S. HRG. 107–730

NOMINATION

HEARING

BEFORE THE

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS UNITED STATES SENATE

ONE HUNDRED SEVENTH CONGRESS

SECOND SESSION

ON

MARK McCLELLAN, OF THE DISTRICT OF COLUMBIA, TO BE COMMISSIONER OF FOOD AND DRUGS

OCTOBER 7, 2002

Printed for the use of the Committee on Health, Education, Labor, and Pensions

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C O N T E N T S

STATEMENTS

MONDAY, OCTOBER 7, 2002

ADDITIONAL MATERIAL

NOMINATION

MONDAY, OCTOBER 7, 2002

U.S. SENATE,
COMMITTEE HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The committee met, pursuant to notice, at 1:36 p.m., in room SD–430, Dirksen Senate Office Building, Senator Kennedy (chairman of the committee) presiding.

Present: Senators Kennedy, Bingaman, and Gregg.

OPENING STATEMENT OF SENATOR KENNEDY

The CHAIRMAN. We will come to order.

It is a privilege this morning to welcome the distinguished nominee to be the next Commissioner of Food and Drugs, Dr. Mark McClellan.

Let me also extend the committee's welcome to his wife, Stephanie, and to his brother, Scott.

Dr. McClellan has an impressive background. He is both an economist and a physician. He is a member of the President's Council of Economic Advisers and is also a major advisor on health policy to the President today. He was an associate professor of economics and medicine at Stanford University. He also served as deputy assistant secretary in the Department of Treasury. And, best of all, he received his medical degree, his doctorate in economics, and his master's degree in public health at Harvard and MIT.

This nomination to a major public health position is long overdue. The question before the committee today is whether Dr. McClellan has the training, experience, and independence to serve as head of the country's most important public health regulatory agency—an agency that serves as the gold standard for the rest of the world.

FDA's mission is to protect the public health. Its mission affects more than a quarter of every dollar spent in the U.S. economy. The products that it regulates—food, drugs, biologics, devices, supplements, and cosmetics—affect public health and safety every day.

The agency also has a long and distinguished history of serving the public interest. It has a proud tradition of promoting the public interest ahead of special interests. It is an agency of skilled professionals who set high standards and demand excellence from the industries it regulates.

Questions have arisen lately about the FDA's willingness to maintain this mission, this history, and this tradition. We have heard that agency morale has suffered in the absence of a commissioner and in the aftermath of a series of recent FDA decisions that

suggest a less exacting, less rigorous approach by the agency in carrying out its mission.

The issue is leadership. In this time of extraordinary medical breakthroughs, as new threats to public health arise, the FDA faces enormous challenges. The American people increasingly depend on the FDA to safeguard public health. Now is not the time for the FDA to retreat from these challenges or surrender its authority over public health.

Dr. McClellan has been nominated to a position of great responsibility. I welcome him here to our committee and look forward to his testimony on these very important issues.

Senator Gregg?

OPENING STATEMENT OF SENATOR GREGG

Senator GREGG. Mr. Chairman, thank you for scheduling this hearing so promptly. It is a pleasure to have Dr. McClellan be the nominee and be before the committee.

The FDA mission is to promote and protect the public health by regulating the safety of food, drugs, cosmetics, and medical devices. The FDA regulates or approves about 25 percent of all consumer products in the United States and as a result is a very high-profile agency with broad and diverse responsibility.

That said, the role of the FDA Commissioner is of vital importance to the public health and, as with any organization, it is less than optimal to have a vacancy at the top of the organization.

Dr. Crawford has done an excellent job since taking on the role of deputy commissioner of the FDA this past year. However, the FDA faces a number of difficult and daunting tasks in the years ahead, and I think everyone will be better served once the FDA has a permanent commissioner at its helm.

Obviously, Dr. McClellan has a tremendous resume—Harvard trained, which is a major plus—even if you come from New Hampshire, we consider that a plus——

The CHAIRMAN. Thank you.

Senator GREGG [continuing]. His experience as a physician as Stanford, his experience as an economist, his experience in the area of health policy have all been exemplary and really extraordinary.

The FDA has a large portfolio, as I have mentioned, but there are a number of issues which we have to address with the FDA today that I think continue to make the issue of how we manage the FDA significant.

First is the corporate culture at the FDA, or the agency culture. Unfortunately, there has been a fair amount of bureaucratic less than effectiveness there that has really increased the amount of time it has taken to get new treatments out.

We also had significant erosion in the staff base as people have moved out of the agency, and that has caused a significant problem with having the technology and the knowledge base within the agency to approve drugs quickly.

The FDA's approval time for new treatments has actually increased in the past year as many of these senior regulators have left the FDA.

We have a big issue in the area of devices, where we need to put in place a user fee model such as we have in the drug approval

area, and I understand the House is going to move on that language this week, and it is something that Senator Kennedy and I have worked hard on, and I hope we can move on it before we adjourn.

Also, the FDA now takes on a major new responsibility in the area of bioterrorism and specifically, for example, in the area of approval of drugs to fight bioterrorist attacks, the most significant example being how we fast-track the approval of a smallpox vaccination so that our population will have that available to them.

And then, of course, the decision to move the biotechnology drugs from the biologics division to the drugs division is obviously going to be a complex process but one which will hopefully, if properly implemented, improve the overall administration of the agency.

So the FDA has many things on its plate. Another thing I should add is the protection of the food supply which has become a major concern in regard to the terrorism issue. So you have a lot of portfolio here to handle, Dr. McClellan, but we look forward to your doing it, and we appreciate your willingness to undertake this kind of task.

The CHAIRMAN. Dr. McClellan, I want to extend the regrets of Senator Frist, who is not here today. He is attending the funeral of a friend. He extends his apologies to you, and his statement will be made a part of the record.

[The prepared statement of Senators Kennedy and Frist follow:]

PREPARED STATEMENT OF SENATOR KENNEDY

It's a privilege this morning to welcome the distinguished nominee to be the next Commissioner of Food and Drugs, Dr. Mark McClellan.

Let me also extend the Committee's welcome to his wife, Stephanie, and his brother Scott.

Dr. McClellan has an impressive background. He's both an economist and a physician. He is a member of the President's Council of Economic Advisers and he's also a major advisor on health policy to the President today. He was an associate professor of economics and medicine at Stanford University. He also served as deputy assistant secretary in the Department of Treasury. And, best of all, he received his medical degree, his doctorate in economics, and his master's degree in public health at Harvard and MIT.

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The issue is leadership. In this time of extraordinary medical breakthroughs and as new threats to public health arise, the FDA faces enormous challenges. The American people increasingly depend on the FDA to safeguard public health. Now is not the time for FDA to retreat from these challenges, or surrender its authority over public health.

Dr. McClellan has been nominated to a position of great responsibility. I welcome him this morning, and look forward to his testimony on these very important issues.

PREPARED STATEMENT OF SENATOR FRIST

I would have liked to have joined my colleagues at this hearing, but I remain in Tennessee to attend a funeral. Still, I welcome Dr. Mark McClellan before the Committee this afternoon.

Dr. McClellan is not a stranger to the members of the Health, Education, Labor, and Pensions (HELP) Committee. During his service on the Council of Economic Advisors, many of us have benefitted from his expertise, clear-headed analysis, and sound advice concerning health policy matters.

Dr. McClellan has served the President well. And I know that he will continue to serve the nation well as the next Commissioner of the Food and Drug Administration.

Mark McClellan is an excellent choice to lead the FDA. He is a talented academician and economist who has helped challenge conventional thinking about important health policy matters through groundbreaking research. He is a gifted health policy analyst who has worked to improve the nation's health care system for all Americans. Perhaps most importantly, he is also a physician who has cared for patients and knows first-hand that there are few greater callings than helping to heal one's fellow man.

Mark McClellan is uniquely qualified to lead this important agency at this critical time.

I want to thank Dr. Lester Crawford for the work he has done to provide a steady hand during these past several months as Acting Commissioner. I know he will continue to provide leadership and guidance during the upcoming transition and beyond.

At the same time, I am pleased that the FDA will soon have a Commissioner confirmed by the United States Senate.

The challenges confronting the next Commissioner of the FDA are great perhaps greater than at any other time in our nation's recent history.

Of course, the FDA has an important, ongoing role to play in ensuring the safety and efficacy of drugs, biologics, food, cosmetics, blood products, and devices goods and products accounting for nearly one quarter of all consumer spending in the United States. But the FDA Commissioner must be more than simply the head of a large, regulatory government agency. He must also provide

strong leadership on a broad range of critical health policy issues that directly affect the lives and well-being of every American.

I'd like to highlight some of the issues on which it is critical that the FDA Commissioner provide leadership, at this time.

The most significant issue we faced over the past year is terrorism. On September 11th we endured the most horrendous attack on American soil since Pearl Harbor. This week, we mark the one year anniversary of the worst attack of biological terrorism in this country. We cannot know when, where, or in what form the next attack will happen, but we must be prepared. This includes speeding the review and approval of rapid assays, vaccines, and other necessary bioterrorism countermeasures. Numerous scientists and research facilities are working to meet the call of the President and Congress to protect our homeland from outside threats. The FDA must help fashion an environment in which these discussions are encouraged and translated to medical practice.

At the same time, we cannot ignore naturally emerging threats to the safety and sustainability of our blood, tissue and organ supply. Last week, it was reported that 40 people were exposed to Hepatitis C from a single organ and tissue donor and Salmonella was transmitted through blood transfusions. This is in addition to the growing body of knowledge we are amassing on West Nile Virus. Considered together with the existing shortage of blood, tissue and organ donors, the need to speed the development of new screening and purification products clearly illustrated.

Finally, I would like to highlight the importance of promoting a regulatory environment that values innovations to improve patient care and consumer safety, while at the same time safeguarding the public health. But this must be done without contributing unnecessarily to overall rising health care costs or allowing basic medical treatments to be forgotten. We presently face just this situation with our nation's vaccine supply. Currently, only four manufacturers produce vaccines and they face the multiple challenges of a growing litigation crisis and changes in the FDA's regulatory oversight. While most of the recent childhood vaccine shortages have been alleviated, our system remains vulnerable to future shortages if we fail to act.

Mark has my full support. I look forward not only to reviewing his testimony from this afternoon as to what his goals and priorities will be for leading the FDA, but also to continuing to work with him to improve the quality of health care for all Americans.

Before we begin I have a statement from Senator Jeffords

[The prepared statement of Senator Jeffords follows:]

PREPARED STATEMENT OF SENATOR JEFFORDS

Mr. Chairman, I want to commend you for the deliberate speed with which you are moving on the confirmation of Dr. McClellan as the Commissioner of the Food and Drug Administration. I have looked over his record and I am looking forward to hearing his statement and reviewing his responses to the questions he is asked today. Although the Administration has taken undue time in nominating someone for this important office. I think it too should be commended for nominating someone with the credentials and experience that Dr. McClellan brings.

Dr. McClellan has earned a respected and widespread reputation across many disciplines in the arena of health sciences and health policy. He has served important roles as an appointee during President Clinton's administration and has continued his commitment to better health police during this Administration as a key advisor on the Presidents Council of Economic Advisors. As physician and as an economist. I think Dr. McClellan can bring an important expertise to the FDA.

The Commissioner of the Food and Drug Administration serves one of the most important roles in our federal government, a role that is vital to maintaining and improving the health and well-being of all Americans. So it is even more important that we have someone with the experience and vision necessary to guide the agency.

During my tenure as Chairman of this committee. I together with Senator Kennedy, had the opportunity to work in close collaboration with previous leaders of the FDA including Dr. David Kessler and Dr. Jane Henney. They worked closely with us as we sought ways to strengthen and modernize the agency. Together we were able to enact the Food and Drug Administration Modernization Act (FDAMA), a law that in part, sought to establish a new culture at the FDA. Through enactment of FDAMA we recognized that the FDA has a greater role to play beyond protecting the American public from unsafe foods and medicines; it also could enhance the public's health by fostering innovation in the medical sciences. It's my hope that as Commissioner, you will continue to uphold FDA's gold standard for safety and efficacy while exploring more ways to expedite products to the market for other serious and life-threatening diseases.

Dr. McClellan, I'm certain that you appreciate the importance of the advances in biomedical research and how they have significantly improved the lives of the American people. While these improvements have not come Without cost, it appears the benefits more than compensate for the increased costs. One recent study concluded that the improvements in survival after a heart attack show that the money spent on innovative drugs and devices was well spent. Advances in cholesterol-lowering drugs, and drugs to treat depression and AIDS also have made significant improvements in quality and quantity of life.

These significant improvements will be all the more important as our population ages and an ever-increasing cohort of Americans become eligible for Medicare. As new treatments for diseases associated with gain" for example Alzheimer's Disease, become more available, will need a commitment from FDA to move these expeditiously through the FDA regulatory pipeline. There have been incredible inroads against diseases of the aged but more needs to be done to get these new treatments approved and to the patients that need them. While there are likely legitimate concerns about the overall cost of prescription drugs. it has been shown again and again that these treatments help reduce or avoid the much higher costs associated with surgeries and inpatient hospital care.

Finally, on the issue of the cost of medicine. I would urge that you look to what processes can be put in place that would provide FDA with the assurance that drugs imported from Canada are safe

and effective for personal use. Companies that manufacture medicines in foreign countries, but that are destined for U.S. consumers, voluntarily allow FDA to inspect its foreign facilities. This is the cost of doing business.

I would hope that you might explore a similar approach for inspecting Canadian pharmacies and drug distributors so that they too might be approved for reimporting medicines into the United States.

Dr. McClellan, thank you for appearing before our Committee today. You are about to engage in one of the most challenging positions in Washington. I'm confident that you will give it your best effort and will do it successfully.

The CHAIRMAN. Dr. McClellan.

TESTIMONY OF MARK McCLELLAN, TO BE COMMISSIONER OF FOOD AND DRUGS, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. MCCLELLAN. Mr. Chairman, Senator Gregg, I want to thank you for your distinguished committee's consideration of my nomination as Commissioner of Food and Drugs.

In my current job and in previous jobs in government and in academics, I have appreciated the opportunity to work with you on a range of health care issues. In the short time since my nomination was announced, I particularly appreciated the time that you have made and that other members of this committee have made to talk with me about critical FDA concerns. It has been a sobering and exhilarating dialogue and one that I look forward to continuing with all of you.

I especially want to thank my wife, Stephanie. If not for her endless hard work and countless sacrifices to get us here, we really would not be here today.

I have come to appreciate through this process more clearly than ever that the professional FDA staff have unique and extremely challenging responsibilities. As new biomedical breakthroughs lead to the development of more diverse, more complex, individualized medical treatments, FDA will face new challenges in assuring their safety and effectiveness without necessarily restricting their access or adding to their costs.

The 21st century has also witnessed a new era of terrorist threats to our Nation's security, and FDA has critical responsibilities here as well. We must take new steps to keep our foods and other consumer products secure by developing new capabilities to prevent, detect, and respond to threats to these products, which are among the safest in the world.

The challenges of transparent and responsive regulation have also never been greater. Consumers are more interested than ever in steps they can take to avoid health risks and to lead healthier lives; yet patients and physicians are often overwhelmed by the volume of information available on medical treatments, and they need help in sorting out reliable, accurate information that they can use. And all of those affected by FDA regulations need clear, predictable, and sensible guidance.

Consequently, the challenges and rewards of working at FDA have never been greater. The need has never been greater for fa-

miliarity with cutting-edge techniques of risk analysis, for clear understanding of increasingly sophisticated food and health sciences, for taking advantage of increasingly rich health information systems, and for supporting the capacity to make informed and timely regulatory decisions.

It is an honor to have the opportunity to help the FDA meet these critical responsibilities as well as many others. But it is a special privilege to be able to do so at a time when Congress and the President, as a result of the bipartisan leadership of this committee, have recently enacted legislation to provide the most significant new resources and tools to fulfill these responsibilities in more than a generation.

It is my hope that the Senate will be able to complete this year's impressive legislative achievements for supporting FDA in meeting the challenges ahead by enacting the Medical Device User Fee and Modernization Act and the Animal Drugs User Fee Act. I understand that the House intends to pass a bipartisan agreement on H.R. 3580 shortly, as Senator Gregg mentioned. The administration strongly supports action this year to resolve the remaining issues in these bills.

If confirmed, my greatest privilege will be to become part of the FDA's main asset—the almost 10,000 professional staff who make it possible every day for over 280 million Americans to have confidence in the foods that they eat, the personal products they use, and the medical treatments that improve their lives.

In recent years, FDA has taken many steps to help make sure that its professional staff have the work environment needed to fulfill these critical responsibilities. But with the new challenges facing the agency, the need to fill literally hundreds of new professional positions as well as to plan for the reality that one-third of the FDA work force will be eligible for retirement as soon as 5 years from now, enhancing the FDA work environment must be a top priority of the Commissioner. There is no element more critical to effective regulation than the FDA work force itself.

In the time since my nomination has been under consideration, I have had the opportunity to talk with some of the FDA professionals as well as FDA veterans, and I look forward to spending a lot more time with them. I am especially grateful to Deputy Commissioner Les Crawford who, as Senator Gregg has mentioned, has done a terrific job so far in managing issues at FDA. Les not only has tremendous FDA experience and expertise; he is also a very effective manager and a friend. I am extremely lucky to have the opportunity to work with him to lead the FDA.

In closing, I wanted to make a couple of promises. First, if confirmed as commissioner, I pledge to listen. Transparency and responsiveness start with the interactions between the commissioner's office and Congress. You should always get clear explanations from me and my staff and a fair and complete hearing of your point of view.

Second, I will make decisions that you will not always agree with. My grandfather, Page Keeton, used to say, "If you haven't made anybody mad, you haven't done anything." I think the lessons he taught me from his experience as a law school dean and an academic expert who often got involved in difficult public policy

issues will be extremely helpful for the pace, the complexity, and the sensitivity of many of the issues facing FDA.

By listening to the points of view of all involved and by ensuring that sound science, careful empirical analysis, and ethical integrity are the foundation for FDA's decisions, I hope to make it possible for us to work together effectively to meet the challenges ahead.

My mother, who has dabbled in politics herself, likes to say, "It is not the dollars you make, it is the difference you make." The 21st century FDA combines a long tradition of excellence in protecting and improving the public health, technical and scientific expertise, and strong bipartisan support for strengthening its ability to carry out its many critical responsibilities. It is a great place to make a positive difference in the lives of all Americans.

I want to thank the committee again for considering my nomination to serve in this important role, and I am happy to take any questions you may have.

The CHAIRMAN. Thank you very much.

We will have 10-minute rounds, and I will ask staff to watch the time.

Dr. McClellan, there have been some disturbing signs that FDA may be backing away from its current authority or that it is not committed to enforcing the legal requirements. A May Federal Register Notice on the First Amendment invited regulated industries to identify regulations that should be eliminated or modified, and this notice has led to industry calls to weaken product warnings.

Today the FDA requires specific warnings on all drugs and devices, including the warning against childhood poisoning on iron supplements, and multivitamins with iron. Iron is the leading cause of poisoning deaths in children under the age of 6.

There are hundreds and thousands of such accidents every year. Do we really want to leave these warnings to the marketplace?

The agency wants to reclassify colored contact lenses as cosmetics, which would leave them basically unregulated even though they pose the same health risks as other contact lenses. These are contact lenses that can cause eye infection, severe pain, and even blindness. A Cleveland teenager, Roby Rouse, was left nearly blind in one eye because of colored contact lenses. Roby has had a corneal transplant, but her doctor says it is too soon to say that she will fully recover.

And The Wall Street Journal reported recently that the number of warning letters from the agency to industry has dropped by well over half after a new requirement that the chief counsel's office review them.

So the question really is about your commitment to using and preserving the full authority of the FDA to ensure the safety and effectiveness of the products it regulates.

Dr. MCCLELLAN. Senator Kennedy, as you noted in your opening remarks, the FDA plays an essential role in American society. It is critical to assuring the public that the treatments, the products, and related issues are safe and effective.

I do not see any intent to move away from the FDA's emphasis on safe and effective treatments being available, safe and effective products. The FDA has a critical role as well in making sure that any health claims made about products are truthful and not mis-

leading. This is, as you pointed out, the core of the FDA's mission, and we need to and I would intend to make sure that that mission is fulfilled.

As we go into the 21st century, and as I mentioned in my opening remarks and you did as well, there are new challenges facing FDA. That means we may need to take a fresh look at how some of these issues are approached. But I think that by applying careful science, including good state-of-the-art risk management techniques, better use of available information to identify risks when they do occur, and hopefully, a collaborative environment between FDA and this Congress in approaching these tasks, we will be able to meet all of those responsibilities.

The CHAIRMAN. So I gather from your response that in any kind of challenge in the courts, you will come out firmly in support of FDA authority.

Dr. MCCLELLAN. Well, I think the FDA's statutory responsibilities from the Food, Drug, and Cosmetic Act are critical to its ability to carry out these functions.

I am concerned that in some recent court cases—Western States is one example—the U.S. Supreme Court has ruled that FDA may have gone in the wrong direction or overstepped some of the statutory or constitutional authorities in carrying out its mandates. That was true in Western States, it was true in a Brown and Williamson decision for tobacco regulation.

