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MEDICAL TECHNOLOGY INNOVATIONS

PUBLIC MEETING

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P R O C E E D I N G S

DR. ZUCKER: Welcome. I want to thank you all for coming here on a Monday morning after a beautiful Washington, D.C. weekend, which we're going to have a few left of these, and I'm sure it's going to turn cold for all of those down here in D.C.

I'm Howard Zucker. I'm the Deputy Assistant Secretary for Health, and I'm joined by Dr. Larry Kessler, who's the Director of the Office of Science and Engineering Labs at the Center for Devices and Radiological Health at the FDA, along with Dan Sullivan from NIH and Jaskins (ph) from CDC, and Steve Phurrough from CMS.

The purpose of today's public meeting is for us to rise to the challenge that Secretary Thompson put forth, a challenge to accelerate the process of medical innovation technology. And what this really involves, as we all know, is the process of moving new therapies to the bedside much quicker and in a much expedited fashion. To accomplish this task, we all must work together all

over at the different agencies here at HHS and the private sector, academia, and all the others who have the great interest in facilitating the world of innovation.

The Secretary formed a task force led by Dr. Les Crawford from FDA with the leadership of many of our HHS agencies. And Larry and I have been involved with the implementation of that process. We put out a Federal Register back in the Spring, and we received comments from many companies and many individuals here in the audience as well as from universities, the public advocacy groups, patient groups, and others from across the country. We collected all that data, we've had multiple meetings, we've had think tank meetings, we've sat down among the different agencies at HHS. We've looked at all the information to try to figure out how we can move this whole process forward. We've collated the data and now what the process is, is to figure out how we could take this information and figure out what would be the best to act as a catalyst to move this process forward.

In order to accomplish the goals and the missions that has been put forth by the Secretary to us, we are planning to provide him with a comprehensive report of what HHS can do as a department, but what we also could do in partnership with some of the other departments across the federal government and in partnership with the public sector as well and how we can help move this whole process forward.

What we would like to do today is hear your thoughts. We are looking for new approaches, to innovation. We are well aware in going through this whole process, as well as other processes in the past, that creativity really requires the input of many individuals, and we hope this morning we'll be able to receive a lot of novel ideas and hear your input about some of the issues that you think are important in an effort to move this process forward.

On behalf of Secretary Thompson and the entire team at HHS I want to thank you for joining us here today, and now I'd like to introduce Larry

Kessler, who's going to give you some logistics about today's meeting. Thank you.

DR. KESSLER: Thank you, Howard, and welcome. This morning we have approximately eight speakers, formally; how have requested time. If any of you in the audience would like time to speak as well, if you have comments on a specific presentation, you're welcome to go to the mike after the presentation. We'll allow a minute or two for that, and at the end of all the presentations, we will allow for open mike time.

The purpose of your being here is for us to listen to what you have to say about issues in speeding medical technology. So we're quite open to your suggestions, as Howard said. We're on a fairly short time frame. We have a report due to the Secretary in the middle of next month, so we've got a lot of work ahead of us yet.

I'd like the three panel members from various agencies to introduce themselves, then I'll go over some logistics for the rest of the morning.

Dan.

MR. SULLIVAN: Dan Sullivan from the National Cancer Institute representing NCI and NIH.

MR. PHURROUGH: I'm Steve Phurrough. I'm the Director of the Coverage and Analysis Group at CMS representing CMS.

MR. WATKINS: I'm Andrew Watkins, the Director of the Technology Transfer Office, representing CDC.

DR. KESSLER: On the committee we also have a representative from the agency for Health Care and Research Quality as well, and we have a representative, interestingly enough, from the National Institute of Standards and Technology who sat in with us.

The project manager for the task force has been Nancy Stanistic. If you have comments that you'd like to pass on to us in writing after this meeting, you're welcome to send them to either Howard Zucker or myself. But if you want to actually make sure we get them and pay attention, that's Nancy Stanistic's job, that's what she does, S-T-A-N-I-S-I-C, and you can find her through the

FDA directory.

Resting about logistics. We're starting our presentations now. Approximately in an hour, quarter of 11:00, we'll take a brief break for about 10 minutes, come back, and we'll see if we can wrap this up, hopefully around 12:30, 1 o'clock. If we go past that--if it looks like we're going to go much past 12:30, we'll actually take a lunch break. But I think we might be able to wrap up all of the comments this morning before we have lunch. But we'll see how that goes.

The first speaker I'd like to welcome is David Gilbert. Dr. Gilbert is from the Infectious Disease Society of America. Dr. Gilbert, welcome.

One more thing--excuse me, one more thing. We are transcribing this meeting, so all your comments will be transcribed for the task force. The video camera that's on, it's actually a private company who takes these things, so this is not actually HHS, but it is a private company, and we're going to try and get the lights down to see if we can see the slides a little better and work

on that.

DR. GILBERT: The Infectious Disease Society wishes to thank acting director, Mr. Crawford, Director Gerberding, Administrator McClellan, Director Zerhouni, and their representatives that are here today to allow us to share an area of deep concern to the Infectious Disease Society an evolving problem that we believe is threatening the public health.

The problem has two facets: the increasing resistance of pathogenic bacteria to the currently licensed antimicrobials; concomitantly, at the same time there's a dramatic decrease and in some instances complete discontinuation of antibacterial discovery and development activities by the pharmaceutical industry. Therefore, there's the need for innovation and speed in the development of new drugs.

The members of the Infectious Disease Society have been most concerned, and over the last year we've met with the leadership of the DFDA, the National Institute of Allergy and Infectious

Diseases, and the CDC. In addition, we've met with over 15 executive leaders of the pharmaceutical industry representing major pharmaceutical companies as well as smaller biotechnology companies. We've met with members of Congress and their staff. The information derived from these interactions led to several proposed solutions which are summarized in our "Bad Bugs, No Drugs" report which was released in July of 2004.

What I'd like to do during this testimony is to focus on antibacterials that we also like to emphasize that the suggested solutions are applicable to bioterrorism issues which I notice made the front page of the newspaper this morning. Vaccine discovery and development and other categories of antimicrobials including antifungals, antivirals, et cetera.

I also would like to emphasize that we are here on behalf of our patients. Our advocacy efforts have not resulted from any financial relationship whatsoever with the pharmaceutical industry. So the details as to increasing drug

resistants are included in our "Bad Bugs, No Drugs" report, and I'm not going to go into great detail there. I'd rather spend the time, and because I believe it's the focus with this group, on suggested solutions to the problem, proposals to remove or lessen the existing disincentives for drug discovery and development.

And that can easily be broken down into two parts: One, changes that might be solutions that might be implemented within existing statutes and then those solutions that would require new legislation. Within existing statutes the CDC does a wonderful job with respect to surveillance of disease burden including epidemiology, detection, and control of resistance; early detection of emerging pathogens for which treatment options are inadequate.

The last bullet point on this slide is an area that we think could be of great help, and that is helping us with what has been called attributive morbidity or mortality projections. In other words, what is the cost in terms of disease and an

economic cost of infection with these resistant organisms, as we seem to be heading down the path of running out of drugs to treat the existing organisms.

Turning to the Food and Drug Administration, we, as well as many other organizations and groups, support the critical path initiative. In addition, in the meetings with the leadership of the pharmaceutical industry, the one thing that comes through over and over again is their anxiety that is created by uncertainty. Anything that would decrease uncertainty with respect to acceptable design of clinical trials would certainly remove a disincentive for drug discovery and development.

There also are new guidance documents that have been approved by the FDA that have been stuck in legal review for a long, long time, some would say an unacceptable period of time. Final release of those guidance documents from legal review would be a welcome advance.

And then, of course, we all agree with

continuous integration of advances in genomic diagnosis, diagnostics in the clinical trials. I suspect some of the other speakers here this morning will address that issue. The more precise the diagnosis, especially in trials as complex as infectious disease, dramatically increase clinical trial study power. We can enroll fewer patients, get crisper answers and, obviously, at less expense.

The National Institute of Allergy and Infectious Disease can also help lessen disincentives. They've already created a study section on point-of-care diagnosis--diagnostics, and identification of new drug targets. There was a meeting this summer that discussed public/private transfer of intellectual property rights.

One suggestion that has come forth out of discussion with the small biotechnology companies is a screening process for candidate new antibacterials. This would be analogous to a program that I believe already exists at the National Cancer Institute where industry can submit

candidate anticancer drugs to the Institute for screening for their anticancer activity. There is no analogous program within the National Institute of Allergy and Infectious Disease for antibacterials. Exploration of this idea would be most welcome.

Now I turn to potential solutions that would require new legislation. The incentives for the large pharmaceutical companies differ from the incentives for the smaller pharmaceutical companies, and so I would like to deal first with some proposed solutions that would be most applicable for large pharmaceutical companies, and these are proposed solutions for pathogens for bacteria, resistant bacteria, bereft of treatment options where the caring physician has few if any drugs left to treat the resistant bacteria.

The idea would be subsequent to Food and Drug Administration approval of a new drug for one of these dangers pathogens for which there are no drugs to provide tax credits for the ever increasing drug discovery and development expense.

Another idea which has been talked about quite a bit is the wild card patent extension. If a new drug is developed for a highly resistant organism, it is proposed that the company that has taken that risk would get patent extension on some other drug in their portfolio of already approved drugs with the understanding that there would be a payback, that is, a substantive percentage of the additional profits made during the patent extension would be dedicated in advance to antibacterial drug discovery and development.

Incentives for small or biotechnology companies are a little different. Again the point is for dangerous pathogens bereft of treatment options. At the time that the small biotechnology company applies for a new drug application, hopefully they would be eligible for small business grants. They also have pointed out some difficulties with FDA of fees that are applied for review of new drug applications. Obviously, they need to pay a fee for a new drug application. The problem comes with supplemental fees when that

original new drug application is modified or a new indication is sought. The companies often have difficulty with capital to afford the repeated fees that have been required.

Regardless of the size of pharmaceutical companies there is one area that resonates with all of the pharmaceutical companies, and that's liability protection for serious, rare, unforeseeable adverse events. Companies will enroll 10,000 patients in a clinical trials for safety and efficacy of a new antibacterial drug.

It's approved as safe and efficacious by the Food and Drug Administration, and then once available for general licensure, it turns out there is a serious adverse effect that affects one in 100,000 patients. There's no way to foresee such an event occurring. Request is that some protection be provided.

There is a example of this injury--this approach--the injury compensation that's provided in the childhood vaccine injury program.

So the IDSA is proposing typing these new

statutory incentives to a list of dangerous pathogens for which we have no effective treatment options. And this is really the linchpin of everything that we're proposing here today; that we need a hit list of resistant organisms that are a threat to the public. We suggest a commission or an advisory committee that lists the--and constantly updates, I'm sure that would be necessary--a list of dangerous pathogens. We suggest that this advisory committee report to the Secretary of HHS and that the statutory changes that are proposed would be tied to this list of dangerous pathogens. Regardless of whatever administrative structure is being appropriate, the need is to identify dangerous pathogens for which treatment options are inadequate.

We can anticipate objections to these proposals. The general drug industry will object to any extension of patent protection; Treasury Department certainly may object to tax credits; consumer advocates will worry about high drug costs, but I think there's a reasonable response.

the attributable additional expense of the care of patient with pan-resistant pathogens can be many hundreds of thousands of dollars. I just left the bedside of my patient yesterday who's been in the hospital for two and a half months with one of these pan-resistant pathogens, a hospital bill as of yesterday was \$630,000.

The Institute of Medicine estimates an annual expense of antibiotic resistance of \$4-5 billion. Pain and suffering, of course, is incalculable.

So what does the Infectious Disease Society of America hope this task force will do? We hope that a high priority will be given to incentives that stimulate drug discovery and development of antibacterials, vaccines, and related diagnostics in the executive branch legislative agenda. We hope that there will be a department level evaluation of the incentives that I've presented and that are included in the "Bad Bugs, No Drugs" report, and we've provided you with copies of such.

