

U.S. Senate Health, Education, Labor and Pensions Committee
Full Committee Hearing
“FDA User Fees: Advancing Public Health”
Thursday, July 28, 2011, 9:45 a.m.

Members Present

- Tom Harkin (D-IA) – *Chairman*
- Michael Enzi (R-WY) – *Ranking Member*
- Al Franken (D-MN)
- Richard Burr (R-NC)
- Kay Hagan (D-NC)
- Johnny Isakson (R-GA)
- Lamar Alexander (R-TN)
- Patty Murray (D-WA)
- Barbara Mikulski (D-MD)
- Orrin Hatch (R-UT)
- Jeff Merkley (D-OR)
- Michael Bennet (D-CO)

Witnesses

- Margaret Hamburg, M.D. – Commissioner, Food and Drug Administration (FDA)

Member Opening Statements

Chairman Tom Harkin

- We convene this hearing today to kickoff the FDA user fee reauthorization process. We will discuss the history and purpose of the user fee agreements between the FDA and the industries it regulates, and we will learn more about the importance of user fees for ensuring that new medical products get to patients as quickly and safely as possible.
- Since 1992, the Prescription Drug User Fee Agreement (PDUFA) has paved the way for quicker and more thorough reviews of applications for prescription drug products. Ten years later, beginning in 2002, the Medical Device User Fee Agreement (MDUFA) has similarly facilitated getting medical devices onto the market. Currently, the drug and device user fees collectively make up 34 percent of the FDA’s overall budget. They are a significant source of the funds that the FDA needs to get its job done.
- Both PDUFA and MDUFA expire at the end of the next fiscal year. Failure to reauthorize them would have significant consequences for the FDA, which would have to let staff go and substantially slows the approval process. Even more importantly, failure to pass the reauthorization legislation would have devastating consequences for patients, whose health and lives depend on new medical treatments. Again, we just can’t let that happen.
- I know that this legislation is likely to attract attention from everyone here who is interested in policy related to the FDA. I have policy priorities of my own, including helping to ensure the

integrity of our global pharmaceutical supply-chain, at a time when our drug products and their ingredients are increasingly being brought to the U.S. from around the world.

- This fall we expect to convene hearings to explore some of these policy issues. Today however, we begin the process with a focus on user fees themselves.

Ranking Member Michael Enzi

- PDUFA and MDUFA programs have been a success, decreasing product review times over the long term, stabilizing funding for the FDA's drug and medical device centers, and decreasing the burden on taxpayers. I do believe, however, that the FDA can do better.
- On the metric most important for patients – the total time to market – the FDA's performance regarding medical devices has declined sharply.
- According to a study by the Boston Consulting Group, by the California Healthcare Institute, overall 510(k) review times have increased 43 percent and PMA review times have increased 75 percent over the past four years.
- Numerous studies have identified serious problems with the Device Center's performance. This is not a partisan issue. Democrats and Republicans, patient and consumer groups, industry, academics and non-profits alike have all raised concerns about the Device Center's performance. The FDA itself has engaged in extensive self-scrutiny, and the IOM is expected to report on several controversial problems tomorrow.
- This Congress, I look forward to working with Chairman Harkin to reauthorize these user fee agreements. We have a few challenges as we try to move this legislation:
 - Timing. We plan to front-load as much of the work as possible to conclude the HELP Committee markup by the spring of 2012.
 - The federal debt is about \$14 trillion and rising, and the FDA is close to a tipping point.
 - In the past few years, Congress has imposed several challenging new mandates on the FDA. The Government Accountability Office (GAO) has put the FDA on its high-risk list because the FDA is overwhelmed by its many diverse public health responsibilities. We need to be practical and strategic about what the FDA can and cannot do.
 - We have a firm deadline. If we don't authorize new user fee programs before the old one expires, the FDA will need to layoff approximately 20 percent of the Device Center and 60 percent of the Drug Center's full time employees.
- Having said all that, I am an optimist. I believe all of us – Congress and the outside stakeholders, alike – can work together to enact a good user fee bill. The last time we did it in the 110th Congress we got a good bill through the Senate unanimously and on time because we all worked together. I believe the way to do that is the 80 percent rule.
- The problem is that the process of finding common ground is hard, slow work. The 20 percent where people strongly disagree is more dramatic. My hope is that the media will focus on the areas of broad agreement, not the 20 percent that might be more interesting for their story.
- This Committee has had great success on FDA legislation when we work together. In 2007, the New England Journal of Medicine said we passed the biggest drug bill in 50 years. We also gave the FDA new authority to regulate tobacco, and just last year we worked hard to give the FDA new food safety authorities.
- We are going to need this kind of bipartisan cooperation to get this done, and I hope today's hearing kicks off a constructive discussion on the serious problems.