I think this goes to the issue that I talked about earlier, that as we learn more from the U.S. Supreme Court and as the challenges facing the FDA evolve, the activities of the FDA need to evolve with it. But that does not mean retreating from the agency's critical mission of making sure that foods are safe and making sure that medical treatments are safe and effective.

The CHAIRMAN. For more than 40 years, the FDA has exercised authority to specify the language of warnings on products, both foods and drugs. Is there any reason that you would take a position to the contrary?

Dr. MCCLELLAN. A key part of the FDA's authority involves regulation of labeling. Regulation of labeling requires that the statements made about the product are truthful and not misleading and that information on warnings are conveyed. I think the question is often in practice for the specific products at stake, how do you convey those kinds of warnings and that information most effectively, and that is where I think a lot of science can come in, both science about the products, science about how the public understands and interprets information on labels and how to make it used most effectively. That is exactly the kind of thing that is an important challenge for the FDA in the years ahead.

The CHAIRMAN. There is a tension between the producer wanting to maximize sales, yet the FDA wanting to minimize risk. So there is a tension involved in the development of mere guidelines for warnings. Are you saying that, although you will consider the best science that is available, you will come down squarely to support safety for consumers and information for consumers.

Dr. MCCLELLAN. The FDA has a critical role to play in making sure that treatments available are safe and effective, and I would come down squarely on the side of defending the FDA's ability to

maintain safe and effective treatments, and also in terms of labeling, to make sure that any kind of health claims are truthful and not misleading.

The CHAIRMAN. Do you believe there is a problem with requiring specific words for warning, and do you share my concern that a company may try to minimize the risk to consumers by artfully wording the warning?

The point I am getting at is, do you agree that there is a value to having the same warning on each product so that consumers will not be confused by differently worded warnings that may be interpreted by consumers to mean that products present different relative risks?

Dr. MCCLELLAN. Well, I think it is certainly critical for the FDA to pay attention to ways to make sure information can be communicated clearly and effectively to consumers. As you know, with the diversity of products on the market, it is very hard to come up with a comprehensive label or set of labels that is applicable to each and every product. You may end up with a laundry list of 50 or 100 specific warnings, most of which may not be particularly relevant to an individual product and which may deter the consumer from focusing on the information that is most relevant to him or her.

So I do believe that the FDA has an important role to play in making sure that information about warnings and health risks is communicated. I am not sure that I can make a general statement about one particular label for the whole diversity of products out there.

The CHAIRMAN. On the issue of off-label use, do you agree with me that while off-label use can be beneficial, it also has great potential to harm the public? For example, the off-label use of some drugs like fen-phen, or the anti-arrhythmic drug Encainide or Flecainide, has caused, as I understand it severe injury or death to thousands of consumers.

Dr. MCCLELLAN. There certainly are examples of off-label uses of drugs leading to adverse impacts on patients. Encainide is one example, fen-phen as well. I think that FDA can do a lot to monitor whether or not drugs in actual practice are causing safety problems and are putting consumers at risk and putting patients at risk.

The CHAIRMAN. As I understand it, when Encainide and Flecainide were used for this off-label use, studies were finally done that confirmed that actually, the drugs caused severe heart ailments. The studies estimated that hundreds if not thousands of patients actually died because of off-label use.

Do you believe that this toll on public health from off-label use justifies FDA requirements that drugs promoted for these uses must be shown to be safe and effective for them?

Dr. MCCLELLAN. I think the FDA does have a substantial amount of authority to work with manufacturers to try to develop better evidence on off-label use. As you well know, Mr. Chairman, the whole Phase IV process in the FDA drug approval process is geared to understanding risks of treatments that are proved in actual practice.

FDA does not regulate as a general matter the practice of medicine, but often has collected or worked with manufacturers to collect more information about off-label use. And as you also know

from the legislation on prescription drug user fees that was recently reauthorized this year, there are some additional provisions related to expanding and increasing FDA's activity in postmarketing monitoring. And I certainly look forward to working with you and the committee in the months ahead to implement those provisions and to find ways to identify safety problems with off-label use as quickly as possible when they do occur.

The CHAIRMAN. The amount of resources and attention to safety it increased very, very significantly in the user fee bill, and this is something that we want to ensure is utilized and utilized effectively.

In 1997, the Congress passed a bipartisan compromise that allows companies to provide off-label information under tightly controlled circumstances if certain conditions are met, most importantly, if the company has completed or commits to completing clinical studies to verify the use.

Will you support and enforce that law?

Dr. MCCLELLAN. Well, the provisions that you are referring to in the FDA Modernization Act as I understand it have been interpreted by FDA to comprise a safe harbor. So a company that is engaged in some kind of promotion of off-label use that also explains a clear plan for providing evidence, Phase IV type evidence, on off-label use, is permitted to go ahead and do so.

As a more general matter, it is clear from the fact that the Prescription Drug User Fee Act included additional provisions related to off-label use and Phase IV testing and postmarket surveillance that more can be done to ensure that we are developing the most accurate information about off-label use and that manufacturers are not promoting that information incorrectly.

I would like to go back to one of the clear themes that I hope will be a hallmark, if I am confirmed, of my work as commissioner, and that is that the FDA is in the business of making sure that information provided about new products is truthful and not misleading. And while there are some gray areas involving some aspects of postmarket surveillance, I think we have the potential to do a lot better in dealing with off-label use, thanks to the legislation that you have passed and thanks to our willingness to try to work together to get better information out about the safety of off-label uses.

The CHAIRMAN. Senator Gregg?

Senator GREGG. Thank you, Mr. Chairman.

The biggest issue would be FDA's approval time and the balance between making sure that the medication or the drug is appropriate and works the way it is supposed to work and getting it out there fast enough so it saves people who need it. We have all heard the horror stories of people who might have been saved by it if the drug had gotten out.

I guess my question to you is how do you see that struggle and how do you see the FDA expediting approval time without undermining the purpose of protecting the public?

Dr. MCCLELLAN. I agree with you, Senator, that giving Americans quick access to safe and effective new treatments is one of the most critical roles at the FDA. There are a lot of statistics cited about approval times and the like.

I think one thing that is clear from those statistics is that FDA has done better over the past decade as a result of the Prescription Drug User Fee Act, and so the reauthorization of that Act with some additional provisions to improve the way that the drug approval process can function at FDA I think will be a welcome help in doing both—achieving the goal of making sure the treatments are safe before they are approved and making sure that they can be provided quickly to the American pubic.

I hope to work closely with staff at FDA on finding ways to improve the process, and I want to go back to something that both you and Chairman Kennedy mentioned at the outset here, which is that it is very important for FDA to have some leadership to help bring this priority home.

Dr. Crawford has done a terrific job of identifying ways to help FDA management work more effectively, and I hope to build on that work as soon as I get out there. This is definitely going to be one of my top goals. And again, I do not think there needs to be a conflict between addressing safety concerns and managing risks appropriately and approving drugs quickly. I think we will have new resources thanks to the legislation that you all enacted to deal with drug approvals more quickly, and I hope to work with you all in the months and years ahead if confirmed to see that that happens.

Senator GREGG. And the same would apply to devices?

Dr. MCCLELLAN. And the same thing applies to devices. And there, as you know, Senator, I think the most important next step that could happen to speed the device approval process is action this year by Congress on medical device user fees and the Medical Device Modernization Act.

We hope that that legislation, as you said at the outset, will pass this Congress and will be enacted into law. This is the right time for us to move forward on this. We have an opportunity to take a new look at as a result of the Prescription Drug User Fee legislation which is speeding and improving the safe approval of effective new drug treatments. This would also be a great time to improve the ability for the FDA Center for Devices and Radiologic Health to work more quickly and effectively as well.

Senator GREGG. How do you see the FDA relating to the international community, especially the European community, in the process, where you are seeing especially in the device area the Europeans moving much faster than we are?

Dr. MCCLELLAN. I think there is a lot that we can learn from the European processes. The FDA has tried to take some steps, as I understand it, in recent years to be clear about when information from drug trials conducted in other countries can be used. There are some important concerns there about making sure that the requisite human subjects protections apply, that the studies are well-designed and well-executed and so forth, and I think that is a good example of where leadership in identifying opportunities for harmonizing clinical trial requirements and the like where we do not sacrifice the importance in this country of making sure that drugs are safe and effective and meet minimum standards, but where we can potentially move more quickly to get drugs approved by working more synchronously with other countries.

Senator GREGG. I am interested in your thoughts on direct-to-consumer advertising.

Dr. MCCLELLAN. Is that just the general thoughts, or——

Senator GREGG. Your thoughts.

Dr. MCCLELLAN. I think direct-to-consumer advertising—the FDA has looked at this recently as well, and FDA, like many independent experts, has noted some significant advantages from direct-to-consumer advertising for treatment of conditions that are seriously undertreated in the U.S. population, resulting in needless reductions in quality of life and even more frequent deaths. Good examples of conditions where direct-to-consumer advertising has led to more treatment of patients who were previously undertreated include high blood pressure and depression.

So direct-to-consumer advertising is clearly playing an important role in helping patients find out about treatments that can be effective for them. At the same time, the FDA does have a critical role in making sure that any kind of advertising is truthful and not misleading, and I think the FDA will continue to make sure that those kinds of conditions are met while encouraging the use of appropriate direct-to-consumer advertising.

Senator GREGG. Well, if a drug works—and it would not be on the market unless it worked—why should it have to be advertised, when that is just going to add to the cost?

Dr. MCCLELLAN. It is a good question, but very often, many patients are not familiar with the treatments that are available for their conditions. Many physicians in advertising to physicians may learn something about the new treatments available for them to use as well.

What is important from the FDA's standpoint is that the information provided to help inform patients and medical professionals about the value of new treatment is truthful and not misleading.

Senator GREGG. What about the issue of using outside experts in the evaluation process? How much more aggressive should we be on that?

Dr. MCCLELLAN. Well, my understanding is that the FDA has actually had some good experience to date in using third parties for independent, careful scientific review of new products. And I know that that is an issue that is currently under consideration in the medical device legislation.

My impression is that to date that program has been quite successful, so it seems like expanding that program in a limited way as part of the medical device legislation could be a useful step forward.

Senator GREGG. Thank you.

The CHAIRMAN. If I could, isn't one of the reasons that direct-to-consumer advertising be accurate is because advertising can raise false hopes among the public, and can create enormous demand for certain products, and can even lead to the use of products that might not be safe? Direct-to-consumer advertising for drug products has increased dramatically, hasn't it?

Dr. MCCLELLAN. Yes, sir. There is a lot of television and radio advertising for drugs. I think something like 80 drugs are the subject of significant advertising today. Again that goes to the point of making truthful information, accurate information, more widely

available to Americans can be a huge help in assisting them in finding ways to treat conditions that they previously may have been suffering through, like depression, diabetes, and the like.

So I think that that goes to the importance of direct-to-consumer advertising but also the importance of FDA's role in making sure that such advertising is truthful and not misleading.

Senator GREGG. In working up that formula as to how you address this, I hope you will also put into that formula how much the consumer pays to resolve the issue of the cost of the advertising.

Dr. MCCLELLAN. That is right. That is part of the calculus. The FDA I do not think has a whole lot of authority to think about the cost implications of direct-to-consumer advertising. I think the main focus of the FDA statutory authority is on truthful, not misleading, advertising. But certainly within that rubric, the major benefits, the major risks of advertising should be brought out, so if there are any significant complications associated with the new treatment, that is something that the public deserves to know about as well as its potential benefits. Those complications can also lead to added costs, too.

The CHAIRMAN. Senator Bingaman?

Senator BINGAMAN. Thank you, Mr. Chairman.

I would like to, Dr. McClellan, ask you a couple of questions in your current capacity and then move to a couple of questions related to the position for which you have been nominated.

As a physician, I am sure you are aware that the College of Obstetricians and Gynecologists and the American Academy of Pediatrics have firm positions that a pregnant woman and an unborn child need to be treated together. And the administration has come out with its new regulations just the other day related to coverage for an unborn child under the CHIP program, but as I understand the position the administration took, it felt that the statute did not allow coverage of pregnant women as part of that.

We have a bill that has been introduced—Senator Bond is a prime sponsor on it—to correct this problem, and it is S. 724, which is "The Mothers and Newborns Health Insurance Act." We tried to get permission to raise that and pass it last week. It came out of the Finance Committee unanimously, and we are trying to pass it through the floor.

Senator Nickles objected on the basis that he believed the administration opposed the legislation. Are you familiar with what the administration's position is on this legislation, and if it is something that is opposed, what reason would be offered?

Dr. MCCLELLAN. Senator Bingaman, let me start by thanking you on behalf of the administration now in the capacity of my current job for the work that you have done for quite some time now to further the interests of the health of pregnant women and their unborn children and, after birth, the young children as well.

The administration completely shares that goal, and we too believe that effective treatment of an unborn child during pregnancy is critical. There is overwhelming evidence that that leads to better birth outcomes and better long-term outcomes for the child.

We know also that there had been a somewhat long-term legislative effort to try to pass legislation like S. 724, your bill—I know that that is something that you have been working on for quite

some time—and the fact that such legislation had not occurred was one of the primary factors that led to the regulatory initiative that Secretary Thompson had announced earlier this year and in turn, it was announced as a final rule last month on coverage for unborn children.

As I think Secretary Thompson has made clear in his comments about that new rule, that rule does provide States with the authority that they need to provide coverage for preventive care during pregnancy and other associated services related to the unborn child.

Because of interpretations of the SCHIP law that this administration has already undertaken, it is already possible for States that wish to enact waivers to do so to cover pregnant women as well.

So I think the administration's position is that we strongly agree with your goal; our concerns about this not being enacted in legislation sooner was what led to HHS' promulgation of a proposed rule to provide coverage for unborn children. That rule is now final, so unborn children can get preventive care, pregnant women can be covered, and States if they wish to do so can also cover infants after birth through CHIP.

So I think we have tried to do the best we can within current law in the face of no action on this issue by Congress in the last couple of years to achieve your goal. And I think our main focus at this point is on seeing if we can go further in the very limited time that remains to do more for providing appropriate coverage. We have a number of initiatives on lowering health care costs and increasing health insurance coverage that we would like to see acted upon before the session ends, and that is where our main focus is right now.

Senator BINGAMAN. But your view is that this coverage of pregnant women under CHIP, that option is already there for States?

Dr. MCCLELLAN. As a result of the final rule that was promulgated by HHS last month, yes.

Senator BINGAMAN. Let me ask about the effort that both the chairman and ranking member of the Senate Finance Committee are making to pass bipartisan legislation entitled "Beneficiary Access to Care and Medicare Equity Act of 2002." This is the legislation that tries to maintain reimbursement levels for some of the providers as well as maintain access. What is the administration's position on that? Do you support that effort or not?

Dr. MCCLELLAN. Well, our first priority on Medicare legislation is improvements in Medicare benefits. Senator Bingaman, as you know, Medicare coverage has become seriously outdated since its enactment over 30 years ago. Even though private plans started covering prescription drugs back in the sixties, Medicare still does not do so.

The administration has had a lot to say about the adequacy of provider payments and various components of Medicare, and I think that our staff would be happy to provide you with some of that information from CMMS, the Center for Medicare and Medicaid Services, if that would be helpful. And no question that very complex administered price systems in Medicare do not function efficiently in making accurate payments to all Medicare providers.

But the President's priority for Medicare this year has been and remains improving benefits for seniors, and we appreciate the efforts by Chairman Kennedy and by members on both sides of the aisle to try to enact legislation to do that, and I think that that is where our focus still remains.

One of the unfortunate side effects of legislation that only or primarily increases provider payments in Medicare is that it also increases beneficiary premiums and beneficiary copayments. So, for example, in the recent proposal agreed to by Chairman Baucus and Senator Grassley, while that bill provided something like $48 billion in additional payments to providers to address some of the concerns that you mention, it also added on something like $13 billion in additional payments in terms of premiums and copayments for beneficiaries, and that is just not the administration's first priority. The administration's first priority is taking steps to make health care more affordable and more accessible for seniors starting with prescription drugs but extending to more affordable health insurance options across the board, and that remains our first priority for new spending.

Senator BINGAMAN. So the bottom line would be that you would not at this time support the Baucus-Grassley proposal.

Dr. MCCLELLAN. Our bottom line at this time is that we would still hope that the Senate can find a way to provide prescription drug coverage and other benefit improvements in Medicare. That is our first priority, and I believe, as I have said on previous occasions, where there is a will, there is a way, and we hope that the Senate leadership can find a way to improve Medicare benefits, that it is overdue and desperately needed by America's seniors.

Senator BINGAMAN. Chairman Kennedy just asked a little while ago about FDA's authority on food labeling, and part of that, of course, is authority to try to promote better nutrition. Would you support special health messages on foods that are particularly high in saturated fat, sodium, added sugars, those types of things that have been shown to lead to particular heart problems and diabetes and other health problems?

Dr. MCCLELLAN. As I understand it, the FDA has been looking at some of those issues, issues such as levels of unsaturated fats in the diet and so forth, that seem to have some important relationships to important medical complications, and that is an issue that I would like to look into further as commissioner.

As always, the decisions of FDA should be guided by the best science on risk management, the best knowledge about how consumers are going to interpret information that is provided, and I look forward to working with you on that if confirmed.

Senator BINGAMAN. One other item the FDA has indicated an intent with regard to is to publish a rule requiring the use of bar codes for human drug and biological products. I guess Secretary Thompson has stated on several occasions that bar-coding is critically important to patient safety and that the FDA is working on such a rule.

Do you support the use of universal product-numbered bar codes on all drugs and biologics at each unit of packaging? Do you think that is a wise action to go?

Dr. MCCLELLAN. I certainly think, Senator—and I know you share this concern as well—that avoidable medical errors are far too common in our health care system, and absent steps in the right direction to reduce risks of errors, as medical care continues to get more complex, and patient treatments continue to become more individualized and customized, the risk of medical errors is going to go up.

Secretary Thompson I think has an appropriate level of interest in the potential for electronic labeling to help prevent medical errors by making sure that the right patient gets the right treatment at the right time. I am not sure whether what he has advocated or what the FDA would consider doing would apply to specific labels on each and every drug and biological product. I think there are important considerations that have to be taken into account with respect to the costs for hospitals and other health care providers to obtain the equipment needed to use the labeling information appropriately, and that needs to be accounted for in any kind of regulation.

But I certainly share the goal of trying to take steps to make it easier for health care professionals to do the right thing. They have a very complex and demanding job that is getting more complex and difficult by the day, and anything that we can do at the FDA to help them out and reduce risk to patients at the same time seems like the right way to go.

Senator BINGAMAN. Thank you, Mr. Chairman.

The CHAIRMAN. We have covered a variety of different health issues. I want to just mention to my very good friend from New Mexico that of course the CHIP program was really just devised for children. I am a strong believer that we need it for expectant mothers, and we have some States that have had some of those programs, including California, and it was cut back. A few of the States have had that program, and it is enormously important.

We do not even have the resources to cover the needy children, and one of the dilemmas that we have is that we are pitting children against children, the children who need attention versus other children, and that is a very, very unfortunate kind of dilemma to be caught up in, and that comes back to the issue of priorities in terms of budgeting.

So hopefully, we can find resources—and I am strongly supportive of what we are trying to do with Senator Bingaman's bill. I am also a continued advocate for trying to make sure that we cover the children who should be covered and need to be covered under the CHIP program and still are not.

Let me just go on to a few other items that are of particular interest to the committee and then come back to clarify a few issues.

One is that my good friend Senator Mikulski, who is so involved in giving the assurance of health care assistance in the TAA, the Trade Assistance Adjustment Act. In the trade adjustment legislation, which passed in July, there are some drafting errors that may prevent any retirees from getting coverage and that leave many eligible workers without benefits. There is a concern about the 3 months of prior coverage that is required in order for much-needed market protections to apply to those seeking coverage.

I know that you share a great interest in seeing the new benefits are made workable, and I know that you have been working on these health care issues as well. And we have enjoyed working with you in a very constructive way. We have not made all the progress that I would like to have made, but it has been a very positive and constructive relationship, as far as I am concerned.

It would be enormously helpful, since you have a good deal of understanding and awareness of this, if I were to be able to tell Senator Mikulski that you will try to see if we cannot get that particular provision worked out in some way.

Dr. MCCLELLAN. I would be happy to talk with her more directly about her specific concerns with the bill. As you know, Senator, we have tried very hard to bridge what many perceive as big philosophical gaps on covering the uninsured, and we have made some real progress this year.

Obviously, we have a long, long way to go, but implementing the Trade Adjustment Assistance tax credit effectively will be an important step in that direction.

The CHAIRMAN. Well, I agree with you that we wrestled around on those issues and then the committee made a judgment. I am not looking to reopen the whole issue. I am really just looking for what was the understanding within the legislation. That is what my remark referred to.

Dr. MCCLELLAN. We will be happy to take a closer look.

The CHAIRMAN. If you could try to do that, I would very much appreciate it.