And we hope that we can garner your help in supporting in Congress enactment of Bioshield II or similar legislation which includes many of these proposed suggestions.

"Bad Bugs, No Drugs" is a major threat to the public health. A recommitment of the pharmaceutical industry is necessary to avoid a future calamity. 2005 legislation will take 10 years to bear fruit. Many of the major pharmaceutical companies have totally dismantled their new antibacterial drug discovery and development programs to gear back up and go through all the necessarily steps to get a new drug to market will take at least 10 years.

Infectious Disease Society of America hopes the task force shares our concern and will provide the necessary vision and leadership to shape the necessary new legislation.

Thank you for this opportunity.

DR. KESSLER: I'd like to make a couple of comments for the panel. If anyone has any questions or comments they'd like to make to Dr.

Gilbert, we'll be able to handle those for a second or two.

First of all, I want to thank Dr. Gilbert for his excellent presentation. Second, I want to make two comments from the task force, and then open it up if anyone else has additional comments.

The focus of the report, and I think that some of the things that Dr. Gilbert spoke to will help us, is a department level attempt to attack the problem of medical innovation, and as Dr. Zucker says, and this has been impaneled across the department, we're looking less for items that apply specifically to the operating divisions of the department. That is, less for something that FDA can do alone or CDC can do alone, and work with things that cross the department entirely. So a number of things that you mentioned, Dr. Gilbert, bit that.

I don't want to be disingenuous. Even if we like some of the legislative proposals, I'm not sure many of them will suffer the bureaucratic process between here and report, but we appreciate

the suggestions for new legislation. I'm just not sure how they can certainly get out of department into report. Thank you.

I want to turn to Mr. Ferguson, and this is an oral presentation, so leave the slides off, and if someone could put the lights up back there, we'll do that. Thank you. Welcome.

MR. FERGUSON: I might note that there are copies of the comments in the back, and I hope that the panel has those, too.

Thank you for the opportunity to appear today. I am Steve Ferguson, Chairman of the Board of Cook Group, Incorporated. Cook is the largest privately held ;medical device company in the world. We sell over 30,000 different products. Our company has been the pioneered in interventional medicine, introducing many new technologies to the marketplace. We manufactured the first catheters used in the Seldinger technique of angiography marketed in the United States; we made the first coronary angioplasty balloon for Gruntzig; we developed and manufactured the first

coronary stents sold in the United States; our company in Australia led in the development of endografts for the treatment of triple aortic aneurysms in the early '90's, and the list goes on.

In August, we submitted our comments to the Department's request for input as to how HHS agencies can work to facilitate the development of new medical technologies. We are honored and grateful for the opportunity to address this task force and further highlight our views.

There are a few things that we thought that sort of our setting around everything that we do, both in the agency and politically, in the suggestions made as far as the legislative process. And, well, I think we need to keep those in mind as we foster and try to foster the development of new innovation, both in the drug and device and biopolitics.

First, device development has moved from really the clinical setting to more science. As Cook grew up, the ideas came from the clinical setting and clinicians, but we're moving more

rapidly to where science is the base of those new ideas and the new technologies.

Second, we're in a world and a global marketplace, but also as part of that the consumer, the patient, has access to a tremendous amount of information. Some of it's good and some of it's bad, but they have the access to that information on the latest therapies for themselves and their loved ones. And how many people do you hear that immediately go to the internet when they've got disease, and I'm sure that everyone here is aware of that.

Third, Americans aren't going to be acceptants, or accept, rationing. If there's a new technology, they're going to want access to it, and once they learn of it they're going to demand access. And that's going to put more pressure on all the agencies and Congress. It's very difficult for a congressman to say to someone who comes in and says, "I've got a particular disease," a child has a particular disease, "but we can't--it's not reimbursed. It's not available in his country, et

cetera.

So there's going to be more and more pressure on our systems to get new technologies to patients that people are aware of. As an informed consumer, you know, it used to be physicians provided most of the information; now people have access to it from a lot of different sources.

There's--finally, there's another concept, and it's been mentioned, but I think it's worth stopping to think about. From all the agencies' point of view, there's more and more we're moving to the gold standard of clinical studies, and I think those are really applicable to disruptive type technologies, and new technologies, or art technologies, coronary--drug-coated coronary stents, but when you look across the device world, those are just not practical. And if you take Cook, we manufacture 30,000 different devices, but as most company the 250 of them are big markets. After you get 250 to 300 in our business in our company, they're less than million-dollar markets worldwide. So you have almost 29,500

devices that sell less than a million-dollar market.

So when you think of a triple-A or aneurysm device, that's one market. A coronary stent with drug-coated, that's a large market. But when you think about devices in general, the need-- and I think that's one of the things that we're seeing in the drug industry, more and more larger trials and larger trials, but the need for that needs to be thought about in the size of those markets in the patient population. You just can't assume that that's wasted effort.

Finally, when we look, innovation is a continuum, and it begins with basic sciences. We know and often in conjunction with NIH or NSF it proceeds through the development of a concept, design, prototypes all the way through reimbursement. When we think about this, there are thousands of suggestions that could be made at each point of that process, and some of them small, some of them are large. But there aren't any major sweeping ones, but there are thousands of them.

I'm going to try and stick, even though you suggested that we go across all the agencies, with the one I know the best, which is medical devices. It's important to recognize that often the burdens, as the first speaker pointed out, are the things that result in products not reaching patients, and so we have to look at both the concept, and in medical devices we talked about leasing (ph) the burdens are the most efficient way. I think at each stage we need to look from the governmental regulatory side how can we most efficiently establish the safety and effectiveness of that particular product.

Finally, when you think about in this day and age the amount of information we got available, and we need to use it efficiently, if the FDA needs and each agency needs to have, CMS needs to have the most up-to-date technologies to handle information and databases and have access to those, and have access across agencies. There's a gold mine of information that's available to us, and our ability to organize and analyze information was

really undreamed of a few years ago. If we work smartly, we can seize upon the scientific breakthroughs, facilitate the development of products, expedite delivery of these products. By properly using information, we can save invaluable time in resource of industry, government, academia, and redirect the energies and profits to developing new devices.

Along this, some suggestions: Permit and enable FDA to utilize and share information that it possesses. And this is sort of a concept of knowing and let FDA use what they know. If they've got knowledge of something, don't force industry to go back and reprove it; don't force each applicant to reprove it. And I think, just if you stop to think about it, a lot of times we think about it, well, that's ours, that's Cook's. We developed and we spent money up front for trials. We spent money on developing that, but it's the basis for the approval process, and it's the basis for clinicians. They're using our product, and we really think those ought to be open to the public,

and it also ought to be open if our competitors come to market that much quicker, then that's the way it is. It's a competitive world, but what we're talking about is service to public health. And we think that eliminating those burdens and using the information that FDA has will be much better.

Obviously, among the data available is the data from physical clinical trials, animal studies, bench testing that apply to the new product application. Information that relies to the materials by clinical standards could also be made available. Using the information will enhance our ability to employ advanced techniques for statistical analyses, including Bayesian statistics.

Finally, it will facilitate the development of more sophisticated methods of computer modeling that in some instances can reduce bench testing, animal testing, and clinical trials.

A second point would be to smartly develop data for evidence-based medicine:

1. Neither government nor the industry, as I've mentioned, has the ability to do extensive studies across all devices and drugs that come to the market, so we need to look for ways to save time in those studies and use historic data or other data that we have available.

2. Allow promising new technologies that have been approved by FDA to diffuse and then analyze the data that is developed.

3. Manufacturers, by working with the government to develop reasonable and practical registries, can provide some of the data. Such registries should be designed to produce the needed information in the least burdensome manner.

4. Data can be significantly expanded by analyzing CMS claims data. This may require more detailed coding for a relatively small number of new technologies which emerge each year. The point is that there are a few that are impact, that are changing and maybe we ought to have coding so that we can identify those and follow those and see their impact within the reimbursement system. It

may also require revision of claims forms and other changes to the Medicare payment system.

5. The data can be further enriched by developing and properly analyzing electronic medical records in communities across the country. We could utilize expertise in the private sector as well as government in this area. And as many know that in Indiana we have the Regenstrief Institute which has been a pioneer in developing electronic medical records.

The organizations such as Regenstrief can provide invaluable advise and assistance in appropriate studies. Indeed, Regenstrief and the Indiana Information Exchange, which really is interesting that all the hospitals in Marion County, and they've got a database of over a million people, and they're all in the same system, so if you go in the emergency room even though these are stacked in individual databases controlled by the Regenstrief, then they merge at the point of care.

And we're trying to expand that across

Central Indiana, but it gives you a tremendous database by the world's best database right there to impact what the various changes are within our system. And they just recently received a grant from AHRQ, and they're already been working with HHS on electronic medical records.

Third, the government should lead the way in exploiting the immense mountain of data available. This includes not only the FDA, NIH, CDEC, NSF, DOD, and perhaps other agencies and departments. We believe governmental entities should do a number of things.

1. They should upgrade to modern, advanced information technology systems that are compatible with each other so they can easily exchange information and use each other's databases. If government solved the problem internally, it will not only increase it's capabilities but also set a standard for the private sector to follow.

2. Greater communication needs to occur across relevant government agencies so that we all

understand the broad scope of what is being developed. Currently, it appears to us--and obviously today is an exception to that--but that we all work in silos. We need to make sure that FDA is aware of what NIH and CMS are doing and vice versa. There are a number--there may be knowledge and data that one organization that could be valuable in the process, or another has that could expedite the evaluation of outcomes.

And 3. Government agencies need to maintain strong lines of communication with the private sector.

And then turning to managing resources wisely, there are a number of steps to be taken to clarify and streamline regulations, reduce the barriers to innovation, and conserve resources that could be focused on new technology. We recommend a series here. Most of them apply to FDA, but some of them have broader application.

The United States should take the lead at the highest levels to harmonize the regulatory and coverage systems around the world. There is a

tremendous waste of resources in bringing products to global markets, country by country, and that waste is growing exponentially. We must set on an agenda and give top priority to leading the global community to accept and help achieve the goals promptly. Specifically, we ought to take the following steps:

1. First develop a system that provides a single approval or clearance for market for low risk devices, in the case of devices and it would be the same application to drugs.

2. We must develop common standards for clinical trials that are universally accepted for approval and coverage process.

3. We need to develop an inspection process that will be accepted by all nations.

4. Develop clear and workable regulatory schemes for combination products and for tissue engineering both domestically and internationally. There is currently confusion and differences across the jurisdiction from country to county.

Internally, the FDA could streamline the

FDA's approval process and conserve resources.

This includes the following suggestions:

1. Simply utilize the reclassification and exemption processes for medical devices. As we gain, if you take an angioplasty balloon or coronary artery balloon, it's now a known technology and is still a DMA product, and those type things ought to be moved down the classification, and those over the 40 years that we've been manufacturing devices, some things that were cutting edge new procedures that were thought of as being really high risk at the time are now known technologies. So we ought to have, keep in our system a way to down-classify and move them out of the system.

2. In the process, especially in the device area, and it's not as true in--because of the evolutionary nature of devices. You learn a lot during the IDE process, and we ought to always be able to make adjustments in that so that the highest quality product comes to patients.

3. We need to develop a clear process to

permit appropriate proof of concept studies. And this is--this, I think, fits across all--all of the various areas in government, but we need to think carefully. A lot of times we get into the process of proving things that are nice to know rather than things that are really essential to bring this drug or device to the market.

We need to devise a process, with appropriate safeguards, which allows for the collection of data, not only in registries but in off-label use.

5. Clinical trials, whenever possible, by using historical data, conformity studies, and the latest technology testing and computer modeling, I think if we consistently don't move forward with what science delivers us for analysis and modeling. And I think government--and I understand the difficulties--but government needs to and the regulatory process needs to stay in the latest level. I think at some point in the future we'll all look--or history will look back on the way we do clinical trials and think that we were pretty

barbaric. And that's sort of the nature of history, you know. At one point in time you think it's the latest technology and the latest way to have a gold standard, and then in the future I think people will look back and say, "Boy, that was pretty crude or barbaric. So we ought to continually think about those things.

