NATIONAL INSTITUTES OF HEALTH

SCIENTIFIC MANAGEMENT REVIEW BOARD

October 26, 2011

Conference Room 6, C Wing
6th Floor/Building 31
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Bethesda, Maryland

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I N D E X

P R O C E E D I N G S

OPENING REMARKS AND AGENDA OVERVIEW

CHAIRMAN AUGUSTINE: Good morning, everyone. Welcome to what I'm told is the 10th meeting of the SMRB. I'm sure to some here it seems like the 30th but, Francis, I'm thinking of you but in any event it has been a busy couple of years.

I hope everybody has had a good summer and that you had a chance for a little bit of a break.

Since we have not met for several months we have a fairly full agenda today.

We have a few members who will be wandering in as the morning goes on and had conflicts to begin with but will be here.

The agenda today begins really with--we're going to ask Dr. Collins to give a little bit of an update on what's happening at NIH in the broader sense and where the Agency sees itself headed into the future.

Then one of the main things we want to do is talk about the recommendations that the committee has provided in the past and focus particularly on three areas, the translational medicine and therapeutics area, the NIH Clinical Center and the substance use, abuse and addiction research at NIH.

And Francis will be giving us a rather thorough update on that supported by the individuals who are most directly involved.

Also those reports are available on the SMRB website and the members can find two of the three reports in the front part of your meeting binder you have today.

Then this afternoon we'll talk about a future task that Francis has asked that we consider undertaking and we will have time to discuss that and any other issues that members want to raise.

We do have a new member who is not here just at the moment but will be shortly. It's Dr. Roderic Pettigrew. As most of you know, Dr. Jeremy Berg left the NIH earlier this year. Rod has agreed to take his place and will join us in a moment and we'll introduce him at that time more formally.

Maybe what we should do is just for the benefit of those who are guests go around the table and introduce ourselves.

As I said, I'm Norm Augustine. I'm chairman of the SMRB.

And why don't we just go around this way?

DR. SHURIN: Susan Shurin. I'm the acting director of the NHLBI.

DR. GREEN: Eric Green, director of the National Human Genome Research Institute.

DR. RODGERS: Griffin Rodgers, director of the National Institute of Diabetes, Digestive and Kidney Diseases.

DR. RUBENSTEIN: Arthur Rubenstein from the University of Pennsylvania.

DR. BRODY: Bill Brody, Salk Institute.

DR. COLLINS: Francis Collins, director of NIH.

DR. CASSELL: Gail Cassell, visiting professor at Harvard University in the Department of Global Health and Social Medicine.

DR. KATZ: Steve Katz, director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

DR. POWELL: Debra Powell, University of Minnesota.

DR. PATTERSON: Amy Patterson, executive secretary for the committee, NIH.

CHAIRMAN AUGUSTINE: Thank you.

Let me also just take a moment to welcome those who are our guests at the meeting today. We appreciate your interest in our work and thank you for taking your time to join us.

I should note there will be public comment periods that are spaced through the agenda. There's a place to sign up out in the hall if you would like to comment on any topic relevant to the SMRB's work. We will take speakers in the order they signed up and, hopefully, there will be time available for everyone to make whatever comments they'd like to make but in that regard we will ask that you hold your comments to five minutes. So if you would be thinking about that as you prepare what you might want to say.

I'd like to emphasize that if you have longer comments you would like to make or more formal comments we welcome letters, email, post cards, whatever, and we will post those on our Web site when we receive them but, as I say, we really do appreciate the comments we get. We have had quite a number and they have been helpful and many have offered constructive suggestions.

The next item of business is the minutes for the meeting of November 10th, December 7th and February 23rd have now been formally completed and I'm told that I should particularly thank Steve Katz, Bill Roper, Susan Shurin and Bill Brody for their inputs on those minutes. You have them before

you. Would anyone want to make a motion to approve those sets of minutes?

DR. : So moved.

CHAIRMAN AUGUSTINE: Second?

DR. : Second.

CHAIRMAN AUGUSTINE: Thank you.

Okay, all those in favor?

(Chorus of ayes.)

CHAIRMAN AUGUSTINE: Opposed?

The ayes have it.

And now we need to go through, as we usually do, the conflict of interest policy for this committee. We do that in keeping with the government regulations in that regard.

Dr. Patterson is the expert on that subject and so we will call on you, Amy.

REVIEW OF NIH CONFLICT OF INTEREST POLICY

DR. PATTERSON: Fasten your seat belts. This is going to be exciting.

As members of this committee you are special government employees and, indeed, members of this committee are very special government employees, and therefore you are subject to the rules of conduct that apply to government employees.

These rules and regulations were explained

in a report entitled *Standards of Ethical Conduct for Employees of the Executive Branch*, and you each received a copy of this document when you were appointed to the committee.

And at every meeting in addition to reminding you about following the ethics rules we also like to pause and review the steps that we take and ask you to take to ensure that any conflicts of interest between your public responsibilities on this committee and your private interests and activities are identified and adequately addressed.

As you know, before every meeting you provide us with a lot of information about your professional, personal and financial interests and, in turn, we use this information as the basis for assessing whether you have any real, potential or even apparent conflicts of interest that could compromise your ability to be objective in giving advice during committee meetings.

If such conflicts are identified we either issue a waiver or recuse you totally from a particular portion of the meeting. We usually waive conflicts of interest for general matters as opposed to specific matters because we believe your ability to be objective on those general matters will not be

affected by your interests.

However, we also rely to a great degree on you to be attentive in real time during our meetings to the possibility that an issue could arise that affects or at least appears to affect your interest in a specific way. And if this happens, please let us know and we would ask you to recuse yourself from the discussion.

And always, if you have any questions about these rules or regulations, we'd be happy to address them.

And that's it, Norm.

CHAIRMAN AUGUSTINE: Okay.

Amy, thank you.

Does anybody have any questions on this topic at this point that you want to raise to the group as a whole?

Hearing none, we'll proceed.

The first item on the agenda dealing with the issues at hand is to call upon Francis to give us his update on where NIH stands and the challenge it faces and the vision for the future.

So the floor is yours.

STATUS OF NIH TODAY AND LOOKING TO THE FUTURE

DR. COLLINS: Thank you very much, Norm.

Good morning to all of you.

I’m a little under the weather with a bit of a virus but happy to be here just the same. I will explain already my unwillingness to shake your hands today because I didn't want to share this particular little bit of DNA with you or maybe it's RNA but whatever it is you don't want it.

(Laughter.)

Sorry that Gail and Bill seem to have drawn the short straws and have to sit next to me but hopefully I will avoid contaminating you or the rest of the room.

But I’m really pleased the SMRB has gathered here again to hear some reports on what's happened with a variety of tasks that you have, I think, nobly and ably assigned us with and which we are nobly and ably trying to follow-up on. And you will be hearing about those in the course of the morning.

The SMRB certainly plunged in to its agenda with great energy and vigor and produced for us no less than four reports in a rather rapid fire fashion, three of which involve substantial investigation of new organizational structures at NIH, some of which turned out to be even more

complicated than those of us who have been here for a while had thought. So we have been very busy and I hope you will get a sense of that this morning as we provide you with some follow-up on those recommendations as they relate to three of those topics.

I thought what I would do though just to get this kicked off is to give you a sort of broader view of where things are in terms of the scientific opportunities at NIH and some of the stresses that we're facing as well.

We have wonderful leadership here and it's my pleasure to have a chance to serve as the person who tries to steer the ship but I would get nowhere were it not for the remarkable talents of the 27 Institute and Center directors and also all of the other senior staff and down through the ranks, the thousands of people who work at this remarkable institution.

By the way, we have one new Institute director in the room that you have not met before that I might want to point out to you. Martha Somerman, who is over here--yes, raise your hand--is the new director of the National Institute of Dental and Craniofacial Research and has been with us since

the last day of August or something approaching that. It's delightful we were able to recruit her from the University of Washington to come and lead that particular Institute. I hope in the course of time you'll get to know Martha a bit.
She's a wonderful talent to add to our ranks.

So yes, we are, I think, at this paradoxical point at NIH where having now been here myself for 18 years I think I could say that the scientific opportunities have never been more exhilarating, never more potential present than there is now for revolutionizing medicine. And that's across the board in cancer, infectious disease, diabetes, heart disease, rare diseases, common diseases, neglected diseases of the developing world.

The potential for make major breakthroughs with profound implications for human health is just around us every day and that’s what makes it exciting to wake up every morning and see what's going to happen in this research agenda that we have the privilege of leading as the largest supporter of biomedical research in the world. But we are faced with a historic challenge in terms of resources so that is the paradox.

I think there has not been a time that people here can remember where the support for biomedical research has been under more stress. And that is of course a consequence, the way in which our country and much of the world is struggling with the difficult economic situation, with large deficits that have to be addressed and so we are, I guess, more than ever in a circumstance of having to choose priorities carefully, being willing to say that there are some things that we're going to have to scale back in order to be able to do new things because if we ever stop innovating then we shouldn't probably deserve to be supported. We have to be out there on that leading edge of the new potential of new things but it is not an easy time to try to make such difficult decisions.

We also, I think, are now in a circumstance where we have to be more effective than ever in articulating the value of what we do and not just assuming that it speaks for itself and that everybody already knows this. And that implies a need to articulate both the medical advances that we have the potential of creating that are going to benefit millions of people but also to be able to explain economic consequences of our research

enterprise in a way that makes it clear that dollars invested in NIH are also a good pathway towards recovery of the economy and support of jobs and so on. And certainly some of us have learned to include those comments in many presentations that we make in order to try to address what's on everybody's mind right now, which is the struggling economy.

I will spare you some of those statistics this morning but I could rattle them off quite readily if you were interested in hearing and, in fact, the economic analyses that have been done, including just in the last few months, are extremely compelling in terms of payback, the return on investment that occurs from NIH investments.

I thought, though, I would focus instead more on scientific opportunities and would do so in a fashion that reflects actually the case that we're trying to make right now because, believe it or not, we're already in the throes of trying to make the case for the FY13 budget even though we don't have an FY12 budget yet.

As you probably know, the budget for FY12 is hanging in the balance of a lot of discussions going on even though FY12 started on

October 1st and we are living in a continuing resolution as we often do at this time of year in hopes that the Congress will come up with some kind of plan between the House and the Senate that the President can sign and then we'll know what our resources are. But meanwhile because of long lead times we are already in the process of defining ways to make our case for FY13.

(Slide.)

And in that regard there are these four themes which cover a lot of territory and perhaps won't surprise you but I think are actually quite compelling in their own way in terms of those extraordinary opportunities. And I just want to touch briefly on each of these and then you'll hear more details about some of them in the course of the day.

(Slide.)

So first of all in basic research I think it is critical to point out that NIH's 52 percent of budget that goes to basic research is the sort of thing which simply will not get done elsewhere if not supported by NIH dollars. These are the kinds of programs that are generally seen as too far away from any commercial output to be supported in the

private sector.

(Slide.)

And there's a lot of excitement about this. And I was very pleased to see the President include this paragraph in a speech he gave about a month ago at Thomas Jefferson high school as part of the Patent Reform Act. And some of us had the chance to be there for that and to meet with him afterwards. And certainly it's helpful to see this very clear statement of the importance of investing in basic research and technology “So that great ideas of the future will be born in our labs and…” he says, “…in classrooms like these at TJ high school,” which is a remarkable magnet school in the Virginia suburbs of Washington.

(Slide.)

Just as an example of something which started out as a very basic science undertaking but which is really gathering more steam almost daily is this whole field of microRNAs. Tiny snippets of RNA that turn out to be real rheostats on the way in which gene expression is controlled at a very refined level so that a particular RNA target of a microRNA may not be translated as efficiently if the microRNA is shutting it down.

And it's clear this is a significant way in which gene regulation is maintained by cells and organisms and maybe even a new way for endocrinology to find a new life because it seems microRNAs can, in fact, be exported by one cell to be received by another, an interesting concept.

There's even a paper, though I'm not quite sure I believe it yet, that suggests that you really are what you eat because a Chinese group studying microRNA circulating in the human plasma discovered fairly significant quantities of plant microRNAs that have somehow made it through the GI tract barrier. And at least one of those very abundant plant RNAs seems to have a target in the liver that affects liver metabolism--I mean lipid metabolism. Now wouldn't that be interesting?

Our diet is in some way now revealing itself on a molecular pathway that nobody could have imagined. The so-called exosome where these microRNAs travel throughout the body may not just be ours but some of those that are around us, including what we put in our mouth. So a fascinating area to be sure and much excitement here, and yet it started as a very back water kind of aspect of basic science.

(Slide.)

Even in the study of genetic factors in chronic unexplained diseases like schizophrenia. I couldn't help but notice the first report in this case where a microRNA turns out to be one of the risk factors for this disease. MicroRNA 137 turns out to have a variant which is associated with schizophrenia risk and that same microRNA turns out to regulate a whole bunch of genes in the brain. So it can make a pretty nice story here so something to watch. Another area to watch, of course, is the induced pluripotent stem cells and the remarkable advances that have happened here.

