing rapid methods such as microarray and biomarkers to screen foodborne pathogens for genetic relatedness. CVM is also developing rapid methods to screen for the carriage of resistance genes in order to measure the migration of resistance genes from the animal production environment to humans where they can cause intestinal illness. This information will help assess the risk associated with antimicrobial use in food-producing animals. CVM's National Antimicrobial Resistance Monitoring System, or NARMS, provides ongoing monitoring data on the antimicrobial susceptibility patterns in common foodborne bacteria. This information can be used to alert the veterinary medical community and regulatory officials about emerging resistance problems that may compromise drug efficacy.

In the area of animal feed safety, CVM is developing and validating methods for detecting prohibited proteins from the United States and European Union sources in animal feeds. The methods will provide Federal and State investigators with rapid and sensitive tools for enforcing the FDA Feed Ban, thus preventing the spread of BSE in cattle and the possible outbreak of variant Creutzfeldt-Jakob disease in humans. We are also conducting residue depletion and toxicity studies associated with melamine and cyanuric acid in animal feeds. Information from these investigations will aid in assuring the safety of animals consuming contaminated feed and humans consuming animal products.

In the area of drug residues and chemical contaminants, CVM is developing methods for use in Federal and State regulatory laboratories to detect illegal drug residues in animal-derived foods such as aquaculture products and honey. Methods are being developed to detect illegal residues, natural toxins, and dangerous contaminants in animal feeds. Significant progress has been made in developing methods to detect melamine and cyanuric acid in feeds, and to develop methods capable of testing for a variety of contaminants in distillers' grains, a byproduct of the ethanol industry frequently used as a component of animal feeds.

NCTR provides research that supports FDA's food safety priorities in three specific areas. NCTR is conducting research to develop, validate, and implement test methods to rapidly detect chemical and microbial contamination of food. The results of this research are evaluated for application in the FDA Office of Regulatory Affairs field laboratories as well as in commercial food facilities. NCTR research also assesses the biological activity of food contaminants. This research includes determining the toxic effects of the contaminants, evaluating methods to neutralize the contaminant, and investigating pathways of antimicrobial resistance. NCTR develops tools that assist FDA to identify high-risk products, and thereby facilitate optimal use of inspection resources. These tools include statistical models and methods to evaluate the risk potential of imported and domestic products. NCTR is also collaborating to develop a database that contains genetic information about bacterial strains that can be used to differentiate between pathogens and nonpathogens and facilitate tracing pathways of contamination.

GENERIC DRUG CITIZEN PETITIONS

Question. Dr. von Eschenbach, you've mentioned in public statements that one significant challenge posed by the Food and Drug Administration Amendments Act is the 180-day deadline for FDA to take final action on certain citizen petitions related to the approval of generic drugs. You've stated that meeting this new deadline will require significant new efforts and additional resources.

For the past 2 years, this subcommittee has provided FDA with more money than was requested in the budget for generic drug review. Is it possible to use these resources to assist with the review of citizen's petitions?

Answer. FDA recognizes the value of the subcommittee's interest and support for the Generic Drug Review program, as represented by the additional resources provided for generic drug review during the last 2 years. The increased funding has been instrumental in ensuring that FDA can continue its performance in expanding the availability of high-quality generic drug products and providing consumers and healthcare providers with information on the safety and effectiveness of generic drugs.

The staff hired with the new funding that FDA received in recent years is not specifically focusing on reviewing citizen petitions. However, increased staff helps to ensure that the Office of Generic Drugs has the expertise necessary to reviewing citizen petitions.

Question. Do you have an estimate of how much would be necessary to meet this new deadline? If so, how much?

Answer. Review of Citizen Petitions subject to Section 914 of the Food and Drug Administration Amendments Act of 2007 involves the work of experts in several offices throughout FDA, including CDER's Office of Regulatory Policy, Office of Generic Drugs, and the Office of New Drugs, as well as the Office of Chief Counsel. We estimate that a total of 40 additional FTEs would be needed to adequately staff all of these offices for this purpose.