We need to adopt more international standards in the area of devices, and especially small markets. We need to look at the humanitarian device exemption as another way of encourage manufacturers to address all markets and eliminate the prohibition of profit on that, streamline the RB requirement, and revue the appropriate size of that portion of market should be.

Thank you very much for the opportunity to share our thoughts. We commend you all for your time and effort and work in addressing the critical issues. We wish you the best in effort, and it's very important to patients. Thank you very much.

DR. KESSLER: Thank you, Mr. Ferguson. Two comments for you. One of the things we've

heard over and over and over again in your testimony and others has to do with the silo effect of the Department of Health and Human Services, so you can expect to see something about trying to continue to build better bridges across the departments. So I'm sure there will be a response to that comment.

If you know when to check, did I hear you correctly that you advocate sharing information so that if Cook does a PMA and submits it to FDA, you'd just as soon have it be open to the public so that other of your colleagues doing trials could learn from that so they don't make the same mistakes? Is that what I understood?

MR. FERGUSON: Well, there are two sides of that question. The--[off mike]--side says keep it secret.

DR. KESSLER: Umm-hmm.

MR. FERGUSON: Okay, the public policy side says it ought to be available.

DR. KESSLER: But you're advocating the latter.

MR. FERGUSON: I'm advocating the public policy side. I'm right here on the public health, public policy side as opposed to what--[off mike]--proposes.

DR. KESSLER: Great. Well, on the slide I can't wait to hear what Batman has to say about that.

(Laughter.)

I don't want to put them on the spot. But it would be interesting anyway. Anybody want to make some comments? Steve?

MR. PHURROUGH: Oh, I think that's a great idea. We would support that highly in being able to take this raw data and analyze it right up front and not have to worry about having to redo that because we didn't see the data when they first got it done. We'd support that.

DR. KESSLER: There are a number of discussions, specifically between the FDA and the Center for Medicare and Medicaid Services to try and use available data in their data systems and possibly in the FDA to learn more about medical

products so as not to repeat or trying to reinvent the wheel over and over and over. So it's a great suggestion. I don't know how far we can carry it.

MR. FERGUSON: We've been first to market in a number of areas over the last 40 years, and we've been or will be the first to market in a number of areas in the future. The question is, is somebody has to reprove what we've already done, and our answer is that's not good for patients' health care.

DR. KESSLER: We agree, thank you.

I want to turn now to--any more comments?

Mandy Raab, Dr. Raab from the MSA Medical Group. Is she here? There you are.

DR. RAAB: Good morning. Today I'd like to talk to you about not an innovative medical device but an innovative medical technology. With each new advance in technology, there is more and more medical data that is produced. This is difficult, every increasingly difficult to analyze. On top of it, the data is often produced across the nation in different locations and, even further,

researchers want to have the ability across the nation to access the research data at any time and at anywhere.

Next slide. MSA has produced, addressed these needs and come up with a new innovative technology. MSA's medical information vision is like a building. You need a solid foundation layer at the bottom, albeit the data management layer, in order for the information layers at the top to be accurate and useful. We focus our efforts on the data management layer at the bottom, however, we do have expertise throughout all of the layers which helps us to produce the most useful data management layer. We take data warehouses of all different types, such as gene expression, proteomic expression, clinical data. We integrate it, we clean it, and then we store it in a data warehouse.

We then create a logical data cube. This logical data cube is then pushed to the next layer which is the technology layer where the data can be viewed through a researchers internal computer or through our software tool called Research Gateway.

At that point the data can be subset, subsetted to the criterion of the researcher and then exported to an analysis package of their choice. The data can then be pushed to the final layer to allow public data to be added to the results to bring new biological meaning to the experiment. Again, the foundation has to be accurate in order for the information at the top to be useful.

Next data. So this is the first problem, disparate data sources. Data sources such as patient demographics, laboratory results, and clinical results are all different data formats and produced in different locations. It is difficult for these data to be structured and architected in order for analysis. MSA's view is to take all of those data sources, link them together so that query can span all of them.

Next slide. As far as functional integration, we believe there is three major medical phases: clinical outcome, health care delivery, and laboratory research. Where these medical areas intersect is some of the major

medical research areas, and that is drug discovery, evidence-based medicine, and molecular medicine. MSA's approach is a holistic approach. We structure the entire knowledge management set so that we can give it to the researchers in total.

Next slide. So how do we do this? We take a patient centric view. We take each patient, we apply the clinical data such as demographics, pathology, and procedures, and then we add public data such as LocusLink and Ref Seq for proteomics. We go ontology, and finally in the end we come up with an enhanced patient view.

Next slide. The second problem that we address is accessing the data. In order for a researcher to explore their data, use volumes and volumes of data, they have to often go to query about complex query and permutation of the query in order to find the substantive data that has the trend or the results that are interesting. This becomes so difficult that they often need a DBA attached at their side. This becomes even the most difficult during grant time, so what MSA has

produced is a Research Gateway tool which allows the researcher to have his own discovery platform on demand through the web that allows him to access in an easy--in an easy tuitive manner his data.

Next slide. So the basic features of the Research Gateway is it has a multidimensional conceptual view, i.e., you can slice the data anywhere anyhow. It's--the data manipulation is intuitive. You can access it through just a simple browser. The calculations, some of them are pre-calculated, but you can always create new calculations "on the fly." You can, of course, apply models and algorithms of your choice, and, of course, it's all transparent to the user.

Next slide. So what does this mean to the researcher? The researcher is empowered to be able to look at their own data and at any given time any given day, based upon his new criteria, look at his research data. They can explore, do virtual experiments if they'd like, and all this can be done without a DBA--without DBA support.

Next slide. You can integrate all types

of databases with the Research Gateway. All it needs to be is ODBC compliant.

Next slide. So in the end you have the power to explore. The researcher can come at this at any perspective. Everything is integrated and at the center is a common ontology. In this example the common ontology would be caCORE or UMLS. Okay? So therefore again, at any perspective, any question where the researcher has a different perspective on a different day, or there are multiple researchers across the nation who have different questions to address, this gives them the platform to do it.

Okay, here's an example of how you reap the benefits of it. With multiple patients you can ask common attributes such as anything from demographics, gender, even what specific gene expression has occurred among patients. And even further, if you do this over for a longer period of time and collect study upon study, protocol upon protocol, you can then start asking questions across protocols, which makes it very powerful, and

you can truly then start to do virtual experiments among the data you've already collected.

Next slide. Here's a snapshot of the Research Gateway. This first snapshot shows you our Explore the Data page where you can subset the data. And here we show you that on the left side we've selected the number of patients in one protocol at a specific Site 002 where their gender is female and their race, I believe is white--I need new glasses--and you're able to count the data. This is important to a lot of clinical trials that go on for so long that the researchers are just chomping at the bit and rightly so. They want to know when they have enough data to do an inter-role analysis. When can I get my data? When can I start looking at the results? This shows them they can count it and figure out what they have, dynamically, again just over the web.

Once you've found out you have data and you want to subset your data to a specific criterion, you can either export the data directly into your statistical package or you can go to our

next slide, where you can take a, as I call it, a quick view. So you can look at your patterns of your data. Again, you can continue to subset the data and spin it even within the quick view and then export it to a statistical package. Here we're showing you the tabular view, and the next slide shows you the graphical view, which is my favorite.

And what I've showed you here is I've taken a lot of pop-up windows up so you can see that you would simply have a drop-down menu, the drop-down box such as a site, and you'd be able to click whatever site you want to look at for those patients. To the right is a field list. You can drag any dimension, any attribute that you want onto the table, and it will dynamically refresh the data.

And this particular graph shows you that you can plot multiple assays. Here we're plotting flow cytometry simultaneously with RTPCR gene expression, and you can plot them simultaneously over time. And what we're seeing here is T-1

helper cells over time simultaneously with the RTPCR gene expression for cell death, genes expressed as associated with cell death as defined by go oncology. And again, you can drag any gene. It's very dynamic, and it's quite addictive.

That's it.

DR. KESSLER: Thank you, Dr. Raab. You'd be glad to know that a number of the comments that we've received in the public docket from the summer also focused on common data systems and trying to be more efficient in sharing data, particularly to make clinical trials more efficient. So it sounds like your comments are undisputed with many others.

If there are no comments, I'd like to move on to Carol Kelly from the Advanced Medical Technology Association after that. Carol.

MS. KELLY: Thank you, Larry, for being my very high-powered tech assistant here this morning. My name is Carol Kelly. I'm an executive vice president with the Advanced Medical Technology Association. My focus at the association is on a health system reform and also on reimbursement

matters. I am joined this morning by AdvaMed staff by Carolyn Jones sitting in the front here with me, and Teresa Lee. They are both associate vice presidents. Teresa works for me in the reimbursement and health system reform area, and Carolyn is one of our FDA experts.

We very much appreciate the opportunity, moving to my first slide here today, to talk to this panel and this program about stimulating innovation within the context of HHS. We'll also talk about some ideas about coordination within the Department and also provide some responses to you here to be summary issues for the docket.

But let me also spend just a moment to introduce AdvaMed to those of you who may not know us as well as some others do. We're the principal trade association in the medical device and technology industry. We represent diagnostic devices, health information technology companies. Our company provides 90 percent of the \$75 billion worth of medical equipment, supplies that are sold throughout the United States each year. We have

about 1300 member companies, and 70 percent of our companies have sales of less than \$30 million in a year.

Moving to the next slide, Larry. Let me provide some--oh, yes, thank you. There is some context here. This is a simplified version of the innovation and reimbursement process as it confronts the companies that are our members, and generally throughout the industry, and it's key to understanding the development innovation process. At the left side of the slide there, you see that the process of bringing an idea, conceptualizing it, and doing preclinical studies can take as long as three years and sometimes even longer, and then working through the FDA process can take another one to three years. So what we're seeing here--and it gets to the issue of working with the Department, certainly, as you conceptualize an idea and move through the process, it can take as long as six years from the conception of an idea moving through FDA, and then based on some work that we commissioned by the Lewin Group, we also know that

the process of working with CMS coverage coding reimbursement can take as long as seven years.

So it can be a very long process from the time that an idea is conceived until it actually gets to the patient. Now, obviously, innovation takes time, regulatory requirements are often the appropriate ones, but innovation and the whole process which takes this time and gives certain signals to those who are involved in it. It gives signals backstream to the investors who decide where and whether to fund innovation. It matters to engineers and scientists who decide what kind of data should be gathered and over what period, and it matters to innovators who evaluate product lines and individual products in deciding where to place their resources, and then finally, it matters to patients, those who are waiting for the next innovation.

Next slide, Larry. Therefore, we welcome this opportunity to share with you some of our ideas about the federal government in making innovation and product development process

smoother. There are many specific and detailed suggestions, and I will go through those as briefly as I can. But I think there are several themes that you will see from these particular ideas that we provide to you here this morning. We recommend greater clarity and regulatory requirements. We recommend greater consistency in regulation coverage and payment. We both believe that steps designed to achieve appropriate evidence standards are very important, and we recommend that there be steps to ensure adequate resources for innovation. because at the end of the day we all know there's only so much in resources that can be put into any one facet of our society. And we think that these kinds of recommendations will make the industry work harder and smarter and suggest additional ways for the industry to partner with the Department.

Moving into the next area, let me compliment HHS's efforts so far to stimulate innovation and accelerate the pace of discovery, and, of course, I'm referring here to the NIH roadmap for medical research and FDA's critical

path initiative. We welcome these initiatives, and both of them are focused on a critical ball to accelerate the pace at which new science and knowledge translate into real-world medical care. Medical companies are engaged in these fields, including genomics, proteomics, and nanotechnology among others. We really appreciate these efforts by the Department to spur development in this area.

One other I would mention here was the formation of NIDIP (ph) which provides us the opportunity to work on a research agenda that's a transnational line, not basic medical research which has been mostly the focus of NIH in the past. But there are key aspects of the innovation process as it relates to our industry that are more incremental in nature and not entirely science-based. Multiple generations of modest and incremental advances come from the basic technology once it is derived, and the hands of practicing health care professionals in real-world setting are key and very important.