(Slide.)

Just to sort of titillate you here, that is a photograph of some induced pluripotent stem cells that have been differentiated in the cardiac myocytes and are sitting there on the petri dish contracting just like they should being cardiac myocytes. And the ability to take skin cells or blood cells from you or I and turn them into pluripotent cells certainly has been a dramatic development.

(Slide.)

And just to draw these two things

together. We now are seeing more and more papers published about ways to create IPS cells that don't involve the use of integrating retroviruses, which has been a bit of a concern. One of which, in fact, brings us back to microRNAs as another way to do reprogramming. Again, demonstrating a connectedness in all this.

(Slide.)

So pretty cool stuff in basic science and certainly something which NIH has stood for, for a long time, as in this quote from James Shannon, whose name adorns the building where I spend my time over there. Building 1 is also called the Shannon Building. And I think we've done pretty well here in demonstrating the effectiveness of this as of this latest season where the three grantees - the three Nobel laureates announced for their advances in immunology had all been at some time NIH grantees. So we claim credit for a lot of what's happened.

(Slide.)

So basic research clearly flourishing. The kind of area where we seek not to be too top down in our motivation of trying to drive the field.

Happy to tell you if you didn't already

see the announcement that we have recruited--and he will be coming in August--in April--a new director of the National Institute of General Medical Sciences where a great deal of basic science goes on. And that is Dr. Chris Kaiser, who is currently the chairman of biology at MIT. A wonderful opportunity to bring somebody with really remarkable credibility as a scientist and a leader into our midst and he will be of course stepping into the role that was previously held by Jeremy Berg who led that Institute very capably indeed. And Chris, therefore, walks into an Institute that is already in great shape but with lots of ideas of his own.

(Slide.)

Of course, technology is playing an increasingly important role in NIH advances. The days where people used to dream about maybe engineers and biologists getting together in greater ways have been replaced by days where they seem to be together on a lot of interesting projects. And no less I suppose than the case of DNA sequencing.

This curve showing you what's happened to the cost of DNA sequencing over the last ten years dropping really at a profound level. That is a log scale on the Y axis. Outstripping Moore's law quite

dramatically with costs now something like 30,000 fold less than they were ten years ago making all kinds of things possible where previously we couldn't imagine. Eric Green, as director of NHGRI, could fill in lots of those examples.

(Slide.)

I'll just give you one where this kind of approach is now opening up a window to discovering the causes of diseases that previously were out of reach because they were too rare basically to allow you to go after the answer.

These two sisters that you see here both suffered from an unusual disorder with progressive debilitating joint pain and calcium build up in the arteries of their extremities but not their coronary arteries. They came to the NIH to the Undiagnosed Diseases Program, which is run here at our Clinical Center by Bill Gall and a cast of about 30 other investigators, underwent some extensive analysis which ultimately resulted in the discovery that they have a new disease. Namely they are both homozygous for loss of function of a gene that codes for CD73, which is actually an enzyme that converts AMP to adenosine. And this both tells us what caused their disease and also points to a pathway involved in

normal vascular homeostasis that we didn't know about and probably has significance for cardiovascular disease in general.

This kind of outcome of being able to come up with an answer to a disease with just two affected individuals was unimaginable a few years ago. And now if you read the pages of *Nature Science, Cell,* the various genetics journals you'll see almost every month three or four more examples of rare diseases that have been unraveled by direct DNA sequencing of affected individuals even if there are few of them available.

(Slide.)

Of course, NIH's mission is both to understand the basics of how life works but to apply that to try to advance human health. This is the translational agenda which has been for a long time an important part of our portfolio, which are now with your encouragement particularly looking at in new ways.

Of course, the SMRB deliberated quite effectively and intensively over the course of several months last year and made a recommendation back in December that NIH might be advantaged by coming up with a new way of encouraging

translational science.

We found that to be very interesting; I accepted your recommendations. We had a lot of follow-up conversations with you and with many other experts in the field, including those in the private sector, in academia, and with advocates.

(Slide.)

This paper, which is in your notebooks, is a summary as of July on my part of putting forward what the opportunities are here scientifically that might make this dream that Arthur Rubinstein and his hardworking working group put forward could look like. And I think over the course of those months this really did mature into quite an exciting set of specific opportunities. Some of which we are pursuing already pretty vigorously.

Kathy Hudson is going to talk about NCATS in a subsequent session and give you considerably more detail about where we are with this so I'm not going to do so at this time to avoid duplication but I think it's fair to say we are all very energized by the potential that this National Center for Advancing Translational Sciences puts forward and grateful to this group for having the wisdom and the vision to be able to sift through those many issues

and make some very helpful and important recommendations.

(Slide.)

Many things happening in translational sciences in the Institutes as well and one just to highlight here. The opportunity to see whether we could get beyond the need for an annual influenza vaccine and come up with an approach that would provide immunity not only against just one particular string that pops up one year but across all influenza strains including not just H1N1 but H5N1.

And this is a very active area of research which has made remarkable progress in the last couple of years. A lot of it happening here at the Vaccine Research Center across campus that Gary Nabel oversees.

The diagram basically points out what the strategy is but generally immunity is generated to the most highly exposed part of the influenza virus hemaglutinin but that's the part that is also highly variable so every one of those red areas are areas that vary from virus to virus and therefore you can see why raising an anti-serum against one may not protect against the other. But careful combination

of structural analysis, immunology, genetics and so on has pointed out that there are parts of this molecule that are not variable and really can't be or the whole thing falls apart and that those could, therefore, be an appropriate target if you could convince the body to generate an antibody against that particular part of the protein. And that is, in fact, vigorously underway with an expectation that this is likely to pan out.

(Slide.)

In fact, Tony Fauci, who will be with us a little later on this morning, has made an estimate here about what the time line might look like. The basic and pre-clinical studies done going back to 2007. Phase 1 human clinical trials are now underway. Phase 2 expected in 2013. Additional studies in partnership with the private sector in 2014 and by 2015 licensure studies and application for licensure.

And given that 36,000 people still die every year of just the usual seasonal flu, and that many of those are people who are unimmunized in part because it's just darned inconvenient to get your flu shot every year, and seems possible that we might be able to make a major advance here with this

particular kind of science.

(Slide.)

I can't talk about translational science and the advances that have happened without highlighting the remarkable event that happened in September with the awarding of the Lasker Bloomberg Public Service Award to the NIH Clinical Center. Some of us had the privilege of being there as John Galen for the Clinical Center received this remarkable award and spoke about the way in which so many people over the course of many decades have contributed to make this so and all of the ways in which this has revolutionized our approach to diseases like cancer and rare diseases and HIV/AIDS and so on. So this is really a wonderful moment to be able to celebrate what this clinical center, the largest research hospital in the world, has been able to accomplish.

(Slide.)

This fourth area is to my mind the most important. We can have lots of great ideas about what might be possible but if we don’t have the investigators to drive that forward and to come up with the ideas that none of us have thought of yet then this will all fail to go forward at the pace

that it could. This again is a constant source of struggle and some anxiety, frankly, right now with resources being tight. It there’s something that wakes me up in the middle of the night, other than having this nasty cold, is thinking about what are we doing to try to nurture and encourage scientists who are maybe just coming into their own independent phase and wondering whether there's a career path for them when things are pretty tight right now.

We have done a number of things to try to encourage innovative ways to support such investigators and here are just a few: We are starting this new program to try to bring clinical investigators into NIH in a fashion that might resemble the things that happened in the '60s and the ‘70s that were so productive in terms of nurturing our next set of talented individuals, many of whom then went on to populate our nation's universities and to lead great programs.

So that in partnership with the Lasker Foundation is to create a program to bring such clinical researchers to NIH to give them a protected period of five to seven years to conduct their own independent research taking advantage of the Clinical Center.

And then if they are successful either to become tenured as an intramural investigator or to have resources to take with them to go elsewhere to a university to start their own program so that they're not caught in this situation of needing support on day one. They will have it as a dowry effectively to take with them wherever they wish to go.

The transformative R01s, the Pioneer Awards, the new Innovator Awards are all programs supported from the NIH Director's Common Fund. Those are difference ways that we encourage investigators to come forward with ideas that have to be innovative that you don’t get into the mix unless what you're proposed is bold and, if successful, would actually change the paradigm. Those are reviewed in a very rigorous way in terms of encouraging the innovation and not worrying too much about the preliminary data or the buffer concentrations.

This new award which we have just announced the first winners about a month ago is affectionately known as the Skip the Post Doc Award which is made available to the most talented M.D./Ph.D. or M.D./Ph.D. graduates who have just

finished their doctoral training and who are ready for a independent role and don't necessarily have the need for a post doctoral fellowship which may take quite a few years and may delay their abilities to do their own creative and independent research.

I had a very good time reading the applications that came in, in this this first cycle of the Early Independence Awards to see what these investigators are proposing and it gave me great optimism about the path that we're on and the talent that is out there. And certainly if this seems to go well we would hope perhaps to see it expanded and perhaps have some of the Institutes adopt similar programs in their own training program. This again at the moment is a fairly small program supported by the Common Fund.

(Slide.)

But we have some other major challenges in our research workforce. And certainly one major one that has been even more apparent in the last few months after the publication of the manuscript which was commissioned by NIH looking at diversity in our workforce, we are woefully short of where we would like to be in terms of having evidence that we are

recruiting the best and brightest from all groups.

Certainly if you look at the representation of African Americans, Latinos, Native Americans in our scientific workforce it is substantially and woefully reduced relative to the general population. And that basically means we're missing out on recruiting some of that talent because we are not seen as a pathway for some of those most gifted individuals and that is a loss to us and to them.

So we clearly need to work on our recruitment programs. Even though NIH has invested substantially in this over many decades it's not clear that we have really developed a sense of what works and what doesn't. And we are embarking upon an effort to try to understand that better.

The paper that came out in the summer, the Ginther, et al. paper in *Science*, the senior author being Raynard Kington, former Deputy Director and Acting Director of NIH, focused on what happens to individuals who do get through the training programs and end up as applicants to NIH for independent research grants, specifically R01s.

And the disturbing aspect of this was that

African American applicants have a substantially lower success rate even when you correct for all of the factors that you might think could potentially account for that, such as institutions where individuals have trained, what kind of training grant opportunities they had and so on. This is just an unacceptable situation and we clearly need to do something to try to change that around.

One thing that clearly correlates with success, and which I think indicates that part of the problem here is a lack of mentoring or a lack of experience is that if one has the chance to serve as a reviewer of other grants early in your career that clearly improves your ability to be successful. And you can see why that would be. The kind of learning experience one has by sitting in the room with other peer reviewers and going through other grants is invaluable.

We also, though, I think have to consider whether there is some inherent bias in the system even though grant applications are not identified by racial or ethnic group. It is possible in many instances, I think, to figure that out if somebody is trying to do so or even not trying to do so. Is there unconscious bias potential here that we have

to be aware of?

(Slide.)

In order to take this on in a most serious way we have already instituted a number of initiatives but one specific group that we're seeking now to try to identify other activities is a working group on diversity and the biomedical research workforce which is going to be part of my Advisory Committee to the Director and specifically looking as you can see here on these transitions points, which is often where we lose people in the training program and we need to understand why that is. Their recommendations are due in the interim form by this December ACD meeting and final ones by next June.

(Slide.)

And you can see this is a very impressive group of individuals who have agreed to take part in this rather intense examination of our programs and to give us recommendations about where to go. The co-chairs being Reed Tuckson, John Ruffin and Larry Tabak, who can tell you much more about this as he has been asked and has willingly embraced the opportunity to put a lot of his time into this effort.

(Slide.)

Another related question, though, and one that I think is on everybody's minds especially in the sort of difficult resource situation we are is what's the right size of our biomedical research workforce?

In any given week I will have somebody say to me, “You aren't training enough doctoral level biomedical researchers. We need more of this and that out there.” And somebody else will say, “You're training too many biomedical researchers. We have a glut of Ph.D.s stuck in post docs and not enough positions to find their ways into.”

Both of those can't be right. Part of it is I think our unfortunate tendency to assume that the only really acceptable pathway for a doctoral trained biomedical researcher is to end up as a tenure track investigator in a top tier university because that's often where they were mentored and that's often, therefore, where they see their role models. And that is a complete disservice to our trainees and to the community and that's something we need to work on.

So, we clearly need a better understanding of the dynamics of the workforce. What is the

supply of talent coming into that? Especially with dynamics that are changing quickly on the international stage where we can't simply count on this remarkable flow of talent coming from other countries or, if it continues to come, we can't count on it staying the way we used to. And why is it that American students are so disinterested in many instances in coming to be part of our workforce? What's that about? And what are those trends looking like?

And then what about the demand? It's not just about universities who need faculty. It's about all of the other places where doctoral trainees are needed. Could we try to come up with a model of this?

(Slide.)