Senator Clinton as well as Senator Dodd and myself and others are concerned about the pediatric rule. You are familiar—the FDA has currently undertaken a regulatory review of the pediatric rule. Can you assure the committee that you will not take action to weaken the protections in the pediatric rule or weaken the enforcement so that pediatric studies for drugs are delayed if completed at all?

Dr. MCCLELLAN. This is another case that I just want to—for those of you who have been following the controversies about this from a distance—not so much you, Mr. Chairman, but others—my understanding is that the pediatric rule is still in full force and effect at HHS and at FDA right now.

The CHAIRMAN. Right.

Dr. MCCLELLAN. My understanding is also that this is another area where the Congress has made substantial progress in improving or giving the FDA the opportunity to improve access to safe and effective new drugs, and there is far too little information available on labeling information, risks, and appropriate use of many drugs in children.

The Best Pharmaceuticals for Children Act passed last year I think will go a long way toward helping to address those concerns. And I certainly look forward to working with you and this committee to make sure we are implementing the goals of that legislation and our shared goal of making sure that children have access to appropriate treatments and safe treatments as quickly as possible.

I want to work together on that.

The CHAIRMAN. Well, that is very helpful, and we appreciate that, because there are enormous challenges, as you have pointed

out, in terms of what the implications have been on children. As you well know, for years, the testing was done on men and not on women, and was not considered in children, and we are trying to bring sound science to these decisions.

Do I understand, then, that your position would be to defend the current authority against legal challenge?

Dr. MCCLELLAN. My position would be—I have not followed the details of the rule and the implementation of the new law as closely as I would like to. I do know that one of the most controversial elements of the pediatric rule, which was the authority that the FDA asserted in the original rule to basically compel manufacturers to do additional testing in children, has not been employed to date, was not employed in the previous administration and has not been used yet.

So my goal is really in making sure that we have the most effective set of policies in place between the pediatric rule and however it can be improved and the new legislation and any additional rules needed to implement that to learn as much as possible as quickly as possible about the appropriate use of drugs in children. I will work with you on that.

The CHAIRMAN. Good. Thank you.

If I could, let me come back to just a couple of other areas. First, on the food warnings, I am a little uncertain about where you stand on FDA's authority to require specifically-worded product warnings.

Let us take the example of food warnings on a food product. In this case, it is multivitamins that contain iron. There were reported instances in which young children ingested these products and died, so that iron poisoning was a leading cause of fatal poisoning in children.

The CDC reported that five children age 11 to 18 died in Los Angeles during a 6-month period in 1992 and 1993, and FDA reports that over a decade, there were over 110 thousand incidents of children poisoned by iron supplements.

FDA required the following warnings on the product: "Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6. Keep this product out of the reach of children. In case of accidental overdose, call"—do you believe there is a problem with requiring specific words for this kind of warning?

Dr. MCCLELLAN. I think it is clearly within the FDA's authority when there is scientific evidence, empirical evidence, of a risk of an adverse event with a product or with misuse of a product to place appropriate information on the label.

I have not looked closely at this particular example, so I don't know at this time whether that specific warning is one that is being implemented as effectively as possible. I would be happy to get back to you in writing on that if I have a chance to take a look at the specifics, if that specific warning is the one that you are interested in.

The CHAIRMAN. Yes.

I mentioned the contact lenses. Do yo believe that colored contact lenses that do not correct vision should be regulated as cosmetics or as devices?

Dr. MCCLELLAN. I know this is a pending issue. It is not one that I have followed closely and certainly, if confirmed, is one that I would be delighted to talk with you about further and work with you on.

On the one hand, as you know, Mr. Chairman, the contact lenses that are used for essentially recreational or cosmetic purposes do have some of the same kinds of health consequences as prescription contact lenses. On the other hand, there are concerns about whether such a lens can be regulated as a drug rather than a cosmetic, and I know that that is one of the difficult issues—one of the many difficult issues—facing FDA, and I would certainly like to make sure that we handle that appropriately.

The CHAIRMAN. The reason I raise this is that the misuse of the contact lenses of inferior quality causes eye infection and severe pain. These are the ones that are used, as I understand, solely for cosmetics, allegedly for changing the color of one's eyes and so on. But even so, these are unregulated lenses that are being made and sold, and teenagers are swapping colored contact lenses as I understand it, with serious risk of infection. As you know, this is something that the division that deals with cosmetics—I believe they are people of good intention and hard work, but there are entirely different criteria, obviously, that are being used, where there is no required testing and no requirement for prescription or medical supervision, no requirement for directions for safe use, and no adverse event reporting for cosmetics.

We have examples of individuals—I mentioned earlier Roby Rouse, who bought a pair of tinted green contact lenses, and as we understand it, the lenses nearly blinded her in one eye, and she had a corneal transplant.

Then, this summer, there was a rash of injuries from contact lenses purchased from unregulated sources. A local doctor said: "Any move to relax regulation would be extremely foolish. This physical device placed in an eye that rubs on the cornea can reduce the oxygen reaching the eye. The repercussions of this are huge. When you let someone think it is an inconsequential novelty, then they treat it with no respect."

So there is quite a bit of information about the dangers of these products, and I would ask you to take a look at that as well.

Dr. MCCLELLAN. I will certainly do that.

The CHAIRMAN. According to the FDA's website, the Reproductive Health Drug Advisory Committee currently has no members. I recently wrote to Secretary Thompson and expressed strong concern about troubling reports in The Washington Post and elsewhere that the Department is handpicking members for its advisory committee not on the basis of best expertise and objectivity but to provide predetermined advice.

With these concerns in mind, we are now hearing that the Reproductive Health Advisory Committee will meet for the first time in 2 years this fall. With issues affecting choice and reproduction, I am sure that you understand how problematic it would be for FDA to have advisory committees which are ideologically suspect and not trusted for their objectivity and scientific integrity.

Can you assure us that each of the vacancies on advisory committees will be filled by individuals who will be selected for their expertise and objectivity?

Dr. MCCLELLAN. I think that expertise and objectivity are important criteria for selection. I would also like to add to that diversity of viewpoints. One of the themes that I would like to stress if confirmed is the importance of transparent and understandable regulation, and transparent regulation cannot happen unless a diversity of viewpoints—informed viewpoints, expert viewpoints—but if there are differences of view, diversity of viewpoints is important.

So I would say number one that my own belief is that scientific expertise and diversity of viewpoints where appropriate are an essential element in advisory committees, and second, my understanding of the Federal Advisory Committee Act essentially requires that we, or HHS or FDA, do not handpick the members but follow an appropriate procedure for making sure that the people selected to an advisory committee are well-respected in the subject matter of the advisory committee and are going to carry out their jobs effectively.

So I think you have both my commitment for making sure that diverse expert views are heard and the law on your side for this one. I do not know about all the—I remember that Washington Post report. I can say more generally that the accusations in there——

The CHAIRMAN. It is troubling.

Dr. MCCLELLAN [continuing]. Well, it is troubling. It just does not really comport with my experience of how HHS is filling its committees, either. I think they are looking for diversity of views and expertise as a general matter. But I will certainly watch that closely.

The CHAIRMAN. On tobacco products, smoking is the number one preventable cause of death in America. It kills more than 440,000 men and women. More than 90 percent of smokers start as children.

Should the FDA, the Federal agency most responsible for protecting the public health, have authority to regulate the most lethal of all consumer products, and would you at least consider the issue. I am not going to ask you about supporting the enactment of legislation that Senator DeWine and I introduced, S. 2626, to give the Food and Drug Administration the power to effectively regulate tobacco products now, because I assume you have not had a chance to review it—unless you want to volunteer that you do support it. But I want to mention that Senator DeWine and I are serious about it, and we are going to reintroduce it in the first part of next year. We are committed to moving ahead.

Have you formed any opinion about the role of the FDA with respect to and the tobacco products?

Dr. MCCLELLAN. Before talking about the role of the FDA, let me just start out by saying as a physician that this is an avoidable health risk that I think it is very important that adults are well-informed about and that the government does at the Federal level to assist States and that the State level and local level does all it can to enforce the laws against tobacco smoking in youth.

I think there are several things that the FDA can do. The reality is that the FDA, according to the recent U.S. Supreme Court decision in Brown and Williamson, cannot regulate tobacco, so that is not going to be on the table at least in the short run.

In my role as commissioner, if I am confirmed, one of the things that I would like to do is make sure that good, accurate information about health risks gets out insofar as that is part of the FDA's jurisdiction, and especially to do what we can to help speed the approval of new treatments to help people quit smoking. There have been some promising developments in new treatments in recent years, new pharmacologic treatments that really do seem to work for people who had been unable to quit by other means, and I think there is more promising science ahead.

I think one thing the FDA can do to help out under current law is to help make those products more available. And I will take you up on your offer of talking as we head into the next Congress about the next steps from here.

The CHAIRMAN. Well, there are a number of different parts to that issue that we have to work on, and we intend to do that.

Let me mention quickly some other areas. On dietary supplements, I expressed to you some concerns about the safety of some of dietary supplements, and you explained to me that the problem comes from the fact that these products are not preapproved, and FDA has the burden of developing the data necessary to take a dietary supplement off the market. But this is increasingly a matter of concern. I do not minimize the fact that this is a red hot issue in terms of the industry itself, but there are important health issues, and we want to be able to work with you on this.

Post-marketing surveillance is extremely important for drug safety, and we have given new authority and resources to be able to do that effectively. We want to make sure that that is going to be a priority.

And we have talked in my office about moving the biological therapeutics from CBER to CDER. If you would like to make a quick comment about that to assure me that there will be no diminution of the safety standards for approval of these products, which have special safety issues.

Dr. MCCLELLAN. That is absolutely right. My understanding of the move is that it only applies to certain activities within CBER. The activities that would move over would be the biological products that are most like prescription drugs, and the hope is that that is going to result in more consistency and economies of scale from being able to integrate the review processes more effectively.

CBER has many other critical roles related to tissues, vaccines, and many other areas that are going to continue, and my understanding is that the transfer is not associated with any reductions in force. Really, the goal is as you said, to help CBER and CDER deal with all of their immense responsibilities more effectively and efficiently.

The CHAIRMAN. On food safety, we have given you additional authority, particularly with the dangers of bioterrorism. Only a small amount of food is actually inspected, and there are increased resources to be able to do that. We want to work with you closely on this issue. It is of great concern to members of this committee and

many who are not; we want to make sure that you have sufficient authority to deal with foreign plants and all of the other kinds of products that need attention.

Our committee, particularly Senator Frist and myself, is interested in antibiotic resistance. This is a matter of enormous concern. We do not really have breakthroughs for dealing with these kinds of issues from our major pharmaceutical companies, and this is incredibly important, and we want to try to work with you to see how we can deal with this issue.

Human subject protection is again an area that Senator Frist and I have worked on. As we have seen the expansion of the life sciences, as we will in this century, we are going to have more research being done and more clinical trials. The protection of human subjects is enormously important. This committee held the initial hearings on the syphilitic study in Alabama, depoprovera in Tennessee, the sterilization of the Ralph girls, the CIA abuse of a substance which resulted in some human tragedies. So the whole area of protection of human subjects is enormously important.

Our committee also held an important hearing with Senator Durbin on West Nile virus. This is an issue where the FDA is very much involved. It is a matter of enormous concern to families all over this country, and there is a promising way to help protect the safety of the blood supply with new technology. We want to make sure that the blood supply is protected, and this is something that is of enormous, enormous consequence.

So these are some of the areas which we have not gotten into but the committee and its members are enormously interested in, so as you well understand, these are matters where the agency has important opportunities for leadership, and we want to be supportive of these efforts on your part.

I am going to ask the members to submit their questions this evening, and we will keep the record open tomorrow. It is my hope that we can have a markup on your nomination on Wednesday. I intend to support your nomination. I think you have a great opportunity to provide important leadership, and we look forward to working with you. Hopefully, we will get this approved so we can get you on the job very quickly.

[The prepared statement of Dr. McClellan may be found in additional material.]

The CHAIRMAN. The committee stands in recess.

Dr. MCCLELLAN. Thank you, Senator.

[Additional material follows.]

ADDITIONAL MATERIAL

PREPARED STATEMENT OF MARK MCCLELLAN

Mr Chairman, Senator Gregg, distinguished members of the committee, thank you for your consideration of my nomination as Commissioner of Food and Drugs. In my current job, and in my previous jobs in government and academics, I have appreciated the opportunity to work with you on a range of health care issues. In the short time since my nomination was announced, I have particularly appreciated the time that you have made to talk with me about critical FDA concerns for the new Commissioner to address. It has been a sobering and exhilarating dialogue, one that I look forward to continuing with all of you.

And I especially want to thank my wife Stephanie. If not for her endless hard work and countless sacrifices, we wouldn't be here today.

I have come to appreciate more clearly than ever that the professional FDA staff have unique and extremely challenging responsibilities. And I am honored to have the opportunity to become part of that workforce.

One of FDA's key goals in making safe and effective new treatments available as quickly as possible, but FDA's responsibilities for achieving this goal are becoming more complex and important than ever before. Many have called the twenty-first century the "health century." Unprecedented progress in understanding the foundations of diseases and the code of life itself holds the promise of breakthrough treatments that can be tailored to the specific needs of individual patients. As these research breakthroughs lead to the development of more diverse, more complex, individualized treatments, FDA will face new challenges in assuring their safety and effectiveness without unnecessarily restricting their access or adding to their costs.

The 21st century has also witnessed a new era of terrorist threats to our nation's security, and FDA has critical responsibilities here as well. FDA oversees the safety of 80 percent of the nation's food, including most of the growing volume of foods imported into the United States. We must take new steps to keep our foods and other consumer products secure, by developing new capabilities to prevent, detect, and respond to threats to these products, which are among the safest in the world.

The challenges of transparent and responsive regulation have never been greater. In part, this is the result of positive trends. Consumers are more interested than ever in steps they can take to avoid health risks, and to lead healthier lives. In addition to assurances that their products are safe, they want more useful information about the health consequences of the products they use. Data that can be used to identify risky treatments and products on the market are improving. Yet patients and physicians are often overwhelmed by the volume of information available on medical treatments, and need help in sorting out reliable, accurate information that they can use. And all of those affected by FDA regulations from the smallest family-run specialty food company to the largest multinational corporation need clear, predictable, and sensible guidance.

Consequently, the challenges and rewards of working at FDA have never been greater. The need has never been greater for familiarity with cutting-edge techniques of risk analysis, for clear understanding of increasingly sophisticated food and health sciences, for taking advantage of increasingly rich health information systems, and for supporting the capacity to make informed and timely regulatory decisions. As I said before, FDA is a unique place to work, one that requires bringing the best technical skills to bear on some of the most complex and important health issues affecting our country.

It is an honor to have the opportunity to help the FDA meet these critical responsibilities, and many others. But it is a special privilege to be able to do so at a time when Congress and the President, as a result of the bipartisan leadership of this committee, have just given FDA the most significant new resources and tools to fulfill these responsibilities in more than a generation. As a result of bioterrorism legislation passed earlier this year, FDA is in the process of substantially expanding and improving its oversight of food safety. This will not only help protect against terrorist threats; it will also provide new opportunities to improve the safety of the foods and consumer products that Americans use. And with the reauthorization and improvement of the Prescription Drug User Fee Act, the FDA has the opportunity to make breakthrough drug treatments available more quickly than ever as well as to use better tools such as enhanced monitoring of drugs after they are approved to detect important safety problems that cannot be detected in clinical trials.

It is my strong hope that the Senate will be able to complete the year's impressive legislative achievements for supporting FDA in meeting the challenges ahead, by enacting the Medical Device User Fee and Modernization Act and the Animal Drugs User Fee Act. I understand that the House intends to pass a bipartisan agreement

on HR 3580 as soon as today. The Administration strongly supports action this year to resolve remaining issues, so that Senate action can also occur this year.

If confirmed, however, my greatest privilege will be to become a part of the FDA's main asset: the ten thousand professional staff who make it possible, every day, for over 280 million Americans to have confidence in the foods they eat, the personal products they use, and the medical treatments that improve their lives. In recent years, FDA has taken many steps to help make sure that its professional staff has the work environment needed to fulfill its critical responsibilities including steps to make FDA a "learning organization" with FDA staff colleges and e-learning programs, and steps to accommodate the needs of a diverse workforce through flexible work hours and work locations, and child and elder care programs. But with the new challenges facing the agency, the need to fill literally hundreds of new professional positions, as well as plan for the reality that one third of the FDA workforce will be eligible for retirement in five years, enhancing the FDA work environment must be a top priority of the Commissioner. There is no element more critical to effective regulation than the FDA workforce itself.

In the time since my nomination has been under consideration, I have had the opportunity to talk with some of the FDA professionals as well as FDA veterans, and I look forward to spending much more time hearing from them and working with them. I am especially grateful to Deputy Commissioner Les Crawford. Les not only has tremendous FDA experience and expertise, he is also an effective manager and a friend. I am extremely lucky to have the opportunity to work with him to lead the FDA.

In closing, I wanted to make a couple of promises. First, if confirmed as Commissioner, I pledge to listen. Transparency and responsiveness start with the interactions between the Commissioner's office and Congress. You should always be satisfied that you get clear explanations from me and my staff, and an opportunity to get a fair and complete hearing of your point of view. Second, I will make decisions that you will not always agree with. My grandfather, Page Keeton, used to say, "If you haven't made anybody mad, you haven't done anything." I think the lessons he taught me, from his experiences as a law school dean and an academic expert who often got involved in difficult public policy issues, will be extremely helpful for the pace, complexity, and sensitivity of many of the issues facing FDA. By listening to the points of view of all involved, and by ensuring that sound science, careful empirical analysis, and ethical integrity are the foundation for FDA's decisions, I hope to make it possible for us to work together effectively to meet the challenges ahead.

My mother, who has dabbled in politics herself, likes to say: "It's not the dollars you make, it's the difference you make." The 21st-century FDA combines a long tradition of excellence in protecting and improving the public health, technical and scientific expertise, and strong bipartisan support for strengthening its ability to carry out its many critical responsibilities. It's a great place to make a positive difference in the lives of all Americans. I thank the committee for considering my nomination to serve in this important role, and I am happy to take any questions you may have.

RESPONSE TO QUESTIONS OF SENATOR KENNEDY FROM MARK MCCLELLAN

Question 1. For more than 40 years, FDA has exercised the authority to specify the language of warnings on products, both foods and drugs. Is there any reason you would take a position to the contrary?

This question was raised during the Senate HELP Committee's October 7 confirmation hearing. At the hearing session I responded to the question when it was asked. Please do not hesitate to contact me again if you need information in addition to the response I provided at the hearing. If confirmed as Commissioner of Food and Drugs I will continue to consider the issues raised by your question.

Question 2. Do you believe colored contact lenses that do not correct vision should be regulated as cosmetics or as devices?

This question was raised during the Senate HELP Committee's October 7 confirmation hearing. At the hearing session I responded to the question when it was asked. Please do not hesitate to contact me again if you need information in addition to the response I provided at the hearing. If confirmed as Commissioner of Food and Drugs I will continue to consider the issues raised by your question.

Question 3. The Wall Street Journal reported recently that the number of warning letters from FDA has dropped by 64 percent since the FDA Office of Chief Counsel has begun reviewing them before issuance. The rationale for this policy is greater uniformity in their issuance.

The Chief Counsel had publicly suggested that, in lieu of serial warning letters, "FDA would likely move directly to litigation after the first [letter]."

Has there been an increase in FDA enforcement actions and referrals to the Department of Justice, which the agency suggested would result from this new policy?

I believe that effective enforcement is supported by consistency in warning letter communications and by ensuring that each letter provides a clear basis for enforcement action if remedial action is not taken. Timely review by the Office of Chief Counsel would seem to support both of these important prerequisites for effective enforcement. With respect to the Wall Street Journal accounts, my understanding is that before Deputy Secretary Claude Allen issued his directive last November, there was no central repository of such letters and no tracking system for them. Accordingly, it is virtually impossible to establish the accuracy of the Wall Street Journal's estimate. However, I understand that the Office of Chief Counsel has refused to concur in only about 6 percent of the 699 warning and untitled letters it reviewed between February 27 and September 5. In the vast majority of cases, the Chief Counsel review resulted in concurrence as well as changes intended to strengthen and improve the letters as a basis for enforcement actions.

Given that OCC only started reviewing enforcement correspondence in March, it is likely too soon to tell whether there has been an increase in FDA enforcement actions and referrals to the Department of Justice, or an increase in the extent to which the letter recipients take corrective actions in response to the warnings. The purpose of the Deputy Secretary's directive is to promote a credible, risk-based enforcement strategy. I am committed to ensuring that FDA policies are designed to minimize risks to the public, including risk minimization through warning letters and an effective threat of enforcement actions. If confirmed, under my leadership FDA will follow up with enforcement actions when companies refuse to follow its regulations.

Question 4. In your oral testimony, you stressed the need for a "diversity of viewpoints" in selecting FDA advisory committee members. Perhaps consistent with your testimony, Time reported October 5 that FDA may be considering selecting Dr. W. David Hager for the Advisory Committee on Reproductive Health Drugs. Dr. Hager reportedly refuses to prescribe contraceptives to unmarried women and recommends Scripture readings for premenstrual syndrome.