IMPLEMENTATION OF THE FDA AMENDMENTS ACT OF 2007

Question. Congress passed, and the President signed into law, the Food and Drug Administration Amendments Act last September. The act is very broad. It reauthorized and expanded FDA's drug and device user fees and included provisions related to food safety, drug safety, research on pediatric products, and advisory committees. According to FDA's implementation plan, the act included 125 separate clauses or provisions that require action.

How are the agency's implementation plans progressing? What would you consider the greatest implementation challenge for the agency?

Answer. FDA efforts to implement the Food and Drug Administration Amendments Act, also known as FDAAA, are proceeding well. After FDAAA passed last year, we determined that there were approximately 125 provisions which FDA needed to implement or would have a role in implementing. These provisions, however, represent many more individual tasks. For example, one provision may take thirty individual tasks to accomplish while another provision may require only two or three tasks. As we implement the provisions, additional tasks are added as the full impact of a provision is not always obvious at the outset of implementation.

There are several challenges in implementing FDAAA. The complexity and breadth of the provisions coupled with various specific deadlines pose an enormous challenge to FDA—one that I believe agency employees are doing their best to meet.

Question. Are you meeting the deadlines set forth in the legislation?

Answer. At the current time we have been able to meet almost all of the specific deadlines required by FDAAA.

MEDICAL DEVICE REVIEW PERFORMANCE

Question. As you know, I've been very interested in the medical device user fee program and I have asked many questions about the performance of the program since it was enacted. In addition, this subcommittee has shown a significant amount of support for this program by providing inflationary increases to fully fund the program.

Can you tell us how the agency is doing in regards to meeting the performance goals associated with the user fee program?

Answer. FDA continues to succeed in improving the process for the review of medical device applications and meeting the performance goals first established under the Medical Device User Fee and Modernization Act of 2002, known as MDUFMA. Title II of the Food and Drug Administration Amendments Act of 2007 continued MDUFMA performance

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goals.

MDUFMA requires close collaboration with stakeholders and increased communication with applicants. FDA is working to clarify its regulatory requirements and make its decisions more transparent through new guidance, educational materials, and meetings. We continually seek to enhance the efficiency and flexibility of our review processes. These efforts help applicants improve the quality of their submissions, and help FDA provide more timely, better-focused reviews. Our ultimate objective is to make important new medical devices available to patients and healthcare providers earlier, while continuing to ensure the quality, safety, and effectiveness of those devices.

I would be happy to provide for the record a table that summarizes FDA's performance on the goals established for the fiscal year 2003-fiscal year 2007 receipt cohorts, showing results achieved through March 31, 2008. The goals applicable to the fiscal year 2008 receipt cohort have been in place for only 6 months, so it is too early for statistical measures to provide useful insights into our progress towards achieving those goals. FDA has, however, taken action to ensure that we are well positioned to achieve the goals for fiscal year 2008-fiscal year 2012. FDA is developing and implementing a new interactive review process that will contribute to better communication with applicants and more rapid resolution of review questions.

[The information follows:]

QUARTERLY REPORT ON PROGRESS TOWARDS ACHIEVING MEDICAL DEVICE PERFORMANCE GOALS SUMMARY TABLES
(Actions through March 31, 2008--Data for FDA)

		Performance Goals and Actual Performance to Date									
Activity	Review Time Goal	Fiscal Year 2003		Fiscal Year 2004		Fiscal Year 2005		Fiscal Year 2006		Fiscal Year 2007	
		Goal	Actual Percent	Goal	Actual Percent	Goal Percent	Actual Percent	Goal Percent	Actual Percent	Goal Percent	Actual Percent
PMAs, Panel-Track Supplements, Premarket Reports:											
FDA decision (approval, approvable, approvable pending GMP inspection, not approvable.	320 days.....		91.8		91.7		87.7	80	83.7	90	100
FDA decision--Percent within 180 days.....	180 days.....		44.9		37.5		29.8		36.7	50	41.2
Expedited PMAs:											
FDA decision (approval, approvable, approvable pending GMP inspection not approvable.	300 days.....		100		92.3	70	83.3	80	100	90	
180-day PMA Supplements:											
FDA decision (approval, approvable, approvable pending GMP inspection not approvable.	180 days.....		94.1		95.3	80	95.0	80	97.0	90	92.8
510(k)s:											
FDA decision (SE/NSE).....	90 days.....		76.1		83.9	75	91.1	75	91.6	80	92.7
Biologics Licensing Applications (BLAs):											
Review and act on standard original BLAs (issue ``complete action'' letter).	10 months.....				100		100	75	97.7	90	97.7
Review and act on priority ordinal BLA submissions (issue ``complete action'' letter).	6 months.....							75		90	
BLA Supplements:											
Review and act on standard BLA efficacy supplements (issue ``complete action'' letter).	10 months.....		100					75		90	
Review and act on priority BLA efficacy supplements (issue ``complete action'' letter).	6 months.....							75		90	
Review and act on BLA manufacturing supplements that require prior approval (issue ``complete action'' letter).	4 months.....							75		90	
BLA Resubmissions, BLA Supplement Resubmissions:											
Review and act on a Class I resubmission to an original BLA or BLA efficacy supplement (issue ``complete action'' letter).	2 months.....					75	100	80		90	100
Review and act on a Class 2 resubmission to an original BLA or BLA efficacy supplement (issue ``complete action'' letter).	6 months.....		100		80	75	100	80	100	90	100