Witness Testimonies

Dr. Margaret Hamburg

- The enactment of PDUFA in 1992 was prompted by concerns that patients in the U.S. were waiting longer than patients in other countries for critical therapies. Through user fees paid by the drug industry, PDUFA provided the FDA with a source of stable, consistent funding to hire additional reviewers, upgrade IT systems and strengthen programs.
- At the same time, the FDA committed to complete reviews in a predictable timeframe, to meet more often with industry, and to provide more guidance.
- These changes revolutionized the drug approval process in the U.S. and enabled the FDA to speed its reviews without compromising the Agency's high standards for safety and effectiveness and our commitment to promote and protect the health of the public.
- The time required for FDA approval has been cut by 60 percent since the enactment of PDUFA, and the U.S. now leads the world in the first introduction of new active drug substances. So far this year, the FDA has approved 21 new groundbreaking medicines; this is the same number of novel drugs approved in all of 2010.
- Despite this positive news, we face a severe productivity problem world-wide in drug development, in which an ever-increasing research and development investment is producing fewer new drugs, and at the same time, the scientific opportunities have never been greater due to new biomedical discoveries.
- The proposed PDUFA enhancements discussed in my written testimony include new steps to incorporate scientific advances into regulations so we can modernize and streamline our processes to the benefit of both patients and industry.
- The enactment of MDUFA in 2002 was prompted by similar concerns about the speed of the FDA review process for devices. User fees paid by the device industry under MDUFA have helped the FDA expand available expertise and staffing, modernize IT systems, and provide additional to industry.
- While the FDA is meeting the vast majority of its goals under MDUFA, we know that the overall time to a decision – FDA time plus the time the manufacturer spends responding to FDA questions – has increased.
- The FDA and industry share responsibility for that increase, and the FDA has been instituting management changes to address our role. As a result, for 2010, total time for lower-risk devices appears to have stabilized, and preliminary data suggests that total time for higher-risk devices is improving.
- We appreciate that AdvaMed is also working to address the part that poor quality applications play in delaying approval by offering training for its companies regarding FDA standards.
- Beyond review times alone, we recognize that significant concerns have been raised about how well the device review program is meeting its two goals: ensuring that medical devices are safe and effective, and fostering medical device innovation.
- In response to these concerns, the FDA conducted an assessment of the 510(k) review program. What we found was that insufficient predictability in our pre-market review programs was contributing to inconsistent decisions and longer times to market. The causes included:
 - Unnecessary or inconsistent data requirements;
 - Insufficient guidance for industry;
 - Insufficient interactions with industry;
 - High reviewer and manager turnover;
 - Insufficient reviewer training;
 - Insufficient managerial oversight; and
 - Rapidly growing workload.
- After soliciting public comment on these reports, we announced this past January 25 specific actions that we will take in 2011 to improve the predictability, consistency and transparency of our pre-market review programs, and have since announced additional actions. For example:

- We have committed to developing updated and new guidances to clarify FDA requirements, and several have been released in recent days and weeks;
- We are enhancing the interactive review process and streamlining the review program for low- to moderate-risk novel medical devices, called the De Novo process;
- We have established a new center science counsel to help ensure consistency in our scientific decision making, and are developing a network of experts to help us to resolve complex scientific issues; and
- We are instituting a certification program and a pilot experiential learning program to provide review staff with necessary training and real-world experiences.
- These and other efforts signify our commitment to improving our pre-market review programs to ensure that patients have timely access to safe and effective devices, and that the U.S. device industry remains innovative and strong.
- PDUFA IV and MDUFA II expire on September 30, 2012, and we're eager to work with you to achieve their timely reauthorization. These are critical programs and make possible the resources and tools that are so vitally needed if we are to provide the American people with the medical products that they need and the safety and effectiveness they count on.

Question & Answer Session

Chairman Harkin – If we did not reauthorize user fees or didn't do so on time, what repercussions would that have for patients?

- Dr. Hamburg – I worry it would have enormous negative implications for patients because we would see significant delays in our ability to review and approve applications of promising medical products that could make a difference in treating, preventing, diagnosing and curing medical conditions from which they suffer. These user fee programs represent a very important component of our medical product review capabilities; they help to ensure, especially at a time of tightening budget constraints, a source of stable, reliable funding for our critical activities.

Chairman Harkin – You mentioned the importance of regulatory science. Can you explain what that is and how it helps to facilitate your innovation, and what you are doing to further it?