In contrast, Time reports that FDA senior associate commissioner Linda Skladany rejected the nomination to this advisory committee of Dr. Michael Greene, director of maternal-fetal medicine at Massachusetts General Hospital and chair of Committee on Obstetric Practice of the American College of Obstetricians and Gynecologists (ACOG).

What are Dr. Hager's credentials for this important committee? Is he being considered, as reported, to serve as chair? And if nominated, would he be recused from consideration of the citizens' petition filed by the Christian Medical Association that requests the withdrawal of mifepristone, which he is reported to have assisted in drafting?

As you can see from Dr. Hager's resume (enclosed), as well as the October 8, 2002 letter to Time.com from Emery A. Wilson, M.D. (Dean and Associate Vice President for Clinical Services, University of Kentucky), his credentials for consideration as a member of the Reproductive Health Drugs Advisory Committee are exemplary.

Dr. Hager and a number of other diverse candidates have been considered as members of this advisory committee. Once selected, all members of the advisory committee may receive consideration to serve as its chair. Accordingly, Dr. Hager would, as a member of the committee, be considered for chair.

Question 5. Do you agree that the Advisory Committee on Reproductive Health Drugs should consist of individuals with an express commitment to protecting and improving women's reproductive health, as well as recognized, mainstream expertise in the fields of medicine or public health?

Can you further assure the Committee that the vacancies on this and other FDA advisory committees will be filled by individuals who are selected for their expertise and objectivity—not on the basis of particular ideology, or views on single issues, such as abortion or the provision of contraceptives to unmarried women?

The Reproductive Health Drugs Advisory Committee will consist of members with express commitment to protecting and improving women's and men's reproductive health, as well as recognized specific expertise in reproductive medicine and public health.

In addition, the advisory committee will be composed of individuals selected for their expertise and scientific objectivity and understanding of public health issues. In accordance with the Federal Advisory Committee Act requirements, the committee will be balanced including as many diverse viewpoints as possible and practicable. To attain fairly balanced membership, the agency will consider a cross-section of those directly affected, interested, and qualified, as appropriate to the nature and functions of the advisory committee.

Question 6. In January 2002, the FDA issued draft guidance on disclosure of conflicts of interest for special government employees participating in FDA product-specific advisory committees. In that guidance, the FDA does not call for web-based disclosure of reported conflict-of-interest information but states that the information will be read into the record at the beginning of advisory committee meetings.

Do you support public access to reported conflict-of-interest information through web-based, e-government strategies such as are implemented at the National Academy of Sciences?

Public access to reported conflict-of-interest information through web-based, e-government strategies is a complex issue involving the Privacy Act, the Freedom of Information Act, and the Ethics in Government Act. At this time, Acknowledgement and Consent to Disclosure documents and Special Government Employee Waiver documents are all available to the public via the Freedom of Information Act; however, requests for these documents through FOIA have been minimal. To support e-government and web-based communication with our constituencies, the Agency provides Acknowledgement and Consent to Disclosure documents on the FDA Dockets Management web-site as a part of the advisory committee meeting transcripts.

FDA staff have spoken with the National Academy of Sciences concerning their e-government strategy for public access to reported conflict-of-interest information; yet, the Academy was unable to direct us to information concerning their model. If confirmed, I will ask FDA staff to continue to look into the NAS strategy and other e-government models as potential benchmarks.

Question 7. I am concerned that the transfer of review of biological therapeutics from the Center for Biologics Evaluation and Review (CBER) to the Center for Drug Evaluation and Research (CDER) will encourage medical officers and scientists at CBER to leave, or even consider leaving, the Agency. If these qualified professionals begin discussions regarding private sector employment, they may be "conflicted" off product reviews under FDA's regulations. Won't this pose a serious risk of delay to biologic product reviews?

First let me say that we value the reviewers and plan to assure them that the transfer of review locations does not minimize their importance to FDA. The conflict of interest laws and regulations help ensure that recommendations given to FDA are free of bias and help maintain public confidence in FDA and the important work of the Agency. To the extent that administering the Agency's conflict of interest obligations present challenges to the flow of work, I will work to minimize problems that may surface and maintain FDA's obligations to conduct a timely review of product applications.

In addition, as a result of the transfer of the review of certain biologics applications from the Center for Biologics Evaluation and Research, where they are currently being reviewed, to the Center for Drug Evaluation and Research, there will be a larger pool of reviewers who are capable of conducting reviews. It is anticipated that this, coupled with the opportunity for CBER reviewers to work more efficiently on the critical programs remaining within CBER, will help to minimize the concerns suggested by your question regarding timeliness of reviews.

Question 8. Since enactment of the Prescription Drug User Fee Act, FDA officials have publicly acknowledged the internal pressures on drug review staff to review applications to meet the PDUFA performance goals. One survey of such staff found that a third did not feel comfortable voicing dissenting scientific opinions, and many felt that approval decisions were too heavily influenced by the application sponsors.

As Commissioner, what would you do to make sure that FDA scientists and review staff are able to openly express their opinions on product safety and other important issues within the Agency and at public advisory committee meetings?

Open discourse within FDA about the safety and efficacy of products under the Agency's regulatory authority is essential to decision-making about these products. While I have not yet identified specific new measures designed to promote this principle, I intend to maintain an atmosphere of open dialogue among FDA's employees.

Question 9. We found earlier this year that the drug industry was not fulfilling its commitments to complete post-market studies of drugs and biological products. Are you committed to seeing to it that these studies are completed, and informing us if the agency needs additional authority to enforce these commitments?

Section 130 of the FDA Modernization Act requires the Secretary of Health and Human Services to publish in the Federal Register a report on the status of post marketing studies. FDA also intends to make information about the status of individual comments available on the FDA Internet site. I understand the importance of this requirement and will work to implement the requirements of Section 130. I am also aware that in Section 130, Congress instructed FDA to bring forward legislative recommendations regarding post marketing studies, and I will assess the need to make any such recommendations.

Question 10. Despite continuing, substantial concerns about the risks of drugs taken during pregnancy, very little is known about the teratogenicity of the vast majority of agents to which pregnant women are commonly exposed. The FDA's Pregnancy Labeling Task Force was first established in 1996 with the mandate to examine current regulations, recommend changes, and consider related needs.

After seven years, the Agency has not fulfilled this mandate by issuing new pregnancy guidelines to replace the current uninformative system. Continuing the current system where more than 80% of drugs, including basic medicines and lifesaving therapies, lack detailed information about the risks to the health of the mother and the child of is unacceptable.

Can you give me an update on the progress of the Pregnancy Labeling Task Force? By what date to you expect them to release new pregnancy guidelines?

I agree with you that far too little useful information is available to women and their physicians about the risks of drugs taken during pregnancy. My understanding is that, under FDA's Pregnancy Labeling Initiative, the Agency is drafting new regulations on the format and content of the pregnancy and lactation sections of the labeling for prescription medicines. The draft regulation has multidisciplinary consensus. I am advised that the goal is to publish this within the next 12 months. In drafting this proposed rule, the Agency has sought external input including a Part 15 hearing and three Advisory Committee meetings to specifically address labeling for pregnancy and lactation.

We also need to develop a better knowledge base on medication risks during pregnancy. On September 23, 2002, FDA published a final guidance to industry on establishing pregnancy exposure registries. The goal of pregnancy exposure registries is to provide clinically relevant human data that can be used in a product's labeling to provide medical care providers with useful information for treating or counseling patients who are pregnant or anticipating pregnancy.

Other pertinent scientific guidances under development address:

The use of animal reproductive toxicology data (draft published November 2001)

The use of human outcome data (draft published June 1999)

The conduct of pharmacokinetic/pharmacodynamic studies during pregnancy

The conduct of studies on the transfer of drugs into breast milk

Risk management of known or highly suspect teratogenic medications.

If confirmed, I will work to build on these efforts to improve the availability of useful information on medication risks during pregnancy.

Question 11. The Public Health Service Act does not include provisions to allow for abbreviated biologics license applications. Some argue that this is appropriate because biotechnology products differ from traditional drug products in several critical respects, including molecular size and complexity as well as the relationship of manufacturing process to product safety and effectiveness. Certainly, biotechnology products that are intended to be similar but made through difference processes are not necessarily equally safe and effective.

At the same time, others argue that the number, cost and importance of biologic products coming off patent in the future highlight the importance of establishing a generics biologics program in the near future.

What are your views on these important issues?

As a scientific matter, it is true that certain biological products, due to their inherent structural complexity, heterogeneity, and manufacturing process do not currently lend themselves to being copied generically. The feasibility of interchangeable or generic biologics should be assessed further and should rely upon scientific knowledge and experience as key factors.

Question 12. The Hatch-Waxman Act creates a number of market exclusivities. Given your impressive economic credentials, and given that tens of millions of dollars or more are often at stake, I am confident that you are not surprised to learn that there has been an enormous amount of litigation over the meaning of a number of the provisions in Hatch-Waxman.

Do you agree that, eighteen years after its enactment, there is a need for Congress to amend the 1984 Act, in a way to state as clearly as possible what the rules are and to reduce the costly legal fights between FDA, brand companies and generic companies—so that the FDA can get back to the job of approving drugs that are safe and effective; the brand companies can get back to the job of finding truly important drugs; and the generics can get back to the job of producing products that will save the public billions of dollars?

I fully support the key goals of the Hatch-Waxman Act, including the provision of incentives for the research and development needed to create valuable new treatments, as well as an effective framework for generic drug competition after a fair patent term has expired. The development of many innovative drugs in the past two decades, as well as the shift of almost half of all prescriptions to generic drugs, is

a testament to the importance of this Act. I also appreciate the goal of S. 812, to improve generic drug competition. As the detailed study of potential abuses of the automatic 30-month stay and other Hatch-Waxman provisions by the Federal Trade Commission has demonstrated, some provisions of the Act may not be functioning as intended. On the other hand, some features of S. 812 go beyond closing loopholes as recommended by FTC and would potentially delay access to new medications, and increase their costs, as a result of much more complex patent filing procedures and new litigation. As Commissioner, I look forward to working with Congress to take steps to address these important issues effectively.

Question 13. Many promising new products combine drug, device or biologic technologies.

How can FDA improve the timely and appropriate review and post-market regulation of such combination products?

As I indicated in my oral remarks, I believe that Congress should adopt the Medical Device Amendments of 2001, H.R. 3580, during the current session. As reported by the House Committee on Energy and Commerce, section 203 of the bill would establish an Office of Combination Products in a manner that is consistent with recent Agency actions to promote combination product reviews.

Question 14. When I expressed to you concerns about the safety of some dietary supplements, you explained to me that the problem comes from the fact that these products are not pre-approved, and that FDA has the burden to develop the data necessary to take a dietary supplement off the market.

How do you propose addressing this problem? Does FDA need more resources or should Congress consider changing the statute?

While my examination of issues relating to dietary supplements has allowed me to appreciate the challenges the Agency faces under the Dietary Supplement Health and Education Act of 1994, at this time I do not have specific statutory changes to recommend. As Commissioner, I will work with the Department and with Congress to implement the Act in accordance with Congressional intent. This includes taking steps soon to implement good manufacturing practices for dietary supplement manufacturers.

Question 15. There have been more than 100 deaths among users of ephedra products reported to FDA. Many of these deaths are well-documented, and occurred at the manufacturer's recommended doses.

Do you support the removal of ephedra products from the market?

As Deputy Commissioner Crawford testified on Tuesday, HHS and FDA recently initiated a number of important actions relating to ephedra. Last June, Secretary Thompson announced enforcement efforts against synthetic ephedrine alkaloids illegally marketed as dietary supplements and a comprehensive review of existing science on ephedra products to be conducted by Rand Corporation and overseen by the National Institutes of Health. More recently, FDA issued a cyber letter to the Internet promoter of Yellow Jackets for promoting and selling this herbal ephedra product as an alternative to illicit street drugs. FDA is also and is undertaking a number of investigations concerning ephedra products and manufacturers. FDA anticipates that the scientific review prepared by the Rand Corporation should be completed in February 2003, I believe that this comprehensive review will provide an important basis for an possible further FDA actions under the Dietary Supplements Health and Education Act.

Question 16. The National Academy of Sciences has warned that each year more than 60,000 children are born at risk for neurological problems due to mercury-contaminated seafood their mothers ate awhile pregnant. For more than a decade the FDA has failed to act on an NAS recommendation and a citizen petition to strengthen the Agency's mercury standard. Instead the FDA has issued consumption advisories, but has done nothing to exercise its legal authority to prevent mercury-contaminated fish from being sold to consumers.

Other than issuing consumption advisories, what steps would you take to ensure that pregnant women and their children are protected form mercury-contaminated seafood?

I agree with you that the FDA has a critical role to play in helping to ensure the safety of foods for pregnant women and their developing children. FDA staff reports that they recently held a public food advisory committee meeting on methylmercury and is including safety initiatives among its FY'03 priorities. Currently they are conducting an extensive public education campaign as well as outreach to physicians. Finally, special funding has been set aside for community outreach efforts in several different geographic locations to insure that the message reaches women in special populations at greater risk for illness. If I am confirmed, I will work closely with you to build on these steps to prevent mercury consumption during pregnancy.

Question 17. FDA has taken recent action on regulating the use of medically important antibiotics as feed supplements to promote the growth of farm animals. This practice increases the prevalence of antibiotic-resistant infections. FDA recently took the positive step of proposing new rules for reviewing future applications for agricultural uses of these medications, but I remain concerned about antibiotics that are already on the market.

Don't you agree that the antibiotics we rely on to protect our health from bioterrorism and other disease outbreaks should be reserved for human use-not fed to farm animals to spur their growth? What is your timetable for taking action on this issue?

Controls to stop the development of antibiotic resistant organisms are an important public health goal embraced by the Department and the Agency, and we need to do more to address this important problem. I understand the draft guidance recently published by the Agency, "Evaluating the safety of antimicrobial new animal drugs with regard to their microbiological effects on bacteria of human health concern" outlines an approach for evaluating antimicrobial resistance concerns associated with the approval of new antimicrobial products for food animals. The guidance also discusses the Agency's intent to apply a similar approach to currently approved antimicrobial drugs. I agree that the importance of a given drug for human medical therapy is a key factor to consider when assessing the safety of using the drug or related drug in animals, and this consideration is reflected in the draft guidance. The guidance applies to currently approved antimicrobial drugs for food-producing animals as well as to future applications. I understand that the Agency intends to prioritize its efforts to reassess currently approved drugs based on their importance to human medicine. If confirmed I would continue to support as a priority protecting the public health by controlling the development of antibiotic resistant organisms from animal and human uses.

Question 18. FDA has an essential role in protecting the safety and well-being of patients who volunteer to serve as human subjects in clinical trials. Due to abuses and lapses in oversight, many patients are no longer confident that their safety will be properly protected in these trials.

What actions would you take to restore that confidence and ensure that patients who volunteer to serve as human subjects are properly protected from harm?

My examination of the issues relating to Human Subject Protection has allowed me to appreciate the importance of these issues, and I appreciate the bipartisan interest in determining whether further administrative or legislative actions are needed to ensure protection of research subjects. I look forward to working with the committee to evaluate what actions may be needed to better protect those who participate in clinical trials.

Question 19. One promising way to help protect the safety of the blood supply is a new technology known as pathogen inactivation, which has the potential to rid the blood supply not only of the West Nile Virus, but also of other dangerous infectious agents.

Should it be a priority for FDA to evaluate this exciting new technology?

Several approaches are currently under study and may be effective at inactivating viruses such as West Nile Virus (WNV). In the event that other responses such as blood screening and testing prove to be difficult to implement in a timely manner, pathogen inactivation may prove valuable as an approach to reducing risk in blood products from high risk of developing severe disease. These approaches, however, must be carefully evaluated for their immediate and long-term safety. I understand that FDA is currently planning to specifically address the inactivation of WNV by such methods in conjunction with its upcoming (November 4 & 5) workshop on WNV donor blood testing. Developing safe and effective methods for detecting and eliminating blood supply risks such as West Nile Virus is a high priority. While the risk of any infection from a blood transfusion in the United States is extremely low, further steps to improve safety and increase the available supply of blood are needed.

Question 20. What would you do to use Internet and other similar systems and standards to enhance the Agency's efficiencies in product approvals, inspections, and in the development of standards and guidance documents?

The awards that FDA's web site have earned from organizations such as USA Today, Dow Jones Business Directory, Parenthood Web, the Emergency Nursing Association, the AgView Internet Search Service and other organizations is a testament to the Agency's efforts to achieve a high degree of openness and communication with the public and regulated industries. The Web pages of FDA centers share similar honors. I intend to build on this record and further enhance Agency efficiency in the areas you have identified.

Question 21. The Center for Medicare and Medicaid Services has initiated its National Coverage Decision process for several new drugs and biologicals in some cases almost immediately after FDA approval of those new therapies.

What role should FDA's decisions regarding safety and efficacy play in Medicare coverage? What is your opinion on whether there should be more interaction between FDA and CMS during the approval process for new therapies? What is your opinion of CMS making national determinations about coverage before new therapies have been marketed for some time?

As you know, FDA does not make coverage decisions. Rather, it approves items like devices and drugs based on their safety and efficacy. CMS must make determinations for coverage based on medical necessity. These are different standards and may require different analyses.

That said, I generally think increased interaction and cooperation among Federal agencies is wise, and I understand that CMS currently works collaboratively with FDA when gathering and considering evidence to make national coverage decisions. In addition, the staffs collaborate through interagency agreements, workgroups and task forces, and in consultative roles with respect to setting and enforcing quality standards, quality improvement and measurement activities, and coverage. I have worked closely with CMS Administrator Scully on many issues during my service in the White House, and if confirmed, I intend to explore additional areas where these two agencies can further improve their working relationship for the benefit of the American public.

Response to Questions of Senator Harkin

Question 22. Do you believe, as the previous FDA Commissioner did, that the Dietary Supplement Health and Education Act (DSHEA) provides FDA with adequate authority to protect the public from unsafe products and false and misleading claims?

While my examination of issues relating to dietary supplements has allowed me to appreciate the challenges the Agency faces under the Dietary Supplement Health and Education Act of 1994, at this time I do not have specific statutory changes to recommend. As Commissioner, I will work with the Department and with Congress to implement the Act in accordance with Congressional intent.

Question 23. Do you agree that all regulatory decisions by FDA related to dietary supplements should be based on sound science?

Yes, regulatory decisions related to dietary supplements should be based on the best scientific information that is available.

Question 24. It has been more than eight years since Congress passed the DSHEA, and there still are no Good Manufacturing Practices (GMPs) regulations, as called for in the statute. What steps will you take to ensure that the proposed rule on GMPs is promptly published and final regulations are promulgated?

Publishing regulations on good manufacturing practices (GMPs) for dietary supplements is a priority for FDA's Center for Food Safety and Applied Nutrition (CFSAN), and I share this view. FDA has forwarded draft proposed GMP regulations to the Department of Health and Human Services. On October 4, 2002, the Department submitted this proposal to the Office of Management and Budget for 90-day review. If confirmed, I will work to implement GMPs for dietary supplement manufacturers as quickly as possible.

Response to Questions of Senator Mikulski

Question 25. I'm concerned about the length of time that it has taken to fund the planned consolidation of FDA's facilities. Your testimony talks about the importance of FDA's employees and the work done by FDA. I've been fighting for the funding that FDA needs to consolidate and upgrade its current facilities. I hope I can count on your support going forward in requests to the Administration for funding this consolidation. Will you advocate within the Administration for full funding of the FDA's consolidated facility in fiscal years 2003-2005 to ensure timely completion of this long-delayed and crucial project?

FDA Headquarters currently occupies approximately 40 buildings in more than 16 locations around Washington, D.C.; from Gaithersburg to Rockville to Laurel to College Park and northern Virginia. While it is not solely FDA's responsibility to ensure that sufficient funding will be available to achieve continued progress on this project during FY 2004, I recognize the importance of this consolidation project for improving the FDA work environment, and will work to achieve the objectives set forth in P.L. 101-635 relating to consolidation.

Question 26. As the architect of the Mammography Quality Standards Act (MQSA), I was troubled to learn of concerns raised over the last few months regard-

ing physician interpretive skills for mammography. I have been working with other Members of this Committee on a bipartisan basis to make improvements to MQSA to help address these concerns. I look forward to building on the groundwork laid this year and enacting changes next year to help improve physician interpretive skills and other areas that may need to be improved. Will you work with me to help make these improvements to MQSA next year?

As you know, the Mammography Quality Standards Act was enacted in response to serious concerns about the quality of mammography. It remains an essential tool for early detection and for combating mortality associated with breast cancer. This issue is of critical importance to millions of women in our country. At the same time, new technological developments such as digital, computer-assisted imaging and telemedicine are augmenting our technical capabilities to provide high-quality mammogram services.

The MQSA authorization expired on September 30. The Administration supports reauthorization of the Act, and I would be happy to work with you to achieve this goal and to explore other steps that FDA can take to help make better mammography tools available to practitioners.