Question. What criteria does the agency use to determine the allocation and priority for the distribution of any increase in staff across FDA components, including offices, divisions, or branches resulting from the medical device user fees and related Congressional appropriations?

Answer. The Food and Drug Administration Amendments Act of 2007, known as FDAAA, was signed into law on September 27, 2007. FDAAA reauthorized FDA's authority to collect fees from the medical device industry under the Medical Device User Fee and Modernization Act, also known as MDUFMA. The activities that comprise the medical device review process are defined in MDUFMA. Medical device review components within FDA that conduct activities that are included in the review process, as defined by MDUFMA, receive increased allocations from device user fee collections.

FDA allocates medical device user fees and other medical device appropriations to best achieve FDA's public health objectives, device performance goals, and other expectations established under MDUFMA, as amended. The allocation between the Center for Devices and Radiological Health, or CDRH, and the Center for Biologics Evaluation and Research, or CBER, is based on the workload balance between the two centers. FDA estimates the percent of the device review workload performed by CDRH and CBER, and allocates MDUFMA resources accordingly. Field resources are allocated among FDA district offices by the Office of Regulatory Affairs according to each district's projected workload. The Centers and ORA apportion their individual resource allocations to their offices, divisions, and branches.

Question. Even though the devices center has received significant increases over the past few years, I understand that the demands on staff are very high. Are there additional tools, such as third party reviews, third party inspections, or fellowship programs available to augment the work of the center? Please discuss the benefits of these programs and why they are important.

Answer. These three programs--third-party review of 510(k) premarket notifications, third-party establishment inspections, and the Medical Device Fellowship Program--provide FDA with important tools that can help us better achieve our public health objectives.

The purpose of the program permitting third-party review of certain 510(k) premarket notifications is to improve the efficiency and timeliness of FDA's 510(k) process. This is the process by which most medical devices receive marketing clearance in the United States. Under the program, FDA has accredited third-parties that are authorized to conduct the primary review of 510(k)s for eligible devices. Persons who are required to submit 510(k)s for these devices may elect to contract with an Accredited Person and submit a 510(k) directly to the Accredited Person. The Accredited Person conducts the primary review of the 510(k), then forwards its review, recommendation, and the 510(k) to FDA. By law, FDA must issue a final determination within 30 days after receiving the recommendation of an Accredited Person. 510(k) submitters who do not wish to use an Accredited Person may submit their 510(k)s directly to FDA. FDA data shows that third-party reviews are somewhat more rapid than an FDA review in some instances. Third-party 510(k)s submitted to FDA are also exempt from any medical device user fee that would otherwise apply.

As of April 15, 2008, FDA has accredited 16 third-party organizations to conduct quality systems inspections of certain medical device establishments. Individuals from eight of these organizations have completed FDA's training requirements and FDA has cleared these individuals to conduct independent inspections. Through April 15, 2008, accredited organizations have conducted six inspections. Although few inspections have been conducted to date, changes specified by the Food and Drug Administration Amendments Act of 2007, also known as FDAAA, have the potential to eliminate certain obstacles to manufacturers' participation in FDA's programs for inspections by accredited third parties.