Moving on to the Medicare program, it

comes as no surprise to anyone here that key aspects of Medicare coverage coding a payment are critically important innovators, and just to sum it up in one statement, I would say we want to ensure appropriate evidence for coverage and appropriate payment level. There's a very simple sounding statement, but much goes into that as an effort on behalf of our association and the industry. And much of this focus is in on the working part of the Medicare program, the machinery of payment and coverage and coding.

Let me take you to the next slide. Your group is very focused quite appropriately on evidence standards, and they have come up here already this morning. And we wanted to provide and embrace Dr. McClellan's vision as it was provided to us about the future of actually collecting evidence for a medical innovation and for patient care. Dr. McClellan was kind enough to come to our national meeting in May, our Medicare meeting in Baltimore, and also to our Board of Directors meeting in September, and he lays this out as his

vision, which we fully embrace, of ways in which to use data for health care innovation. And it is thus, once a product clears FDA, it would obtain prompt Medicare coverage, it would be used in real-world settings by practicing physicians and routine patients everyday practices. Once this is provided for, the data would be collected and fed back through information technology. And Dr. McClellan's vision in this context, the data would allow better judgment about a product's effectiveness in the real world.

We believe that this vision has much merit and great potential. We would also note that it is not vision; it is not something that can be done immediately. It permits--and these are reasons why we find it so attractive--it permit broad effusion, treatment in real-world settings applied by practicing physicians with continuous information-gathering. It limits the current local Medicare coverage process in our minds, which is prompt and provides a quick coverage for Medicare beneficiaries.

Moving on to the next slide. Despite this vision, we also see a number of issues that are very important to address now as we move into this vision of the future. We don't have electronic health records, and e-prescribing and connectivity from providers to hospitals and the system and the way in which he would in order to do this well.

So the issues we have now have to do with the way in which evidence was collected at the present time as we move towards this vision. Everyone knows that the randomized control clinic will try and list the gold standard for evidence-gathering. But there's also information from real-world practice, and there's also guidelines from medical societies.

We would also note it's unrealistic to expect complete and comprehensive evidence on every question that may arise. Our industry is very interested in being a science-based, and is a science-based industry, but we'd also note that seeking absolute information or ever changing demands for information can also yield delays in

time to patient care.

A second major step that we believe that can stimulate innovation as I mentioned before is the Medicare local coverage process. For many of the reasons that Dr. McClellan focuses in on it, it allowed technology to diffuse to generate data in everyday setting, and to prove its value while being used by practicing physicians in real-world settings.

Another area I would focus on briefly is utilizing guidances. This is an area in which the guidance practices in which FDA has a long history of working with my industry, and that is now being translated over as a result of the Medicare Modernization Act into the national coverage process over at CMS. And to Steve and to Sean Tunis (ph), we welcome the efforts that you have done with having a workshop and working with the FDA staff to try to understand best how this can provide not only guidance to the industry, but I think it could, potentially, be a fundamentally different approach to the way in which we work with

the national coverage process at CMS.

Next, I would note the indication by indication MCDs that have been done that noncover all other indications, unless those decisions for noncoverage are clearly data-driven, we believe that new indications should be decided by the local coverage process as the national one continues with decision-making.

Another that is really important is communication. We certainly welcome the open-door forums and a number of the workshops and activities that the agency has been engaged in, and I notice that the, as I just mentioned, the good guidance process, process itself, may yield a better communication between the industry and the agency.

A few other quick mentions on the Medicare coverage process. We would recommend that for Medicare technologies that are received humanitarian (ph) device designations and device exemptions from FDA, that they move through the Medicare national coverage process quickly. That will send a clear development signal to innovators

that these are important to do. And I would also note that we are working with the agency around the implementation of the Category A routine patient care costs that arose as a result of the Medicare Modernization Act and also appreciate the Category B coverage for routine patient care costs and also for the device at the discretion of the local contractor as being very important to spurring innovation.

Let me quickly mention in the next slide a few Medicare payment concerns. I've mentioned that innovators respond to financial and reimbursement signals. We've had some critical discussions and important ones with the agency on outpatient payments as relates to assuring that device, the amounts of the device attached to an APC in the particular payment grouping are appropriate. The outpatient perspective payment system was legislated by the Balance Budget Act in 1997. It's had kind of a rocky start here. I think we're getting more on a path of understanding, though, how to make sure that the reimbursement amounts are

more appropriate over time, though work remains to be done here.

In the inpatient prospective payment system, I would note that we were delighted that when the Beneficiary Improvement Protection Act provided additional payments for new technologies in the inpatient setting, we think that the agency has been overly conservative in the way in which it's gone about setting these limits on this program, the reimbursement amounts. There are only three technologies in the program after about 40 years, so that's another area of concern to us.

On coding issues, we welcome the HICPIX (ph) coding changes that were recently announced by CMS and by the Council on Technology and Innovation and LIDA HERPOON (ph) in that regard, and we will be making additional recommendation on coding to the agency.

On competitive bidding, we appreciate the fact that the agency made larger its initial advisory council and included a representative of AdvaMed, D.M. Waldman with Johnson & Johnson. We

think that competitive bidding should start with those items that have been already tested in the demonstration processes, and we recommend an open and transparent process throughout the competitive bidding.

And then finally, I would mention two other items in the recent position payment reg the agency suggested a face-to-face physician prescription in regards to all DME prescriptions and any changes in the use of the equipment or renewals, and in the final position regulation they are--decided to rethink that, which we applaud and would be happy to work on equality standards that are not as burdensome as the ones originally proposed.

And finally on the Clin Lab fee schedule, I think we need processes to provide for revisions when mistakes are made and some kind of a reconsideration process to the extent that there are problems, and also we are looking at fundamentally different ways to pay for lab tests.

On to the next slide. Well, what I've

walked through in all these details really matters, and I appreciate your patience with hearing them from me. In a survey of medical device companies done by the Lewin Group in 2003, some 70 percent of the companies rated Medicare coverage and reimbursement as very important or extremely important factors affecting their product development. Forty-four percent of responses indicated that the length of time it takes to secure coverage had hindered their ability to bring innovative new technologies to patients and more than 12 percent of revenue-earning companies said that these requirements had forestalled them from actually pursuing and developing a technology.

So in addition to the new science and transnational research issues which we think are critically important here at the Department, I'd also note as relates to the Medicare program and now a bit more as relates to FDA some of these more procedural and evidence-related matters, let me turn next to the FDA, briefly. Recommendations here have to do with data development, improved

communication and clarity, and we will also make some recommendations regarding in vitro diagnostic policies of payments.

Moving on to the next slide on data issues, we believe FDA can make data development and data-gathering smoother and more efficient. We note that the industry has a long history of working with the FDA in a cooperative fashion, and we are looking to build on it. We suggest developing criteria to determine when computerized and statistical models are appropriate as a substitute for clinical testing. With remarkable sophistication and power, today's computers computerize modeling can provide extremely valuable data quickly and at less cost.

Second, we suggest FDA use--allow use of data collected from independent formal clinical trials in approving new uses of existing medical products.

Third, we suggest FDA Center for Devices and Radiological Help, they're a data summary template for each standard that it recognizes and

publish it along with the datasheet on the recognition of that standard.

And, finally, we recommend development of a product to more fully explore the many feedback paths and information loops that occur in the use and diffusion of medical technology. We believe that will benefit not only the government but also the companies as they are trying to understand the safety and use of their products in the marketplace posts FDA approval.

Another quick--another couple of quick comments around FDA. We, as I mentioned before, welcome the good guidance process at FDA. We think FDA should be commended for its work in this area. We also think that there could be improvement in FDA in engaging the public to work with the agency to develop first draft of guidance documents.

Secondly, we urge greater attention to educating and updating FDA reviewers on rapidly changing innovations and medical products. These need to be carefully designed education and training programs, and they would serve as an ideal

vehicle for collaboration among academia, our industry, and the FDA staff.

And let me turn to my last two slides, one on IVDs and the ideas from the docket. There were some suggestions around IVDs that we wanted to discuss and comment on here today. As a first matter, we recommend consistency in regulation by HHS. Tests developed by and performed in laboratories do not require a prior proof of or by FDA or tests developed by manufacturers and sold to labs do. We don't impose a new set of regulations, but we do believe that there should be some consistency in regulation here and welcome an opportunity to work with FDA in that regard.

On another issue having to do with IVDs, we recommend that FDA take steps that would allow a greater use of identified--unidentified or unlinked tissue samples to permit quicker determination of a test sensitivity and specificity. These studies utilize left-over or banked samples and require little or no personal health information. The specific recommendation here would be for FDA to

set guidelines for waiving IRB review and informed consent requirement so that this can move forward.

And finally, we also recommend enriched base approaches for IVD product development.

And I conclude with this slide, which ties together the important role of FDA regulation and Medicare policies in influencing innovation. This is from a survey of our members done by Lewin Group in 2003. As you can see, the very factors that we've talked about today influence directly the decisions that are made about products in development. When asked, the top 10 factors that affect their ability to develop new medical technologies, device firms answered as you see here: FDA regulatory requirements, the close of clinical research, Medicare coverage and reimbursement requirements all topped the list.

I show this to reinforce the simple point that the procedures, the processes, the rules and requirements of HHS play out in real-world decisions as innovators. There are, as we were talking about in here, what's really critically

important for us is well-known pathways and evidence standards being key, we also suggest that voluntary pathways that might coordinate the various operating divisions of the Department could be of interest and promise for some of our members, depending upon what kind of product development they are engaging in.

And I appreciate your time and attention this morning. I would be happy to answer any questions that anyone has.

DR. KESSLER: I have a question, if you'd just stand there.

MS. KELLY: Sure.

DR. KESSLER: I have one question because we've heard this before to one area that is a little bit paradoxical for me which maybe Steve has more clarity about.

You mentioned in one of your slides about Medicare coverage issues that you strongly believe that local coverage helps spur a nation. At the same time at the bottom of that slide you mentioned consistency, but one of the hallmarks of local

coverage practice out in the--among the contractors is the lack of consistency. So it seems paradoxical, and I can't quite figure out which of these plays into helping medical innovation, and it hurts because it looks like local coverage is your consistency problem but consistency in nature that you strongly advocate that we do better on.

MS. KELLY: That's a very good question. Thank you for asking it, Larry.

I think that our companies appreciate the opportunity to work to the local coverage process because it is very responsive to them, and I know that that also raises the issue of consistency across the country. We think greater attention could be given to the fact that often the local contractors work through matter more quickly and with a great deal of consistency as we look at what's happened for products throughout the United States. So I don't think it, as we have been thinking about this more, and we actually plan to do some more analysis in this area, that having the companies work at the local level gets you

inconsistency necessarily at the local level, it often gets you a more flexible process that operates more quickly and also provides information that can be used in a national coverage process since the people in Baltimore and Dr. Tunis' staff and Dr. Burroughs' staff are trying to look for information and data. So that's an area that we're looking into.

DR. KESSLER: Okay, and a brief follow-up. It seems to us one of the things you mentioned is that medical device companies, the hallmark of that industry is to have many, many small companies. So, for example, 70 percent of your members you said, I think in that revenue was something like 39 million.

MS. KELLY: In the left, yes.

DR. KESSLER: So you're talking about a lot of small companies who now have to deal with 50 local contractors. Isn't that a hard burden on small companies that may have 10, 20, 30 and 40s versus Cook, and Medtronic and the big guys?

MS. KELLY: Yes, that's also a very good

question. I will also note that the Medicare local medical directors do talk among themselves and do share information with one another. So once a company's dealt at the local level with certain--a number of local medical directors, it's my understanding that often that information is shared among the different plants that are actually looking at making their own decision.

The other thing that is also a hallmark for industry is that some of the smaller companies often partner with the larger companies when it comes to actually marketing and providing, you know, actually rolling and industrializing a particular technology so that if you're a small company you often do those partnerships with larger ones that permit you the opportunity to have greater access to the fuller resources of the company.