Question 27. This week, the House of Representatives will pass the Medical Device User Fee and Modernization Act of 2002 (H.R. 3580). This is important legislation to improve the FDA's review and approval of medical devices and provide FDA with additional resources for medical device review and approval. Under this legislation, FDA would receive additional funding for medical device review from user fees from manufacturers and an additional authorization of $15 million per year for the Centers for Devices and Radiological Health (CDRH). Do you support adding the $15 million to the device center's budget in fiscal year 2003? Will you work to ensure that the President's budget for fiscal years 2004 and subsequent years includes this $15 million?

The user fee program that has been negotiated over the last five months and that is a $50M program by year five. The goals that FDA agreed to meet are contingent on the Agency receiving $50M by year five. The industry agreed to fund up to $35M in user fees by year 5 and the remaining $15M is to come from appropriated dollars. I strongly support enactment of a new device user fee program in this session of Congress. If Congress passes the law that creates this user fee program for medical devices, I plan to work to ensure that the device program receives the funds it needs to adequately implement the program and meet the goals that are laid out in the draft goals letter.

Question 28. I am pleased to see that your testimony underscores the importance of FDA's employees. They are dedicated and hard-working. Without them, FDA would not be able to carry out its mission to promote and protect public health. What steps would you take as Commissioner to help ensure that the FDA will recruit and retain the best and brightest employees in the coming years?

Thank you for acknowledging the hard work and dedication of FDA's work force, and for your efforts to help improve the FDA work environment. FDA strives to hire the best and brightest people; this is essential for carrying out FDA's public health mission of consumer protection.

In recent years, FDA has implemented a number of programs to help recruit and retain a high-quality work force, and I intend to build on these programs. Over the last five years FDA's recruitment tools have improved and the hiring process has been streamlined. These changes have allowed the Agency to hire people more quickly. The FDA Centers and the Office of Regulatory Affairs are active in recruiting people to work in their specific specialty areas.

FDA has just completed its first full year of using the Automated Candidate Evaluation System (ACES). Major benefits of ACES include (a) the acceptance of online employment applications via the Internet; (b) improved applicant pool through exposure to the Internet; (c) automated applicant ratings and rankings through applicant responses; (d) automatic acknowledgement (via e-mail) to all applicants; and (e) through e-mail, a fast and easy method for communicating with all applicants. In addition to expanding its library of rating questions from 20 to 65 occupations, ACES was an instrumental tool in helping FDA to meet its critical staffing needs as a result of September 11. With respect to Office of Regulatory Affairs' (ORA's) Consumer Safety Officer hiring initiative, over 3,000 applications were handled for vacancies announced in 155 locations nationwide. The delegated examining unit issued hundreds of selection lists in a matter of weeks. It has been estimated that it would have taken (6) months to handle this workload under the manual process. Approximately 500 selections were made for Consumer Safety Officers under this hiring initiative, with approximately 300 additional selections made for a variety of other occupations within ORA.

All of these ongoing efforts are important steps forward. If confirmed, I intend to work with FDA's human resource programs and other programs to improve them further and to take additional steps to recruit and retain the best possible workforce.

Question 29. Since its creation in 1994, the FDA Office of Women's Health has sponsored research, conducted public education campaigns, encouraged the participation of women in clinical trials, and served as an advocate for women's health in agency decisions. Recognizing its important work, this Committee, as well as the House of Representatives, recently passed legislation that would statutorily authorize the Office of Women's Health at FDA.

As Commissioner, will you support legislative efforts to authorize this Office? When appropriate, will you seek the advice and recommendations of the Office of Women's Health?

I appreciate your recognition of FDA's Office of Women's Health (OWH) and your support for their activities. The proposed legislation is largely consistent with current program and activities of the office. OWH is an integral part of the Agency and I look forward to working with OWH to improve FDA's recognition of important women's health issues.

RESPONSE TO QUESTIONS OF SENATOR JEFFORDS

Question 30. As I mentioned in my opening statement, I am increasingly concerned that the FDA will be prepared to review treatments that become available for our aging populations. For example, Alzheimer's Disease is a serious disease that is afflicting the elderly in our country. The Alzheimer's Association estimates that 4 million Americans have Alzheimer's Disease, and that number will grow to 14 million in 2050 unless a cure or prevention is found. My question is this how will the FDA handle treatments for diseases like Alzheimer's under your leadership? What will you do to make certain that the FDA speeds its review for safety and efficacy of any promising therapies for aging populations? Will you make sure that FDA uses the regulatory tools such as—"accelerated approval" and "fast track" and "approval based on surrogate markers"—on products for diseases like Alzheimer's Disease?

As I expressed in my opening statement before the Senate Health, Education, Labor and Pensions Committee, I believe that giving Americans quick access to safe and effective new treatments is one of the most critical roles of FDA. The Agency already has established several procedures to accomplish this. If confirmed, one of my top priorities will be to work closely with FDA staff on ways to improve these procedures.

I am very concerned about the plight of patients who suffer from serious illnesses, such as Alzheimer's Disease, but I am encouraged by recent progress and potential future developments in biomedical research in this area. FDA is continually striving to expedite the approval of safe and effective treatments for these conditions. I will work to ensure that the criteria for accelerated approval or fast track procedures are used appropriately for these treatments, in order to help expedite relevant approvals.

Question 31. Thousands of American citizens are increasingly looking across our border to Canada to purchase the medicines they need at a price they can afford. Traditionally, the FDA has chosen to "look the other way" with respect to these elderly citizens as they bring medicines back into the U.S. for personal use. Despite efforts of the drug industry to portray the specter of counterfeit drugs smuggled into the U.S. by terrorists, there has been little, if any evidence to show that people taking medicines obtained in Canada are at any increased risk for adverse reactions than U.S. consumers. In the first instance, I would like an assurance from you, that under your leadership at the FDA, citizens will not be unduly encumbered from obtaining medicines from Canada for their personal use. Second, please describe what steps the FDA might take, or what legislative authority might be needed, so that FDA can make the practice of personal reimportation of prescription drugs acceptable to the Agency from the perspective of ensuring safety and efficacy.

From a public health standpoint, importing prescription drugs for personal use is a potentially dangerous practice. Neither FDA nor the American public have any assurance that unapproved products from foreign sources are effective or safe, or have been produced under U.S. good manufacturing practices. Because FDA does not regulate foreign distributors or pharmacies, these products may not have been stored under proper conditions, or may not be the real products. I am wary of subjecting patients to these risks.

The Federal Food, Drug, and Cosmetic Act prohibits the importation of unapproved new drugs, including foreign-made versions of U.S. approved drugs, that

have not been approved by FDA for marketing in the United States. I understand that FDA does allow Agency field personnel to use their enforcement discretion and allow entry of unapproved prescription drugs for personal use in limited circumstances. However, my belief is that legislation to provide better prescription drug coverage with more effective price competition in the United States legislation such as you and the President have supported is a much more effective solution to the problem of high prescription drug costs for many seniors and others in the United States.

Question 32. I was glad to read in your statement of your support for the legislation currently under consideration that would strengthen the Agency's ability to review medical devices. As you know, the Food and Drug Administration Modernization Act (FDAMA) sought to provide the Agency with new tools to address the rapidly changing technologies associated with medical devices. Please describe for which class of products the Congress should consider extending the use of third-party reviewers and third-party inspectors. Also, please describe what steps you think are necessary to prepare the Agency for these rapidly changing technologies, for example: should the Agency establish an Office of Combination Products and, if so how should it function?

I support using third parties to supplement the Agency's medical device good manufacturing practice inspections. Due to resource constraints, the Agency has been unable to inspect device facilities as completely as desired. A third party program would supplement the Agency's efforts and provide greater coverage. As with the current third party review program, adequate protections must be in place and there must be an opportunity to evaluate the success of the program. Further, as FDA gains additional experience with the third party review program, I believe it would be appropriate to evaluate additional use of outside experts in this area.

Finally, the Agency has recently taken steps to facilitate the review of combination products by the Agency. FDA has established a Combination Products Program within the Office of the Ombudsman. The new program serves as a focal point and advocate for combination product issues. The goal is to develop policies and procedures that facilitate the review of combination products and to monitor the progress of premarket reviews of combination products. I support these efforts and intend to build on them if confirmed.

Response to Questions of Senator Bingaman

Question 33. As a physician, you certainly are aware that the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics believe that a pregnant woman and the "unborn child" must be treated together. As you are aware because of your role as advisor to the President on health issues, in regulations that the Administration recently published as a final rule on October 2, 2002, the Administration allows for coverage of an "unborn child" through the State Children's Health Insurance Program (SCHIP) but felt the statute did not allow coverage of pregnant women.

In issuing the regulation, the rule acknowledges the problem of not providing coverage to the woman as well. As the rule reads, "We welcome all of these suggestions for expanding health insurance coverage [to pregnant women] and indeed States and the Secretary have already used the flexibility in current regulations. However, there are still gaps. We also welcome support for the action of the Secretary in granting waivers to States But the Secretary's ability to intervene through one mechanism (a waiver) should not be the sole option for States and may in fact be an inferior option. Waivers are discretionary on the part of the Secretary and time limited while State plan amendments are permanent, and are subject to allotment neutrality."

Among other things, the rule notes that if you are only covering the fetus then women lose a number of important aspects of care during all the stages of a birth pregnancy, delivery, and postpartum care. As a physician, do you agree with the clinical guidelines of the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics that it would be preferable for both the pregnant woman and the "unborn child" to receive health coverage?

Do you acknowledge the a woman could very well be denied the following services:

During Pregnancy: Cancer, medical emergencies, accidents, broken bones, mental illness, or even life-saving surgery of a pregnant woman if the fetus is determined to be viable?

During Delivery: Eepidurals in current circumstances in certain states?

During the Postpartum Period: All health coverage from the time the child is born, including but not limited to treatment of hemmorage, infection, episiotomy re-

pair, C-section repair, family planning counseling, treatment of complications after delivery (including, once again, life-saving surgery), and postpartum depression?

Senator, thank you for raising the important issue of prenatal and maternal care at the hearing on October 7. I stand by the response I gave at that time, and I look forward to working with you on this and other issues, should I be confirmed.

Question 34. Secretary Thompson has made a number of statements over the past year in support of passage of legislation, including specific references to S. 724, the "Mothers and Newborns Health Insurance Act." The Senate is now trying to pass the legislation and we heard on the Senate floor from Senator Nickles that the Administration may be opposing this legislation.

Dr. McClellan, what is the position of the Administration on the passage of S. 724? If opposed, what are the specific reasons for this change in position and who made this decision.

Senator, thank you for raising the important issue of prenatal and maternal care at the hearing on October 7. I stand by the response I gave at that time, and I look forward to working with you on this and other issues, should I be confirmed.

Question 35. The Chairman and Ranking Member of the Senate finance committee just introduced bipartisan legislation, S. 3018, the Beneficiary Access to Care and Medicare Equity Act of 2002. In your current capacity, can you tell us whether the Administration supports this legislation. If not supportive, can you specifically tell us what the Administration is objecting to in the bill?

Senator, thank you for raising this important issue at the hearing on October 7. I stand by the response I gave at that time, and I look forward to working with you on this and other issues, should I be confirmed.

Question 36. In your current capacity, can you tell us if the Administration supports the extension of the QI-1 program? If so, will the Administration support an extension of this important program to low-income seniors and people with disabilities immediately as a free-standing piece of legislation or part of a bigger Medicare/Medicaid package?

The Administration strongly agrees with you that the QI-1 program provides an important protection for our nation's most financially vulnerable seniors and disabled citizens and the President included an extension of the program in his budget request. The Administration would not object to the Senate taking this measure up as a free-standing bill.

Question 37. According to the Department of Health and Human Services, Americans' poor diet and sedentary lifestyles cause between 310,000 and 580,000 deaths annually.

How would you use FDA's food labeling and other authority to promote better nutrition? Would you support special health messages on foods high in saturated and trans fat, sodium, added sugars, and other constituents that promote cardiovascular disease, diabetes, and other health problems?

I believe that Americans want more reliable and useful information to help guide their dietary choices. To help Americans get the information they want to make informed dietary choices, I will consider ways to provide more effective labeling information and will encourage efforts by the Agency to use additional resources to better educate consumers on how to use the information available on food labels to improve their diets, and, thereby, their health. These efforts are particularly successful when done in collaboration with other federal and state agencies, food industry, public health, and consumer organizations who share a desire to promote better nutrition across America.

Question 38. A factor that may be increasing antibiotic-resistant infections in people is the widespread uses of medically important antibiotics in food animals. A recent review of the literature by an expert panel convened by the Alliance for the Prudent use of Antibiotics concluded that antibiotic use in agriculture posed a health risk and should be strictly controlled, particularly for healthy animals.

What role do you believe that antibiotic use in livestock and poultry plays in the emergence of resistant bacteria in people, particularly foodborne bacteria? What is your view of the recent FDA's Center for Veterinary Medicine (CVM) draft guidance document "Evaluating the safety of antimicrobial new animal drugs with regard to their microbiological effects on bacteria of human health concern?" Will you push for a rapid finalization of this document, and when would you anticipate a final document would be ready? Once finalized, in what timeframe would currently available antibiotics be considered using this guidance document? Does CVM have adequate resources to complete its assessment of virginiamycin in a timely manner, while still participating in the hearing on the proposed ban of fluorquinolone use in poultry?

The development of antibiotic resistance is an important public health priority. If confirmed, I would continue to support as a priority protecting the public health by

controlling the development of antibiotic resistant organisms from animal and human uses.

FDA believes that a great deal of scientific evidence exists showing that food-producing animals serve as reservoirs of both commensal and pathogenic bacteria that may be transferred to humans by consumption of contaminated food products. Additional evidence has shown that with the use of antimicrobial drugs in these animals, the bacteria may become resistant to drugs that are also used to treat human illness, potentially making human illnesses more difficult to treat. The new draft guidance document that CVM published on September 13 represents the Agency's approach to dealing with this public health concern. The goal of FDA's approach to the issue is to protect public health by preserving the long-term effectiveness of human antimicrobial drugs, while providing for the safe use of antimicrobials in food-producing animals. FDA's draft guidance is consistent with the approach advocated by the World Health Organization and other international health organizations.

I understand that the draft guidance document published on September 13, 2002 has a 75-day comment period. CVM held a public meeting on October 2 to further explain the draft guidance and encourage comments. CVM expects that all comments can be addressed and the guidance revised by Spring 2003. Currently available antibiotics will be reviewed in priority order based on their importance in human medical therapy, as resources permit. CVM anticipates having available for comment a draft assessment of the risk from use of virginiamycin in food-producing animals contributing to Synercid resistant Enteroccocus faecium in humans later this year.

Question 39. The FDA has stated its intent to publish a rule requiring the use of bar codes for human drug and biological products. In addition, Secretary Thompson has stated on numerous occasions that bar coding is critically important to patient safety and that the FDA is working on a rule. The FDA believes, according to documents included in the Federal Register, that the use of such technology will reduce medical errors.

Do you support the use of universal product numbered bar codes on all drugs and biologicals at every unit of packaging? If so, are you committed to publishing a rule in the very near term?

Senator, I appreciate the discussion we had of this question during my oral testimony. If you need additional information, please let me know. I look forward to working with you toward our shared goal of eliminating avoidable medical errors.

RESPONSE TO QUESTIONS OF SENATOR MURRAY

Question 40. Will you as the head of FDA work with those of us in the Senate who hope to codify the Pediatric Rule? If not, what steps are you planning on implementing to ensure that FDA aggressively fights to implement the Rule and defend the Rule in court?

I know that the health of America's children is a top priority of the Department and I share this priority. We are determined to make certain that children's medications are safe and effective. I will work to see that by having drugs available that are properly studied for use in children, our nation's children will receive the safe and effective medical care they deserve.

With the Best Pharmaceuticals for Children Act (BPCA), Congress provided the government with a very important tool to address specific pediatric needs. This law and its new tools resulted in questions being raised regarding the continued need for the Pediatric Rule promulgated by FDA in 1998. On April 19, 2002, the Department strongly reiterated a commitment to further ensuring the safety and effectiveness of drugs used to treat children, including continuation of the Pediatric Rule. As Commissioner, I will continue to enforce FDA's rule requiring companies to take steps to ensure drugs are properly labeled for pediatric use based on scientific studies.

In an advance notice of proposed rulemaking published on April 24, 2002, FDA sought public comment on how best to implement the BPCA and what additional steps, if any, need to be taken to ensure that drugs in children are adequately studied. The comment period has closed and FDA is currently reviewing the submissions. I will certainly support these efforts.

Question 41. Safe and effective drugs are the gold standard of the FDA. However, we know there are risks associated with almost any drugs. It is important for the FDA to evaluate the risks v. benefits of any drug. Different representatives of this Administration have made conflicts statements with regard to the official position on the drug mifepristone. A drug that has been safely used by more than a million women, but anti-choice organizations that fought the approval of this drug, have

now called for the FDA to reverse it's position and pull the drug from the market. The petitions also call on FDA to impose much greater labeling restrictions that would make the drug all but unavailable in most parts of the country.

The FDA has already ruled on safety of this drug. However, I am concerned about efforts by this Administration to turn the clock back for women.

As the new Administrator of FDA what criteria will you utilize in reviewing these petitions? Will science remain the guiding force or with this be a political decisions? If the FDA does review the drug, will the risks of unintended pregnancy be part of the evaluation? There are significant risks for many women from an unintentional pregnancy. This drug offers a safe and effective method of terminating a pregnancy. The risks of carrying the pregnancy to term must be part of any science-based review.

The Agency's review and approval of any drug adheres strictly to its statutory mandate and mission as a science-based public health regulatory agency. The appropriate legal and scientific standards are applicable to the review of all citizen's petitions, including this one. If confirmed, I intend to carry out my important statutory responsibility to monitor the safety of all approved drugs in actual practice. The enhanced post-marketing surveillance provisions in the recently-enacted Prescription Drug User Fee Act provide new tools and opportunities to do so.

Question 42. As you may know, medical device technology has a very short life span. Timely approval of new life saving medical devices is important for both the manufacturer and the patient. Increasing delays only deny access to these new devices and delay the development of even better, safer technology. As the new Administrator of FDA, will you be supportive of an FDA device user fee to provide additional resources? What measures will you implement to ensure that devices are approved or reviewed in a timely manner? Can the Agency rely on third party reviewers or experts without jeopardizing the integrity of the FDA approval process?

I support Congressional action in this session to enact device user fees, building on the intense and productive negotiations over over the past five months. The device review program is in great need of additional resources, which that program would provide. These additional resources would go a long way toward helping the responsible Centers review new technologies in a more timely manner. Moreover, the program would permit the Agency work with the device industry to improve the quality of device applications, potentially reducing costs as well as time to approval.

My view is that the Agency can and should take advantage of outside expertise, especially when that expertise can supplement our own experts. I believe that, with adequate procedures in place, the use of such third parties would enhance rather than jeopardize the review process.

Question 43. One of the areas that I have focused a great deal of my energies has been in the area of gender bias in research and development of new drugs and devices. Beginning in 1993, we have seen a dramatic improvement at NIH of support for research involving women. Women are no longer simply "little men," but include in more and more research supported by NIH. We have a long way to go but we have made some progress. FDA plays a critical role in this process. FDA must approval research protocols involving human subjects and must work to ensure that drug manufacturers conduct Phase III and Phase IV Clinical trials, often involving women.

However, without the leadership and pressure from the FDA, many drug manufacturers will not include women in clinical trials or seek FDA labeling approval for drug impact on women, especially pregnant women. As the new Administrator of FDA, what leadership role will you play in eliminating the gender bias in research? Will this Administration continue the work of the previous Administration in working with the manufacturers to ensure proper labeling for women?

The enrollment of women volunteers in clinical trials for medications and devices will help assure the safety of these products in female populations. I understand that FDA recently provided a report to Congress describing the development of a demographic information and data repository. If fully developed, this database will increase the Agency's ability to consider pharmaceutical effects not just by gender, but by race, ethnicity and age. As we move into an era in which medications can be tailored increasingly to the individual characteristics of patients, I believe that developing such tools is important for FDA to fulfill its responsibilities effectively. I also understand that FDA's OWH, in partnership with the National Library of Medicine, is initiating activities related to electronic labeling. I look forward to working on these and other important women's health issues while at FDA

In terms of improved maternal and neonatal health, FDA has proposed a new pregnancy labeling rule for improved communication about medicine used during pregnancy and lactation. I will work to implement and build on this effort to provide more useful information about medication risks during pregnancy.

Question 44. In our new focus on homeland security and bioterrorism, FDA will play a key role in approving new vaccines or treatments. In an effort to expedite this process, FDA may use a lower safety standard for approval. While I support the need to review and

approve new treatments or vaccines to prepare against a deadly bioterrorism attack, I am concerned about special or vulnerable populations like children and pregnant women.

What safety standards will you implement at FDA to ensure that new treatments or vaccines to fight a bioterrorism attack are safe or as safe for children and pregnant women. We know that Cipro, the only antibiotic approved specifically to treat Anthrax, has never been approved for use by children or pregnant women. How do we protect vulnerable, special populations in the event of the unthinkable?