- Dr. Hamburg – This is an area of science that I have become deeply compassionate about since I have become FDA Commissioner. It is clear that we are not adequately harnessing advances in science and technology to really promote the development of new medical products and the knowledge and tools to enable their swift and meaningful review and approval. From the perspective of the FDA, regulatory science is the knowledge and tools that we need to effectively and efficiently review for safety, efficacy, quality and performance. It's increasingly recognized within the scientific community as a critical gap. The NIH, FDA and other scientific agencies within government need to come together to really build this area of science to, for example, give us the ability to usher in the era of personalized medicine (PM). There are a host of ways that targeted investments in regulatory science can enable us to bridge that gap between investments in biomedical research and the opportunities that exist today, and the translation of those discoveries into real-world products.

Ranking Member Enzi – A *Wall Street Journal* opinion piece yesterday talked about genomic sequencing and other new technologies that will usher in this era of PM. Last year the FDA approved 20 new drugs, but in the future it may be necessary to target hundreds of drugs for specific patients. How is the FDA's pre-market approval system preparing for that future?

- Dr. Hamburg – this expansion of knowledge through investments in regulatory science and partnership will be very important. The models for drug development are certainly changing, and we’re recognizing that the future of serving patients is to better understand what therapies work for certain patients and why. Within recent weeks we released a new guidance on companion diagnostics to help us move into this era of PM.

Ranking Member Enzi – The Institute of Medicine (IOM) is expected to make their recommendations tomorrow on how the FDA should change the 510(k) process. What process will the FDA use to evaluate and act on those recommendations, and will you have a notice and comment period?

- Dr. Hamburg – We welcome the IOM report, but they are just recommendations. We will review them internally and engage with stakeholders to get their perspectives on the recommendations. Any actions that we would take in terms of program or policy change that would emerge from the IOM report would be done in an open and transparent process with lots of opportunity for discussion, notice and comment.

Ranking Member Enzi – The last PDFUA reauthorization contained some new rules on conflicts of interest for the advisory committees. Are these rules making it harder for the FDA to get qualified experts on the advisory committees, especially for the rare diseases?

- Dr. Hamburg – This is a very important question, and whatever groups I meet with express that same concern. We work very hard to get the appropriate experts, and in rare instances we can waive conflict of interest requirements in order to get the experts that we need. But I think it’s a dynamic process we need to keep looking at, especially when you’re talking about rare diseases. We are certainly talking with our various stakeholders about exploring this issue.

Senator Franken – I think we can all agree that patient safety is a priority of Congress and the FDA. When I talk to patients they tell me they also want to be able to access medical devices that have been developed, but too often they haven’t been approved by the FDA. I believe we can make the FDA processes more efficient and predictable. I have three areas I want to address today: (1) improving coordination between the FDA and the medical device industry; (2) dealing with the overly-strict FDA rules on conflicts of interest; and (3) humanitarian use devices, and how it has worked in limiting profits on the sale of these devices. So given those three areas, here are my questions. How can the FDA do a better job of working with the industry to answer questions, make the review process more predictable, and restore trust between the FDA and the industry?

- Dr. Hamburg – It’s so important and it’s something that we’re very actively engaged in. Myself and other leaders of the FDA are trying very hard to reach out, listen to, learn from and work with members of the industry. In the last 10 days I’ve been traveling around the country to meet with CEOs of device companies and entrepreneurs involved in the device industry. There are some critical areas that we need to work on: communication in terms of both formal and informal mechanisms for sponsors to meet with us; being able to provide more guidances, and adding clarity to what our expectations are; ability for the FDA to make sure that our own staff are adequately trained and we are as explicit as possible about our standards.
- Senator Franken – I’ll submit my other two questions for the record. Going forward, I plan to work on the three policy areas that I touched on in my questioning. I hope we can work together to address these issues.

Senator Burr – Do you have any idea how many drugs and devices bypass the American market now and seek approval in Europe, Asia and South American because of time delays or the cost of approval in the U.S.?

- Dr. Hamburg – I am very concerned about the strength of the U.S. industry, and the ability of American companies to deliver drugs and devices that American people need. But it is important to step back and look at where we are. On the drug side, we are the first to approve drugs in more than 50 percent of the cases.
- Senator Burr – Why should we reauthorize user fees for pharmaceuticals and devices when, in the case of devices, the length of time has gone up since we instituted user fees?
- Dr. Hamburg – Showed charts to try to answer the question.

Senator Hagan – To follow up on the medical device questioning...we are hearing that companies are taking research overseas because of some of the unpredictability. In particular, I'm hearing from medical device companies that the review of the 510(k) products has become particularly burdensome causing product approval delays and the frustration for the manufacturers, providers and patients. So anything that would delay the review process really concerns me at this time of job losses. So the industry plays an important role in our economic recovery and I want to support their growth. I also continue to hear from constituent companies that the FDA's medical device review process is pretty unpredictable. How can we improve this situation? What I'm particularly interested in is the concerns I have heard about the FDA stopping the clock when more questions about more data are brought forward. Can you discuss whether the FDA has thought about providing early feedback to companies prior to application submissions, or adjusting how the FDA measures time in relation to the user fee goals?