DR. KESSLER: Thank you. Steve?

MR. PHURROUGH: Carol, I think she feels spied on locally.

MS. KELLY: Sure.

MR. PHURROUGH: Just a moment. One of the things the agency has not done well over the last several years is we have attempted to be more open and transparent with particularly the technology industry companies in our coverage process as we've done that. We have not involved the beneficiary or beneficiary's advocates as well as process. So we have over the last several months a significant initiative to bring in patient advocates that are in our--in our coverage and payment process to get their view.

And as I've talked about the coverage process to these groups over the last several weeks to months, the number one concern they have is the local coverage process, that there are inconsistencies and some of their advocates in Texas may not get the same coverage as their advocates in Oklahoma. Or, in fact, some of their advocates in New York City may get something different from across the street, depending upon who the particular local carrier is.

So there's this real conflict where our

patient advocates are strongly telling us that we should do away with the local coverage process, and all policies should be national and they also have a bit of direction from Congress in the Modernization Act that we need to be a bit more consistent in our local coverage policies. So we do have this dichotomy, this conflict, so how do we resolve it? What do you think the next steps are for the agency to attempt to resolve this sort of conflict between the two views?

MS. KELLY: I think, as you well know, Steve, when we've had these conversations before with Sean Tunis as well, I mean the agency, your staff isn't really equipped to do everything at the national level. So the question there's not the staff, the time, the resources, nor would I think you probably want to have all decisions made at the national level.

So the issue becomes what decisions are going to be made at the national level and what decisions are going to be made at the local level. And, certainly, we would welcome working with you

on--and this is one of the things we've talked about--in good guidance practices kind of format when the agency has established how that will work. We might sit down and roll up our sleeves and discuss what are kind of the indications for doing things on a national level and what decision-making might very clearly be left to the local level.

There's no question that if you have a number of academic centers that are involved in, and local physicians are involved in actually the creation of an idea and bringing it to the patient at a local level, that for some period of time, that may not be diffusing throughout the country immediately, but I'd also point out that the national coverage process can take a while, too, as the M-Tech (ph) decisions are made and technology assessment goes on. So it's always a balancing act.

But I would certainly--we would certainly welcome with you sitting down and talking about kind of the national coverage process and what makes sense to do at the national level maybe under

a heading of good guidance practices, if that makes sense to you.

DR. KESSLER: Anything to--thank you, Carol.

We'll take 10 minutes and begin again with Dr. Sundwall. He's around somewhere.

[Recess.]

DR. ZUCKER: Ladies and gentlemen, we're going to start again. I'm looking for Mr. Podraza, Ronald Podraza.

Mr. Sundwall--Dr. Sundwall from the American Clinical Laboratory Association will start.

DR. SUNDWALL: Well, good morning, and thank you very much. I'm David Sundwall, the senior medical and scientific officer for the American Clinical Laboratory Association, and along with other speakers, I want to compliment those who put this event together. I think it's timely, and I'm very impressed. I don't know how on earth you're so intellectual you get an editorial in The Post the very day of your meeting. I mean this is

absolutely on point to what we're talking about. I thought you guys are really powerful: influence at The Post. I'll reference that in a minute.

I understand as a clinician and as someone who's worked with the clinical laboratory industry now for about 10 years the challenge facing our policymakers. It's really tough, and that's why I commend your reaching out to try and do things differently, because, ideally, we would embrace the new and improve patient care, and do that in a quick way. But at the same time, you have the challenge of then parting with the old and the inefficient and also at the same time considering the Medicare Trust Fund and taxpayers' interests. So this is really a difficult challenge, and the tensions are understandable. And no matter what we do they'll be there, but I appreciate the effort to try and make it work better.

My comments are just going to be a summary of the written comments that are available to you in the back of the room. Much of what I have to say or which is printed in our comments are rather

specific regulatory issues, and I don't think I'm going to go over those in detail, but I am just going to give you the general overview of what my written comments have said.

I do want to commend Carol Kelly and AdvaMed. I thought your presentation gave a very nice overview of the complexity of the issues that we all face in this area. I think we may have some difference of opinion on actual coverage policies. We would be glad to be engaged with you on that discussion, but at the same time we understand the dynamism of having it a local, maybe stimulating things earlier.

Let me just say a word about the clinical lab industry. Clinical labs provide information for clinicians as they attempt to diagnose disease, monitor treatments, and is screaming for preventive medicine. I'm still a clinician. I volunteer once a week, and I can tell you that this data is arguably the most reliable, the most affordable, and the most widely available information in health care. It's certainly better than my ability to

extract accurate information from a physical--from a history or even a physical exam.

But what a lot of people don't understand is clinical laboratories are also innovators. They are all often engaged in the development and performance of new laboratory testing. These tests are usually developed utilizing something called "analyte specific reagents" or ASRs, and I mention that because it's relevant to the regulatory scheme and also utilizing a new technology called "multiflex testing" or "multiplex technology."

So what are the barriers if we are innovators and we provide such useful information? What hampers us? We believe that there are many different kinds of barriers to the process of bringing new clinical laboratory tests to the market, and therefore to the benefit of patients. And these include threats of higher standards or more burdensome regulations being considered for ASRs by the FDA and for multiplex testing. A lack of clarity and consistency related to the assessment in new technologies and insufficient

funding for developing information that would help policymakers as they make decisions on coverage and payment.

Specifically, let me just mention briefly some of the barriers that we experience. The Food and Drug Administration, we believe the regulations that apply to clinical laboratory testing are illogical and outdated. Consider, if you will, a clinical diagnostic test in the 21st century being regulated based on whether or not there is a similar product in commercial use in 1976. It just kind of defies logic.

Also, if you think about it with the recent mapping of the genetic code and the effort to translate that into clinical utility, a lot of that is totally dependent on clinical testing, diagnostics, and it just doesn't apply to the current regulatory scheme. We would strongly recommend that HHS consider light regulatory and legislative reforms that would decrease the focus on pre-market review and instead take into account more fully what occurs once the medical technology

is in the marketplace. I think this compliments what AdvaMed has said, that it makes just an awful lot of sense for us to monitor things in post-market surveillance once there's been the safety and efficacy issue or if it even applies. But we think that needs to be streamlined.

FDA regulations, and especially the fear of more stringent regulations, is slowing the adoption of new technologies in a number of areas, but, specifically, like I said in genetic testing and proteomics. This is particularly relevant to ASRs multiplex testing, and the reason I mention that is because we have been told repeatedly that FDA is considering regulating ASRs and, specifically, genetic tests. And the Secretary's advisory committee on genetic testing, the predecessor of the current advisory group called for FDA to regulate genetic tests as part of the medical device amendments. Although that didn't happen, there was that recommendation.

There's also recently been published a draft guidance on multiplex testing. Although it

hasn't been implemented, we think that dampens innovation using this kind of technology.

The bottom line is there's uncertainty, and it does indeed slow down innovation on the part of labs because they're not certain of the costs or the complexity, or what regulatory scheme we're going to be subject to.

I'd also just like to mention, as we do in our written statement, that the FDA and others need to understand how regulated labs already are. Under the Clinical Laboratory Improvement Act regulations and the law, there is a complex regulatory scheme; there is oversight of the quality of laboratory testing, and our fear is that it is FDA's attempts to expand their regulatory reach that it would be overlapping and unnecessary regulation and oversight.

Another point I just want to mention briefly is what others have said is this inability--an apparent inability to rapidly respond to rapidly changing medical technology. ACLA would love to work with the FDA, with CMS, and also a component

that we've heard referenced here, but not enough, the AMA/CPT process. This continuum, as was illustrated in the slide Carol showed, is really an amazingly complex set of barriers, and we think this could be more seamless, it could be more efficient and more consistent.

I just this weekend participated in the AMA/CPT editorial panel meeting in Florida, and there were over a dozen specific laboratory codes under consideration and review. And it was just a great illustration of how complex this process can be. And while much of what was proposed was eventually adopted, after years and how knows how many dollars of effort in going through this process. So we would hope that this might be considered as how do you factor in the CPT, the FDA, and then the eventual payment process?

CMS has indeed improved in its reaching out to us and to others and how they go about setting payment policies. But at the same time, still there's much to be done. I think their annual meeting which they have convened to set

payments levels for newly-approved CPT codes is commendable, and I believe the result is some amendments requiring they do this in a more open process, and we're glad to participate in that, but, unfortunately, the process that they use is pretty much what's considered crosswalking. They will get a new CPT code for a new test and then be asked to identify what's an appropriate payment level based on older similar tests. The fact is this often results in a level that's woefully underpaid given new technology or the cost of providing that test. So there has to be some way whereby we have better information on making those decisions. But we commend them for their progress in that area.

Finally, let me just say a word about data. The Washington Post article today gets into this information. I thought it was fascinating if you haven't read it, but it does say that Medicare and Medicaid are going to try and be smarter about the way they make decisions, making them more evidence-based. But to do that is expensive, and

they propose possibly partnering with industry to help pay for such studies, which I found relevant to our discussion today and a creative way to do things, maybe the user fee like FDA has used or whatever.

I certainly can't say what ACLA's position is on this, but I welcome this evidence-based using information that's current and making the process something where there's an opportunity for the industry to participate in.

So, in closing, I'll just say I think it's great what you're about, and we want to be partners in this process. And if you'll read my paper, we have some good suggestions. Thank you very much.

DR. ZUCKER: Thank you, Dr. Sundwall. I just had a comment for you, or a question, really. You mentioned that the predicate system the MTA has, and I don't want to be defensive about it, but, and although it still exists and I recognize-- and the FDA recognizes that various something of an archaicness in making a device equivalent to something that was on the market prior to '76. But

the Congress did, in its infinite wisdom, add a provision to allow for de novo classification so that it's no longer necessary for any company with any product come to the FDA to have to adhere to the older predicate system. There's now a new avenue for approval, and I believe, in fact, we've used it in the in vitro diagnostic area at least-- at least once recently. Can you comment on that? Are you familiar with that?

DR. SUNDWALL: Well, I think you're talking about the Roche product. Is that the--

DR. ZUCKER: I'm not talking about a specific product, but the process that allows you to bring a new product to market that would be called a de novo classification. So a classification unique or not to your bidding its own certain risk factor profile.

DR. SUNDWALL: Right. I think any mechanism that's offered to us to avoid that regulatory process is fine. I recall when the effort on the part of not Teeter (ph) but Seeberg where they were going to regulate in vitro HIV

testing according to Medical Device Amendments. It felt to me--and this is--and some if it goes with a little history with respect to Medical Device Amendments in 1980s but when I was working on the Hill, but anyhow, it seemed to me like they were trying to shoehorn in these diagnostics into this category.

And it was a reach that we did not quite understand. In theory I guess it's reasonable, but in practice it doesn't make sense. So I would welcome any kind of de novo or other way to get around this, but please understand that we have for the last three or four years had hanging over us very real threats or promises that they were going to regular ASRs more stringently without our appreciation that it wasn't already being regulated sufficiently if you're looking at it from a public health standpoint or protecting the patient.

DR. ZUCKER: Thank you. Any comments or anything, Steve?

(No audible response.)

DR. ZUCKER: I'd like to call Caroline

Loew, if she's arrived.

DR. LOEW: First of all, thank you very much to HHS and today's panelists for the opportunity to speak today on this important initiative which I can say at the outset PhRMA strongly supports.

My name is Caroline Loew. I'm the vice president of Scientific & Regulatory Affairs at PhRMA, the Pharmaceutical Research & Manufacturers of America. We represent the U.S.--pharmaceutical industry that last year alone invested \$33 billion in R&D.

Have the next slide, please. The pharmaceutical industry is highly innovative, and, historically, this innovation has resulted in treatments and cures for complex diseases and has the potential to do so in the future. This innovation not only transforms the lives of many patients; it also reaps economic benefits by reducing in numerous instances nondrug expenditures in the health care system.