As a general matter, FDA cannot license or approve "new vaccines or treatments" using a "lower safety standard for approval." FDA must follow the statutory standards for safety which are set out in the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act and which are described in FDA's implementing regulations. Second, if a sponsor seeks FDA's approval of a product for use in bioterrorism preparedness by an expedited approval mechanism, such as accelerated approval or the Animal Efficacy rule, FDA will apply all appropriate safety standards.

Finally, in terms of special or vulnerable populations, my understanding is that FDA has done the following: the Agency published a final rule in May of 2002, effective June 2002, entitled "Evidence Needed to Demonstrate Effectiveness of New drugs When Human Efficacy Studies are Not Ethical or Feasible", and also known as the Animal Efficacy Rule. This rule provides explicit conditions under which studying the effectiveness of products used to reduce or prevent the toxicity of chemical, biological, radiological or nuclear substances can be performed in animals when studies in human are not ethical or feasible. These conditions includes a well-understood mechanism of toxicity of the threatening substance, an animal model known to be predictive for human response, and sufficient information on the way the product is metabolized to allow for the selection of an effective dose. These studies can include non-adult animals to provide effectiveness and dose selection data for children, as well as studies on the reproductive toxicity of these products. The Agency published guidance in August 2000 that provides advice on how to design reproductive toxicity studies in animals for preventive vaccines for infectious disease indications. If confirmed, I will obviously pay close attention to the effectiveness of this guidance.

Response to Questions of Senator Reed

Question 45. One of the recommendations made in a recent GAO report to help increase the pipeline of new vaccines would be to have FDA review vaccines under its "fast track" or "priority review" authorities. Is this something you would consider as Commissioner?

FDA has reviewed, and will continue to review, license applications for vaccines in the most expeditious manner possible. Often, shortages are temporary and are over before even the most expeditious review can be completed. In such cases, the formal designation for the review process has little impact on the shortage. Thus, as a practical matter, it will be infrequent that a new vaccine will become licensed expressly and in time to alleviate a shortage. However, FDA will consider fast track and priority reviews designations whenever it appears that FDA can facilitate increased supply of vaccine through such actions. I also intend to examine the factors responsible for vaccine shortages to determine if further steps may be possible to prevent shortages in the first place.

Question 46. In light of the focus on bioterrorism since September 11, 2001, do you believe that FDA's relationships with other HHS and government agencies and with industry are sufficient to allow FDA to deal adequately with the drug- and device-related efforts necessary to America's safety? If not, have you considered what other partnerships FDA might need to establish or what other resources it needs?

Effective coordination with other agencies, hopefully including the new Department of Homeland Security, is a critical task given the terrorist threats that we now face. It is my understanding that FDA has strong relationships within the HHS, and government agencies and with industry which are necessary to deal with bioterrroism issues. Even before September 11, 2001 FDA worked closely with its sister agencies within HHS - for example Center for Disease Control and Prevention on the anthrax attacks and many food illness outbreaks as well as with other agencies on bioterrorism-related issues. I am encouraged by work that CDC Director Gerberding is undertaking to improve our monitoring capabilities; these efforts may have spillover benefits for other FDA activities in monitoring food and drug safety.

FDA also has worked with many local and state health agencies on food issues and has had long-standing and well-developed relationships with various law enforcement agencies, particularly important in tracking counterfeit drugs. There has been extensive work with industry to respond to the need for new vaccines and to expedite development of needed countermeasures. But terrorist threats are a new and evolving priority for all government agencies, and so effective coordination will demand ongoing attention. If confirmed, I will work with Congress and outside groups, as well as government agencies, to ensure that we identify and respond to new opportunities to work together to protect against bioterrorism.

Question 47. There has been growing public concern about dietary supplements. Do you think that the regulation of dietary supplements should be revisited or is the current framework sufficient?

While my examination of issues relating to dietary supplements has allowed me to appreciate the challenges the Agency faces under the Dietary Supplement Health and Education Act of 1994, at this time I do not have specific statutory changes to recommend. As Commissioner, I will work with the Department and with Congress to implement the Act in accordance with Congressional intent.

Question 48. Currently both the FDA and the USDA lack the legal authority to recall contaminated food. But food recalls conducted voluntarily by companies don't always work. For example, an August 2000 General Accounting Office report identified several instances in which the FDA believes that food companies delayed initiating a recall of their products. Do you support mandatory recall authority for the FDA? If not, how will you deal with instances where companies refuse to recall an adulterated or misbranded product or to provide distribution information?

My understanding is that FDA, through its authority under the Federal Food, Drug, and Cosmetic Act, can remove a violative product from the market by using its seizure authority. It is also important to note that the new Bioterrorism law signed by the President this year (P.L. 107-188) grants substantial new powers to FDA to administratively detain foods for which there is credible evidence or information that the food presents a serious adverse health consequence or death to humans or animals. This authority is coupled with additional authority to detain imported foods at ports of entry for a period of time sufficient to enable their inspection. FDA is currently working on regulations to implement these new authorities. It will be important to assess the potential need for mandatory recall authority in the context of these new and expanded food safety authorities once they are implemented.

Question 49. Federal food safety responsibilities are divided among twelve different agencies and governed by 35 different statutes. President Bush, Health and Human Services Secretary Tommy Thompson, and Homeland Security Director Tom Ridge all have publicly discussed combining federal food safety responsibilities into a single agency. Would you support efforts to establish a single, independent food safety agency? If so, but you do not believe that an independent agency needs to be established, where would you suggest housing a single food agency within the current government framework?

There has been much discussion about consolidating all food safety, inspection, and labeling functions into one Agency to increase the effectiveness of the food safety system. My view is that what matters most are food safety results, not organizational changes.

Last year, the White House established a Policy Coordinating Committee (PCC) led by the Domestic Policy Council and the National Economic Council to work on this issue. This group did not support the development of legislation to create a single food agency. In my view, the more important and urgent question is whether coordination amongst various Federal agencies with food safety authorities is working effectively, and whether and any new steps are necessary to improve that effort in order to advance food safety. To accomplish this goal, the PCC is continuing to explore ideas to better enhance our nation's food safety systems. As Commissioner, I would continue to enhance the close cooperation FDA has with its food safety partners.

Question 50. It was recently disclosed that the FDA failed to make public industry-submitted findings about the adverse effects of Celebrex compared to alternatives drugs. This and other cases have given rise to concern that FDA's protection of industry trade secrets makes it easy for companies to conceal safety concerns from the public and mislead the public with overly-optimistic public statements about a drug's prospects.

How would you propose to address this concern about trade secrets? What is your view on the relative priority of disclosure and protection of trade secrets? What, in your view, is the best process for determining what constitutes a trade secret?

At the core of FDA's public health mission is its responsibility to assure the safety and effectiveness of medical products. At the same time, the Agency is required by statute and its own regulations to safeguard trade secret and confidential commercial information submitted to it by sponsors of premarket approval applications, which in turn helps encourage the development of new treatments to improve the health of the public. I believe that FDA takes both responsibilities seriously, and that it should be possible to both protect trade secrets and take rapid action where there is clear evidence of significant adverse effects. FDA should respond to sponsor concealment of safety information using the full extent of its legal authority. If the concealment were uncovered following approval, for example, FDA could take a variety of actions, ranging from issuance of a public health advisory, to requiring labeling changes, to withdrawal of approval.

For products under review that have not yet been approved, FDA is not charged with policing the marketplace for false or misleading statements or omissions from the standpoint of protecting individual investors from financial losses. Instead, Congress has assigned this responsibility to the Securities and Exchange Commission (SEC), which is entitled to initiate enforcement action against a firm for making false or misleading statements or for failing to disclose material information in connection with a securities transaction. Depending on the circumstances, this could include concealment of material safety information about an investigational new drug. My understanding is that FDA refers cases of suspected false or misleading statements concerning investigational products to the SEC for prosecution and assists SEC in investigating such cases. If confirmed, I will work to make sure that FDA provides such information in a timely and appropriate fashion.

RESPONSE TO QUESTIONS OF SENATOR CLINTON

Question 51. FDA is currently undertaking a regulatory review of the pediatric rule. Can you assure the Committee that you will not take any action to weaken the protections in the pediatric rule or weaken enforcement so that pediatric studies for drugs are delayed, if completed at all?

I know FDA is committed to make sure all drugs for pediatric patients are properly studied. I share this goal and will work to make certain that children's medications are safe and properly studied. With the Best Pharmaceuticals for Children Act, Congress provided the government with a very important tool to address specific pediatric needs. In an advance notice of proposed rulemaking (ANPR) published on April 24, 2002, FDA sought public comment on how best to implement the BPCA and what additional steps, if any, need to be taken to ensure that drugs in children are adequately studied. I certainly support these efforts.

Question 52. FDA is defending its current authority against legal challenge to the pediatric rule. Is it also your view that FDA has authority to carry out the pediatric rule, and do you intend to exercise and defend that authority?

On April 19, 2002, the Department strongly reiterated that it is committed to further ensuring the safety and effectiveness of drugs used to treat children and will continue to enforce FDA's rule requiring companies to take steps to ensure drugs are properly labeled for pediatric use based on scientific studies. I share this commitment to ensuring that FDA is using all of its statutory authorities as effectively as possible to improve our understanding of the appropriate use of pharmaceuticals in children.

Question 53. Different representatives of this Administration have made differing statements with regard to the official position on the drug, mifepristone. It has now been safely used by more than a million women, but anti-choice organizations that opposed its approval in the first place have now called for the FDA to reverse its position and pull the drug from the market. What is your view on the safety and efficacy of this drug? Do you believe it is appropriate for FDA to add any new criteria in its evaluation of drugs and devices now on the market?

Please see above.

Question 54. FDA's capacity to enforce regulation of prescription drug promotion has not kept pace with the increased volume of prescription drug advertising. One study has found that more than half of direct-to-consumer advertisements contain misrepresentations, another that 38 percent of advertisements directed at doctors violated five or more FDA regulations. Examples of repeat offenders, who continue to run false and misleading ads despite multiple enforcement letters also raise serious concerns about the adequacy of FDA's enforcement of existing regulations on prescription drug promotion. Claritin for example was asked to change its advertising at least 10 times since 1997, and Celebrex was cited 3 times.

A) What actions would you take or recommend to assure compliance with existing laws and regulations governing prescription drug promotion?

B) The benefits of prescription drug advertising are enhanced if patients are directed the most therapeutically appropriate medicine, rather than a therapy that involves no advantage, or may even be therapeutically inferior to its alternatives. What action will you take to assure that comparative information for drugs and non-drug therapies for the same indication(s) is disseminated, rather than obscured?

A: One of the FDA's important responsibilities is to ensure that the public receives truthful and nonmisleading health information on drugs. The Division of Drug Marketing, Advertising, and Communications (DDMAC), in the Center for Drug Evaluation and Research (CDER), FDA, is responsible for regulating prescription drug promotion. DDMAC's mission is to protect the public health by insuring that prescription drug information is truthful, balanced, and accurately communicated. This is accomplished through a comprehensive surveillance, enforcement, and education program, and by fostering optimal communication of labeling and promotional information to both health care professionals and consumers. Section 522 of the Bioterrorism Bill will provide additional resources for DDMAC beginning in FY-03. If Congress passes appropriations for DDMAC as specified in Section 522 of the Bioterrorism Bill, the additional resources will be especially useful for regulation of direct-to-consumer advertising. Thus, if confirmed, I believe I will have an enhanced ability to help ensure that consumers receive accurate information on drugs.

B: Advertising needs to be truthful, balanced, and not misleading. Presentation of a discussion of alternatives to the treatment being promoted may be especially important in achieving this goal in cases where the product is harmful to people who can't use or have failed to benefit from an alternative therapy. In that case, my understanding is that FDA's regulations currently require that the promotion should recognize that limitation of use.

Question 55. It was recently disclosed that the FDA failed to make public industry-submitted findings about the adverse effects of Celebrex compared to alternatives drugs. This and other cases have given rise to concern that FDA's protection of industry trade secrets makes it easy for companies to conceal safety concerns from the public and mislead the public with overly-optimistic public statements about a drug's prospects.

How would you propose to address this concern about trade secrets? What is your view on the relative priority of disclosure and protection of trade secrets? What, in your view, is the best process for determining what constitutes a trade secret?

At the core of FDA's public health mission is its responsibility to assure the safety and effectiveness of medical products. At the same time, the Agency is required by statute and its own regulations to safeguard trade secret and confidential commercial information submitted to it by sponsors of premarket approval applications, which in turn helps encourage the development of new treatments to improve the health of the public. I believe that FDA takes both responsibilities seriously, and that it should be possible to both protect trade secrets and take rapid action where there is clear evidence of significant adverse effects. FDA should respond to sponsor concealment of safety information using the full extent of its legal authority. If the concealment were uncovered following approval, for example, FDA could take a variety of actions, ranging from issuance of a public health advisory to requiring labeling changes to withdrawal of approval.

For products under review that have not yet been approved, FDA is not charged with policing the marketplace for false or misleading statements or omissions from the standpoint of protecting individual investors from financial losses. Instead, Congress has assigned this responsibility to the Securities and Exchange Commission (SEC), which is entitled to initiate enforcement action against a firm for making false or misleading statements or for failing to disclose material information in connection with a securities transaction. Depending on the circumstances, this could include concealment of material safety information about an investigational new drug. My understanding is that FDA refers cases of suspected false or misleading statements concerning investigational products to the SEC for prosecution and assists SEC in investigating such cases. If confirmed, I will work to make sure that FDA provides such information in a timely and appropriate fashion.

Question 56. The Best Pharmaceuticals for Children Act, passed by Congress last year, provided explicit authority and support for the work conducted by the Pediatric Subcommittee of the Oncologic Drugs Advisory Committee including work to help evaluate and prioritize new and emerging therapies for treating pediatric cancer so that pediatric cancer patients have timely access to the most promising new cancer therapies. Because the population of pediatric cancer patients is relatively small in number, limiting the number of therapies that can be studied for that population, and because the studies have very high stakes, the decisions about which therapies to study are important and should be deliberate and scientifically sound.

Do you support these functions of the Pediatric Oncologic Drug Advisory Committee and how would you assure the facilitation of these functions?

I support the Pediatric Subcommittee of the Oncologic Drugs Advisory Committee and its ability to carry out its important functions. Related to this important area of oncology, FDA recently co-sponsored a workshop on pediatric oncology drug development with representatives from the American Academy of Pediatrics, the National Cancer Institute, and pediatric oncology organizations listed in the Best Pharmaceuticals for Children Act. The workshop provided perspective from advocacy groups, interested health care providers, academia, and industry organizations on various aspects of drug development in pediatric oncology, including prioritization of new and emerging agents, clinical trial design, and access to new therapies. The input received from this workshop has been used in developing topics for discussion at future meetings of the Pediatric Subcommittee of the Oncologic Drugs Advisory Committee. If confirmed, I look forward to receiving further input through the subcommittee.

Question 57. Prescription drug use for children under nineteen grew twenty-eight percent last year. Prescriptions of Ritalin grew 122 percent over the past four years, and a recent House Government Reform Committee hearing raised continued concerns about over prescription of this drug, especially because it is easier to write prescriptions than to use behavioral therapies that may be as effective, if not more.

As much as 70% of funding for studies psychostimulant medications come from pharmaceutical companies. Investigators who have been funded have raised concerns about undue influence on trial design and reporting of results. This has prompted the Journal of the American Medical Association to stop publishing studies without full disclosure of pharmaceutical companies' role in the study design. This intervention has helped, but researchers continue to face legal intimidation and other difficulties because of dependence on pharmaceutical financing. How do you plan to ensure that the role of other effective non-drug treatments to be addressed adequately in ADHD drug studies that lead to FDA approval?

Pharmaceutical companies are targeting ADHD drugs directly to consumers, and some suggest that the consumer marketing promotes these drugs to patients who may not meet ADHD criteria, and de-emphasizes the role of non-pharmacologic interventions for ADHD. What, in your opinion, is the FDA's role in ensuring fair marketing of drugs to consumers, especially for ADHD drugs?

The Office of the Surgeon General, together with the National Institute of Mental Health (NIMH) and FDA, coordinated a Conference on Children's Mental Health: Developing a National Action Agenda that was held on September 18-19, 2000. Pharmaceutical manufacturers, academic and other investigators, advocacy groups and Pediatric Pharmacology Research Units participated in this conference. In preparation, FDA had a meeting in April 2000 with the NIMH to discuss issues that were brought to the conference. In addition, at the Pediatric Advisory Subcommittee meeting September 11 and 12, 2000, a session was held to update the Committee on issues being developed for the conference.

Many topics, including the use of Ritalin (methylphenidate) to treat ADHD, were examined and discussed at the conference. The information generated from this meeting will help answer questions about appropriate trial designs and the needed research in this area. If confirmed, I will work to make sure that FDA continues to collaborate with sponsors to ensure the appropriate labeling of these products.

Question 58. Currently both the FDA and the USDA lack the legal authority to recall contaminated food. But food recalls conducted voluntarily by companies don't always work. For example, an August 2000 General Accounting Office report identified several instances in which the FDA believes that food companies delayed initiating a recall of their products. Do you support mandatory recall authority for the FDA? If not, how will you deal with instances where companies refuse to recall an adulterated or misbranded product or to provide distribution information?

My understanding is that FDA, through its authority under the Federal Food, Drug, and Cosmetic Act, can remove a violative product from the market by using its seizure authority. It is also important to note that the new Bioterrorism law signed by the President this year (P.L. 107-188) grants substantial new powers to FDA to administratively detain foods for which there is credible evidence or information that the food presents a serious adverse health consequence or death to humans or animals. This authority is coupled with additional authority to detain imported foods at ports of entry for a period of time sufficient to enable their inspection. FDA is currently working on regulations to implement these new authorities. It will be important to assess the potential need for mandatory recall authority in the context of these new and expanded food safety authorities once they are implemented.

Question 59. As a result of heightened concerns about food bioterrorism, the FDA received funding to hire more than 600 new food-inspection personnel. But even with this funding, the Agency can only inspect around two percent of the millions of food shipments imported to the U.S. each year.

With much of FDA's funding prioritized for drug approval, or other important FDA missions, FDA's food inspection capacity has struggled even to remain steady relative to inflation, much less keep pace with the growth in imported foods, and when there are occasional increases in funding, FDA has frequently been unable to capitalize on these increases by building those increases into the baseline for the following year. Do you support increased resources for FDA food inspection, incorporated into the baseline, and will you be an aggressive advocate for this funding?

What other plans do you have for improving the safety of imported foods? Do you believe that the FDA should have the authority to go to foreign countries to inspect the plants that are shipping foods to the U.S.?

I consider the safety of imported food a very high priority and will work to ensure that food safety activities are funded at the appropriate level. As you note, the bioterrorism bill has provided valuable new resources for food safety activities. As you know, minimizing food risks is a complex undertaking that involves many issues besides inspections. The Agency staff reports that due to constantly changing environments of operation, for example, counter-terrorism and BSE, FDA's domestic inspection and import strategy cannot be defined in terms of a percentage of coverage through inspections, physical examinations, and sample analyses. It needs to be a flexible blend of the use of people, technology, information, and partnerships to protect Americans from unsafe imported products.

An important part of the long-term solution to a higher level of confidence in the security and safety of food products lies in information technology that will merge information on products, producers, and intelligence on anticipated risks to target the products for physical and laboratory examination. This solution relies on data integrity activities that reduce the opportunity for products to be incorrectly identified at ports. It also relies on cooperation from producers so that FDA can identify sources that are unlikely to need physical testing. Foreign inspections are an important aspect of FDA's approach. If confirmed, I will work to implement these improvements in food safety activities.

Even with such targeting of products to be more closely examined, improvements are limited by the available methodologies for assessing threat agents and the Agency's ability to predict which tests ought to be used. I understand that the Agency is also using funds to work to further improve targeting and using force multipliers such as information technology.

Question 60. Following a General Accounting Office report that was highly critical of the FDA's efforts to regulate feed mills, the Agency in 1997 inspected all U.S. feed mills to ensure feed segregation. Since then, the FDA has promised annual inspections of feed mills that handle mammalian materials. Did the Agency meet its inspection goal for FY2002? How many firms remained out of compliance with the Agency's feed ban? What enforcement actions, if any, were taken against non-compliant firms?

The European Union has banned animal protein in both ruminant and non-ruminant feed, while FDA allows mammalian protein in non-ruminant feed. However, because feed is a high-volume, rather than precision product, studies have shown that large numbers of feed mills lack systems to prevent commingling of ruminant and non-ruminant feed. What actions would you take to protect the American public an/d the American farmer against the fatal and economically devastating outbreaks of BSE that can result from inappropriate contamination of animal feed by mammalian protein?

FDA's Center for Veterinary Medicine and Office of Regulatory Affairs advise me that as of October 2, 2002, FDA and its state counterparts have completed over 15,000 inspections of approximately 11,000 firms. FDA's FY 02 goal of inspecting all renderers and feed mills handling prohibited material should be met. Currently 85% of the inspections have been completed and entered into the FACTS data system with the remaining inspection information expected by the end of October. According to FDA, less than 1% of the renderers and feed mills handling prohibited material are out of compliance and appropriate enforcement action will be taken. To date FDA has issued over 50 Warning Letters and classified 31 recalls of more than 240 products.