- Dr. Hamburg – We are very committed to trying to streamline the review process and make it easier to navigate for companies. I do think that in the MDUFA process we have an opportunity to really act in some key areas that will provide us with the necessary tools to make significant strides forward in key areas, whether it's in terms of the review teams, ability to provide guidances, ability to ensure consistency of decision-making, etc. That said, I think it is important to look at the present time, as we are currently meeting most of the agreed-on goals with industry. But we're committed to further improving this process. AdvaMed is moving forward with working with industry to train them to FDA standards.
- Senator Hagan – I am out of time but I'd like to submit some questions for the record because I'm concerned that there's a proposal to regulate laboratory diagnostic tests as medical devices, and they're already regulated under CLIA. I worry about the impact of the additional and duplicated requirements that the industry would have to meet.

Senator Murray – One issue that is of concern to me is the safety and effectiveness of drugs used in children. We have passed two laws: the Best Pharmaceuticals of Children Act and the Pediatric Research Equity Act. They have dramatically increased the amount of information that we do now have on drugs for children. Studies conducted under those two laws have led to almost 400 pediatric label changes. The laws have historically been reauthorized along with PDUFA, so I hope we can reauthorize them again in 2012. A GAO report published in May found that 130 additional products have been studied in children since these laws were last reauthorized in 2007, and as a result, all 130 products were revised with important pediatric information. Can you tell us about the importance of these laws and whether you support reauthorization?

- Dr. Hamburg – These laws have been very important and in many ways have changed the landscape in terms of deepening our understanding about the use of drugs in pediatric populations. We strongly support reauthorization of the laws.

Senator Mikulski – I am so glad to see you, Dr. Hamburg, and I welcome you with the same enthusiasm that I feel with pride that the FDA is located in my state. I would like to welcome the Committee to go out to the FDA to see what it actually does and the wonderful people that work there. In your testimony you raised the issue of innovation and you have a series of recommendations. As you can see, there is an

inherent tension between innovation and regulation, and we shouldn't have to pick one side or the other. What should we do in PDUFA to make sure we promote adequate regulation, but we do not stifle innovation?

- Dr. Hamburg – You're absolutely right that we need to marry safety and innovation. I think there are a number of things that are underway and a number of elements in the PDUFA V negotiation package that will help us to strengthen those activities. One is building out some of these scientific capabilities so we can really use science to identify where are the critical opportunities; how we can do clinical trials that are meaningful but shorter and more cost effective; and how we can look out across the whole lifecycle of a drug to ensure safety and effectiveness by using data mining and monitoring available information in the real world.

Senator Mikulski – In your testimony you talk about how you want to streamline the regulatory process but make sure we ensure safety, and you have several recommendations. Were they supported by the private sector and have you begun to implement them?

- Dr. Hamburg – Yes. I think one area that has been very exciting is the opportunity for public/private partnerships to really address these critical issues in terms of the gaps in science. I met recently with R&D directors from some of the major pharmaceutical companies, and we all really see this as a critical need. In terms of the device program – it is very important that we have a flexible regulatory process that recognizes that innovation is so dynamic in that area, and we really need to be able to support industry as it develops an idea and tests it and puts it into the marketplace and continuing to monitor it as innovation occurs going forward. It requires that we have adequate support for science within the FDA (in terms of reviewers who understand the complexities of products coming before us).

Senator Mikulski – On page 25 of your written testimony you share with us the private sector's views and recommendations on how to improve the process from drug review to regulatory science to others. Have you incorporated these into your recommendations for the Committee for reforming and refreshing?

- Dr. Hamburg – These are the seven categories of enhancements that were agreed to within industry as part of the PDUFA V negotiations. There was enormous enthusiasm and support for these recommendations. We do think that these elements will really strengthen our programs and activities and our ability to deliver.

Senator Hatch – I would like to see our medical device industry match what Europe does. The FDA is a great agency that handles a tremendous amount of commerce in this country, and I think you should call on us to help where we can. But it's clear that in the area of medical devices we're losing ground to other countries, in part due to increasing difficulties in getting new products approved by the FDA in a timely and efficient way. What are you doing to get us at least back to where we were several years ago in terms of speed and consistency of review, and how are you attracting manufacturers to come to and remain in the U.S.?