In the past 10 years in the U.S. alone,

there have been about 300 new drugs and devices approved for over 150 diseases ranging from diabetes, cardiovascular disease, schizophrenia, Parkinson's disease and HIV, and in many of these cases the treatments changed dramatically the standard of care.

Next slide, please. However, the reality is that the barriers to innovation have grown over the same period, particularly as more complex diseases are tackled. PhRMA is currently completing a study examining the clinical and regulatory barriers, drivers of R&D performance, and I'll share some of this data with you, PhRMA's study, with you today in the next few slides. However, the bottom line is very simple. It takes 10 to 15 years to successfully discover and develop the drug. Based on the study, we see that amounting to something around a \$1.1 billion investment per successful drug that comes through the marketplace. However, in spite of this enormous investment both scientifically and financially, output is declining.

Next slide please. So as I said, historically, while the industry has been highly productive, it is facing numerous challenges, driven in part by the shift, as I noted, to research our more complex diseases. Although this is, in fact, just one of several drivers, these drivers collectively are using a significant challenge to R&D productivity.

In the study that I just mentioned, we have several top line--several top line outcomes. Firstly, we see, as illustrated here that there's been a significant increase in clinical development times, particularly we see a step increase from the '90s to 2000 almost approaching a year in clinical development.

Secondly, we're seeing a significant increase in clinical development costs. From the period '96 to '99 as compared with the period 2000 to 2003, we're going to see a doubling in clinical development costs for a successful drug candidate, and it's important not to forget, of course, that this is just a fraction of the total cost of

bringing a new drug candidate to marketplace.

So instead of these additional investments and additional research time improving research productivity, we're seeing instead an overall decline across the development cycle. I'm going to delve into this a little more in the next slide.

Looking at this attrition data in more detail, we see--and basically the bottom line here is where to focus--with the reduction in Phase 1 and Phase 2 success rates, we would have to today increase the Phase 3 success rate to almost 120 percent to be able to attain the success rates we were achieving in development in the late 1990s. This really is, at least by our assessments and we believe are shared by the HHS innovation initiative, a call to action.

Could I have the next slide, please? So while the data itself is very concerning, the positive aspect that we found from our study is that there are a number of major drivers of this decline. We understand clearly what the impact of these, and this in turn points us to, we believe, a

solution set that we can work from both as an industry but also, hopefully, in partnership with HHS and various agencies, including NIH and FDA.

The slide shows on the left-hand side both the primary drivers and their impacts, and, as I said, points us to a solution set. Take as an example the top two implications that we're finding it increasingly difficult to differentiate products during development, and that we're seeing a significant change in how companies are focusing their development pipelines, focusing on much more complex disease areas, as I indicated.

This points to both the need to work on innovative clinical trial designs and also to incentivize the developments of new technologies. Both of these are areas that have been identified through the FDA and NIH innovation-related initiatives.

So in fact what we're seeing is that many of the potential solutions to this problem fall well under the rubric of the HHS innovation initiative, and we hope that this study and its

results can lend further weight and energy to that initiative.

Next slide, please. So clearly, with this backdrop PhRMA supports the HHS innovation initiative, and we would welcome a systematic solution-based approach to the drivers of this decline. We specifically consider that the Department can lead and coordinate an integrated approach to these issues across the various HHS agencies, and in the next few slides I'm going to highlight some areas where we think this would be particularly valuable.

Next slide, please. First of all, at the highest level we believe that there are some clear policies that HHS could follow that would support innovation, which are listed here. Firstly, we would like to see HHS fully support the FDA's critical path initiative.

Secondly, we would like to see HHS initiate an activity to facilitate the identification and validation of biomarkers and surrogate endpoints.

Thirdly, we would like to encourage NIH basic research into disease mechanism of action.

Fourthly, we'd like to see HHS facilitate research and reimbursement for primary prevention products.

Fifth, we believe that HHS should actively support payment policies that encourage continued innovation, and, finally, we believe that it's very important--and it's important not to forget this--there should be an active program to educate both the public and policymakers about the need for innovation-friendly public policies. We'll explore each of these in areas in a little more detail in the next few slides.

FDA's role in a drug development and approval process puts them in really a unique position from our perspective to address these issues in a way that we consider both relevant and implementable. As we look at FDA's critical path initiative, we consider the following points to be extremely important:

Firstly, we'd like to see the FDA's

critical path initiative be the focus of HHS's efforts. Again this is because of its unique role that the FDA has facilitating the development and approval process of production in the marketplace, essentially facilitating the innovation cycle.

Secondly, we would like to see FDA's activities associated with the critical path initiative being adequately funded because we believe that without adequate funding, it is likely that these initiatives will not succeed.

Finally, we believe that it's important-- and this is probably a key role for HHS--that the various related activities across HHS and FDA be coordinated. The research and the general work done in this area should be complimentary, not duplicative, and in each case it should underscore or be based on respective missions and areas of expertise of the NIH and FDA.

Formatively, actively participating in FDA's consultative process on the initiative, and we strongly support the direction that it's taking. We hope that HHS will lend its way to this

important work.

Next slide, please. Biomarker research is another area that we consider to be extremely important. The value of biomarkers in drug development is already being seen in a very limited sense, but we believe that it needs considerable development. Biomarkers have the potential to streamline clinical testing and approval pathways for many drugs and ultimately to get drugs to patients faster and more economically.

While the industry will continue, clearly, to work in this area within companies, we believe that larger collaborative efforts between FDA, NIH and industry could reap significant rewards. The capabilities for research and analysis in this area are clearly at NIH, while FDA can ensure that regulatory validation of biomarkers for their ultimate use in developments, in the developmental drugs.

The key areas then, as we consider this area up close, firstly, that it needs to be appropriate selection of candidates for biomarkers.

Secondly, the process to develop these biomarkers needs to ultimately ensure their regulatory validation so that they have some relevance to the drug development process.

There are many models by which this work can be done, and we believe that they need further exploration before one is decided on. However, the industry is extremely keen to participate in work in this area.

Next slide, please. We also see a very important role for basic research at NIH. For many debilitating diseases there is currently a very limited understanding of the mechanisms of disease progression. This is clearly an area that could benefit from basic research. Such research ultimately stimulates innovation as the basic knowledge acquired helps the industry to develop drug products to treat these diseases by identifying new targets for new mechanisms of action for attack.

Already we see NIH conducting a lot of research in this area, and it really is perfectly

placed to do so. This work needs to continue and expand. If it's done in consultation with FDA and the industry, we believe it will ensure and focus on the relevant disease states, and we see again this is an important area for coordination by the Department.

Next slide, please. For many diseases, the most cost-effective treatment is prevention. However, the reality is that few of these products ever make it to market because of the regulatory reimbursement, rather, hurdles that are placed across the developments and approval pathway. We'd like to see the development of possibly of an FDA guidance that could help clarify and streamline the approval process for these products and, in addition, we would also like to see HHS encourage reimbursement policies and support the effective delivery of intervention products to patients.

Next slide, please. Clearly, another important area are the reimbursement and payment policies to support innovation. There's a body of literature supporting the idea that the current

payment policies are, in fact, acting as a barrier to the diffusion of innovation and access to recommended care.

There are several key points in this area. Firstly, choice and competition must be valued and any policies in this area need clearly to be patient-focused.

Incremental innovation is also very important and should be valued and rewarded. There are many examples such as medicines, new medicines in an existing therapeutic area--new treatments added to an existing therapeutic area--also treatments perhaps that facilitate ease of administration. Those are all important, have important patient benefits, and should be valued equally as a new production in a new cause.

CMS processes should also be timely, transparent, and open in the areas of coverage and payment decisions. And, finally, we'd like to see causes in this area keeping pace with technological devices such as concepts of personalized medicine and also general disease management areas.

Final slide, please. Unfortunately, the complexity and the fragility of innovation is poorly understood among policymakers and the public. Such innovation requires dedication, hard work, resources, and a willingness on the part of the industry to accept significant risks. We feel that HHS can play a very important role in protecting and spurring future innovation by educating policymakers and the public in this area.

I'd finally like to thank again the panel and HHS for the invitation to speak today, and I'd also like to say again how keen PhRMA is to support this initiative as it moves forward. Thank you.

DR. KESSLER: I have one question maybe you can answer it. One of the issues that has come out of this is a lot of the concerns about intellectual property issues in different companies, and while we're working to and discussing some of the issues that can move this process forward, within the government people are talking about is there a way that some companies would be able to not so much share the knowledge

that they've learned about their own particular product but the knowledge that they've learned about the process with other companies so that they don't end up having to deal with the same issue, and maybe that will speed up the process? If it's what we do at our end, but is there something that could be done at the other end that could help move this forward?

DR. LOEW: Are you talking more about a kind of pre-competitive technology knowledge or about a specific therapeutic area of class for example?

DR. KESSLER: Well, not really anything that specific but more in the sense that if Company A has--is making trans X (ph) and they go through the process at HHS and we help to--[off mike]--this whole process.

And then Company B is making trans Y which is unrelated, but maybe falls within the cracks of their--[off mike]--or, you know, sort of in the same realm, whether Company A would be barred to work with the other company and say, "Here are some

of the catches that we ran into, nonspecific to their product, but just in general these are some of the issues that we've had to deal with, and maybe that would help move it forward than having each person to have to learn--[off mike]--

DR. LOEW: This isn't something that we've specifically discussed with our membership, and certainly, an idea that we can explore. However, I know there's a little bit of sensitivity around this in some areas, particularly--and it's typically arisen in how FDA provides guidance to companies, maybe a second follower, or a third follower, and a therapeutic cause where they've already seen the first drug come through and have some--gained some--applied some--[off mike]-- through that.

I think that more generally, if you--there are certain--there are certain bodies of knowledge which companies would be prepared to share in a collaborative sense, and they relate to areas that one might consider, as I mentioned, to be more competitive in nature. And all of this comes down

to there are concepts such as, you know, sharing information on pharmacogenetics, pharmacogenetics, toxicogenetics (ph) where data could be shared in a blinded sense in a column database and allies to inform much better. For instance safety decisions in the preclinical and anticlinical development arena.

So I think that the industry is moving to a point where it recognizes that there is some information that is traditionally considered competitive in the area such as I indicated--that I just indicated, but it may well be worth exploring a model to share that information collaboratively.

So I don't know that we've necessarily got to perhaps quite the point that you all are suggesting, but there are certainly areas where I think we will be very interested in exploring some kind of public/private partnership to share that type of information, ultimately, to further the science for everyone's good.

DR. KESSLER: I will try one more time. Is Mr. Ronald Podraza in the room? Okay, well,

that all gives us 10 more minutes to our lives, so we'll go to Gerald Finken. Mr. Finken, Dr. Finken.

DR. FINKEN: Good morning. Thank you for this opportunity to present to the task force and to each of you. I'm here today as a pharmacist representing a small group of pharmacists who participate in pharmaceutical care for patients in clinical trials. I'm hoping that after today and in a few years from now that I'll be representing an association or be part of an association that deals in this area. Today one does not exist.

We are here today to weigh new ideas and promote new solutions, and I'm hoping that through the presentation today that I will be able to provide a novel idea that will provide some solutions across the various agencies, specifically, right now, of course, with the NIH and FDA. But I believe just as you have done in first things first is a model that I like to use. You've already taken the first step to provide the step for innovation and stimulating new technologies. I, too, believe that this step of

what I'm going to go over is a first things first, but with far-reaching--with far-reaching attributes.

As this task force gets together and they go through their various ideas that are presented today and have been in writing, I would hope that you would take this idea that I'm about to present and consider it to its fullest extent. And what I need to do and why it's unique is that I'm going to spend most of my time today explaining what this idea is as a new concept and then discuss ways that I feel that the agencies can use that concept.

Please, next slide. That concept that I'm talking about is what I'm calling centralized subject monitoring. This centralized subject monitoring is a very simple, innovative solution I think that has been overlooked in clinical research.

Please, next bullet. It's a service.