CDRH established the Medical Device Fellowship Program, also known

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as MDPP, to increase the range and depth of collaborations between CDRH and the outside scientific community. The MDPP offers short and long-term fellowship opportunities for individuals interested in learning about the regulatory process and sharing their knowledge and experience in the many specialized fields that concern medical devices. Physicians with clinical or surgical expertise, engineers in biomedical, mechanical, electrical and software areas, and individuals from many other scientific disciplines have participated in the fellowship program. Opportunities are available for students in many other areas as well. This collaboration improves FDA's review processes, postmarket surveillance, and science base, all of which contribute to efforts to ensure patients and health care professionals have timely and continued access to safe and effective medical devices.

ROLE OF PHYSICIANS IN MEDICAL DEVICE DEVELOPMENT

Question. As you know, I've been very interested in the medical device user fee program and I have asked many questions about the performance of the program since it was enacted. In addition, this subcommittee has shown a significant amount of support for this program by providing inflationary increases to fully fund the program.

The role of physicians in medical device development and utilization is often not well understood. Can you comment on the role that physicians play in the development of new technologies? Does FDA ever require device companies to train physicians in the use of new technologies?

Answer. A physician may play any number of roles in product development and use, including developer, researcher, investigator, instructor, as well as end user. For example, a physician may identify a problem in medical care, which could initiate the development of a new device. Physicians may also be involved in the conduct of research on a device, including serving as primary investigators, on Institutional Review Board committees, or as monitors of large clinical trials. A physician serving as an investigator may participate in data collection and data analysis for a device premarket submission and may also represent the company in presenting this information to FDA. Once a device is cleared or approved for marketing, physicians may also have a role in teaching other physicians about device use, for example, as a means of promoting safe and effective use.

Yes, FDA has required training as a condition of approval included in premarket approval application orders. For example, carotid stent approval orders require that labeling specify the training requirements that apply to practitioners before they may use these stents. Also, many firms voluntarily provide training for physicians.

OFFICE OF GENERIC DRUGS PRODUCTIVITY

Question. The subcommittee is sympathetic to the workload that the Office of Generic Drugs (OGD) is facing. We all understand and appreciate that generic drugs are cost-effective alternatives that save consumers billions of dollars a year and we appreciate the work that OGD is doing.

With respect to FDA's performance goals, in your most recent budget justification, you indicate two factors have served to lower your productivity. You said that the move to the White Oak campus is "expected to cause a disruption in productivity." You also indicated that working under a Continuing Resolution during the First Quarter in fiscal year 2008 has caused a delay in hiring and training new staff at OGD.

Given that you have now announced OGD's move to White Oak, please provide the Committee with an update on your projected productivity at OGD? In addition, we appreciate your providing an update on the number of new staff hired and trained with the funding the Committee provided last year.

Answer. OGD will remain in its current Metro Park North buildings for the immediate future. OGD currently occupies three buildings on that the Metro Park North complex.

Overall productivity remains high. However, it is still difficult to keep pace both with the incoming applications and with other matters requiring OGD resources such as Citizen Petitions, lawsuits challenging the approval of generic drugs, and providing guidance to the industry.

In the period from October 1, 2007 through April 15, 2008, OGD has been able to hire 31 new staff representing a variety of scientific and clinical expertise. These new hires are undergoing training. Once that training is completed, OGD expects them to make significant contributions to review performance.

GENERIC DRUG APPLICATION ACTIONS

Question. You have advised the Committee that the OGD target is 1,900 actions for fiscal year 2009, including approvals, tentative approvals, not approvable, and approvable actions on applications. You have also said that your target approval time for the fastest 70 percent of original generic drug applications approved for the fiscal year 2003-2005 cohort is 17.8 months, an increase of 1.8 months from the fiscal year 2002-2004 cohort of 16.0 months. This, of course, is contrasted with the statutory review time of 6 months.

Will the new staff you have hired and trained affect these projected times?

Answer. OGD believes that it will make the goal of 1,900 actions in fiscal year 2009. The Office is on track to exceed the fiscal year 2008 goal of 1,780 actions. As recently hired staff becomes fully trained, OGD will be more confident in its ability to reach these goals. Current performance is based on many overtime hours.