- Dr. Hamburg – A recent industry study showed that for lower-risk devices that don't require clinical data (about 80 percent of the devices we review), the U.S. is in fact as fast as, or faster than, Europe in bringing those products to market. For the higher-risk devices we are slower than Europe, but it's important to recognize that we have a different regulatory framework. In Europe they don't require safety and effectiveness like we do – they require safety and performance.
- Senator Hatch – So would it be better for us to switch to the European performance language?
- Dr. Hamburg – I think Americans really count on the fact that medical devices that they will use are safe and effective and will benefit them in terms of the intended use. I think that the device industry leadership agrees that we should not change the standards for medical device approval; AdvaMed recently put out a press release speaking to that. But I think what we can and must do

is work together to make sure we have the most streamlined and modern regulatory systems possible. At the need of the day, absolute speed is probably not the ultimate criteria.

Senator Merkley – I want to start with an article that came out yesterday regarding an IOM report that is anticipated tomorrow. For the report, the IOM was hired to analyze regulatory proposals related to medical equipment. Even before the release of the report there has been a lot of controversy. Could you comment on what the issues are here?

- Dr. Hamburg – The IOM is a branch of the National Academies of Science. We actually asked the IOM to put together a committee and do a study about important issues involving the 510(k) regulatory process, which is the largest component of our medical device review activities. Their report will provide us with recommendations and we will review them and get feedback in terms of whether or not we want to pursue aspects of them. I think there was concern expressed by some components of the device industry about whether their perspective was adequately represented on the committee. Various lawyers have looked at that and feel that the composition of the committee is sufficiently diverse.
- Senator Merkley – My impression is that people are upset because they disagree with what they think will be in the report. What is the heart of the actual policy issue that is being wrestled here?
- Dr. Hamburg – I think the heart of the policy issue is the adequacy and the appropriateness of the 510(k) process. The report obviously will speak to very important issues and the concerns have to do with whether the committee was properly constituted.

Senator Merkley – Sometimes problems develop after a product is introduced that weren't caught in the clinical trials. Can you address how well the MedWatch system is publicized or being used by consumers? Could it be improved?

- Dr. Hamburg – I think we need to strengthen many components of our post-market surveillance activities. Also, in large part due to efforts by Congress, we are strengthening our broader activities in the post-market period, including our ability to target in on emergency safety concerns through changes in labeling, changes in data collection, and in mining existing databases and creating new databases to inform our decision-making.

Senator Merkley – Given new forms of advertising (e.g., the Internet, social media) and the types of cautions that are normally embedded in advertising, are those presenting new issues?

- Dr. Hamburg – Certainly the age of the Internet has created vast new challenges for us in terms of monitoring what information is out there about products in terms of advertising and its accuracy, and also products that are being advertised for sale that are fraudulent or counterfeit. We are working very hard to get a better handle on the scope of the problem and identify solutions that will work.

Senator Bennet – I want to make one observation about the tension that I think exists around some of these issues. The mission statement of the FDA is pretty clear that it's both about the public safety and about supporting innovation in our medical device industry. The tension that people in my state feel who are doing this work is rising, I think as a reflection of the globalization of the industry; the concern that a lot of us have is that we may not own this industry in the 21st century. One thought that I have is whether we want to consider changing the FDA mission statement to recognize the global economy we're in and the importance of the U.S. of driving this, or maybe that's not the right place to do that, and maybe it's somewhere else. Are we moving at a rate of speed that will get us to a place where we can compete in real time with the rest of the world, or not lose the advantage that we have?

- Dr. Hamburg – I certainly share your concerns. We see our mission as doing our very best to assure the safety, effectiveness and quality of the products that we regulate, but also to help

support and facilitate the translation of opportunities in biomedical research into products that people need, and also to try to provide some sort of recognition of the need to match unmet public health needs with opportunities that exist in terms of available science and technology. I have actually created within my office a special focus on innovation, trying to support all of the good ideas, programs and policies that are spread throughout the FDA with a focus on advancing innovation. I also have been trying to work hard with my colleagues within and outside of government to see what we as a nation can do to strengthen our programs and policies of innovation.

Senator Bennet – We’re now at a point where 80 percent of our drug supply-chain is coming to us from offshore. Could you talk about whether we’re doing everything we can to try to inspire international cooperation around that issue?

- **Dr. Hamburg** – You’re absolutely correct that it’s such an important problem. We need to recognize that the supply-chain for these products has gotten very complex and much more complicated with many points along the way for potential unintentional or intentional contamination. So we need to transform and move beyond the borders in terms of how we inspect and ensure quality in products coming into this country. We also have to work in much closer partnership with industry, which needs to be accountable for the supply-chain of their products, and through working together we need to be able to assure the integrity of the supply-chain. We’ve also now set up offices in many countries that provide a regional presence for inspections.