FDA and its state counterparts conducted initial inspections of all renderers, protein blenders, and feed mills, as well as a representative number of distributors and ruminant feeders starting in late 1997. In FY 02, FDA focused its inspection effort on renderers and feed mills handling prohibited material. Any firm found to be out of compliance in its last inspection was placed in first priority to be re-inspected.

In addition, FDA prioritized its inspectional coverage to include for-cause inspections (e.g., as a result of a sampling assignment). During FY 2002 FDA developed a comprehensive Compliance Program to provide clear instructions to the field staff for conducting inspections and appropriate enforcement. In addition, the Agency conducted numerous training sessions for Federal and State investigators in order to enhance the conduct, quality, timeliness and accuracy of inspection findings and reporting; and provide updates on the science of BSE and animal protein detection methods. This included 2 major national meetings with 300 participants. These meetings included participants from USDA and Canada.

BSE is a very important issue for FDA and I will continue to devote time and attention to this as Commissioner.

Question 61. The Food and Drug Administration is charged with insuring the safety and efficacy of drugs. The same quality standards to generic drugs as to brand-name drugs. All available evidence demonstrates that generic drugs are medically equivalent to their brand counterparts. One analysis has suggested that a 1% increase in generic substitution rates could result in more than $1 billion in additional savings annually for consumers. Yet, the brand-name companies sometimes wrongly suggest that generic drugs are inferior. Do you agree that there is no basis for that charge? When false claims are made about the equivalence of generic drugs, are you, as Commissioner, prepared to work to set the record straight?

FDA approves generic drugs that are therapeutic equivalent to brand-name drugs. The quality, strength, and purity standards for approval of drugs sold in the United States are uniform, whether they are for generic or brand-name drugs. Generic drugs contain the same active ingredients as the brand-name drug and are just as safe and effective.

RESPONSE TO QUESTIONS OF SENATORS GRAHAM AND NELSON

Question 62. Most food inspections in the country are done through state food regulatory programs at both Departments of Agriculture and Departments of Health. It is important that such partnerships remain strong and continue to grow. What are your suggestions for ways to strengthen partnerships with the states? (Barnes/Oliver)

I agree that such partnerships are critical and should be strengthened. FDA works with the States through a combination of partnerships and contracts and since the passage of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 will also be utilizing cooperative agreements and grants. I look forward to working with you on this issue if confirmed.

Question 63. In today's world of biotechnology and genetic engineering, the position for which you have been nominated is that of the top administrator in the nation setting standards and approval processes for new drugs and bioengineered foods. How will you approach the development of safety standards and the approval of new products?

I believe that the safety standards for all of the products FDA regulates must be based on sound science. This is true for foods and for medical products, and for products developed through bioengineering or by other technologies. The Federal Food, Drug, and Cosmetic Act, and the Public Health Service Act lay out the safety standards that foods and drugs, including biological products, have to meet, and I believe that FDA has done a good job in ensuring that they do.

Drugs and biological products manufactured using biotechnology must meet the safety and efficacy standards set forth in the statues and implementing regulations. I believe that it is important for patients to have access to safe and effective therapies as expeditiously as possible through an efficient review process. I plan to work with CBER and CDER to ensure that new drug and biologics applications receive the highest quality review for both safety and effectiveness, and that these reviews are performed as efficiently as possible.

Regarding bioengineered foods, FDA currently has in place a science-based process to evaluate information concerning the safety of these foods. This process permits FDA scientists to evaluate safety tests conducted by developers to ensure that relevant safety, nutritional, or other regulatory issues are resolved prior to marketing. My understanding is that this process has been successful, and the bioengineered foods that have entered the U.S. market have been evaluated by FDA and found to be as safe as other foods. I also understand that the Agency is taking steps to keep pace with the latest scientific advances. FDA has established a new advisory committee for food biotechnology, and the Agency is developing new guidance to assist industry in the early stages of product development. FDA believes that these and other initiatives will ensure that the Agency is ready for new developments and will enhance consumer confidence and enhance the safety of the food supply.

Question 64. How do you propose to establish close liaisons to coordinate on food security and food safety with the proposed new Department of Homeland Security?

FDA has close ties with the law enforcement and intelligence communities through its Office of Criminal Investigations. Those interactions have been strengthened since the events of September 11, 2001. FDA has already established or participates in a number of interagency committees to coordinate food safety and security activities. These interactions are anticipated to continue and expand when the Department of Homeland Security is established.

Question 65. Most states have enacted the Model Food, Drug, and Cosmetic Act and work closely with FDA to ensure uniformity and consistency. There have been past attempts to enact a more stringent federal preemption statute that some fear could thwart state programs for food safety. Many state legislature are questioning whether to fund state programs if these are preempted by federal law. What is your position on federal preemption?

State programs play an important role in promoting food safety, and as Commissioner I intend to build on efforts to work with states cooperatively to ensure uniformity and consistency. As I learn more about this issue, I will work with the Administration and other interested parties on developing a position on the issue of whether federal preemption is appropriate in certain circumstances.

Question 66. There has been numerous reports of adverse reactions associated with herbal supplements on the market. In light of these reports, what are your thoughts on how best to address adverse reactions occurring with herbals and dietary supplements?

Dietary supplement safety is one of FDA's key responsibilities. As part of FDA's Dietary Supplement Strategic Plan, the Agency is developing and will soon implement the CFSAN Adverse Event Reports System (CAERS). This comprehensive system will track and analyze adverse event reports involving cosmetics and foods, including dietary supplements. CAERS will replace the patchwork of existing adverse event systems that are currently maintained by individual offices within CFSAN.

Publishing regulations on good manufacturing practices (GMPs) for dietary supplements is also an important initiative related to the safety of dietary supplements. FDA has forwarded draft proposed GMP regulations to the Department of Health and Human Services. On October 4, 2002 the Department submitted this proposal to the Office of Management and Budget for 90-day review. If confirmed, I intend to work to implement GMP regulations as quickly as possible.

Question 67. The FDA has long endeavored to get mercury out of other health products and devices, yet in docket # 01-N-0067 and 01-D-0064 declares that mercury dental fillings are safe. The Dental Devices section failed to have a current scientific advisory panel examine the proposal, nor has it held public hearings on the proposal, which has drawn overwhelmingly negative responses during the public comment. The regulation would preempt state consumer protection laws, a move out of step with the general position of this administration. Dr. McClellan, will you ensure that any actions taken by FDA with respect to mercury in regulated products comport with the position of the White House Task Force on Mercury, the general FDA policies against mercury in health products and devices, and FDA policies on up-to-date scientific review of its proposed regulation?

I will work to make sure that actions FDA takes on mercury in regulated products are guided by the recommendations of the White House Task Force on Mercury, the general FDA concerns about health problems associated with mercury, and FDA's reliance on up-to-date scientific information for decision making. The comment period on this proposed rule has just recently closed. The Agency will carefully review all comments to the proposed rule and, if confirmed, I look forward to acting based on these comments.

RESPONSE TO QUESTIONS OF SENATOR GREGG

Question 68. Do you share the view that FDA and CMS have distinct regulatory missions and that any harmonization of their responsibilities should be approached carefully? Given your background, how are the missions of these agencies similar and distinct? How can FDA and CMS work together to speed access of safe and effective medical technologies for Medicare beneficiaries without delaying access to those same technologies by the rest of the American public? Can you assure me that you would oppose efforts to involve FDA in collecting data related to cost, cost effectiveness, value, and other reimbursement considerations in an effort to address concerns with the CMS coverage process, which responsibility is outside the current scope of FDA review, and which responsibility would inevitably only result in delaying public access to medical technology?

Certainly, FDA and CMS have distinct roles. As you know, FDA does not make coverage decisions. Rather, it approves items like devices and drugs based on their safety and efficacy. CMS must make determinations for coverage. These are different standards and may require different analyses. From the perspective of CMS' authority, just because an item is safe for marketing, it is not necessarily the most medically appropriate item for a beneficiary, or a good use of taxpayer funds.

That said, I think increased interaction and cooperation among Federal agencies is wise. I understand that CMS currently works collaboratively with FDA when gathering and considering evidence to make national coverage decisions. In addition, the staffs collaborate through interagency agreements, workgroups and task forces, and in consultative roles with respect to setting and enforcing quality standards, quality improvement and measurement activities, and coverage. I have worked closely with CMS Director Scully over the last 18 months, and if confirmed, I will work with him to explore areas where these two agencies can further improve their working relationship for the benefit of the American public.

The activities that you identify relating to cost and reimbursement are not primarily within FDA's mandate under the Food, Drug and Cosmetic Act.

Question 69. User Fees. Dr. McClellan, the Senate now has before it legislation to reduce delays in FDA review of innovative medical technologies by giving it user fee resources. The user fee agreement recognizes that CDRH's base has been substantially eroded over the years. In order for the public to obtain the full benefit of the performance goals outlined in the user fee deal, the CDRH needs both the fee revenue from manufacturers and an additional $15 million in appropriations added to its base in 2003 and carried forward in each of the subsequent four years. Do you support adding the $15 million to the device centers' budget in FY'03? Will you work to ensure that the President's budget for FY '04 and subsequent years includes this $15 million?

The user fee program that has been negotiated over the last five months is a $50M program by year five. The goals that FDA agreed to meet are contingent on the Agency receiving $50M by year five. The industry agreed to fund up to $35M in user fees by year 5 and the remaining $15M is to come from appropriated dollars. I strongly support enactment of this new user fee program in this Congress. If Congress passes the law that creates this user fee program for medical devices, I plan to work to ensure that the device program receives the funds it needs to adequately implement the program and meet the goals that are laid out in the draft goals letter.

Question 70. It is an unavoidable fact that FDA cannot keep pace with rapid advances in medical technology without more help from outside experts. This is not a criticism of the hardworking reviewers at FDA. Even with its limited resources, it would never be practical for FDA to have the expertise on staff to properly assess the most recent innovations from the frontiers of medical technology. In 1997, Congress gave FDA explicit authority to use outside experts to help with all or portions of a product review. To date, FDA has seldom, if ever, used this authority. Needless delays in product reviews could be avoided if FDA brought in an outside expert to help reviewers understand the scientific issues behind a product application. In addition, legislation now under consideration would authorize the Agency to make use of independent outside experts in the facility inspection process. It is important to stress that what FDA needs in these situations is not more resources but more expertise. Dr. McClelland, what are your thoughts on how FDA can make greater use of independent outside experts to augment FDA's in-house review and inspection programs?

I believe that appropriate reliance on outside experts can augment and strengthen FDA's internal capabilities. I understand that FDA is making greater use of independent outside experts, and the activity at the Center for Devices and Radiological Health (CDRH) is a good example of this. CDRH is working to enhance scientific decision-making and expand the Center's capacity to evaluate and ensure the safety and effectiveness of medical devices. The Center is engaging outside experts to assist with pre- and post-market product review. Clinicians, surgeons, engineers and scientists from academia, other government agencies, and the military are providing needed medical and scientific expertise on a wide range of increasingly complex medical devices. As Commissioner, I look forward to having the opportunity to further evaluate this matter and to support collaborations with outside experts where appropriate.

Question 71. We have seen recent reports raising concern about a drop-off in the number of warning letters that FDA field offices are issuing on drug advertising and other issues. Yet FDA leaders highlight the need to bring greater consistency and predictability to the process of issuing warning letters for violating FDA rules,

which in the past has varied widely from district to district. As Commissioner, how do you plan to ensure appropriate, yet consistent, enforcement of FDA rules?

I believe in credible, risk-based enforcement. I also believe FDA should speak with one voice and be as consistent as possible, to help make sure that the threat of an FDA enforcement action is taken very seriously. It is my understanding that this was why, in November of 2001, Deputy Secretary Claude Allen directed that the Office of Chief Counsel review all enforcement correspondence. Before this directive, there was no central repository of such letters, no tracking system, and little coordination. Letters were often issued long after the deadlines set in the Regulatory Procedures Manual. (RPM).

It is my understanding that there had been complaints that, in some cases, different districts were taking varying positions on the same issue. There had also been complaints that FDA would not follow up on many of the letters. Moreover, there were assertions that some of the letters were not legally sufficient, and some did not reach the threshold of regulatory significance.

I intend to examine this issue more closely if I am confirmed, and thanks to recent FDA actions, I will have better and more timely data to do so. FDA now tracks such letters, and has recommitted to the deadlines in the RPM. Between February 27 and September 5, OCC reviewed and disposed of 699 letters. It refused to concur in only 6 percent. The vast majority was concurred in subject to various changes meant to strengthen and improve the letters.

In fact, my understanding is that, on occasion, OCC has urged that the district or center consider bringing an enforcement action instead of sending a letter. OCC has even refused to concur on the grounds that an actual enforcement action, rather than a letter, was the appropriate response.

FDA's mission in protecting the public health is so critical that its enforcement capabilities must be taken extremely seriously. When the Agency takes a position, companies must believe that FDA can and will back it up by going to court if necessary. I believe that the OCC review policy is consistent with this goal, and I intend to make sure that it works to increase FDA's consistency and credibility. I would like to state very clearly that, if I am confirmed, I will work to ensure that FDA takes action when companies fail to comply with warnings.

Question 72. A challenge facing every head of a science-based regulatory agency is how to effectively communicate to the American public about the risk and benefits of regulatory decisions. The vast majorities of new medical technologies perform as intended and deliver life saving and life improving benefits to patients. Yet medical technologies can be inherently dangerous and on rare occasions, a serious problem arises. Dr. McClellan, how do you propose to balance the occasional need to alert the public to real and potential product-related threats without undermining the public's well placed confidence in the medicines and foods they use on a daily basis?

Communicating effectively with the public about risks and benefits is one of FDA's most important and challenging tasks. FDA already has a well developed system to alert and advise the American public about the risks that may come to light with FDA regulated products. The Agency uses different modes of communication in an effort to achieve a rational, balanced presentation of the facts. The Agency makes extensive use of the Internet, issue talk papers and press releases regularly distributed to the media as well as a system to alert healthcare professionals and industry as necessary.

As good as any system for communicating risk may be, there is always room for improvement and, as risks and available methods of communication change, good reasons to take a fresh look at the issue of effective risk communication. As Commissioner, I will work with the FDA Centers to explore such innovative approaches. Where appropriate, I will examine ways to improve communication approaches across the Centers. I look forward to discussing any additional recommendations from you and other members of Congress in this important area.

Question 73. An increasing number of breakthrough medical technologies are based on tissue-engineered technology. I believe that, based on the primary mode of action of these technologies, they must remain under the purview of FDA's device center, and that there is no public health reason to move these products to another center. I am concerned doing so would introduce needless delays in the review process. Would you agree that tissue-engineered medical products should continue to be regulated as medical devices?

You have highlighted an important example of how FDA's regulatory capabilities need to adapt to new kinds of biomedical innovation. FDA's device center has clearly developed unique expertise that will be relevant to many new tissue-engineered technologies. In my oral remarks I urged that Congress adopt the Medical Device Amendments of 2001, H.R. 3580, during the current session. As reported by the House Committee on Energy and Commerce, section 203 of the bill would establish

an Office of Combination Products in a manner that is consistent with recent Agency actions to promote combination product reviews. As Commissioner I will work with Congress and others to evaluate the most appropriate approaches for addressing tissue-engineered medical products, and I will ensure that the expertise developed by FDA's device center is used to ensure timely and consistent review of such products. Obviously, enactment of H.R. 3580 would be a great help in achieving this goal.

Question 74. The U.S. is the world leader in developing new medical device, drug, and biotechnology products. These products contribute $7.2 billion annually to our balance of trade. The market for these products is truly a global one and the regulatory systems our manufacturers face can be quite varied. Patients around the world, and our own US based companies will be better off with greater convergence among the regulatory models around the world. Achieving mutual recognition agreements with trading partners is one important step FDA can take in this regard. As Commissioner, will you work to implement existing MRAs quickly and reaching additional agreements with our major trading partners?

As you note, there are enormous benefits for American workers and our national economy from a greater ability to export our world-leading medical products. Mutual recognition agreements are important for the Agency because of the leveraging it provides for FDA's inspectional resources and assisting the Agency in its public health mission. If I am confirmed as Commissioner, I will certainly investigate expediting implementation of current MRA's and working on additional agreements.

RESPONSE TO QUESTIONS OF SENATOR FRIST

Question 75. The Administration is, reportedly, developing a plan to allow individuals to choose to receive smallpox vaccinations in advance of any potential smallpox attack by a bioterrorist. The Administration already has asked states and localities to develop plans to vaccinate individuals in the event of a smallpox outbreak. What role do you expect and believe the FDA should play in supporting the Administration's plans to protect the American people from a potential smallpox attack?

FDA will play an important role in providing guidance, technical assistance, and product review for the smallpox vaccine and other bioterrorism-related products. The Agency has embarked on an expanded program of regulatory and scientific assistance to industry and to state and Federal public health agencies. I have also been advised that FDA is expediting its review of new products, new uses of approved products, including products to address a smallpox attack, and new manufacturing sites for counter-terrorism products.

Finally the Agency is working with the Department of Defense to develop test methods for investigational products suitable for large scale military and civilian health emergencies. I believe that these are appropriate actions to respond to such threats.

If confirmed, I will work expeditiously on these and other steps to develop safe and effective bioterrorism countermeasures.

Question 76. Currently, we do not have vaccines for a number of the deadly potential agents that may be used in a bioterrorist attack against Americans. What responsibility do you believe the FDA has to ensure that additional vaccines, assays, and other bioterrorism countermeasures are rapidly developed? Are there any legal changes that you believe are necessary in this area to ensure that we are able to develop necessary countermeasures to protect the American people?

FDA's role in the development of medical countermeasures to combat terrorism is a proactive stance in the provision of regulatory guidance to see that vaccines, drugs, and medical products developed for these purposes are safe, effective, and available to the public when they are needed. Activities include regulatory guidance for products under development, communication with manufacturers to address shortages and inventory concerns, and regulatory guidance for the deployment of products for which outcomes data collection is a legal requirement. FDA has many important responsibilities, but the development of bioterrorism countermeasures must be given a very high priority. I assure you that I will devote significant attention to this task while at FDA.

Question 77. The bioterrorism legislation was completed in record time. Do you have any recommendations about how we could improve upon that bill. Are there actions you believe the FDA Commissioner can take administratively to further improve our bioterrorism preparedness or response capabilities?

This is landmark legislation that gave the Food and Drug Administration new responsibility and authority with respect to ensuring the safety of the food supply and rapidly approving vaccines and other countermeasures. FDA is currently involved in a number of rulemakings with respect to this new authority. I am not aware of

the need for any major amendments. If I learn of the need for changes, I will work with the Administration to notify Congress. As for administrative changes, preventing bioterrorism and protecting the food and drug supply will certainly be a major focus of my tenure at FDA. As the Agency identifies administrative actions to improve our bioterrorism preparedness, I will work to implement them and work with Congress to ensure they are consistent with our specified statutory authorities. I appreciate the committee's leadership in enacting this important legislation, and look forward to working with you to achieve our shared goal of protecting the nation from new bioterrorist threats.

Question 78. Are there actions the FDA could take to alleviate existing shortages of childhood vaccines and prevent future shortages?

Beginning in 2001, there was an unanticipated shortage of some of the recommended vaccines in the United States. Through concerted efforts by suppliers, FDA, and other HHS agencies, my understanding is that this situation has eased considerably. Supplies of these vaccines returned to normal by the summer of 2002, with the exception of the Pneumoccal Conjugate Vaccine. Because of manufacturing challenges as well as the large demand, this vaccine is still in short supply.

An ample supply of influenza vaccine is currently available for the 2002-2003 influenza season, and there are no delays at this time.

In the future, as in the past, FDA will work with manufacturers to anticipate shortages, to encourage increased production of needed vaccines when shortages are anticipated, and to expedite FDA review of any pending applications or submissions for vaccines in short supply. If confirmed, I intend to work with you to explore new ways to prevent vaccine shortages in the future.

Question 79. Broadly thinking, what changes in FDA regulation and policy are necessary to ensure an adequate, stable supply of needed vaccines?

We must look first to the causes of past shortages. These have been addressed recently in detail by the GAO and by the National Vaccine Advisory Committee; the causes are complex. Shortages caused by such events could be mitigated, in part, by maintaining stockpiles of essential vaccines, and by improving incentives for adequate participation and production in the vaccine industry.

Currently, there is no mechanism for FDA to get reliable reports from vaccine manufacturers, even sole manufacturers, of projected shortfalls in production or a decision to stop manufacturing or distributing a vaccine. Advance notification to FDA by vaccine manufacturers would facilitate timely and effective agency actions. For now, FDA must rely on information voluntarily provided by vaccine manufacturers to help mitigate any shortages.

Question 80. In addition to prioritizing the review and approval of emerging technologies, what action can the FDA take to further ensure the safety of blood, tissue and organ supplies?