The fiscal year 2003-2005 cohort approval time is 16.6 months. The cohorts for subsequent years are not sufficiently populated to make a determination. OGD does know that its yearly median time to approval has increased due to the escalating workload. OGD continues to endeavor to take first action (approval, not approval, or tentative approval) within the statutory timeframe but the volume of applications often thwarts OGD efforts.

As background regarding Abbreviated New Drug Application (ANDA) review times, the Food, Drug, and Cosmetic Act states in section 505(j)(5)(A), "Within 180 days of the initial receipt of an application under paragraph (2) . . . the Secretary shall approve or disapprove the application." Therefore, either an approval or not approval or similar action not resulting in approval is considered by FDA to be an action that meets this statutory timeframe. FDA makes every attempt to meet this statutory timeframe. However, for a number of reasons it is not always possible to do so. After receiving a disapproval action, manufacturers frequently resubmit applications that address the deficiencies identified in the disapproval action.

Question. Can you provide the Committee with information on the 30 percent of generic drug applications that are outside your "70 percent measure"? For example, could you provide us with information on the most speedily approved and the most delayed in approval ANDAs (e.g. how fast ANDAs outside the 70 percent cohort have been approved, and how long others have been delayed)?

Answer. Generally, the quickest ANDA approvals or tentative approvals have been applications submitted under the President's Emergency Plan for AIDS Relief (PEPPAR). Traditionally, the review of these applications is expedited.

In general, applications that take longer to review and approve are from less experienced manufacturers, cover highly complex products or dosage forms, or are related to products that are the subject of Citizen Petitions challenging FDA's approval requirements for the drugs. Applications can also take longer to approve if concerns are raised during facility inspections. For example, applications from one firm were on hold for about 2 years because the manufacturer had been unable to address inspection issues. These cases can delay a number of applications and affect the overall average time to approval. In addition, delays are often caused by the applicants themselves. For internal business reasons, firms may not place high priority on certain applications and may not respond to deficiency letters in a timely fashion. This can considerably delay approval time.

Also, please note that some applications may never be approved because the applicant cannot demonstrate to OGD that the proposed product meets all of the requirements for approval. It is important to understand that part of OGD's mission is fulfilled by preventing inferior, unsafe, and dangerous products from entering the market. Whether a product is approved and how quickly it is approved is

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controlled by both OGD and other supporting FDA organizations, and the applicants themselves. Poor submissions or inadequate proposed products can result in substantial delays to approval time or in a proposed product never being approved.

Question. How long have the oldest ANDAs which are still under review been pending before the FDA?

Answer. There are two unapproved applications for a product that were submitted 8 and 9 years ago. However, that product has a long and complicated regulatory history that has affected the review of the applications. The new applications were received about 4 years ago. Action on those applications has not occurred because FDA must consider issues raised in citizen petitions that relate to the approvability of the products.

Also, please note that some applications may never be approved, because the applicant cannot demonstrate to OGD that the proposed product meets all of the requirements for approval. It is important to understand that OGD's mission is fulfilled by preventing inferior, unsafe, and/or dangerous products from entering the market. Whether a product is approved and how quickly it is approved is controlled by both OGD (and other supporting FDA organizations) and the applicants themselves. Poor submissions and/or inadequate proposed products can result in substantial delays to approval time or a proposed product never being approved.

Let me now turn to one example of what appears to be an extremely long delay in approval of an Abbreviated New Drug Application that has been brought to my attention. We are aware that the agency has had under review for several years one or more ANDAs with respect to enoxaparin, a low molecular weight heparin, which, some scientists believe has a better safety profile.

Question. Given the recent heparin recall, without revealing any confidential information, could you outline the efforts the agency is making to approve generic substitutes on a priority basis, if any? Is the agency close to giving final approval to generic alternatives?

Answer. OGD has not approved an abbreviated application for enoxaparin. Therefore, the Office may not discuss the manner in which any review is handled nor may OGD indicate how close any potential approval might be. OGD will expedite the review of any new applications for heparin in an effort to alleviate a possible shortage situation. However, we cannot comment on the existence or status of pending applications.

Question. If a shortage of any drug becomes critical, what steps is the agency taking to make certain adequate alternative supplies are available to patients? Are generic alternatives included in these steps?