Senator Bennet – I just want to let you know that I have asked the device companies in Colorado to give me the 9-10 “pain points” that they have, and I will get those to you in an effort to not have this same conversation again next year. I hope this will make it easier for you.

Second Round of Questioning

Chairman Harkin – In response to Senator Bennet’s comments, we will have hearings this fall on that very subject of the supply-chain, so I will look forward to working with you then on that.

Chairman Harkin – We all want better devices and innovation and we’ve made great strides in this country. But let’s face it – there’s a lot of money to be made in devices. I do want to make sure that we have an agency that is independent and that is able to withstand the tremendous firepower of an industry that has a lot of money and obviously wants the least amount of regulatory oversight. I think it is a gross disservice to many of us who have been supportive of the industry, as I have been, when an article like this appears in the *New York Times* this morning, saying that ‘allies of the medical device industry are waging an extraordinary campaign in Washington to discredit a coming report by one of the country’s pre-eminent scientific groups that examines possible new regulations on the industry.’ That scientific group being the IOM, which is scheduled to release a report on Friday that could propose a tougher approval process for a wide range of devices. I say to the device industry that you are doing a disservice to your industry, patients, and our country because the FDA is charged not only with making sure that products are safe but they are effective, which is different than what they do in Europe. I want the FDA to continue doing that, and I want them to continue to be an independent agency. I want you to continue to be independent and use the best science available to you.

Ranking Member Enzi – The last PDUFA law authorized the Risk Evaluation and Mitigation Strategies (REMS) to speed access to drugs with risk concerns. But in many cases, REMS just ended up slowing

down the review process. Can you fix that process administratively or could small statutory fixes help you to effectuate legislative change?

- Dr. Hamburg – The authority to pursue REMS was given to us in 2007 and we had to develop strategies that would enable us to better monitor safety in the post-market period. As we have implemented it, it has put new burdens the FDA and on industry, and we are looking now at ways we can systematize ways we can do it. We can move forward and improve REMS. It does give us a set of important tools that actually does give us more confidence on the front-end as we approve promising candidates that may have safety concerns. So I think we can continue to strengthen and streamline the program. At the moment, I am not aware that there is any particular need for a legislative fix, but I think that we recognize that the program has been somewhat cumbersome.

Ranking Member Enzi – A June 2011 report from the GAO found that the Device Center is not overseeing recalls effectively. The FDA already has a clear statutory authority to mandate device recalls, but the average time that it took for the FDA to effectuate a Class I recall – the highest risk type of recall – was 516 days. In addition, the GAO found that the FDA does not use recall data to identify systemic safety risks. What steps are being taken to address those problems?

- Dr. Hamburg – We do need to strengthen our programs and reduce our response times. There are a number of important activities underway, including the creation of a unique device identifier that will enable us to more effectively track devices. We have to also look at our systems to make sure that we are responding to emerging concerns in as timely a way as possible.

Ranking Member Enzi – Also referring to the GAO, in 1998 they called for the FDA to implement a series of recommendations to respond to challenges posed by the globalization of drug manufacturing. What progress has the FDA made on the GAO’s longstanding recommendations?

- Dr. Hamburg – This is a huge and growing area of focus. We are trying to extend our capabilities in terms of our foreign inspections, working with counterpart regulatory authorities to share information about the inspections they’re doing and information about supply-chain integrity and the quality of products. We are also working with industry, because at the end of the day, their knowledge and accountability around the supply-chains and the manufacturing practices in these overseas spots is critical to our shared goal of achieving integrity and safety of the supply-chain. You mentioned some interest in the reorganizations that I recently did; one of the areas was to try to bring greater integration of our Office of Regulatory Affairs activities with our Office of International Programs so that we can really use our resources in the most coordinated way possible and really focus on strategy that takes into account risk.

Senator Burr –If the IOM report triggers a change in process, do you commit to making sure that the process includes notice and comment period?

- Dr. Hamburg – Absolutely.
- Senator Burr – I heard you say to Senator Merkley that the 510(k) process looks at safety and effectiveness. Is that correct?
- Dr. Hamburg – Yes, through the 510(k) process we are trying to assess safety and effectiveness.
- Senator Burr – In reality, the process for 510(k) is substantially equivalent. If the FDA has made a shift on assessment of safety and efficacy of 510(k)’s, this would be an earth changing move.
- Dr. Hamburg – It’s clearly a different process than when you talk about the drug evaluation process and the way that we look at data and require information to demonstrate safety and effectiveness. We’re looking at predicates and we’re looking at a different model with the goal of supporting the assessment of safety and effectiveness of that product.