Blood, tissue, and organ safety is an important FDA responsibility, and I intend to build on some recent programs implemented by FDA to improve safety in these areas. FDA has created a new office that oversees tissues as well as cellular and gene therapies. Close coordination with the Office of Blood Research and Review within the Center for Biologics Evaluation and Research (CBER) will help ensure that consistent donor testing is performed on potential blood and tissue donors. For example, development of West Nile Virus screening tests will be used not only for blood donors, but also for human tissue donors. Human organ transplantation is regulated by the Health Resources and Services Administration, with which CBER has close coordination. FDA continues to increase its capacity to inspect human tissue banks to bring inspections on par with blood bank inspections.

Additionally, FDA continues to work with the tissue industry and the Centers for Disease Control and Prevention to provide guidance on procedures to minimize the chance for cross-contamination of tissues with pathogenic organisms during processing. The Agency intends to work with the medical community to enhance the sharing of information concerning potentially contaminated tissues and to provide guidance on the submission of INDs for new cellular and tissue-based products.

Question 81. FDA plays a critical role in protecting individuals participating in clinical trials. What actions do you believe FDA can take to strengthen protections today, and what legislative steps do you believe are necessary in the future?

My examination of the issues relating to Human Subject Protection has allowed me to appreciate the importance of these issues, which are vital to the integrity and validity of clinical research. As Commissioner I will work with you and others in Congress to assess the need for potential changes to the law or regulations in order to better protect those who participate in clinical trials.

RESPONSE TO QUESTIONS OF SENATOR COLLINS

Question 82. Dr. McClellan, over five years ago, the Food and Drug Administration (FDA) examined the health issues that tissue transplantation could pose to the public and concluded that the existing regulatory framework was insufficient. Subsequently, FDA notified the industry that it intended to impose regulatory changes to strengthen oversight of tissue banks and processors, through the "Proposed Approach to the Regulation of Cellular and Tissue-Based Products." Yet, five years later, the majority of the regulatory changes are not final, and the Agency cannot even state when the remaining regulations will be implemented.

In August 2002, Secretary Thompson advised me that while the department is giving publication of the final rules high priority, they are not able to forecast a specific date. When do you anticipate the regulations will be finalized?

I agree with you that improving the safety of tissue banks and processing is an urgent priority. FDA is giving publication of the final rules high priority as indicated by the current listing in the Unified Agenda (67 FR 33072) and expects to complete its rulemaking process within the next 12 months. I will work to expedite this process, and will continue to work closely with you and others to help ensure that all tissue banks and production processes meet the new FDA standards.

Question 83. Dr. McClellan, in May 2001, as Chair of the Permanent Subcommittee on Investigations, I held a hearing that examined the efficacy of the current regulatory framework. During the hearing, Dr. Kathryn Zoon, Director of FDA's Center for Biologics Evaluation and Research, testified that FDA is committed to establishing a regulatory framework that will ensure the safe use of human tissue for transplantation. Dr. Zoon estimated that the Agency would dedicate $4.35 million in resources in fiscal year 2002 to the regulation of human tissue. She also testified that cost estimates of the implementation of the tissue regulation would be developed as part of the fiscal year 2003 budget. No estimates have yet been provided by FDA or the Department of Health and Human Services (HHS). Furthermore, in January 2001, my colleague Senator Durbin sent a letter to FDA requesting a breakdown of costs for implementation of the proposed regulations, and has never received a response.

It is impossible for Congress to provide the necessary resources unless the figures are identified. Would you please provide an estimate of the costs associated with implementing the regulations?

Thank you for your efforts to promote safe tissue transplantation policy. If confirmed, I look forward to working with you to ensuring that all tissue banks and processors provide safe tissue products.

Question 84. Dr. McClellan, in my bill, S. 2531, The Tissue Transplant Safety Act of 2002, I included a provision that would require the Commissioner of FDA and the Director of the Centers for Disease Control and Prevention (CDC) to jointly develop a single reporting mechanism for use in reporting adverse reactions of tissue. I believe there is a need for a centralize reporting system because the CDC does not currently have access to the same information as FDA. In fact, CDC must now rely on information it solicits from FDA ans state health departments. A central repository of adverse reaction information would be very useful in order for CDC to perform timely investigations of public health threats.

When FDA was asked to comment on my bill, the Agency did not take a position on the requirement other than to suggest that it might be a cumbersome process. What is your position on a central reporting requirement?

My understanding is that FDA currently receives voluntary reports of adverse events related to tissue through FDA's Medwatch System. FDA's proposed Good Tissue Practice rule would require tissue establishments to report adverse reactions and product deviations to the Agency. FDA also recognizes the importance of sharing and coordinating this information with CDC and is committed to working closely with CDC on this issue. If confirmed, I will work with you to ensure that this important goal is achieved.

Question 85. Dr. McClellan, included in my bill, S. 2531, The Tissue Transplant Safety Act of 2002, is a provision that would require tissue establishments to submit a registration request to the Commissioner of FDA that would identify the principals of the establishment and the scope of its operation. Upon approval, a covered entity could then engage in activities related to human cell, tissue, or tissue-based products. An entity's registration could however, be suspended or revoked if found not to be in compliance with tissue regulations.

When FDA was asked to comment on the bill, the Agency responded that the provision conflicts with FDA's current registration requirement, which is a simple notification to FDA that allows the Agency to communicate with and inspect establishments that engage in tissue activities.

Unfortunately, a major gap in the current oversight regulatory scheme has been the haphazard inspection cycle with which FDA has examined tissue establishments. The ability to suspend or revoke registration would be a powerful means by which FDA could use to ensure greater compliance with safety standards and tissue regulations.

What is your opinion with respect to strengthening the registration requirement?

I agree that inspections and strong enforcement tools are important to help protect the public from unsafe tissues. FDA's recent Establishment Registration and Listing Final Rule requires tissue establishments to register with FDA and list their products and will increase the effectiveness of our inspection program. The Good Tissue Practice Proposed Rule includes inspection and enforcement provisions to ensure compliance. These provisions would allow FDA to order, as needed, the retention, recall, and destruction of products that present a communicable disease threat to the public. The proposed enforcement provisions would also permit FDA to order the cessation of one or more steps in the manufacture of tissue products, as needed, to protect the public health. These are powerful enforcement tools. FDA has successfully ensured compliance with other regulations using similar tools, without linking registration with the right to conduct business. If confirmed, I will examine whether these compliance tools are working effectively to achieve our important goal of tissue safety, and whether additional measures are necessary.

RESPONSE TO QUESTIONS OF SENATOR HUTCHINSON

Question 86. Recognizing the potential for prescription to nonprescription drug switch to further develop consumer empowerment and lower the costs of health care, would you describe the level of emphasis that you would place on Rx-to-OTC switch and the approval of new OTC drugs?

Over-the-counter (OTC) drugs play an increasingly vital role in America's health care system. As Commissioner my goal is to be proactive in identifying Rx-to-OTC switches of drug products that will provide consumers an enhanced role in their health care decisions.

Question 87. Nonprescription or over-the-counter (OTC) medicines serve important benefits for consumers, empowering them to treat certain conditions that can be self-diagnosed without the intervention of a physician. Do you agree that OTC medicines provide value for the public health delivery system, and if so, do you support giving greater emphasis to programs that focus on OTC medicines and consumer self-care issues?

Over-the-counter (OTC) drugs play an increasingly vital role in America's health care system. As Commissioner my goal is to be proactive in identifying Rx-to-OTC switches of drug products that will provide consumers an enhanced role in their health care decisions.

Question 88. Based on recent actions by FDA relating to dietary supplements, such as the development of a more rigorous adverse event surveillance system and several enforcement actions relating to safety and claims, do you agree that the Dietary Supplement Health and Education Act (DSHEA) provides FDA with adequate legal authority to regulate dietary supplement products?

While my examination of issues relating to dietary supplements has allowed me to appreciate the challenges the Agency faces under the Dietary Supplement Health and Education Act of 1994, at this time I do not have specific statutory changes to recommend. As Commissioner, I will work with the Department and with Congress to implement the Act in accordance with Congressional intent.

RESPONSE TO QUESTIONS OF SENATOR FRIST

Question 89. Background: On September 28, 2000, the FDA approved RU-486, mifepristone (Mifeprex), for termination of early pregnancy (49 days or less).

The drug is distributed by Danco Laboratories, and manufactured in China for distribution in the United States by Hua Lain Pharmaceutical Company. FDA contends that the manufacturing site was inspected by the FDA to make sure it met FDA's requirements under Section 510 of the Federal Food, Drug and Cosmetic Act.

Many question the safety of RU-486 to the health of the mother. According to the FDA medication guide that is required to accompany each physician's distributing of RU-486, patients should visit their provider three times throughout this treatment and that 5-8% of women will need surgery to end the pregnancy or stop chronic bleeding.

The drug must be supplied directly by qualified physicians, and will not be available through pharmacies or the Internet. Physicians administering the drug must be qualified to provide any necessary surgery, or have made arrangements for any necessary surgery.

Recent Events: April 19, 2002, Danco Laboratories, working with the FDA, issued a letter to health care providers regarding postmarketing adverse events of ectopic pregnancy (including one case of ectopic pregnancy resulting in death), sepsis, and a single case of heart attack. The letter reminded providers of the approved regimen for Mifeprex and of the need to report any serious adverse events associated with Mifeprex.

On September 13, 2002, Governor Davis of California signed into law a bill that would allow nurses to prescribe abortion pills, such as Mifeprex, as long as they are under the supervision of a physician. However, the law does not require the physician be present, and may be read to conflict with the approval guidelines laid down by FDA.

On September 25, 2002, Danco Laboratories stated that more than 100,000 abortions had been completed in the U.S. since approval of the Mifeprex in 2000, that sales have increased significantly this year and that they have begun to see the drug used in private physicians' offices, as well as abortion and family planning clinics.

Questions. What do you believe are appropriate circumstances under which to withdraw a drug from the market?

Along with Senator Jeffords, I introduced legislation to improve patient safety. The House has passed two similar bills, and Senator Kennedy has even introduced such a bill. A common provision in all the bills would create a voluntary reporting system to track patient errors and adverse events. As you know, FDA already has such system for reporting adverse reactions to medications. What else do you think should be done to improve patient safety?

a. As you know, the circumstances under which the Commissioner of Food and Drugs has the power to withdraw the approval of a drug are specified by section 505(e) of the FD&C Act. These circumstances include: 1) new evidence shows that the drug is unsafe for use as approved by the Agency, 2) new evidence that either was not considered or was not available at the time of approval demonstrates that the drug is not shown to be safe for use as approved by the Agency, 3) new evidence indicates that there is a lack of substantial evidence that the drug will have the intended effect under the conditions of use in the labeling, 4) the sponsor fails to file patent information required under the Act, or 5) the application contains an untrue statement of material fact.

Additionally, mifepristone was approved for marketing under 21 CFR Part 314, Subpart H. Under Subpart H, FDA may withdraw approval of an application approved under that Subpart if: 1) a post-marketing clinical study fails to demonstrate clinical benefit, 2) the sponsor does not perform a required postmarketing study with due diligence, 3) post-approval use of the product demonstrates that post-marketing restrictions are inadequate to assure safe use of the drug, 4) the sponsor does not follow agreed-upon postmarketing restrictions, 5) the promotional materials are false or misleading, or 6) other evidence demonstrates that the drug is not shown to be safe or effective as approved.

b. As you know, I appreciate your leadership and Senator Jeffords' leadership on the important problem of patient safety. Indeed, I believe that a major step that this Congress could take before adjournment to reduce errors is to enact your bipartisan bill, or the very similar bipartisan legislation that has been reported out of the Ways and Means and Energy and Commerce Committees in the House.

If confirmed, I look forward to working with you and other members of Congress to building on this legislation with further administrative actions to help improve patient safety and eliminate avoidable complications of drugs and devices. More complete information on adverse events will help achieve this goal. As you know, FDA's voluntary system focuses on adverse events, which may or may not be the result of medical errors. FDA has undertaken efforts to encourage increased reporting of adverse events and medical errors.

FDA currently is working on several additional patient safety initiatives, such as a proposed rule to require bar-coding of prescription drug products. I will look for more opportunities for FDA to take action to improve patient safety.

RESPONSE TO QUESTIONS OF SENATOR WELLSTONE

Question 90. FDA officials have been working hard to improve the speed of the review process for drugs and biologics, and if there is new medical device legislation that provides FDA's Device Center more resources, those reviews are also likely to be faster in the coming years. Speed of approval must be balanced ,of course, with patient safety. Many patient and consumer groups are worried that FDA has become more focused on responding to industry's concerns rather than rigorously assuring patient safety. In order to assure patient safety, what will you do to improve

resources needed to monitor adverse reaction reports, Phase IV trials, and other safeguards that protect patients from potentially dangerous products?

The enactment of PDUFA III allows resources from user fees to be used for enhanced risk management resources for the human drug and biologics programs. These additional user fee resources should enable the Agency to add additional staffing to the Agency's risk management efforts, including those efforts that occur up to three years after a new drug is approved. These additional PDUFA resources will enable the Agency to add about 100 additional staff years to drug and biologic risk management efforts by 2007. The PDUFA resources are clearly designed to enhance patient safety.

As I indicated in my oral remarks, I believe that Congress should adopt the Medical Device Amendments of 2001, H.R. 3580, during the current session. H.R. 3580 defines the process for the review of medical devices, upon which device application fee revenues may be spent, to include both the evaluation of postmarket studies required as a condition of approval and compiling, developing, and reviewing information to identify safety and effectiveness issues. If this legislation is enacted, it will permit FDA to use some of the resources to enhance patient safety.

Question 91. The FDA usually follows the recommendations of their advisory committees when decisions are made about approving new drugs, biologics, or medical devices. However, sometimes FDA approves products that the advisory panels do not recommend. For example, in a recent case involving a type of jaw implant (TMJ Implants Inc. Fossa Eminence implant), FDA approved the device even though the advisory committee unanimously opposed approval and the FDA's scientists pointed out the deficiencies of the safety research. The FDA stated that the patient and surgeon should share the risk of this device, instead of the FDA deciding for them whether the device is safe. Patient groups point out that the company heavily lobbied FDA to get their product approved. What will you do to ensure that decisions about the approval of new drugs, biologics, or devices are made on the basis of scientific evidence, not political pressure?

FDA is a scientific regulating agency that makes decisions on the basis of science. The Agency's review and approval of medical products must adhere to its legal mandate and mission as a science based public health regulatory agency. Open discourse and information gathering within FDA about the best available evidence on the safety and efficacy of products under the Agency's regulatory authority is essential to creating the appropriate decision-making atmosphere to fulfill this mandate. I will work to maintain an open atmosphere within FDA for dialogue about products under FDA review. At the same time, I will also work to promote predictability and transparency about FDA decision making processes.

Question 92. In the last few months, several investigative articles have criticized the lack of safeguards in FDA's regulation of implanted medical devices. There have been examples of implants being withdrawn from the market after patients died or were seriously harmed by implants. Some of these implants were approved through the 510K process, which is supposed to be limited to products that are "substantially equivalent" to other products on the market. However, the FDA determined that some implants were "substantially equivalent" even if they were made out of a different material,or used in a different part of the body.What will you do to make sure that implants reviewed through the 510k process really are substantially equivalent?

Substantial equivalence determinations are intended to be sufficiently flexible to allow product change and improvement, so long as the new product is at least as safe and effective as a product already on the market. In accordance with the statute and its regulations, FDA does require the submission of a new 510(k) for changes or modifications to an existing device, where the modifications could significantly affect the safety or effectiveness of the device. Changes in materials may be handled under the 510(k) process. However, I understand that the Agency has the discretion to require clinical data to support the use of new material in that implant in order to establish that the new product remains as safe and effective as the "predicate" product. Obviously, if confirmed, I will work to make sure that the Agency continues to collect such information when appropriate.

Question 93. A new GAO report recently concluded that post-market surveillance has suffered as a result of the Prescription Drug User Fee Act (PDUFA). Post-market surveillance is needed to make sure that drugs and other medical products are safe when available to the general population, and not just in premarket clinical trials. It is also important since so many drugs are taken for many, many years to treat chronic conditions. And of course, patients with implanted heart valves, knees, and other body parts may lives for decades. What is your view of requiring registries for implanted medical devices, and long-term safety studies for implants and drugs used for chronic diseases? How long-term should those long-term studies be?

I understand that FDA has some experience utilizing registries for issues related to medical devices. I also understand that when Congress required the Agency to use a pacemaker registry in the mid-1980s, the Agency encountered reluctance on the part of health professionals and patients. However, I will continue to be open to explore the use of registries, as well as other tools to develop more accurate and timely information on the safety of drugs and devices in practice. As you know, recent changes in the law (Section 522 of the Federal Food, Drug and Cosmetic Act) permit the Agency to request postmarket studies for up to three years. The Agency considers the use of registries to be a postmarket study tool. While the current law establishes three years as the ordinary limit on postmarket studies, the Agency may require longer studies if the manufacturer consents or the issue is resolved by a scientific dispute resolution panel. Finally, as part of the FDA drug approval process, the Agency may also obtain a commitment from the drug sponsor to perform Phase IV clinical trials, including long-term studies. These studies occur after a drug is approved. Finally, other electronic data sources may provide useful sources of information on long-term safety.

It is my understanding that some manufacturers of drugs for which long-term use has been proposed have committed to follow several hundred patients for at least one to two years. How long the studies should be would depend on the particular drug and patient population to be followed.

Question 94. Biologics can involve live cells that need nutrients such as bovine serum to survive. What safeguards does CBER use to make sure that those live cells and serums do not harbor dangerous infections such as Mad Cow Disease? Now that CDER will take over some responsibilities from CBER, what will you do to make sure that these safeguards are still in place?

FDA's vigilance and procedures will not be changed after the transfer of the review of certain biological products from CBER to CDER. I understand that, through issuance of several letters and guidance documents, FDA continues to recommend that manufacturers of all vaccines and other biological products eliminate the use of bovine-derived materials obtained from high-risk bovine spongiform encephalopathy sources.

Since 1989, and most recently in January 2002, FDA also has issued numerous Guidance documents recommending that human blood and blood products and other biologic products containing or prepared using human blood derivatives not be obtained from donors at increased risk of transmissible spongiform encephalopathies, including variant Creutzfeldt-Jakob Disease. If confirmed, I intend to continue and, where necessary, enhance such steps to ensure the integrity and safety of biologics.

Question 95. When the Prescription Drug User Fee Act (PDUFA) was coming up for re-authorization in the past year, FDA officials met with industry representatives in a series of meetings, where the outlines of the user fee agreement was hammered out. Consumer groups were invited to a few meetings with the FDA officials, but were not part of the meetings where decisions were made. A similar scenario took place when FDA negotiated with device manufacturers to develop user fees for medical devices.

In your view, what is the appropriate role of patient and consumer organizations when policies affecting consumers are being developed?

FDA values the input of all interested stakeholders as the Agency carries out its mission to promote and protect the public health. If confirmed, I intend to explore ways to enhance opportunities for such external input; it is valuable in making sure that FDA's decisions are as well informed as possible.

This approach is consistent with the FDA's governing statute. Section 505 of Public Law 107-188 requires the Secretary of Health and Human Services to consult with a broad spectrum of stakeholders, in developing proposals for reauthorization of the Prescription Drug User Fee Act (PDUFA). This section further provides that recommendations for reauthorization of this Act be published in the Federal Register. Finally section 505 provides that following discussions on the proposal with the regulated industry, the recommendations be presented to Congressional committees, that a public meeting be held, and that comments be accepted on the proposal. I think this is an appropriate structure for consulting with all stakeholders during PDUFA reauthorizations. However, I welcome suggestions for improving the input process from patient and consumer groups.

CONSUMER HEALTHCARE PRODUCTS ASSOCIATION,
WASHINGTON, DC 20036
October 4, 2002.

Senator Edward Kennedy,
U.S. Senate,
Washington, DC 20510.

DEAR SENATOR KENNEDY: On behalf of the Consumer Healthcare Products Association (CHPA), I am writing in support of the nomination of Dr. Mark McClellan as Commissioner of the U.S. Food and Drug Administration (FDA). Dr. McClellan's distinguished career in public service and his knowledge of healthcare issues make him an excellent candidate for the position.

Founded in 1881, CHPA is the national trade association representing U.S. manufacturers and distributors of nonprescription or over-the-counter (OTC) medicines and dietary supplements. CHPA today represents over 200 companies involved in the manufacture, distribution, advertising, and research of consumer healthcare products. Our industry is heavily regulated by FDA, and the Association has a lengthy history of working cooperatively with the Agency to assure that consumers have safe and effective products.

In supporting the nomination of Dr. McClellan as FDA Commissioner, we particularly would like to note his active knowledge and involvement in issues that are important to us, such as the Prescription Drug User Fee Act and bioterrorism preparedness. We also appreciate his understanding of the important role of nonprescription medicines in the healthcare delivery system, and his commitment to the Administration's development of a proposed rule on Good Manufacturing Practices for dietary supplements.

Based on his academic background, knowledge of healthcare policy issues, and his commitment to public health and public service, we support the nomination of Dr. Mark McClellan as Commissioner of FDA.

Sincerely,

LINDA A. SUYDAM,
President.

[Whereupon, at 2:45 p.m., the committee was adjourned.]

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