Answer. It has been the practice in OGD to expedite reviews of applications for products that may prevent or remedy potential shortages or in matters affecting the public health. This practice is reflected in a Manual for Policies and Procedures for OGD which states: "Certain applications identified at the time of submission for expedited review. These include products to respond to current and anticipated public health emergencies, products under special review programs such as the President's Emergency Plan for AIDS Relief (PEPFAR), products for which a nationwide shortage has been identified"

Questions Submitted by Senator Arlen Specter

GENERIC BIOEQUIVALENCE

Question. The FDA's Office of Generic Drugs has not provided a public process for the development of new bioequivalence methods for locally acting drugs. Bioequivalence is used to ensure that a generic drug will be equivalent to a brand name drug. FDA should not develop new scientific methods without transparency, or use those methods to review drug applications until the methods have undergone public and peer review.

In a May 1, 2007 policy statement, the FDA stated that the development of "methods for the assessment of bioequivalence of locally acting drugs" is an area where "additional discussion and collaboration about the science" are needed. The expected result of that statement would be an open public process when developing new bioequivalence methods for locally acting drugs. However, the approval process for Vancocin and Lidoderm continue to be developed without transparency.

Generic drugs are an important part of our healthcare system. Currently, over 60 percent of the prescriptions written in the United States are for generic drugs. Critical to ensuring the safety and effectiveness of generic drugs is the science used to establish bioequivalence of these generic drugs. I have spoken with you on a number of occasions regarding the need for a public process for development of new bioequivalence methods for locally acting drugs. Further, I have sent five letters regarding this issue. They were sent on: December 29, 2006, April 3, 2007, September 26, 2007, and March 28, 2009. On March 28, I sent two letters one regarding locally acting drugs the other specifically on Lidoderm.

Will you commit to developing a process that ensures public review of the data and rationale behind new bioequivalence methods for locally acting drugs before those new methods are used to review or approve generic products?

Answer. In response to your April 3, 2007 letter, FDA advised that notice-and-comment rulemaking is not necessary to ensure that the standards applied by FDA to the approval of generic vancomycin products are scientifically sound and have been thoroughly reviewed by appropriate medical and technical experts. Since the passage of the Hatch-Waxman amendments in 1984, FDA determined the bioequivalence criteria for hundreds of products without notice-and-comment rulemaking. These products included products to treat cancer, HIV/AIDS, and other serious diseases. Just as in assessing whether the sponsor of an innovator drug has submitted adequate studies to establish that its product is safe and effective, FDA relies on the most up-to-date and rigorous science available in assessing whether an Abbreviated New Drug Application, known as an ANDA, sponsor has submitted adequate evidence of bioequivalence.

FDA can obtain public input regarding applicable bioequivalence criteria through a number of mechanisms. Currently, whenever possible, FDA is making bioequivalence recommendations available to industry as guidance, to assist in the development of new generic products. The guidance is initially available in draft and public comment is invited. FDA develops guidance based on procedures set forth in regulations which establish Good Guidance Practices. As a general matter, these regulations provide for a process by which the public can comment on draft guidance and suggest alternative methods. FDA has also sought input from the Advisory Committee for Pharmaceutical Science on recommendations for bioequivalence studies for locally acting drugs related to the products you mentioned. We are considering holding an additional Advisory Committee meeting in the near future at which these issues will be examined. As we have stated in the past, we continue to consider your concerns as we address these scientific challenges.

PRE-EMPTION

In recent years, the FDA has made clear in final and proposed regulations, and in amicus briefs submitted to courts, the agency believes its decisions regarding approval of drugs, medical devices, and the labels on the drugs and devices pre-empt State law tort claims against manufacturers. On this basis, many courts are dismissing negligence and failure to warn claims against drug and device manufacturers if the FDA has approved the device, drug or label. Some argue that State tort claims are the only means for consumers to seek redress for injuries caused by insufficient warnings on drugs or malfunctioning devices.

Question. Given the FDA's unsatisfactory track record of making certain that drugs are safe and that consumers or physicians are warned of all possible consequences of taking drugs, how can you justify the FDA's recent attempts at asserting pre-emption of State tort claims? What is the harm in allowing the injured, or families of those who have died, from seeking redress based on State law?