So that's what we're trying to do seeking some stakeholder input with an RFI, which has already happened. And this group, ably led by Shirley Tilghman, President of Princeton, and Sally Rockey, our chair here of extramural research who you'll hear from this afternoon on a different topic, and with this pretty impressively diverse group of experts is going to be looking at this from the perspective of what's the right size and what

are the levers that NIH could pull systematically to try to address these situations.

Recognize that we do not train all of the biomedical researchers in the U.S. but we train a lot of them, both in terms of people who are listed on grants of principal investigators that we support through our grants program, those frankly we have a little less control over, but then there's another fraction where we have rather direct input because their individual or institutional training grants pre-doc and post doc.

And there we could clearly, if we knew what the right thing to do was, have an impact on both the quality and the quantity of trainees that are coming through. And the quality of training clearly needs to be attended to as well. It’s not, not sufficient to say how many people we need. It's also critical to say and how should we be training them to be ready for the kind of opportunities that are out there.

(Slide.)

So all of these things give you a snapshot, I guess, of the great opportunities in science that are in front of us right now but here is the reality check that causes us to actually have

some considerable concerns about how to support this and that forces really serious consideration about priorities.

In the blue bars here is the appropriations in dollars for NIH since 1998. You can see the doubling that happened between '98 and 2003 that put us in a very strong position to have a lot of exciting research going on that otherwise might not have been possible to start. But then you can see the flattening of the budget that happened after with the exception of the Recovery Act dollars in '09 and '10.

In yellow, though, is what happens when you apply to this the Biomedical Research and Development Price Index, the BRDPI. And you can see that that has eroded our buying power quite substantially since 2003. And, in fact, if you draw a line there, assuming that we get the President's budget for FY12, which would be quite optimistic at this point, we would still be back somewhere in the neighborhood of where we were ten years ago as far as our buying power even as the scientific opportunities have grown and expanded quite dramatically.

The consequences of this to a parameter

which many of our applicants are concerned about, namely success rates, are clear and are deeply disturbing.

(Slide.)

You can see since 1978 the success rates for a grantee coming to us have tended to be in this zone between 25 and 35 percent which most of us would say is fairly healthy. But it has become less healthy in the last seven or eight years. And as that budget flattened off in 2003 you can see what has been Happening. As our buying power has decreased the cost of research has been going up by inflationary index. And then in 2011 the current estimate is that the success rates were 17.4 percent. It’s the first time in history they have been less than 20 percent.

And, of course, we don't know in 2012 what to expect or what will happen beyond that. Much of that now rests in the hands of the super committee because if they are unable to come up with a plan for cutting the deficit and the so-called sequesters kick in we could see an extremely Draconian outcome for all aspects of government support, including the National Institutes of Health.

Again, this then forces all of us to look with great care at all the things we're doing and I guess one can think of various strategies for dealing with these budget challenges.

Of course, as I said at the beginning, one thing we must do is to make the case for NIH as articulately as we can just in case people aren't aware of just what the value is of what we do and we have to work even harder with all of our other advocacy groups to try to be sure that message is getting across.

What we have been doing, of course, by necessity as these dollar figures have begun to get tighter is to trim spending across the board. This year--this past year, FY11, for the first time we effectively reneged on out year commitments to multi-year grants in order to try to keep monies available for new grants. And even so we did not end up, as you saw there, with a very good outcome as far as success rates.

Then, of course, we do have to evaluate and rearrange our research portfolio focus on both programs that are perhaps less productive than they used to be as well as areas of research that perhaps need a boost or not. And every Institute director

is deeply engaged in that process. Perhaps this is one of those circumstances where one could say we shouldn't waste a good crisis and we should make some very difficult decisions about priorities that would be harder perhaps to institute in better times.

Then there are much more, sort of controversial but I think we have to consider them, ways of managing NIH resources that potentially could be considered. Such as do we really need to think about whether every principal investigator ought to have some sort of limit on how much resources they are given in order to spread the money around a bit more? Should we say, for instance, that no individual should have more than three R01s? There are people who have more than three R01s. They are generally very productive though.

And having talked about these--some of these issues in front of AAU presidents and chancellors it was clear there were deep concerns about stepping away from NIH's perspective which is basically meritocracy, and applying any other specific rules even though it might seem to be the way to provide a broader number of investigators

with support. Is that really what this is about?

So lots of things on that list that we are thinking about and we have put some data up on the NIH Home page for people who are interested in providing advice about this so that one can, for instance, figure out how many dollars do you actually free up if you make one of these decisions. If you decide to say no investigator can have more than three RO1s, what does that really do? Does that make that big a difference in the number of new and competing grants you're able to give that year?

That data is up there for people to look at. We have made no decisions about this but we think it’s a good time to have a conversation with our most important constituents, the universities, institutes and the grantees. And we look forward to having more of that in the next few months as we try to figure out how to negotiate these troubled waters. So your suggestions in that regard would be welcome as long as you're willing to wade into that territory.

(Slide.)

And again here is the website which has a lot of the data on there if people are interested in having a look and trying to see what the

consequences might be of pulling some of these levers that we potentially have access to, but we want to do so only with great care because obviously almost everything we would do will have both the expected results and some secondary consequences, and you don't want to be surprised by those. You have you want to have your eyes wide open.

(Slide.)

So I will basically stop there and quote the President here in terms of another thing that he said a month ago. “If we're going to create jobs now and in the future we have to out-build and out-educate and out-innovate every other country on earth.” We, at NIH, would like to contribute to that and aim to do so as vigorously as we can with the resources we are given.

So thank you very much for giving me the chance to put forward these ideas and I’ll be glad to answer questions if that will be good and I’ll come back to my place to do so.

CHAIRMAN AUGUSTINE: Thank you, Francis.

We'll open the floor to questions from the members.

DR. RUBENSTEIN: Francis, I know there was a fair amount of opposition to the translational

research center around Congress and various constituencies which I think at least from my vantage point you handled extraordinarily well. I just wonder what your reading of it is now and now that you have got it in place how the scientific and other communities are thinking about it?

DR. COLLINS: Kathy Hudson will say a bit more about this but, briefly, I think as the concept of what the translational center's goals were going to be became more clear in people's minds, and the notion that this was a drug discovery company or a drug development company for NIH became clearly not the plan, the embracing of the overall plan has grown substantially. And I think my experience now talking to biotech and pharma, and there's a wonderful recent report that Kathy will mention from a group chaired by Maria Freire that we asked to look at this, and was very strongly supported, is that there is a lot of receptivity to this from those who have actually managed to get the chance to see what the real intentions are.

In terms of the administration the President spoke strongly about support for this in September. The Senate in their mark for FY12 have language that is quite supportive of NCATS. The

House has not yet come up with a bill that has been voted on by their committee.

There is some considerable concern though about whether this is sufficient to get this started in FY12 with all of the other uncertainties that are out there, but I think it--it's gone down an interesting path to put it mildly. There was a lot of misunderstanding at first but I think clarity is now coming pretty far along.

DR. GREEN: Can I make a--To amplify one point, so, Tom Insel and I are co-chairing the search committee to identify the director of NCATS when it comes to existence and we have a very active--we have a superb committee, a very active committee and we're making lots of phone calls. And I will tell you
the response we're getting with basically cold phone calls to perspective candidates and some of the real leaders in that general area is a remarkable amount of positive feedback.

In fact, lots of messages we're getting, "Oh, make sure you tell Francis or make sure you tell everyone we think this is a great idea. This is long overdue." You know, despite any of the negative publicity that came out initially, that's —

it’s all melted away. Huge amounts of enthusiasm and I think we’ll get a lot of good candidates as a result.

But even the people that said we’re not interested in being candidates were very, very positive about this development.

DR. RUBINSTEIN: That’s my reading as well, so that’s very good. (Not at microphone-inaudible).

CHAIRMAN AUGUSTINE: Yes, that is really good to hear.

Sol?

DR. SNYDER: I was just curious about what level of funding there can be and was that bill in Congress that you're talking about have anything to do with moving money around or adding money?

DR. COLLINS: Again I don't want to preempt what Kathy is going to say. It’s the very next agenda item but basically the Senate approved the formation of NCATS by bringing programs from other parts of NIH together under this new structure, including the CTSAs and also added $20 million for the Cures Acceleration Network which is something that was authorized in the Healthcare Reform Bill but had not yet been appropriated.

Again, the House doesn't have a voted upon proposal. The chairman is still somewhat skeptical about NCATS but we're hopeful that can be overcome.

CHAIRMAN AUGUSTINE: Francis--Gail, please?

DR. CASSELL: I think along those lines it would be helpful if maybe members of the committee could have some of the economic--recent economic analyses that you have referred to as talking points perhaps.

DR. COLLINS: Have we got those.

DR. CASSELL: Alright, I knew you did but it might
be nice to have them; we can further share them with others as well.

DR. COLLINS: We'll be glad to provide those for you.

CHAIRMAN AUGUSTINE: Yeah, that would be helpful.

DR. COLLINS: There's a particularly good report from May from United for Medical Research that went through a fairly rigorous economic analysis and we can get you that plus some additional material.

DR. : (Not at microphone-

inaudible).

DR. COLLINS: There are slides and there are also reports. We'll get you both.

CHAIRMAN AUGUSTINE: Terrific.

DR. CASSELL: I think, along those lines too, Norm, if there were some easy way that we could get the data in terms of comparison with other countries' investments, especially those that are going way up
while we're going down, might also be really helpful and make good arguments. I don't know if the data contain that kind of information but--

DR. COLLINS: We have that and it is pretty breathtaking when you look and see particularly what China and India are doing but also what Europe is doing.

DR. CASSELL: Oh, yeah.

CHAIRMAN AUGUSTINE: Francis, I had a question on the funding rate for grants, the 17 percent projected number. If you just judged the applications or proposals on merit alone without a funding issue what percent would you feel would be appropriate to fund?

DR. COLLINS: It probably varies quite a bit from topic to topic but, in general, I think the

experience over all these years has been about a third are the ones that you really feel, yes, this is good stuff and we should do this. Maybe even a little more than a third. And that's being pretty stringent. That's not just doing everything that comes in the door that might give value.

So we're clearly way below that now with only about one in six instead of one in three finding their way into getting support. And you can imagine the consequences for investigators who then spend more and more of their time writing, rewriting, and trying to come up with something else to submit to try to keep the lab going instead of doing research.

CHAIRMAN AUGUSTINE: That was the point I was going to make. I'd also suggest like 20 percent of the people who should be getting awards are basically wasting their time writing proposals. Gail?

DR. CASSELL: Two thoughts.

One is, Francis, how do you make a compelling argument that the overall quality of the grants today that are not being funded are as high as they were when fewer applications were being submitted by individual investigators? I think this

is a concern that people have had all along but do we have data to support the fact that that’s--you know, that the quality, in fact, is higher?

A second thought is that with all the emphasis that we all have on innovation and transformative research, I worry that some of the really basic problems that are rather mundane but very important from a public health standpoint, like sepsis is an area that's understudied and yet the deaths due to sepsis continue to go up in this country in all age groups--and I just am choosing that one because it happens to be an example fresh on my mind but there must be others--how do you protect those rather mundane areas of investigation at a time when study sections are so focused on the need to really be creative and innovative?

DR. COLLINS: Both very important questions.

You know, it is difficult to come up with a metric to evaluate quality of applications across say 20 or 30 years. My own sense is that the quality is going up and not down in terms of the rigor with which people are approaching problems and the way in which they're defending their

approach.

I saw Steve raising his hand as if he might want to weigh in on this.

DR. KATZ: I would say that from the standpoint of the evaluation of 20 years ago versus today obviously we rely heavily on peer review. And nowadays the exceptional and outstanding applications which are not being funded are clearly something that would not have happened years ago and it’s not just a matter of the study section thinking well, this should be funded but there is a certain pride in saying, yes, this is an exceptional or outstanding application. And you're not going to say that unless you really mean it.

DR. : Yes, and yet not all of those are getting funded.

DR. COLLINS: In terms of the areas that you mention that might be neglected, I think this is a big job for all of the 27 Institute and Center directors to look across their portfolio to try to see are there areas which are critical for public health but perhaps are not getting the attention they deserve and, if so, then to identify an opportunity to encourage that field with a specific RFA. And it would be interesting if Tony was here

what he would say about the sepsis question and whether that's something that he--

DR. CASSELL: Oh, and I—-I really only, I said sepsis, as I just said, because it was just fresh on my mind having a recent experience there but it also comes to mind at a time when the foundations are having such struggles in terms of their amounts that they can invest. Is it time to maybe rethink or consider different types of partnerships, especially with the different patient advocacy groups now that are funding research, some pretty significantly really.

DR. COLLINS: I think this is a great time to look at new models for partnership between NIH and foundations, between NIH and the private sector.

In fact, some of us are spending a lot of time doing just that. I'll be jumping on the train as soon as this meeting adjourns to go to New York for the board meeting of the Foundation for NIH, which is a mechanism we have to try to encourage those kinds of consortia with foundations and the private sector.