Next bullet. What I want to point out is that it's a service and not a technology. I know that most of the critical path initiatives and a

lot of the ideas that are being presented are technology-based, because that is where the revolution is in the basic sciences. This is more on the applied sciences, if I can extrapolate that, the applied science of just a new service that I think has been overlooked.

I think that this service addresses some of the issues again in its infancy. I see many areas that this service can assist in the critical path research as well as in the critical path initiative; that I see that it can decrease development costs, I think at an impact of what it can do to help the first time FDA successes, and, of course, support other initiatives that occur even today.

Next slide. So what is centralized monitoring? How does it work? It's a very simple process. You've seen it out in the community time and time again if you just have your pharmacists, your nurses, your physicians performing what we call pharmaceutical care, disease state and management. You get your prescription filled, your

pharmacist counseled you on how to take that medication.

We've taken that and extrapolated it back into clinical research, and it's a simple thing of just that each subject in a clinical trial is contacted and coactively counseled on the use of the medication in the clinical trial as one aspect of it.

Please, next bullet. The subject's response was a series of open-ended standard questions on pharmaceutical care, and questions are answered.

Next bullet. It's a proactive and a reactive that--and a proactivity is critical to the success of this, is that we don't wait to get calls back when there's a problem. We try to prevent those through a proactive mechanism.

Please continue. The information that we're provided by the subject is fed back through the investigator, back to the CRAs, back to the sponsor and vice versa that information that's presented or that needs to get to the individual

patient is it also comes back through the process. So there's a very good feedback loop.

And the basic analogy is like when I think about Phase 1 trial, the communication is pretty simple. You know, the sponsor has their site monitor who goes out to investigate, and then the investigator has their, you know, closed environment for those, you know, 10 to 12 to 20 patients that they're--that are involved in it in the clinical study. It's a very simple communication.

Please, next slide. But as we move up into the Phase I or Phase II, Phase III type studies, I mean just look at this. There's only 320 patients in this trial. Imagine how this box looks. It's like a, as a communication flow network. It starts very simple with the sponsor and just expands exponentially almost as you get out to the individual patients. And this does not include the various mid-manager levels of communications that it would have to go through.

And, of course, it's, you know, this is

very unique that all sites would have all patients. But the idea here is that if I took an individual to the far right-hand column side, how does that information get fed back to the sponsor? Or the first patient of the first investigator at this site, how does that information get fed back?

And this is all people. It's all about communication. When you look at this, each one of those site monitors have various degrees of training and experience. Each one of those investigators have various degree of training and expertise. And, of course, the patients as well. There may be multiple studies, there may be one or two studies. But the amount of communication that flows back and forth between that is enormous.

Next slide. The proposal is very simple, is that you take this mass flow of communication out, and you bring it back under to a few individuals, and that is that those few individuals, as it occurs in the community setting today, is that the subject monitor--is what I'm looking here--it's a centralized individual, a few

individuals who can take care of the population of this size. It's being done.

That information that's found out by the patient in the far right-hand corner and the information up above is funneled back through so that one individual can interpret, or assist to interpret, what the patient--the issue the patient has. Most important is the compliance of the study medication that they're taking. This is not to usurp the responsibilities of any of the individuals that are participating in the trial today. This is in addition to.

I want to point out that this is not occurring. Please understand, as I preach--as I preach, that this system, you would think that again it's a simple process you think does exist, that there is communication and there is communication between the investigator and the patients, and there is communication in those channels that I said, but this communication is in addition to that, this service.

Next slide. I wanted to put up some

examples of just some statistics of the few studies that we've done so far. You know, of course, what we're looking at is like the patient--the sample set that we chose, a couple thousand patients we're making approximately six calls per patient, and of those numbers we have notable interactions, you know, of almost 69 percent.

Now, this is information that may or may not go back to the investigators, and I want to point out not all of this information is captioned on the case report form, you know, that quantitative data, and that this counseling interventions are those items that do affect the protocol. The 28 percent again may or may not be caught.

Next slide. I'm sorry, can you go back one? A point that I want to make here is that like counseling interventions. And I want to use an example of a simple thing. It's going to be proactive, or it can be reactive. If you start a new study and you think you have it all down and the site you tell them--to give to tell the

patients to take their medication at breakfast and dinner, and you think you're covered, and it's not a medication where you give 10 and 10, you know.

That's not real, so you advise all the patients to take their medication at breakfast and dinner. We're fine, correct? Right, on the East Coast when are you taking your medication? On the West Coast when are you taking your medication? Morning and evening. In the mid-West you're taking it at lunch because it's breakfast, dinner, supper. All right, simple things like that are what we're finding out early on in the process.

Now, it may or may no come out. What happens if the CRA and the investigatory all believe that living in the Midwest don't understand that dinner on the East Coast is at the evening meal or, you know, during the evening, just as an example. I could go on and on with examples.

Please go on.

There are many questions that get asked that go back and forth with some of the intangibles. The idea is that you empower the

patient to be part of the trial, to answer their questions. There is also the self-reporting of adverse events, not again through the sequence that we get--we get--it's discussed many times about the adverse events have to go back to the investigator, and that still happens. What we're finding out is that when you send home on medication for four weeks, how long does it take before they forget about what just happened?

So you can time that about proactive communication in between visits to capture information that's slipping past, and not intentionally. But if you look at the paradigm that we've shown, or the flow chart of the information, the information is missed.

Next slide. The impact of utilizing centralized subject monitoring is, of course, the increased compliance and accuracy to study administration, disease state and management imposed for the protocol for the entire project and for that therapeutic area. Of course, the data improves, and again with better data you're

hopefull that you're going to be able to make better decisions about moving forward. And, of course, improving subject well-being is very important because I think it's imperative that we empower the patients in our clinical trials to participate, not in the study they're currently on but to talk to their friends, talk to their relatives to improve that process and say, you know, being in clinical trials is not a bad thing.

Next slide. There are other--I'm sorry--there's other additional impacts of, you know, of improved site and site monitor training. When we started, we were patient advocates but found in the sequence of events that the sites and the investigators themselves started to rely heavily on the individual to gather information or to ask information.

There's improved use of technology through, you know, the current diaries that are out there, electronic forms of IVRS, RFID tags, that type of information can be greatly improved with this type of service being put in place. And, of

course, the end result of that is improved evaluation, as I stated, to improve protocol and program predictability and efficiency.

The key element of this that I think that's a little bit intangible right now, and this is where I get back to the first things. First, is it started--I believe there's cognitive data set out there, and that is that we're gathering information through intuition, and I'll give you an example.

You know it was only about five years ago, 10 years ago that they only created a computer that could beat the chessmasters, and that's because as a human being we can bypass the standard--not decision tree, but the communication flow of how many steps would it take. If you fill a case book of questions or a diary of how many questions you have everything answered, you couldn't do it. There wouldn't be a computer big enough. But you have a professional out there who, intuitively, can go to, when someone says, "I'm feeling great," that means an awful lot. You know, how do you capture

that in an electronic diary, whereas a professional king the right questions can go to the point of where data can be captured.

So the cognitive database is something I think that is missing, currently, in the current quantitative sense of our clinical trials.

Next slide, please. And, of course, to apply what strategies. The strategies that I see is, of course, is that I'd like this task force and the agencies themselves to consider this concept, as we've considered about how it affects the current research. But I think it's far-reaching than that. I think that I'd like to see, of course, the HHS and its various agencies accept this idea and, of course, provide incentives and guidance to where this needs to go to affect, you know, the industry as a whole.

Next slide. I can't say enough that first things first, that it does start with the NIH through grants and basic research, and, of course, goes to the FDA clinical research. But I see this far-reaching. I think as a pharmacist I know that,

you know, physicians conduct trials that you choose the position because they're going to be prescribers of your medication.

And so physician to physician, there's information that flows from research to the practical community setting. But I, as a pharmacist, especially, I never had a pharmacist come and tell me that they learned in counseling patients in pharmaceutical care or a study nurse come out and present those ideas or concerns that patients are going to have. There's disconnect. How do I learn? I learn through journals, I learn, you know, through sales representatives. I learn through other means, and a drug is on the market for a year or two years before we finally understand, you know, the proper use of the medication.

So I think there's a profession that's, or professional information that could be utilized in the community setting. Thank you.

DR. KESSLER: Thank you. Douglas Cary from Cary Pharmaceuticals. As Mr. Cary comes up,

this is the last scheduled presentation. After that we'll leave the microphone open for people that would like to make other comments.

MR. CARY: Thank you. On behalf of Cary Pharmaceuticals, I would like to thank the organizers for coordinating this important meeting on a very timely topic.

As we know, Congress spends over \$20 billion a year on basic research at NIH and universities. As a result of the BioDole (ph) Act, this creates thousands of patents that are not being developed, as commercializing these inventions is not the role of NIH. This is left to the pharmaceutical industry to fill this role.

As we've heard previously, the pharmaceutical industry also spends billions of dollars on basic research. So while they're interested in licensing technologies from universities and in NIH, they would prefer that they license it after Phase II clinical trials because at that point the risk in time to market has been reduced. So this creates what we perceive

as a funding gap between the transitioning of innovation out of the laboratory and into a clinical development path.

Companies such as ours, especially a pharmaceutical company, is attempting to bridge this gap by in-licensing technologies from NIH and universities, advancing the technology through Phase II clinical trials, and at that point out-licensing to a strategic Pharma marketing partner (ph). Cary Pharmaceuticals has been in operation for six years and is applying this business model: We currently have three products under development. The first we licensed from Georgetown University, and patents have been issued in the United States and Europe in the Department of Biology and Hypertension (ph) that Georgetown is conducting research on Tempol for oxidative (ph) stress and hypertension under a five-year \$10.5 million NIH grant.

Our second product, QuitPak, is a unique, nonnicotine product for smoking cessation consisting of two components previously approved by

the FDA. Patents have been approved in the United States, Europe, and other major market with completed pharmacokinetic trials, and we will be conducting Phase II clinical trials next year. The regulatory path is a 505B2.

In February of this year, the company entered into an agreement with a major health care development company, and under the terms of this agreement, that company will become a strategic development partner for QuitPak. It will invest \$2.8 that will take the product through Phase II-B clinical trials.

The success for any of these ventures is very dependent on raising capital, and traditional wisdom is that venture capitalists are the source of this funding. Our many venture capitalists avoid investment in pharmaceutical types of deals because, as we've heard earlier, they perceive a long lead time to market in too many dollars to get to a decision point.

Venture capitalists also receive up to 2,000 business plans a year, and they fund fewer

than 10. A headline in The Washington Post business section in August helps define this lack of funding. It says, "Venture investing in region start-up firms falls to seven-year low."

Also a web site for a venture capitalist that is considered to be a potential funder for pharmaceutical deals describes their investment focus in these terms: They say they're "a venture capitalist expecting large returns with minimal risk." They invest in early-stage investors in therapeutics targeting major aging disorders and cancers. Target companies will have most if not all of the following characteristics:

Outstanding management team led by energetic proven entrepreneurs, leadership potential in a large and/or rapidly growing market segment; strong business plan including solid marketing and sales plan; strong intellectual property position and compelling technology; the capacity to leverage new technology and/or productivity enhancements; key strategic partnerships; annual revenue potential of more than

\$100 million; and potential for liquidity in three to seven years. Remember, this describes an investment in an early-stage therapeutic company.

SBIRs are also proposed as viable funding sources, but as the name implies, the focus is on funding research and not development. I am not aware of many, if any, commercialized pharmaceutical products whose development was funded by SBIR grants.

So a recent UPS pharmaceutical--next slide--UPS distribution states, "A critical drug discovery is worthless until it gets into the hands of the people who need it." This is the focus of the public meeting, how to provide funding and incentive to transition critical discoveries out of the laboratory and into a clinical development path so that the products might be commercialized to the benefit of the public health.

The following recommendations are provided for consideration:

First, establish an NIH funding mechanism for pharmaceutical development. For lack of a

better term "Small Business Innovation Development."

Second, require small business investment corps to provide funds to venture capitalists--to venture capital funds specifically for investment and pharmaceutical development.