If the courts continue relying on rules and regulations issued by the FDA and dismiss cases on pre-emption grounds, the FDA really needs

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to ensure that it is making the correct decisions. The American people will be counting on the FDA more than ever before.

Answer. FDA shares your concerns about drug safety and the ability of consumers to seek redress for injuries caused by drugs and devices. However, FDA is also concerned that State product liability lawsuits that challenge FDA's careful determination of safety, efficacy, and appropriate labeling can have detrimental effects on public health in a number of ways. Examples of detrimental effects include limiting patient and doctor choices, decreasing patient access to beneficial drugs, and creating confusion over warnings or statements that can deter the use of beneficial drugs.

It is vital to public health that labeling neither underwarns nor overwarns. The public health risks associated with overwarning can be as great as the health risks associated with underwarning. Overwarning can cause patients not to use beneficial medical products and doctors not to prescribe them. Underutilization of a product based on dissemination of scientifically unsubstantiated warnings, so as to deter patients from undertaking beneficial, possibly lifesaving treatment, could frustrate the purposes of Federal regulation as much as overutilization resulting from a failure to disclose a drug's scientifically demonstrable adverse effects. Further, allowing unsubstantiated warnings may also diminish the impact of valid warnings by creating an unnecessary distraction and making even valid warnings less credible.

In making these crucial balancing decisions, FDA abides by standards set forth in regulations and guidance documents that are issued through a public process. FDA is the scientific regulatory body that is publicly accountable for effectively executing its mission of protecting and promoting the public health. FDA believes that State court actions that undermine FDA decisions may have the consequence of serving to hinder, rather than help, public health.

Question. Does the FDA have the resources to adequately protect consumers of drugs and medical devices? Given the recent, highly publicized safety issues with drugs and medical devices, how can you assure the American people that the drugs they are prescribed are safe enough to justify pre-empting State law and denying access to the courts when people are injured or killed?

Answer. Congress has charged FDA with the responsibility to ensure that drugs, biologics, and devices are safe and effective, and that the labeling of these products adequately informs users of the risks and benefits of the products. FDA considers not only complex clinical issues related to the use of a product in study populations, but also practical public health issues about the use of a product in day-to-day clinical practice. FDA examines the nature of the disease or condition for which the product will be indicated, and the need for risk management measures to help assure that the product maintains a favorable benefit-risk balance. FDA believes, based on the authority that Congress has given it and the scientific expertise that resides in the Agency, that it is uniquely qualified to make important judgments about the safety, effectiveness, and labeling of medical products.

FDA extensively reviews drugs and devices for safety and efficacy using standards specified in the law. FDA doctors, chemists, statisticians, microbiologists, pharmacologists, and other experts evaluate whether a product is safe and effective. In addition to its comprehensive pre-market review of medical product safety and efficacy, FDA engages in post-market surveillance to detect and respond to emerging information about products after they have been on the market. Manufacturers must review and report to FDA any adverse events associated with use of a drug in humans, and must periodically submit any significant new information that may affect FDA's previous conclusions about the safety, effectiveness, or labeling of a drug. Device sponsors have similar obligations. FDA is currently modernizing its post-marketing surveillance and risk communication efforts through implementation of the Food and Drug Administration Amendments Act of 2007 and other major initiatives. FDA believes its teams of scientists are unsurpassed in ensuring that labeling meets patients' needs.

On September 27, 2007, the President signed the Food and Drug Administration Amendments Act into law, also known as FDAAA. FDAAA reauthorized two important user fee programs, the Prescription Drug User Fee Act, also known as PDUFA, and the Medical Device User Modernization Act, also known as MDUFMA. PDUFA and MDUFMA provide FDA with the resources to assure the safety and effectiveness of human drugs and medical devices. For fiscal year 2008, FDA will receive \$459.4 million in PDUFA fees and \$48.4 million in MDUFMA fees. These additional resources will help FDA to achieve its mission of assuring the safety and effectiveness of human drugs and medical devices.

CONCLUSION OF HEARINGS

Senator Kohl. This hearing is recessed.

[Whereupon, at 11:05 a.m., Tuesday, April 15, the hearings were concluded, and the subcommittee was recessed, to reconvene subject to the call of the Chair.]