And we're running a meeting next week, a major meeting with a pharmaceutical company R&D chiefs about target validation and exploring ways

that we might in a very unprecedented and, I think, pretty creative way come up with an approach to target validation based on human data that might have considerable value.

CHAIRMAN AUGUSTINE: Susan?

DR. SHURIN: Gail's raising some important questions that we need to have answers that are out there sort of right up there with the economic impact. One of the measures of this quality issue actually came up during ARRA, and which many of us--NHLBI was one of them--took about a third of the funds that we had and just lowered the pay line. So we funded a whole bunch of grants which had already been peer reviewed which we would have funded had we had enough money. And we're tracking all of those. And I can tell you that as of right now in terms of productivity, which I am going to have to measure by publication rate particularly in high impact journals, they are at least as good as the ones that we funded getting to the pay line.

CHAIRMAN AUGUSTINE: That's really important.

DR. SHURIN: The more important issue, of course, in the long term is impact but you have to

go further out to really see scientific impact. But looking at productivity they're clearly just as good.

And I think that the other key issue that we get very concerned about is that as resources get tighter the study sections get more and more conservative and so it gets harder and harder to fund high risk/high reward research. And going to a pay line in the general vicinity of about 30 percent enables us usually to fund a significant amount of research which may or may not pay off but sometimes when it does pays off it is extremely high impact.

CHAIRMAN AUGUSTINE: I suspect we should proceed.

And the next speaker, of course, is the NIH Deputy Director for Science, Outreach, and Policy.

We've been talking about NCATS.

Dr. Hudson, I think we have pretty well covered your presentation. But welcome.

(Laughter.)

ADVANCING TRANSLATIONAL SCIENCES

DR. HUDSON: Thank you. Thanks.

(Slide.)

What I would like to do this morning is to remind you of some of the problems that the TMAT Working Group sought to address and then update you on the actions that we have taken at NIH subsequent to receiving your thoughtful recommendations to try to move forward and implement those.

(Slide.)

So the problem that your working group and your committee were addressing was the very high attrition rate of compounds going down the therapeutics development pipeline where that entire process is error prone, failure prone, slow, and extraordinarily expensive. So despite the fact that we at NIH are investing considerable resources and pharma is investing considerable resources, we have a very low rate of new medicines entering our medicine cabinet.

(Slide.)

In 2010 there were 21 new molecular entities that were approved by the FDA for use to treat various disorders and diseases.

(Slide.)

And a similar landscape is seen with recombinant biotech medicines and biologics. On the right you can see the orange bars indicating the

rate of approvals of new biologics from the FDA over time with 2010 being on the right. And again notice that on the Y axis here we're in the single digits for approvals. So this is sort of a depressing landscape that your committee sought to address.

(Slide.)

So in May of 2010 Francis gave you a charge to give us some suggestions on how we could better support translational and therapeutic sciences and six months later in December of 2010, not yet a year ago, you delivered to us this report on translational medicine and therapeutics with its extensive recommendations and thoughtful analysis for us.

(Slide.)

Very quickly on the heels of receiving that report Dr. Collins recommended and Secretary Sebelius agreed that a new center should be created at the NIH to support translational sciences and she, as required by law, notified the chairmen of the various--and ranking members of the various committees about her intention to establish this new center.

(Slide.)

Also at the same time Francis set up an

internal committee to really try to hash out some of the details about how would this new center work, how it would interact with other translational science activities at the NIH, what is the mission statement, what is the organizational chart, et cetera. And this is a list of the members of that committee who worked for several months to develop a recommendations and a mission statement which has evolved a little bit since that working group concluded its work.

(Slide.)

And the mission statement is “to catalyze the generation of innovative methods and technologies that will enhance the development, testing and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions”. And the emphasis here is obviously on the catalyzing the development of new approaches and new methods and not in moving individual compounds down that drug development pipeline. And that really turned on the point that we talked a little bit around this table a few minutes ago about the communication challenge early on to distinguish what we're trying to do here in enabling therapeutics development from doing therapeutics

development.

(Slide.)

So NCATS will facilitate and not duplicate the research activities and the other Institutes and Centers. It will complement and not compete with the private sector, an important message that I think we have now effectively conveyed. And importantly especially in these tight budget times we need to emphasize that NCATS will reinforce and not reduce our commitment to basic research. So the level of support for basic research at the NIH, a little over 50 percent, has been pretty stable over time and it will remain unchanged by the creation of this new Center.

(Slide.)

So this is a list of NCATS research programs that will be moving into the new Center once it is formally established. And all of these except one were programs that you recommended be imported into the Center upon its creation.

The internal committee of Institute directors recommended and Francis supported including the Office of Rare Diseases Research in NCATS. That office is currently within--reports to Jim Anderson and DPCPSI and reports to Francis

directly in the Office of the Director and we felt that it would be a good addition to move into NCATS.

(Slide.)

One thing that I didn't put into this presentation is a summary of some work that we have been doing and has just recently been concluded to look at how the CTSAs, the Clinical and Translational Science Awards, will be integrated into this new Center in a smooth and effective way in order to support the very important work that those centers do now, numbering 60, across the country and being able to have them maximally support the mission of NCATS.

(Slide.)

And so Steve Katz chaired a group of Institute directors, largely made up of folks who have been advising NCRR on the CTSA program since its inception, Susan Shurin, Jim Anderson was on that group, Griff Rodgers is on that group, and ably led by Steve Katz and staffed by Lyric Jorgenson, and they delivered recommendations to Francis recently which he adopted on how to make this integration and
fusion most successful.

(Slide.)

And Francis mentioned the Cures Acceleration Network and I'll just say a word about that. It was established by the Affordable Care Act but had interesting language embedded within it which basically said that we couldn't undertake any of these activities until we had a specific appropriation for the Cures Acceleration Network or CAN.

It includes a number of interesting features. One, a board of directors or board of advisers that has an interesting composition as compared to the normal Institute or Center council. So it includes a large number of private sector folks, venture capitalists, and patient stakeholders.

It also includes three authorities. The one that we have spent a lot of time thinking about how to use in interesting and novel ways is the flexible research authority which is a DARPA-like authority allowing other mechanisms of supporting research other than traditional grants, cooperative agreements, or contracts. And so we've been trying to identify unique opportunities to be able to use that authority once an appropriation is in hand.

The other authority here is Partnership

Awards. And I think particularly in this budget climate finding opportunities to be able to partner with the private sector in developing resources in a pre-competitive way and partnership to leverage each other's resources and know-how is particularly important.

(Slide.)

Francis mentioned this group. So we had lots of committees and working groups targeting specific parts of NCATS and giving us really stellar advice to build on your own advice. This group was largely comprised of folks who have--are either in the private sector or who have had private sector experience and they gave us some high level advice about how NCATS could operate in general and specifically how NCATS could interact--interface with the private sector. And this group also recently completed their work and delivered a report to Francis, which is on the website.

And I'll just mention that on our Home page now, NIH's Home page, at the bottom of the page is a blue button that says "Promoting Translational Sciences" and if you click on that button everything having to do with NCATS is sort of gathered together in one place and easy to find.

(Slide.)

And this report from the ACD is there as well.

(Slide.)

So Francis mentioned his article in which he laid out his vision for NCATS and that has been very useful particularly in correcting misimpressions about what NCATS would do and sparking ideas about early priorities for this new Center.

Dr. Collins and many of us have spent a lot of time recently talking to groups of pharma companies, biotech companies, venture capitalists, academic health centers, and others to try to identify what are those bottlenecks in the drug development pipeline that we could usefully attack and try to overcome.

(Slide.)

So this is the proposed organizational chart for NCATS and I would point out a couple of things about this organizational chart.

First, unlike the organizational charts of most Institutes and Centers, the primary bifurcation is not one of extramural and intramural. So we're going to try to have a more porous interface between

intramural work and extramural work in this Center and that’s represented by not having that fundamental division at the get go and high up in the organizational chart.

The two fundamental research divisions are the Division of Preclinical Innovation and the Division of Clinical Innovation. Also you see there the Office of Rare Diseases Research which we decided to put into NCATS.

I’ll point out that the council that--we are trying to put together a council slate currently for this new Center and we are hoping that this council can both fulfill the statutory requirements for an advisory council for an Institute but also fulfill the statutory requirements for the CAN board so that we don't have multiple different groups opining on the same subject matter but rather an integrated whole. That will be sort of a large council which is atypical but we're looking forward to that novel mechanism.

(Slide.)

This is the requirements for the CAN board and, as I mentioned earlier, it's quite distinct from the standard council for an Institute.

(Slide.)

So we are, and Eric mentioned this, we are currently soliciting applications for NCATS Director. This person should have expertise that transcends a single discipline, preferably have experience both in academia and in the private sector. And a large number of the folks on our list do have both those backgrounds--backgrounds in both of those sectors. And this person really needs to be willing to engage in disruptive innovation and has an exciting challenge to be the first leader of this new Center.

(Slide.)

The search committee is listed here. The members of the search committee are listed here and again Eric and Tom Insel are the search committee co-chairs. If you have ideas for folks who they should reach out to and touch, please send a note to Eric or Tom Insel and we'll make sure to try to lure them in.

(Slide.)

So there was some mention of the Senate appropriations bill and where it stands in terms of NCATS.

So the Senate bill does provide $582.4 million for NCATS, that is the sum of all of the

programs that are being imported plus an additional $20 million for the Cures Acceleration Network, which we would be able to use, as specified in the Affordable Care Act, 20 percent of that or $4 million for the flexible research authorities.

The report language that accompanies the bill says that NCATS is a far-reaching example of how NIH can refocus its mission in a difficult fiscal time and so we have strong support from the Senate in their bill that has been marked up and approved by both the subcommittee and the full appropriations committee.

(Slide.)

As Francis mentioned, the House has not yet marked up a bill through its subcommittee and so we are waiting for what the House action will be and what the agreement will be between the House and the Senate at the end of the day. But we don't want to waste time. While we're waiting we're starting to launch design programs that can be pilot programs that can be taken on by NCATS early on in its life.

One of those is a project that Jim Anderson is leading in DPCPSI, which is a partnership between us and DARPA, which will have all sorts of interesting aspects to it. One of

which is that we will be able to sort of learn how they do project management at DARPA by being able to work closely with them.

The other is the science here which is the goal of developing a chip that will mimic the physiological processes of various organ systems interacting with one another. And DARPA is focused on the bioengineering aspects of this project, our RFA is not yet on the streets. It's in development but is expected out sometime this fall. Will be focusing, as you might expect, more on the biological side of this and what kind of readouts would you want to be able to get from such a tissue on a chip mechanism.

(Slide.)

The second pilot project--we have several ongoing but the second one that I'll mention is an effort to identify what role NIH could play in being sort of a matchmaker for rescuing and repurposing efforts. And so we would like to be able to match compounds that are abandoned in pharma's medicine cabinets and be able to match those with our investigators who have good ideas about new indications for those compounds.

We're in negotiations now with a company

to be the initial pilot and hope to expand that to many, many companies who would be willing to provide their compounds in exchange for us being able to basically crowd source their compound for really great ideas of rescue and repurposing.

(Slide.)

So--So since you delivered to us your thoughtful report, we have been very busy and we have gone through lots of stages in the process of standing up this new Center.

We still have a couple of check boxes that await Congressional approval before we can stand the Center up but we're eagerly waiting that day when we can cut the ribbon and we hope you all will join us for that.

And, as Francis mentioned, the President has indicated that he is strongly supportive of this new Center and, in fact, at this event I invited him to come to NIH for the groundbreaking of NCATS, the ribbon cutting, and he indicated that he would like to do so. So we are looking forward to that.

And I would be happy to answer any questions or listen to your discussion.

DISCUSSION

CHAIRMAN AUGUSTINE: Thank you.

Gail?

DR. CASSELL: Kathy, Francis and others, I am really excited. I think that it's obvious you have made a lot of progress. The two projects that you have just described, especially the one with DARPA, I think is really very exciting and important. That's an understatement.

I wonder about the regulatory science FDA-NIH project. As you well all know all too well, the amount of monies there are really small, especially monies that FDA can contribute to such a joint effort. And I wondered if you could comment on this particular program and how you see it growing and how you see the interface between FDA and NIH. It's extremely important and I hope that FDA will be a strong arm and not tagging along just because of lack of resources.

DR. HUDSON: So thank you for the question and comment.

We have been working really closely with Peggy Hamberg and her colleagues since Francis arrived certainly and we were excited to launch the regulatory science initiative with them. We are moving that into NCATS and actually are sort of putting the toxicity tissue on a chip program under

that general rubric. And that actually I didn't mention that and I should have, I apologize. FDA is involved in that and they have been really instrumental in sort of advising that program. DARPA and NIH are putting the dollars in but the brain power is coming from all three agencies. So that's an exciting opportunity.

And then, Amy, do you want to say anything about the regulatory science work that we have underway in the grants?