Third, FDA to establish incentives for developing medical technologies from NIH and universities similar to the Orphan Drug Program.

Fourth, incent the Small Business Administration to provide assistance to private technology companies, not just a small or retail--a small service or retail establishments.

Fifth, encourage state governments to allocate portions of the State Pension Fund and/or tobacco settlement money to fund development of medical technologies. Pennsylvania is a good example of a state that's doing this sort of thing.

Encourage NIST to provide funding for medical pharmaceutical technologies that have commercial potential; as a result improve the public health. Our company's experience with NIST

application was that the smoking cessation product was not speculative enough to be considered for this type of funding.

And, finally, establish tax benefits for parties who invest in companies that develop NIH and university technologies.

Thank you.

DR. KESSLER: The mike's open. I think, Teresa, you want to make a comment? Do me a favor. If you do go to the microphone, please provide your name and your affiliation so we can get it in the transcript.

MS. LEE: Hi, my name is Teresa Lee, and I'm with the Advanced Medical Technology Association. Earlier in the day we heard some comments regarding permitting and enabling the FDA to utilize and share information that it possesses, and on behalf of AdvaMed we just wanted to point out that device innovation at its core is highly iterative with very short product cycles, and as a consequence, many manufacturers are highly sensitive to market signals related to disclosure

of such information.

As a result, release of clinical trial information and other proprietary information can be a significant disincentive to innovation and may impair the government's ability to obtain such information in the future.

Where, however, CMS and FDA are able to retain information as confidential manufacturers are often willing to come forward voluntarily, and the policy of protecting trade secrets and proprietary information as confidential will actually promote constructive public/private sector cooperation as part of the Department's operations. Thank you.

DR. KESSLER: Thank you, Teresa.

MR. WALKER: Hi. My name is Stephen Walker. I'm with the Abigail Alliance for Better Access to Developmental Drugs. We're a group that focuses on, essentially, the end of the translation process trying to get the drugs from the development process out to the patients when they need them.

I think there's something that quite a few presenters here have touched on today, but haven't really taken on head on, and I think it's because in some cases a fear of a cult-like belief, and in other cases a fear of being perceived as being sacrilegious. I think it's my job to be sacrilegious on this.

You can't think about innovation without thinking about the whole critical path because innovation is--is at the upstream end of a pipe, and if there's back-pressure even with great innovation, it can't get through the system to the patients, and so you end up with resources idling trying to get through the system. And from our perspective, having lost relatives and seen what the system does to cancer patients, and then worked with many other patients trying to get what they need for them, there's a big stagnation point in the approval process and in the development process that has to do with human clinical trials.

Our current system of statistically-based clinical trials in which all of the approval end

points are related to P-values and confidence limits, essentially banished as science and knowledge from the process. And it creates a situation where you must maintain a large pool of desperate cancer patients, for example, to populate these trials.

I heard earlier today, and I've heard a lot of very good things today, by the way--I heard earlier today that history is going to look back on the way we do clinical trials as being crude and barbaric, and I can tell you, as someone who's been in chemo lounges for about 1500 hours, they're already viewed that way by patients. We need to start thinking about different ways of deciding when things work and when they don't that have nothing to do with statistics.

In fact, as an environmental scientist with 20 years of experience cleaning up super-fund sites, I can tell you that the cult-like and straight-line belief in statistics is the only way to make a decision in a clinical trial is unprecedented in any other field of science. No

one else does it. The reason we do it in this field is because in the 1960s when we started doing this, we didn't know anything about the science. We need to start using the knowledge we have now. We're inventing drugs using knowledge-based thought processes. We're developing in that way, and then when sponsors come to the FDA, it's almost--there's almost an aversion to putting in the science because the only thing it can do is hurt you.

So the FDA needs to figure out how they're going to look at science and how they're going to start making decisions based on sound professional judgment, some clinical judgment, and we just heard a presentation a few minutes ago about how to collect more of that information from a clinical trial.

You need to take all this information you're getting and put it into a system where we are using the information we are now capable of collecting to make better decisions faster. And, by the way, as you think through the critical path initiative, we need no off-ramps to patients. It

can't be just one at the end accelerated approval and an access program that doesn't work. We need off-ramps to patients that really work. Thank you.

DR. KESSLER: Thank you for your comments. You might want to know that a number of those comments have been made over the past couple of months from a variety of sources in the task force about making clinical trials more efficient, about making much better, much more intelligent use of data in a variety of means by increasing the accrual to clinical trials. As you may or may not well know, one of the problems that hampers development is that accrual to trials can be so painfully slow so it's hard to get up numbers, even tell what's going on let alone whether or not you're depending on a P-value. You can't even get a trial done. P-value can be--

MR. WALKER: I'd like to follow up just a bit.

DR. KESSLER: Sure, you may, but use the microphone, please.

MR. WALKER: My personal experience with

why accrual to clinical trials--and, by the way, I'm absolutely certain this is correct--is that the reasons given by clinical researchers and the FDA completely missed the target. Having tried for two and a half years to get into clinical trials with a patient with a very common disease, metastatic colon cancer, the majority of patients do not qualify. The restrictions that are imposed by the statistical approach makes it almost impossible to enroll some of these trials, and as we see in post-market clinical trials, if you're going to use statistical type decision in-points for those trials--in other words, if we're going to pursue the survival benefit in a post-approval setting, we're going to be doing these trials where refractory patients are getting placebos and allowed to die on them because crossover screws up the statistics. You can't expect those trials, number one, to be useful or meaningful nor can you expect them to be completed unless you go overseas.

And that's happening right now. We're pursuing these meaningless clinical in-points, but

that's a different subject for a different day.

The fact is patients either can't get in, they can't get to them, or it's not a good option. And there are many trials that are not a good option. The statistical-based clinical trials really should not be viewed as dumb science, and we should be trying to get away from it. And everyone here needs to understand that when patients are diagnosed with a serious disease--and this doesn't apply, for example, to a painkiller for which there are already 20 available drugs on the market. This applies to the ones we really need.

Patients are not struck dumb. There are still engineers and doctors and lawyers and, you know, people with educations of various levels, but they're not stupid. And they know that when they're being offered a bad option, they know it's a bad option, and they will go if it's the only one they have. But if that have another one, they won't.

So we need to get real about that end of the critical path, because those patients need this

to work a lot better, much more than you do, and it's--that's all I have.

DR. KESSLER: Thank you.

MR. BURROUGHS: I'm Frank Burroughs. I'm president of the Abigail Alliance for Better Access to Developmental Drugs. Once people get to know us they call us the Abigail Alliance, but from our name, the Abigail Alliance for Better Access to Developmental Drugs, you can tell what we're about. A lot of you in this room have heard about us, read about us in various newspapers, or seen us on The Today Show or whatever.

But we're working on basically--and I don't want to take a lot of time here, I want to make just a few important points that are relevant and--but I do want to say that we're working very hard to help people get to drugs sooner. Of course, that's related to innovation, getting to patients sooner, products getting to the market sooner.

Let me give you a really compelling story here. The Abigail Alliance is working on a lot of

issues related to better access or earlier access, better innovation. Here's an interesting story.

Kiana is a 41-year-old woman with a little boy four years old and a little boy six years old. She's dying--I hope not--but it seems like she's dying of kidney cancer. There is a promising drug on the horizon that, statistically, with the data they have so far is very promising for kidney cancer. On a minor technicality she can't get not the clinical trial. This drug is show very--in Stage II trials--Stage I and Stage II trials are showing very high safety and efficacy.

Here's the irony: We may lose Kiana. Her father, who used to work--who I knew when I first spoke before the House Government Reform Committee, is alive today four years later after getting into a clinical trial. I wanted to make the point about how important it is to get early innovations to people sooner, get treatments to people sooner when their only option is certain death.

I want to leave that message. We're talking about people, not just Abigail, not just

Jennifer McNealy, Steve's deceased wife, but tens of thousands of people every year.

Again, I don't want to take too much time, but I was very impressed with everybody who was speaking here today, impressed with the U.S. government HHS's concern about this issue. I did want to make a comment. Douglas Cary of Cary Pharmaceuticals made some very important points along with everybody else speaking here today. Something the Abigail Alliance is working on that we've been pushed is what we call the Maryland Model. As a matter of fact, I've spoken to a lot of people on Capitol Hill about it, and actually testified on Capitol Hill about it a couple of years ago.

What is the Maryland Model? Back to The Washington Post again. About two years ago there was an article in The Washington Post about the University of Maryland setting up equipment labs with small biotech companies, pharmaceutical companies could share the university laboratories because the university had set up some small

production labs, and this is greatly helped the pharmaceutical industry in the state of Maryland.

It's called the Maryland Model because this could be applied nationally. Using existing federal infrastructure facilities, we could add the labs and the small production facilities to existing federal facilities around the country. For example, right here in the Washington area it could be Walter Reed. It could be--it could be and, of course, NIH, or it could be on the West Coast, it could be Stanford University or other private or public facilities, and it wouldn't cost a lot of money, and it would help us get innovative products from small companies to the market sooner.

Thank you very much.

DR. KESSLER: Thank you for your comments. Are there other comments for today?

(No response.)

DR. KESSLER: Then let me make a final statement, and then Dr. Zucker can wrap it up. I want to appreciate all the speakers. We have all of their handouts. There's a few to be picked up

at the back. I can't promise you what will be in the eventual report that's released by the Department. What I can promise you is that every member of the task force, those of us who are here up front. Dr. Sullivan has just stepped out for a minute, but he's been here for the rest of the time, Shana Christup from CDC who's back here over on one side of the room, and Elise Berliner from AHRQ who's on the other side of the room; that we will listen to every comment that you've made today, those that were made in public, those that were made to the mike, it'll be in the transcript, and we'll take those under consideration and try to put as many of the good ideas as we can into the report.

We appreciate your time. I'll turn it over to Dr. Zucker to close out the panel for the day.

DR. ZUCKER: Thank you, Larry. I just want to echo Larry's words. I thank everyone for being here. We very much appreciate this information. And as Larry has mentioned, trust us

that we will incorporate into our discussions all the discussions that took place here as we move forward with the report.

As I mentioned at the outset, the objective is to provide the Secretary with specific action items that HHS can implement really in a relatively timely fashion. And we all in the task force believe that if we can identify four or five or six, or just a handful of items that steps can be done now which will serve very much as a tipping point so that this tipping point in medical innovation technology, which will allow the entire process to move forward much quicker. And as I had mentioned at the beginning, something that will accelerate this whole innovation process that we seem to all feel is a little bit in stalled patent.

On behalf of Secretary Thompson I would like to thank all of you, and I'd also like to thank all my colleagues both here and, as I mentioned, colleagues who are in the audience who are working on this task force, and they are very much instrumental in this whole process in moving

this program forward.

And lastly, I'd like to thank Nancy Stanistic from FDA who has been the eyes and ears for Larry and I for the last several months in moving this forward.

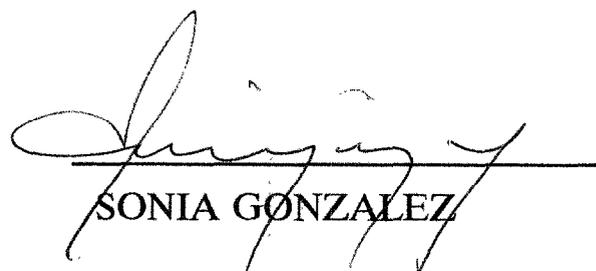
If there's anything else you'd like to bring out, we'd be around for a little while as well. Thank you.

DR. KESSLER: Task force members, if you'd come up, I'd appreciate it.

(Whereupon, at 12:22 p.m., the meeting concluded.)

C E R T I F I C A T E

I, **SONIA GONZALEZ**, the Official Court Reporter for Miller Reporting Company, Inc., hereby certify that I recorded the foregoing proceedings; that the proceedings have been reduced to typewriting by me, or under my direction and that the foregoing transcript is a correct and accurate record of the proceedings to the best of my knowledge, ability and belief.



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