- Senator Burr – Let me say: the statute that’s applicable there is substantially equivalent. Are you telling me that’s not the threshold?
- Dr. Hamburg – It’s a different model of regulation from the drugs. It does build on track records of prior products.
- Senator Burr – I’ll certainly follow-up on this with additional questions. But I would question whether you have the authority, without a change in rules, to do exactly what you’re stating. If it does, it may explain a lot as to why there has been an increase in the times that it takes for device approval.

Senator Burr – Has the increase in fees resulted in fewer review cycles per submission compared to previous user fee agreements on devices?

- Dr. Hamburg – The review cycles have increased somewhat over time, and it’s something we want to bring down. We think that by working together with industry to address the issues within the FDA, and issues around the quality of applications and response to information requests from the FDA, we can continue to move in the direction of bringing those review cycles down.
- Senator Burr – Industry says the FDA is moving the goalpost; the FDA says that this whole process is the result of poor-quality 510(k) applications. Do you want to comment on this?
- Dr. Hamburg – I think that is a very stark view of the conversation. We recognize that it’s a combination of factors. The FDA has a role to play, and that’s why we have undertaken this fairly self-critical internal review. But it is the case that the delays in the time of getting a new product to market do also reflect the time taken by the submitter, whether it’s because the quality of the application wasn’t adequate, or because we have asked for information that in fact wasn’t necessary. We need to make the overall time as short as it needs to be to achieve the goals.
- Senator Burr – You are in the middle of negotiating the device user fees. Would you consider a new structure with device user fees where the industry would pay at different intervals based on FDA performance?
- Dr. Hamburg – Right now the model really does focus on FDA review time. I think what you’re saying is, would we look at it in terms of the overall performance of the system.
- Senator Burr – The whole user fee foundation was built on ‘if you supply us this money, we will become more efficient at what we do.’ Were I in the industry, I would be very reluctant to come to the table to talk about even reauthorizing the fees because of the performance that I have seen. Dr. Coburn and I have asked the GAO to examine the performance goals so that Congress can be fully informed when we consider the user fee reauthorizations. I look forward to reviewing those GAO recommendations because it is an independent assessment of how well the industry is meeting the performance goals.
- Dr. Hamburg – I can assure you that we track our performance on the existing MDUFA goals, and those were negotiated with industry. At the present time, we are meeting 95 percent of the goals in the 510(k) process. I think the larger concern, which is one that we share, is are we doing an adequate job getting products to market as quickly as possible, and that involves both the time taken by the submitter and the time taken by the FDA. The MDUFA goals only focus on that FDA component.

Senator Hagan – I mentioned in my earlier questioning about the laboratory diagnostic tests (LDTs), and I would like to go back to that. I have heard concerns about the FDA’s proposal to regulate those tests as medical devices. I am concerned that this added regulatory process will further slow innovation. It is my understanding that the FDA is in the process of developing guidance to regulate LDTs as medical devices. Where is the FDA in the development of this guidance?

- Dr. Hamburg – LDTs clearly are devices. Given the realities of the world that we’re in today and that these LDTs are being done in commercial labs and treating patients in facilities that are wide-

spread, it is important that there be a common standard of review and approval for those tests along with other comparable diagnostics. We are going to be putting out several guidances to help the LDT industry understand what will be expected of them in terms of regulatory oversight. It actually will create for industry a level playing field in terms of the companies that are involved in LDTs specifically, or diagnostics more broadly. I think the draft guidances will all be put forward quite soon, and then there will be opportunity for public comment.

Senator Hagan – In North Carolina we have about 19,000 biopharmaceutical jobs; it is such an important part of our economy, and I want to make sure we do all that we can to invest in this sector. The main concern coming from these companies has been the FDA’s issuance of a complete response letter, and the fact that once the FDA issues this letter, the Agency is no longer bound by any deadline to make the decision on the product. The crux of the problem seems to stem from inadequate communication between the Agency and the company at all stages of the process. I would urge you to help improve upon the efforts to provide frequent, transparent communications. Is the FDA providing early feedback to companies to ensure that their application submission contains all the necessary data, and what is the FDA doing to provide companies with feedback when the FDA issues this complete response letter, or doesn’t approve the application?

- Dr. Hamburg – One piece of good news is that we actually are approving more things in the first cycle rather than using the complete response letter. From the early days of PDUFA we have gone from 46 percent approval in the first cycle to now 68 percent. In the PDUFA V categories of activity, we do include a focus on strengthening communication at various stages in the cycle.

Chairman Harkin – I appreciate all the time that Dr. Hamburg has spent with us. I’ll submit some questions in writing, and relinquish my time to Senator Burr.