DR. PATTERSON: Well I think Gail is correct that what's underway right now is a beginning but I do think a very notable and unprecedented feature of that collaboration is that FDA is integral to the peer review process. So they have actually been at the table helping to evaluate proposals and make decisions. So it's--they are not just tagging along. They are--they're contributing--they are contributing resources but, as you said, they may be more limited but they are contributing their insights and expertise.

DR. CASSELL: So it would be great to include on your slide just so that people realize they are involved, especially in the DARPA project. They have wanted for a long time to be-- have a

study to look at why drugs fail and this will certainly help do that.

I am aware that in response to the FDA Science Board Report on science and technology at FDA, Jessie Goodman told me just recently they have been able to squirrel away a little bit of monies for academic centers of excellence in regulatory science. So it would be nice to see again more collaboration if at all possible in this area.

DR. COLLINS: Your point is very well taken. I couldn't help but notice that something happened in converting the slides to this current format where the FDA logo on the slide faded away.

(Laughter.)

I almost think there was something suspicious going on there. It was right there but--

(Laughter.)

DR. : You're in trouble now.

DR. COLLINS: Be sure to bring it back.

DR. RUBINSTEIN: I know it may be difficult because of the multiplicity and small size of biotech companies but having some input from them as well as venture capitalists and pharmaceutical companies because there's a lot of innovation going

on in very small companies. So I don't know exactly how to do it but I would just like to bring that up because in my view a lot of the new innovation in drug discovery is happening there rather than in big pharma at the moment.

DR. HUDSON: Indeed. And, in fact, we were just out in San Francisco two weeks ago at the personalized medicine Burrill conference and spent time a lot of time with individual companies and them as a group collectively seeking their input and ideas, yeah.

DR. COLLINS: We also had a wonderful meeting in San Francisco in July that was organized by Sue Desmond-Hellmann and Brooke Byers where they brought in a bunch of entrepreneurs partly from therapeutics but also from diagnostic and devices. And we had a very interesting day where they were quite revved about what NCATS might be able to contribute from the different perspective of biotech entrepreneurs.

CHAIRMAN AUGUSTINE: Gail?

DR. CASSELL: So I wonder--you didn't mention the SBIR/STTR program and how it might could interface getting to Arthur's point. And it would be really exciting if there were some way in maybe--

I don't know if you're reevaluating your SBIR program and if that's why it's on the agenda but I think--

(Laughter.)

DR. COLLINS: What a great foreshadowing.

DR. CASSELL: --it just seems that this could really help do a lot of things. I was on the phone until 1:00 this morning with a young faculty member at Stanford. I agree with what you're saying, Arthur, and they're going great guns on some really exciting things but can only get it so far so this would be great.

DR. HUDSON: Right. We're excited about having a strong SBIR program in NCATS and we'll be looking forward to deliberations of this committee in terms of what kinds of enhancements might we contemplate for this program in order to make it even more fruitful than it already is.

CHAIRMAN AUGUSTINE: Well, thank you for that report.

We’re close to on schedule so why don’t we go ahead.

Yes, Bill, please?

DR. BRODY: I wanted to make a comment after Francis' presentation and I’m not exactly sure

how to say what I want to say.

And I'm not speaking for the extramural establishment but I'm observing the extramural establishment which I think is fundamentally in denial about the macroeconomics of what's going on. And I don't--everybody has expanded or is expanding, continuing to think that build it and they will come, whether you're at small research institutes or at large universities.

The macroeconomics are simply not going to support the research establishment the way it is. The level of stress--this is my third downturn in NIH funding but this one feels fundamentally different from the other ones.

And the impact of the stimulus funding--I was interested in your comments, Susan. Although our ability to predict success is very limited and, in fact, I mention this morning an article in Sunday's *New York Times Magazine* section by one of my heroes, Daniel Kahneman, who is the only non-economist to win the Nobel Prize in economics, who talked about the inability to predict success in a variety of fields.

Nonetheless I think what it did is it postponed a period of pain which then comes back

afterwards where the same--many of the same people, not all, are again faced with the challenge of getting grants.

I don't know what the solution is but it can’t be more and growing--and economic arguments notwithstanding, we obviously need to make those and to push Congress but the budget is fundamentally going to change.

One of my faculty said I’m Dr. Revision. I’m spending all my time apropos of your comments. Is it worthwhile for our top scientists to be spending--we have post docs who, you know, we impose rules but somehow people get around them and we’ve got post docs eight to ten years in the system.

I don't have any solutions but I do think it's worthy of significant discussion about are we going to make any fundamental changes to the research establishment.

On the one hand it's like managing a snake farm. You want to move ahead but you want to move slowly. So I fear that NIH or Congress might make changes very drastically. We’ve all made long-term investments and if you make changes to facilities, administration, recovery, for example, you need to do them slowly otherwise you'll really

impact.

On the other hand we need--I think the system has to washout some people. I was in New York yesterday in one of these limo cars or whatever and I asked the driver how long he had been driving and he said, “About four months.” I said, “What did you do before that?” He says, “Pharmaceutical chemist for 31 years and I got laid off with the merger of pharmaceutical companies. The pharmaceutical companies are down.” I mean it's happening everywhere. And my fear is that we die a thousand deaths as opposed to sort of taking some big hits. I mean there are some things we can do more abruptly.

So I don't have a solution. I know you're doing your darnedest to figure how to negotiate through this and you have got 10,000 constituents, including my vocal faculty, who think that theirs is the only voice that needs to be heard. But, anyway.

DR. COLLINS: I’m glad to have you raise this, Bill. And I guess I’d just like to ask your advice in terms of how to be sure that the denial doesn't get in the way of finding solutions.

I--We have sort of tried to organize this fall opportunities to meet with the leadership that

you would think would most need to get their minds around where this is going.

And I had this very interesting meeting with AAU presidents and chancellors. And my sense was it didn't take me telling them that things were going to go into potentially a bad decade. Maybe the fact that Jack Lew talked to them right before I did had something to do with their smelling the coffee.

And Larry is speaking to the APLU and I'm speaking to AAMC and I have already spoken to IOM. We are sort of having this collection of opportunities to lay out the seriousness of the situation to make it clear that NIH doesn't want to do things that will be causing harm that we couldn't have sort of anticipated and prepared for.

But at the same time that the simple Darwinian approach might not be sufficient in terms of just allowing success rates to fall, fall, fall because we know that our particular brand of natural selection is not very good when it drops below the 25 percent or so success rate.

CHAIRMAN AUGUSTINE: Sol?

DR. SNYDER: Yes. In trying to figure out what's going on and what to do about it, one thing

that is confusing is-- because Elias Zerhouni used to say one of the big problems of not funding grants is because the stimulus plan brought all these enormous numbers of applications out of the woodwork. I don't if it was the same people making lots of applications or a lot of new people coming in. And that, therefore, when we say the funding rate is very low it's really sort of artificial in that there's a lot of funny stuff out there, which perhaps talking about some analysis the NIH could do to see what's going on. I don't know--I don't have any answers but there's something about that.

DR. COLLINS: Yes, we certainly have a lot of data about that and when Sally Rockey is here this afternoon she can no doubt reel off some of those statistics.

We were worried that there might be a big bolus of applications coming in in '11 and '12 for people who were funded through the recovery dollars and then with only two years of support wanted to come back and keep going. It was not as scary as anticipated. There's--the total number of incoming grants, while it has gone up a bit, has not been drastically upward.

So there are many drivers of why the

success rate is falling. The main problem, of course, is the purchasing power that we have to deal with is 20 percent down from where it was in 2003 and the average cost of a grant has been trickling upward because it's more expensive to do research, and that’s despite NIH's efforts to do downward negotiation with almost everything we get, assuming that whatever is being asked for they could probably do it with a little bit less.

So there are several factors. Yes, there has been an increase in the number of grants but that actually kind of got triggered by the doubling way back in '98 to 2003 as the number of faculty who are ready to do great research increased. The cost per grant has gone up and our buying power has gone down. It’s the sort of perfect storm. No single thing explains all of it but it puts us in a tough bind.

Should we push even harder to insist that the average cost of a grant can’t grow even though the BRDPI is? The only way you can do that is by more systematic downward negotiations which are already pushing people kind of to the limit of what they can actually do. That's on the list of possible levers we might pull but it's not an easy

one.

There are even suggestions that the nuclear option of thinking about indirect costs ought to be on the table.

Can NIH afford to pay the current allocated rate when things are so tight? But let nobody imagine that that wouldn't have consequences for science. Indirect costs actually support science.

And many fear has been expressed that if you start tinkering with that you put universities, many of whom are already in deep trouble, especially those that depended on state appropriations that are being cut back pretty drastically and then what lever do they have left to pull? Well, it’s to increase tuition. That doesn't feel right at a time where we want to see more people having an opportunity for education.

So there's no magic here. There is a need, I think, therefore, particularly for all of us to own this. What I don't want is to have this sort of come forward as, okay, NIH has got the problem and NIH is going to make some suggestions and either you'll like them or not. That's not the way we can do this.

We have to really, as a community, get together and look at what those options are, decide which of those make sense and then own them collectively even though they will be unpleasant and there will be consequences that many people will find really quite difficult. It's where we are.

CHAIRMAN AUGUSTINE: Arthur?

DR. RUBINSTEIN: I just want to support what both said. I think there is an unreal feeling around that it's not going to affect our institution but it will affect everybody else and we'll get an increased amount. And everybody says we will but that's the top 20, 30, 40 places, and it doesn't add up.

So, you know, when you look at what's happened in the pharmaceutical industry, I don't think it's that farfetched that as these numbers go down dramatically there's going to be millions and millions of dollars left in research institutes and universities.

And, you know, to push for a plan now rather than a catastrophe of laying off people which is likely, I think, is really important.

And just so you know, when I preach about that at our place they just laugh at me so you

should know that. Although I'm coming here and preaching the same so you can laugh at me, too.

(Laughter.)

CHAIRMAN AUGUSTINE: Gail?

DR. CASSELL: I think along with Elias's slides that he used to talk about he also had slides showing the building construction especially within the medical schools.

I haven't seen any of that recently but wonder again if in the economic analysis it wouldn't be good to have that to show what the consequences are.

Certainly to share it at the state level and I'm sure you will do that in spades but at the same time I think there has to be some consideration for the indirect cost and improved efficiency at the university levels in terms of management and the use of those indirect costs.

As you know, the--since OA21 was kind of renegotiated I'm not aware that there has been a big effort to really relook at how the monies are being allocated and utilized. I'm not saying that that's something that should happen but I think maybe one should at least begin to ask the question anyway.

DR. COLLINS: Well, certainly this is also

a moment where perhaps we can make an even more effective case about the aspects of administrative costs that are imposed on institutions that don't make a lot of sense and that have just sort of crept in to the way that business is done. Effort reporting comes quickly to mind as an area where a great deal of time and money get spent on an auditing process that nobody is really quite sure has any real value and yet it has become the norm and the IG looks at it. So maybe there's an opportunity to do something about that.

Human subjects, as you have probably seen there’s an advance notice of proposed rulemaking to essentially come up with a very different way of implementing the Common Rule that we believe could provide an opportunity for considerable less burden on administrative functions related to low risk research, which currently still goes through an awful lot of oversight steps and also would push very strongly for single IRBs in multisite trials instead of the current system which is terribly duplicative where many IRBs are looking at the same consent form, tinkering with the language, and wasting everybody's time.

So, yes, we are, I think, quite with you here that in addition to thinking about ways to reorganize the funding formulas, we also have to figure out ways to unload tasks that aren't really at the present time serving the purpose of promoting research and protecting the public.

CHAIRMAN AUGUSTINE: I feel very much like I have heard this discussion before. In the field I come from we lost 700,000 people out of a million-and-a-half in five years. And the initial discussions--they had a dinner. I have always referred to it as the last supper--

(Laughter.)

--where it became apparent that when the people left the dinner who could do something about this, the feeling was very much, boy, you've got a problem but not 'I've got problem.

And really your point about moving the snake farm--in my view of snakes I empathize with your point but I think the biggest lesson I learned out of that episode was don't cut the cat's tail off an inch at a time. If you've got to do some tough things get on with it, get it over with. I found that people can stand change. They just can't stand uncertainty. And not to practice psychology but

that was really the lesson I learned out of that.

Also, this has great implications for the earlier topic of how do we encourage people to go into this field. And we went through the same thing but if you don't encourage any young people to come in all of a sudden you have a very aging group of talent. All of which is to say it’s not easy but having solved that problem I think we need to move ahead.

(Laughter.)

All right.

The next speaker, of course, is the principle Deputy Director of NIH, a member of the SMRB alumni group--

(Laughter.)

--and you’re going to give us an update on the a--what’s properly known as SUAA committee.

(Laughter.)

OPTIMIZING SUBSTANCE USE, ABUSE, AND ADDICTION RESEARCH AT NIH

DR. TABAK: Right. Although I’m not going to use that term this morning.

(Slide.)

So thanks for the opportunity to give you a very succinct update on where we are with the

throes of having a single institute devoted to substance use, abuse, and addiction research.

(Slide.)

And so, as you know, this board made this recommendation to Dr. Collins, which was accepted, and I just would like to give you the update as to where things stand.

So beginning of the calendar year 2011, there were a number of internal discussions with NIH scientific staff amongst those ICs that could be potentially affected by the proposed changes, and then a task force developed some guiding principles informed by those initial discussions. And where we are now is we are in the midst of completing a very detailed portfolio analysis amongst all the potentially relevant Institutes and Centers looking at grants, cooperative agreements, contracts and as well as intramural research because, as you well know, there is a significant amount of research in this area in our intramural programs. And it is through this process that we hope to develop a final portfolio integration plan.

Simultaneously with this, hearing from many, many stakeholders, we decided to launch a scientific

strategic plan. And so just to be absolutely clear, this is not a reprise of should we have a new institute or not. That decision has been made. Rather this truly is designed to be a scientific strategic plan where the gaps and new opportunities that would emerge as a result of the creation of this new institute will be explored by both experts here at NIH as well as relevant stakeholders from around the country. And this group has begun to meet internally and is developing the plans for the stakeholder outreach and this should be available shortly where we begin to engage individuals either in focus groups or interactive town meetings and other vehicles and modalities to ensure that we get maximum input about the scientific opportunities.

Now, we're fast forwarding a year from now to the fall of 2012 where we will release both the portfolio integration plan and have a public comment period. And concomitant with that will be the release of the scientific strategic plan also soliciting public input. All this designed to enable us to provide final recommendations to Dr. Collins by the end of the calendar year 2012, which then in turn allows us to incorporate our plans to be included in the

President's FY2014 budget.

Now, whilst this is being developed we will begin implementing the portions of the scientific strategic plan that are not dependent on the formal reorganization. And in that regard I will tell you that almost by self-assembly the intramural programs of NIAAA and NIDA have really made outstanding progress towards this goal and, again, with no coercion but rather just simply understanding what the scientific opportunities would be by working more closely together. And so both the scientific directors of these two intramural programs together with Michael Gottesman, who is the deputy director for intramural programs at NIH, have been working beautifully and so they actually may be close to finished by the time we get to the more formal stages.

And then the expectation is that with the beginning of fiscal year 2014 we will have a new institute. This is a place holder. Please do not send me hate mail about this. You can send me hate mail about anything else you want but this is the proposed name: National Institute of Substance Use and Addiction Disorders. But this name is strictly a place holder and we will of

course entertain other suggestions from the community, from stakeholders and so forth.

So just to summarize bottom line, we have shifted the implementation by one year. In part, a reflection of the complexity of the portfolios across the Agency and, in part, a desire to ensure that sufficient public comment is made available from stakeholders particularly with regard to the science, the scientific opportunities. So it will not be a redo of the strategic plans that are extant but rather it's a look at the interfaces, the new opportunities and ways to go forward in creative ways.

(Slide.)

Now, I am not a visual person which may seem odd to you for a dentist but, for those of you who are visual, this Gantt chart describes everything that I just said in words and you have it in your handout.

So with that I'll stop and entertain any questions that you may have.

DISCUSSION

CHAIRMAN AUGUSTINE: Thanks, Larry.

Questions? Please?

DR. POWELL: Well, Larry, I'm just very

pleased especially that you're taking the time to do this right and especially with all of the challenges from the stakeholders that this group heard as this deliberation was taking.

And I think the idea of developing not just the integration plan but the scientific strategic
plan is a really good one. And so if it's worth doing, it's worth doing well and I think you've embarked on that.

So congratulations.

DR. TABAK: Well, thank you.

And I should say that it's only possible because of the very strong leadership that both Ken Warren and Nora Volkow and their many colleagues have been providing, as well as the other potentially affected Institutes.

I think internally this has been very much a community effort and I think that will be reflected by a very strong outreach gathering the relevant stakeholders from around the country.

CHAIRMAN AUGUSTINE: Deborah, thank you.

Other comments?

All right, hearing none, Larry, thank you.

We will proceed ahead.

The next item on the agenda is an opportunity for public comments. This is a relatively short period but we wanted to pick up a few comments that relate directly to the briefing you just heard. There will be another period later on for additional public comments.

As I said, we'd ask that speakers limit their time to five minutes out of respect for the other speakers.

The first speaker is Dr. Mark Goldman who represents the Research Society on Alcoholism.

We welcome you. If you'd like to use the podium that would be great.

PUBLIC COMMENTS

DR. GOLDMAN: Thank you. Thank you all for hearing me. You may remember I spoke about a year ago about this as well.

Actually Dr. Tabak's comments set the perfect stage for what I want to say in that he quite correctly identifies the kinds of interactions and discussions and things that have happened all across the field. As the president of RSA, I know I have been recently talking to my counterparts at some of the drug groups, CPDD and Nicotine and others, and these discussions have taken place.

But one thing that I want to put out for you all to consider is this: The original report from the SUAA never really defined what the scope of this problem is. We don't really know what it is that we're talking about and that's not a failure of the group. That's the nature of the field. The nature of the field is that we're not sure how far and wide this phenomenon of excessive behavior that doesn't--is not well controlled by people. We know that in the report we have things like tobacco, alcohol, drugs, some discussion of obesity, gambling, all these kinds of things that come together.

Based upon the discussions that we've already had in the field I think it would be of great moment, of great importance, the opportunity is there to actually not just get strategic feedback in these kind of--I don't mean to denigrate the process, but small bore kinds of ways, local groups, discussion--focus groups, that kind of thing. I think in this field the kick off to a new institute would be best served by a consensus conference putting together people from all these different fields to discuss what it is that, in fact, is the core of what we're talking about and set this new

enterprise off on a good course because otherwise this discussion, this uncertainty is going to actually become a problem for the institute, the new institute, itself as its trying to decide on allocations of resources, allocations of budgets, what are the scientific new opportunities and such.

You know, it comes down to very simple thing. In some ways as much as we do know, in some ways we don’t really know even what we're talking about. And I hope that this is something that this group will take into consideration.

Thank you.

CHAIRMAN AUGUSTINE: Thank you, Dr. Goldman. We appreciate your comments.

Next we'll hear from Dr. Johnson, University of Virginia School of Medicine.

DR. JOHNSON: Good morning and thank you for allowing me to speak. And I hope everybody is having a great morning.

I listened with great interest to the previous speakers and I want to echo some of the things that they have said but most importantly I want to probably focus on some of the details which a new institute should incorporate and some of the thoughts and ideas to make sure that the new

institute works as well as we would expect it to.

As we go through this process I was very happy to see that there was considerable deliberation on what the scientific portfolio would be but I would encourage that there also should be a similar deliberation in terms of a focused cost analysis in terms of how this will be proposed in budgetary terms and to be able to explicitly talk to the researchers and other stakeholders on how that would affect their grants or their budgets in terms of the future.

The second thing that I'd like to talk a little bit about is the portfolio structure itself. I think that, as Mark said, one of the problems with substance abuse and addictive disorders is that it can become all encompassing. And you can imagine a time in which almost every behavior possible could be described as addictive. And, therefore, there needs to be some focused thought as to what the structure of the different disease entities and addictive behaviors might well be. And a consensus approach would be the best way to look at that. Now, that might be to understand the epidemiological impact of some of these diseases and disorders and how those epidemiological translate into the budget

of the new institute.

So, for example, NIDA currently does have a--basically a structure for recognizing HIV research which is very important in terms of the consequence of drug abuse but you could also do the same thing looking at what the relative impacts of alcohol and tobacco and other drugs are to make sure that the emphasis of the institute does fit the national need.

There needs to be some consideration, I hope, given to the idea of trying to have a consensus amongst directors of various institutes to be able to contribute to this new enterprise and to be able to allow some merging of their portfolios to be able to get this to occur. And, in particular, the nicotine and tobacco portfolio is very important because it's so much as--a component of the comorbidity of alcohol and other disorders.

I think, finally, I think I would like to just talk a little bit about building consensus with not only the stakeholders who are researchers and scientists but also with industry. One of the concerns that obviously occurs with the merging or with the development of a new institute is how would we develop new drugs, new treatments and how that

would be applied in the real world. And it would make sense to also involve at some point deliberations with biotech or industry as appropriate to understand how the new institute can take opportunities that present itself and seek ways of collaborating.

I think, finally, there will need to be some consideration of how this Organization will be driven and led. And I think that Mark said it best that some kind of consensus conference to decide what type of people or person or groups of people should direct this organization at the start and how that should come to pass will be very important in it being able to gain credibility and consensus amongst everyone.

Thank you so very much.

CHAIRMAN AUGUSTINE: Dr. Johnson, thank you very much for sharing those views.

And our next speaker is Dr. Martin Woodle of the Institute for Translational Biomedical Science.

DR. WOODLE: Thank you very much for the opportunity to speak.

Just a very quick introduction to myself. I--After a post-doctoral studies I went to biotech

industry in California where I was part of the development of a pegylated liposome that is now a drug that is marketed by Johnson & Johnson as Doxil. And following that I have had experience in other small biotech companies as well as large pharma and spinoffs from Novartis to venture capital financed biotech. And I've started the Institute for Translational Biomedical Science recently as a means to try to help address some of this problem that you have clearly identified and recognize.

I'd like to thank Dr. Rubinstein for his comment about the key role of small biotech and their innovation and I would like to emphasize that. I think that my feedback for you to consider is finding ways to augment and utilize that small biotech resource which I sense is somewhat overlooked and not fully drawn into your attempts to address this problem of translational research.

I'd like to point out that translational activities are by their nature rather mundane and boring and there's very little that is considered innovative in that.

Even when bringing things together that have never been together, and thus are new, they are very often not considered innovative. And so that's

a real dilemma and challenge as we face this field of the NIH attitude and expectation of innovation as it applies to translational activities is really a challenge and a problem to be addressed.

So I just wanted to thank you for your efforts to address this problem and finding the ways. I think the institute is very attractive and has lots of aspects and I would like to encourage you to look for ways to utilize that early biotech resource which is not funded by venture capital because the timelines are too long and the risk levels are way too high.

So thank you for your time.

CHAIRMAN AUGUSTINE: Thank you for raising that point.

And as I understand it, there are no further public comments at this point and so we're just a couple of minutes ahead here.

I think what we should do is go ahead and take our break now if that's okay with everybody. And so let's see--we should meet back here about 10 after if everybody will do that. So we’re now on break.

Oh, I’m sorry. I forgot an important point. Let’s make that--our group here is supposed

to get a photograph taken and we'll be taking it over in that corner. We'll do it right now so that this is--if everybody--it's like herding cats. Steve, nothing personal here but if everybody would get over where Steve is right away.

So let's make it 11:20 the break will end then so we have time to get a picture.

(Whereupon, at 10:54 a.m., a break was taken.)

CHAIRMAN AUGUSTINE: Okay. If everybody is back; we will continue. Steve is going to give us an update on the recommendations on the Clinical Center.

Steve?

NIH CLINICAL CENTER: ORGANIZATIONAL AND BUDGETARY CHALLENGES

DR. KATZ: So, thank you. It's my pleasure to provide this update since the SMRB has made many recommendations with regard to the operations and governance of the Clinical Center.

(Slide.)

I would refer everyone who is not at the table--everyone at the table has this little pamphlet, the Scientific Management Review Board Report on the NIH Clinical Center. And I can tell

you that we spent, as a subcommittee, with Arthur's leadership, we spent a lot of time in making recommendations with regard to the Clinical Center governance. And the SMRB really established this SMRB to simplify the Clinical Center governance.

(Slide.)

And the responsibilities of those, as you can see on this slide, they complement those of the Advisory Board for Clinical Research, which is a board that advises John Gallin directly on the operations of the Clinical Center but this provide— this advisory--this Clinical Center Governing Board provides strategic and operational policy direction and oversight for the Clinical Center, also strategic and operational oversight over the changes to the mission of the Clinical Center, should there be any, and to implement those recommendations of the SMRB.

It also provides recommendations on the optimal size and scope of the Clinical Center and how best to maximize the quality of research conducted in the Clinical Center. It provides policy and operational recommendations on crosscutting scientific and administrative issues that affect both the NIH's Institutes and Centers and the

Clinical Center, and also provides recommendations on the Clinical Center's annual budget request after considering the recommendations of the ABCR and the overall NIH budgetary environment.

So this was — this was a group that was set in motion to really provide recommendations to the director of NIH taking into account not only the recommendations of the Advisory Board to the--for Clinical Research but also the NIH budgetary environment.

(Slide.)

The members of the CCGB are shown on this slide. There has been--we have had many meetings to discuss many of the issues dealing with budget first of all and, second of all, with what some of the next steps are.

(Slide.)

With regard to the budget issues and the funding source for fiscal year 2012 and 2013 the Clinical Center budgets will continue to be funded internally. The intent was to implement the SMRB proposal to fund the Clinical Center as a line item in the Office of the Director appropriation for fiscal year 2013. And you will recall we had many options. We had options one through five. There

was almost unanimous agreement that the option to put the budget of the Clinical Center in the Officer of the Director was overwhelmingly embraced.