Senator Burr – I want to get back to a conversation that you had with Senator Hatch. In PDUFA we created the opportunity for the FDA to use outside review for predominantly Class I devices with accredited institutions that the FDA could exercise who to accredit. The objective was to try to move things out of the FDA so we could stay focused within the FDA with the limited number of reviewers on the most sensitive and potentially difficult devices. In addition, that part of PDUFA also gave the authority for the FDA to include foreign clinical data in submissions of applicants. The first one with the devices was never fully fleshed out; the second one was never used. Do you see an appropriate use of either one of those options?

- Dr. Hamburg – We do use data from foreign clinical trials in our drug review process.
- Senator Burr – I would love for your staff to highlight any of that to share with me.
- Dr. Hamburg – We do seek outside expertise in our device review programs as well, and it is actually one of the areas that Dr. Shuren has identified as a priority for strengthening, as well.

Senator Burr – Much of your testimony today highlights certain data-points and performance goals reports; however, the time to market is probably the most important metrics for patients waiting for life saving products. How would moving from FDA days to calendar days help to ensure that the review clock is not skewed and the performance goals truly reflect the time that it takes for life saving products to reach patients?

- Dr. Hamburg – At the end of the day I think we all agree that what really matters is what American consumers can access in the marketplace. There are different strategies in terms of identifying the performance goals to get there, and that can be discussed as part of the MDUFA negotiations. We want to see a program where industry and the FDA are working together with clearly defined, achievable goals.
- Senator Burr – Would you be supportive of eliminating FDA days and going to calendar days?

- Dr. Hamburg – It is hard for us to be held completely accountable if you’re trying to achieve a program that really works.
- Senator Burr – My attempt is not to hold you completely accountable, but for Members of Congress to understand how long the approval process actually takes.

Senator Burr – I am increasingly concerned that the FDA is not striking an appropriate risk/benefit balance for patients. The California Healthcare Institute recently reported that the FDA is focused “less on the benefits of new products than on potential risk, and to try to mitigate the risk by demanding larger, more expensive and more costly clinical trials.” In 2007, Congress gave the FDA post-marketing risk evaluation mitigation strategies (REMS) authority to address theoretical risk in an attempt to help the Agency strike the risk/benefit balance. I’m concerned that this authority is not being used appropriately.

- Dr. Hamburg – We always do look at the risk/benefit balance and we recognize that patients are willing to take very significant risks when they face a very serious disease. We certainly approve drugs all the time that have known associated risks. I do think that in the PDUFA V plan, we have an opportunity to address risk/benefit in a more systematic way. One of the categories of focus is going to be to strengthen our activities in that area. On the device side we will be putting out guidance very soon on how we think about the risk/benefit equation and recognizing the complexity of the problem.

Senator Burr – I would like to make one thing abundantly clear to you and to the Chairman: this Committee, as well as one in the House, has the policy responsibilities for the FDA. No matter what you negotiate with the industry on user fees, it has to pass through Congress under reauthorization. I have raised issues today regarding measurement tools. If in those agreements there is not something that addresses, to my satisfaction, the ability to measure, whether it is devices or pharmaceuticals, this will be a very slow and laborious process. If we don’t have measurement tools to determine whether a fee system produces a better outcome, then I’m not sure why we would sign off on it as policymakers.

- Dr. Hamburg – I do feel obliged to respond. If you look at the PDFUA program, you can see dramatic changes in our drug review programs that have really changed review times and enabled us to address what was an early concern about Americans not getting access to drugs as early as people in Europe and elsewhere. We have seen the dramatic shifts as a result of PDFUA; I think industry would agree that it has made a real difference having that source of stable and predictable funding and the ability to identify together key areas of priority for action. We are earlier in the MDUFA process, but I think we have the opportunity to really transform that review process as well and to support the industry in its critical goals, so I’m very optimistic about what we can achieve through this reauthorization process.

Chairman Harkin – I have a few closing remarks:

- I do not believe that time to market is the most important metric. I believe safety and effectiveness are the most important metrics;
- When we talk about FDA days, I understand why we stop the clock until we get requested information. The clock should not continue to tick if the FDA asks for additional information from industry and they don’t get what they asked for;
- On the more money and better jobs issue: I think if we look at the staffing of the FDA prior to PDUFA and look at the amount of things they were involved in approving, and then compare that to today when they have PDUFA and MDUFA as well as other things (e.g., food safety), I can tell you that I want the FDA to do all of that. If you look at all the things that we have asked the FDA to do in the past 20 years and the staffing, I think you will realize that if we had kept the staffing at that level to respond to all of the incoming issues, we are currently understaffed and underfunded at the FDA; and

- I hope that both the drug industry and the medical device industry, as we're reauthorizing this, don't get the mistaken idea that somehow if you provide the money, you get to provide the outcome. I want the FDA to be as independent as possible and scientifically based.