But the implementation was more legally complex than anticipated and right after I talk perhaps we'll ask for some of those legal complexities to be brought forth by Barbara McGarey.

And the issues could not be resolved within the fiscal year 2013 budget. As many of you know, we're already dealing with the 2013 budget so that timeline has really passed.

(Slide.)

The Clinical Center Governing Board has reviewed the Clinical Center funding request based on the current patient census. We have provided recommendations to the director of NIH and actually at tomorrow's IC director’s meeting we're going to be discussing them and Francis will be making a decision very shortly.

The recommendations attempt to balance the need to provide quality research and patient care with the need to seek efficiencies given a difficult financial environment.

Concurrently we have initiated collaborative efforts with the Office of Intramural

Research to seek further budgetary efficiencies.

(Slide.)

Now, in addition to the budget issues we've also addressed other recommendations and other priorities that came from the discussions at the SMRB.

And one of these was to better utilize or to better have a chance to utilize the clinical research center for the extramural community. So consistent with the SMRB recommendation to enable use of the Clinical Center by extramural investigators we have developed a new bench to bedside program. There is one currently existing. It’s one that relies really almost on a tin cup from the various offices within the Officer of the Director. And this will consist--this new bench to bedside program will consist of cooperative agreements between intramural and extramural researchers utilizing the Clinical Center. The applications will be subject to peer review and will be funded by appropriate ICs. The other bench to bedside program was subject to peer review as well.

So we have developed a basic outline of the program and actually issued a request for information to further shape this RFA.

(Slide.)

The program outline is called the NIH Clinical Center Cooperative Program of Bench To Bedside Research Projects and will be published either late in 2012 or early 2013 for funding, hopefully, in 2013.

There will be some unique Requirements. And here you can feel some of our discussions that we have had at the SMRB. Extramural investigator must have an intramural collaborator; applications must be submitted by extramural PI; the project must use the Clinical Center resources; the project must be signed off by the Clinical Center, the IC scientific and clinical directors; and awards will be for three years at more dollars than the current bench to bedside program up to $500,000 per year in direct costs; and the IC director will determine the exact funding source, how much comes from intramural and how much comes from the extramural.

(Slide.)

We've also put out a request for information. John and Sally Rockey co-chair a committee that worked with the CCGB on this request for information. And it really is request for information on how the community views the

utilization of the Clinical Center. So it solicits input from extramural investigators on partnerships with NIH intramural investigators utilizing the Clinical Center. And what this RFI consists of are many of the potential uses and resources of the Clinical Center that can be utilized by the extramural community.

(Slide.)

Some of the other activities of the CCGB are to explore the total cost of the Clinical Center funding provided for ICs for services beyond those included in the Clinical Center budget to really have a sense of what it really costs to run the Clinical Center and also to begin formulating longer term efforts to assure protocols conducted at the Clinical Center are of the highest quality.

And going back to, I think, what Norm said, this is not something that we can just snip a bit of the tail off at a time. We really need to look at new ways for funding the clinical research center utilizing as background many of the recommendations that we heard from the SMRB.

So I'll stop here. Perhaps the best place to start would be with Barbara McGarey to just--if you would, in just a few minutes, discuss the

complexities, the legal complexities of implementing exactly what the SMRB recommended.

DISCUSSION

MS. McGAREY: Sure.

Thanks, Steve.

While the principle--it's really one overarching principle and it has to do with the first bullet on Steve's last slide, nine, related to exploring the total cost of the Clinical Center.

Recall that as the Clinical Center is managed now within the management fund costs can be supplemented by the ICs and there is not necessarily one total number. As we move to a line item in the OD appropriation you have to identify a total budgetary number for the Clinical Center that we propose in the budget and then, if Congress accepts it, it goes into the actual appropriation. Once that happens, that number cannot be supplemented. So, you know, by going into the OD appropriation we're really fundamentally changing the legal framework of how the appropriation works.

And I think at this time NIH was--we're just not there yet in terms of understanding what that number is and we didn't want to, you know, remove flexibility from the Institutes in fiscal

year ’13, you know, without understanding really what that number might be.

DR. KATZ: I should add that the directors tomorrow--the steering committee last week and the directors tomorrow will be discussing with Francis the implementation of some of the recommendations--of that recommendation from the SMRB but done in a little different way so that it doesn't involve the clinical center appropriation within the Office of Director.

Richard?

DR. HODES: Just a question for Barbara.

So we understand this prohibition against augmenting an appropriation.

On the other hand Institutes and Centers with their own appropriations certainly do find ways to collaborate by co-funding certain efforts.

Is that not the kind of flexibility that could be used to address this constraint?

MS. McGAREY: If those--if those co-funding--if those projects were deemed to be part of the Clinical Center--either the infrastructure or the research activities there--then you’d have to really look closely at that and make sure that you weren't--I mean it--to some extent it has to do with

how the appropriation is actually written and what that line item specifically says. So those projects could conceivably be included in that line item and then you would have a problem.

DR. CASSELL: Steve, could we hear more about what may discussed tomorrow as an alternative to the SMRB recommendations as far as the funding through the director's office?

DR. KATZ: So it is possible to do as was recommended by the SMRB to take a very small amount of the total NIH budget and put that into the management fund and gear that towards the clinical research center. That is it would end up being--if you look in the booklet actually I have a table that was--I think convinced the group that this could be done at very low cost but it would just be done physically in a different way. So it would be keeping with the idea that the clinical research center was going to be utilized and opened up to the extramural community and, as a consequence, there would be a very small amount of money in the--to the tune of .02 or less percent for the utilization of the Clinical Center by the extramural community.

DR. FAUCI: So functionally the effect

will be the same--

DRS. KATZ: Speak up, Tony.

DR. FAUCI: I think it’s on. But functionally the effect will be the same that the additional delta of--just to refresh--I don’t know. I think we need to refresh everybody's memory that we were talking about that if the Clinical Center might need as a delta increment in a given year, not the whole thing of the Clinical Center, the delta increment in a given year, an amount that's more than the percentage of the NIH increase. Let’s say the NIH is flat and they need two percent increase. That two percent we were discussing as a mechanism of how do you get that two percent taken out of the totality of the NIH budget versus the intramural program. One of the ways was to make it a separate item and then Francis could do that.

So what Steve is saying is that functionally you could do the same thing by taking a small amount of money out of the totality, putting it in the fund and then have that fund be--if necessary, utilized at two percent.

DR. KATZ: And that--that two percent that Tony is talking about is two percent of the Clinical Center budget so it’s not two percent of the total

NIH budget.

And for those of you who want to see the example it's in that booklet on page 18. That was the--that was the example that was used as to what--how little of that moneys would be utilized to keep the vitality and the functioning of the clinical research center.

CHAIRMAN AUGUSTINE: Arthur?

DR. RUBINSTEIN: So I saw the request for information and I was very pleased about that I must say and I showed--it came out, I think, a week ago or something like that. I showed it around to some of the key people at Penn and they were quite excited by it. So I think it was a really good step. We'll see, you know, what feedback you get but I was encouraged by the thought that this was a new and important initiative. So.

The other thing is--and this is probably a stupid comment. So you went through all the stuff with congress getting the NCATS approved and all that difficulty, one thing or another, can't you just persuade them to be a little more flexible about the Clinical Center instead of going through these hoops and putting some language that they will support?

Excuse me if that's stupid.

MS. McGAREY: No, no, no not at all.

The—right, so the fundamental--the fundamental principle is one of general appropriations law so even Congress can't get around the principle. But I see what you're saying, which is, you know, couldn't we come up with language that would say, you know--you certainly--usually it's up to a certain amount or not to exceed. You still have to come up with an amount.

DR. RUBINSTEIN: Yes, but if said that wouldn't go up a lot more than .023 of the NIH budget or whatever, I think you could do it, right?

MS. McGAREY: You'd still need to know what that--yes. So of course but you need to know what that benchmark amount is and I think NIH is not ready to say what that is because of the--you know, the prior funding has been really from all the Institutes and core funding, et cetera.

DR. PATTERSON: Norm had to step away for just a moment. So, Gail, I know you were asking to say.

DR. CASSELL: But I, actually was going to make the same stupid recommendation that Arthur made. It does seem to me to be reasonable given the

establishment of NCATS and how closely linked the Clinical Center is to translation, and I realize the hesitancy to put a number on it but maybe there could be some way to phrase it so that it would give you protection but also flexibility.

And, I guess the question I have for everybody is how much of a problem is this lack of flexibility that you had before in terms of an Institute being able to supplement in the event that there was an emergency need or something else.

What I worry is if there were a disease outbreak where you need to do studies in the Clinical Center and then you get locked in to this mechanism and you can't supplement the Clinical Center to do what needs to be done without compromising either already ongoing studies or ones that were already planned.

And I really haven't thought this through too carefully but it seems like you should be--one should be able to make it work.

MS. McGAREY: Yes.

DR. KATZ: So this presentation doesn’t necessarily preclude our doing this in the future at all, number one. And, number two, the specific example, Gail, that you give does still allow

Francis the flexibility of addressing that particular need in an urgency in addition to his director’s discretionary fund. He can move that kind of money if needed.

DR. FAUCI: But--and you don't even have to invoke the discretionary--the director’s discretionary fund in this, Gail, because the way the proposal is, is either put it as a line item in the OD, which you heard the reasons why that would be tough, versus allowing money to come from the broader NIH mechanism to go through the standard institute way that we feed money into the Clinical Center and then the Institutes can decide which of the mechanisms that they'll use to do that. That if there is an emergency they could just get more money in that group and in that arena without having a line item.

So it's really a question of a line item versus non-line item, not flexibility because, I think, as Steve alluded to, we still have that flexibility to do things more or less depending upon the situation.

DR. COLLINS: So I appreciate the suggestions from Gail and Arthur that one nice way to think about this is if you could really do it the

way you would like to and organize an effort to try to make that clearly documented in legislative terms or at least in appropriations language terms. That might be ideal.

I guess what we have learned in the NCATS experience is it takes a long lead time to be able to try to encourage those kinds of changes to happen and there's a lot of unpredictability of the outcome. And this is, I think, another reason why we're not trying to do something for FY13 but instead considering all of the options for 14. And your words are very helpful in that regard.

DR. KATZ: But implementing the recommendations of the SMRB in a very similar light earlier on for ‘13.

PUBLIC COMMENT

DR. PATTERSON: Any more comments from SMRB members?

Any questions from the audience?

Okay. We were scheduled on the agenda to have another public comment. We don't have anyone formally signed up for comments but I’d like to open the floor.

Is there anyone in the room who would like to approach the mike right now and make comments?

Anybody?

(No response.)

Larry, are you standing up to volunteer?

DR. TABAK: No.

DR. PATTERSON: No.

(Laughter.)

Okay. All right. Well, we are now going to take about a 45 minute break to get lunch.

There are boxed lunches available here in the room next door for board members and there's also a cafeteria on the first floor if you'd like to go there.

And we'll convene--reconvene at 1:30 and we'll be talking about a new tasking for the--I'm sorry. 1:30. That was wishful thinking. 1:30, 45 minutes.

(Simultaneous discussion.)

Oh, ok. Well, we need to check. Well, could people be back here say at 12:30? Okay. All right, 12:30. We're ahead of schedule. Okay. Good.

(Whereupon, at 11:45 a.m., a lunch break was taken.)

A F T E R N O O N S E S S I O N

CHAIRMAN AUGUSTINE: Ok, why don't we start out?

We're going to turn this afternoon to future tasks for the SMRB and there's one in particular that Francis is going to describe to us.

And I would just note as a way of background that we have put a pretty good load on the NIH at this point in time and, as you can see, they're working mightily in the face of great bureaucracy to bring about some of the suggestions that we've made.

At the same time, given the requirements on us to meet five times on every issue as a Board, in addition to all the times we meet as working groups, if we do have other things we'd like to address we probably need to get on with it or there will be a very long down time here, which assuming there are constructive things to be done would not be a good outcome.

So this afternoon we'll talk about the one proposal that Francis has and as a way of background Dr. Sally Rockey will be presenting information to us.

And as you probably know she's the Deputy Director in the Office of Extramural Research here at NIH.

And Francis, you're not scheduled to say anything at this point but do you want to say something in the way of setting the stage here?

DR. COLLINS: Let me just tee this up very briefly and then Sally has some real content to put in front of you that I think will be interesting and will inform the discussion about a possible charge for the SMRB.

Clearly at a time like this we have to be sure that every aspect of our portfolio is being efficiently allocated to produce the greatest possible scientific results.

The SBIR and STTR programs which Sally will describe to you are, in fact, congressionally mandated and occupy a certain percentage of our budget. And Sally will go through that. And we are proud of some of the accomplishments of those programs which particularly support research in small business but we're not convinced that they are absolutely optimized.

And at a time where again resources are tight and also where we're trying to do everything

we can to contribute to the encouragement of the economy and everybody agrees that small businesses are crucial for that, we thought it would be timely to take a look at the SBIR and STTR programs and assess what might be done to make them even more effective than they have been. And, hence, bringing this to you as a pretty authoritative and distinguished and experienced group to seek your advice about what we might be able to look at in terms of potential changes in the program that would make it even more effective.

So we gave a lot of thought to topics that the SMRB might be particularly well situated to address and came up with this one as certainly the top of my list at the present time for you all to consider today.

I thought in preparation for that it would be good for Sally to lay out some of the specifics of this program not down into the real details because that would take quite a long time, and if you decide to take this on as a task there will be time for that in those five meetings that you've already referred to. But I thought you needed to have a pretty good sense of the landscape and that's what she's prepared to put in front of you and then

we can have some discussion about this.

So thank you for your consideration of this as a potential charge and thanks to Sally and her team for organizing a presentation that I think you'll find to be pretty interesting.

OVERVIEW OF THE SMALL BUSINESS INNOVATION RESEARCH (SBIR) AND SMALL BUSINESS TECHNOLOGY TRANSFER (STTR) PROGRAMS AT NIH

DR. ROCKEY: Thank you very much for having me.

(Slide.)

I just wanted to mention to you starting off that I have my very capable SBIR team here with us today who will be able to answer with more detail some of the nuances of the program.

(Slide.)

The SBIR and STTR stand for Small Business Innovation Research Program and Small Business Technology Transfer Research Program.

(Slide.)

The purposes of the program and the congressional goals are to stimulate technological innovation, use small businesses in order to meet the federal research and development needs (so that's a very critical aspect

that we are targeting towards a sector of our economy), foster and encourage participation by minorities and disadvantaged persons in technology and innovation (and I will tell you that we have abilities in this program to target women and minority-owned businesses), and increase private sector commercialization. That's a critical aspect of the program, including when companies apply for the program they have to talk about the potential for commercialization in these programs.

(Slide.)

Now, the program has been around a long time. It’s been around since 1982 is when it was authorized through the Small Business Innovation Development Act in 1982 for the Small Business Program.

(Slide.)

The STTR program is--has many of the same attributes. In fact, it's about stimulating and fostering scientific technological innovation like the SBIR program. This is more a program that is targeted towards cooperative research, so research between small businesses and research institutions, primarily academic institutions. So that is a difference. And that program was authorized in 1992

so there was a ten year difference.

So this is--both these programs are long term programs that we've--that have been in place 30 or so years. And over the course of the years many things have been tweaked, many different types of SBIR programs have been developed and we'll talk a little bit about that.

(Slide.)

So how do we get funding for these programs?

First of all there is a set aside. So any organization or agency in the federal government who has over $100 million of extramural, that’s outside of the organization, R&D funds is required then to set aside 2.5 percent of these funds for the SBIR program. So every single agency, Department of Defense, DOE, USDA, NSF, et cetera, has a small business program.

That percentage has actually increased over the years. With some of the reauthorizations they actually went from an earlier amount, which I believe was 1.35 when it first started out to 2.5 over time. The Small Business or the STTR program is much smaller than that. It requires that if you have a billion dollars in extramural R&D that you

set aside .3 percent of your extramural dollars towards small businesses.

(Slide.)

So here is a brief history of our re-authorization. And you can see all this in yellow because what's happening now is that while we had reauthorization in ’88, 2000 and so forth and so on, we have been caught in a quagmire in the last--since 2009 of trying to reauthorize the program. There is some focuses about the program that there has been some discussions up on the hill and with the federal agencies of how best to reauthorize this program, including what should be the level of set aside, what should be the amount of venture capital that’s allowed in the program, et cetera, et cetera. So we have been on this reauthorization treadmill for--and dealing with only temporary extensions of our authorization since March 20th of 2009. Again we have another temporary extension right now on November 18th, 2011. But for the community this is a lot of uncertainty for the community when they don't see a real reauthorization conducted for the program.

(Slide.)

I was wondering--did I skip a slide?

I'm sorry.

Here is the participating agencies. You can see that HHS, which is primarily an NIH, is one of the large contributors of $682 million a year. DOD is $1.4 billion. Again remember it's based on your extramural funds and a portion of your extramural funds.

NIH is probably one of the most active federal agencies in regard to the small business program and, in fact, we oftentimes are asked to come to the table to talk about our policies and our directions for our programs as a driver for the SBIR program across the federal government.

(Slide.)

So here are our Institutes and Centers. All of our Institutes and Centers except the ones at the bottom – the Clinical Center, CIT, and CSR - who have funding authority, participate in the SBIR/STTR programs, except for Fogarty. The idea about the SBIR program is that it is a domestic program and that's why Fogarty does not participate.

(Slide.)

So there are some unique management implementations of the program. And this is

important to recognize because the SBA, the Small Business Administration, has quite a bit of oversight for the program across the federal government so it oversees and coordinates all the programs at the 11 agencies. And it also develops the policy directions based on legislation. So it sets ground rules for the program.

So, for example, we used to allow venture capital backed companies to participate in our program to a greater degree than we currently allow. That was, in part, by a policy analysis done by the SBA back in 2003 which then excluded certain types of venture backed companies to participate. So they can drive the implementation of the program at the— at the agencies.

We have a central office that is responsible for the--here in OER that is responsible for coordinating across the ICs and reporting and also producing our parent announcements or our funding opportunity announcements. Each IC has a lead program and usually grants management are points of contact because making SBIR grants because of the requirements of dealing with small businesses often requires difference types of expertise to issue those types of awards. And we also serve as

our sister agencies in HHS, CDC, FDA with review and other types of announcements for their SBIR programs.

(Slide.)

This is the current budget allocation for the SBIR across the ICs. So remember because the ICs receive appropriation they are then thus expected to spend a certain percentage of their funds. This just gives you an idea across the IC how much each of those ICs devote to the program.

(Slide.)

So how do we construct the phases of this program?

The first is a Phase 1 feasibility study. There is a budget guide of 150,000K and 100K for STTR of total Costs. They can have a six month period or a one year period for STTRs. And the average though for SBIR is--actually we exceed the guidance that's put out by the SBA. Our--generally our average award of a Phase 1 is 214K; for STTR it's 200K. So that’s the first part. So when they come in they compete for a Phase 1. It's a competitive process like all of our programs. They go through peer review and we award them.

Then they have what is called the Phase 2.

This is the first--the full research R&D portion of the program. They can have up to 750K for STTR and one million for SBIR over a two year period. But again we have exceeded the guidance on the awards. The average is $1.2 for SBIR and $1.2 for STTR. So that is the Phase 2. They come in and they now are conducting the research on the road to commercialization we hope of a product, a service, a technology, et cetera.

We have what’s called a fast track. We're one of the few agencies that has this where we combine the Phase 1 and Phase 2 application and review process. One of the things that's a difficulty for our businesses is that they are in our typical peer review process that can take a long time. The Phase 1/Phase 2 is for those that we feel quite assured that they're going to be--that we are assured that the feasibility of the project will lead to an appropriate Phase 2, therefore, we combine them. They do go through a competitive review. They have to be part of this and not all of our Institutes and Centers participate in this.

And then we also have a Phase 2b competing renewal. This is also unusual for our program because we often times fund very long term

technology development for some of these products or services that we allow them to come back and compete for a renewal of their program. Again not all the ICs participate. It varies in its size. It can be up to three years. And generally it's for the more clinical side of things when there's complex instrumentation or tools and they have to get through FDA and things like that, we will grant them a competing Phase 2.

(Slide.)

So what is--then there's the Phase 3, which is the commercialization stage. Now, the commercialization stage is really we give them some technical assistance in this phase but we at NIH do not fund this phase. You can, however, fund it. Some of the other agencies like DOD, who usually is the customer of these small businesses--in fact, DOD is buying much of the technology that their small business program is producing. They will invest with non-SBIR funds in Phase 3, the commercialization stage.

What is commercialization?

What's the definition?

Reaching the market. We base it on sales or license revenues, R&D investments and research

contracts and sales of equity, investment by a third party, sale/merging of a company, et cetera, et cetera. So it's a typical definition of commercialization.

(Slide.)

So this just gives you a history within HHS how much is spent in both the SBIR and the STTR programs. Most of our sister agencies do not have an STTR program because of the limitation of a billion dollars in order to have a STTR. And this gives you averages for Phase 1 and Phase 2.

(Slide.)

And I will mention that the guidelines are upped each March--were upped just this last March to increase the size of our awards. So we do usually try to implement the new guidelines whenever they come out from SBA.

(Slide.)

Now, what is the eligibility?

First of all, small business concern--you'll see me use this acronym in the slides--is they must be a small business. A small business is one that's organized for profit. So this is a for profit program. You cannot be a non-profit organization in order to be a recipient of the SBIR

program.

They must be small, of 500 or fewer employees, and that includes their affiliates. So this gets complicated when they have venture capital backing how the size of the venture capital company can, in fact, impact the size of their own organization.

Now, the interesting thing is that we've looked at the average size of the companies that we support and on average our companies that we support have ten employees. So you can imagine these are quite small companies.

The principal project director or principal investigator must have primary employment, 51 percent or greater, with the small business concern. So in other words you have to be--you cannot be a university scientist with most of your salary coming off the university and then be a PI on an SBIR grant. You have to be employed by that company.

And then 51 percent--and this is where we get into the venture capital question. At least 51 percent U.S. owned by individuals and independently operated or at least 51 percent owned and controlled by another one business concern that it itself is at least 51 percent owned and controlled by one or more

individuals. This is very complicated. So eligibility for SBIR when there's joint ownership of small businesses and other complications we often have to send this off to SBA to get an agreement of whether or not a company is eligible.

(Slide.)

Now, STTR is much—is similar except that it has to be a formal cooperative R&D effort. So at least a minimum of the effort has to be by the small business, at least 40 percent, and 30 percent by a U.S. research institution. So that's the minimal. So the research institution can have a higher percent under these circumstances. The U.S. research institution can be a college or university, other non-profit research organization or federal R&D center.

There is a requirement for some sort of intellectual property agreement between the small business concern and the research organization, and the PI is not required to be employed by the small business so they can be at the research organization but that PI must commit at least a minimum of 10 percent of their effort. So you can see now how this is very important that many of our small businesses, even in the SBIR program, have involvement with

universities but in this case you see all of them do--or with another research organization.

(Slide.)

So just to tell you again this is just the major differences. SBIR permits partnering and the primary employment must be the small business. STTR requires partnering and they can be employed by the research organization. But remember the small business is always the official awardee so the small business--even though you have a partnership in the STTR program, the small business still receives the award.

(Slide.)

So let's talk about success rates. This just shows you on the greenish line that the success rates of the SBIR program. Now this is SBIR/STTR combined. This is also Phase 1 and Phase 2 combined. And this we're comparing with the success rate of RO1s. And as you can see back in the early 2000s we had a success rate about the same and then the SBIR program started going up quite dramatically. The reason this happened is that the number of applications that we received in SBIR were going down quite dramatically at this time. And then you can see what's happened in 2010. We had

suddenly a big drop in the success rate of our SBIR program, and that is primarily due to the Recovery Act funding and I'll explain that in just a moment.

(Slide.)

So what happened with ARRA? When we received our 1 point or $10.2 billion in the stimulus package in 2009 there was as part of the legislation that authorized the stimulus package and set aside--and appropriated the funds for the stimulus package, we received an exemption from having to set aside a portion of our funds for SBIR/STTR. Small businesses, however, were not excluded from competing in our programs and actually they competed and did very well in our programs in the Recovery Act.

However, we felt that it was important to support the small businesses as economic growth so we developed two funding opportunity announcements for small businesses. One was a catalyst award where it was basically a Phase 1 award for those kind--those organizations that had yet participated in our program. So we were trying to get new entrants into the program to broaden the base of small businesses that we had to choose from. And the other was called the Bridge Span Program, which was

really this program to gap--to bridge the gap, the valley of death gap. We really wanted to--between innovative R&D and the commercial market. We encouraged third party investment, which we're not really technically allowed to do in the SBIR program but in this Bridge Span Program we did. And we don't have an evaluation of this program yet but it could serve as a model for going forward with some of the ways that we might want to use the SBIR funds. However, it's just now really into a second year and so as these projects go forward we'll be closely analyzing this.

(Slide.)

So this again just shows you the differences in our success rates in 2009 and 2010. There is some difference between STTR and SBIR. Traditionally, STTR had a smaller success rate or a lower success rate than SBIR. That sort of flipped in the post ARRA period. However, we saw--one of the reasons that we saw so many applications come in that reduced our success rate was because of the advent of these new programs. We went out and advertised them across the country to bring in small businesses and we had quite a few applicants who were either not successful in their program or

became more knowledgeable about NIH's SBIR program, and we saw those numbers come up dramatically in the number of applications we received in 2010. So that's our explanation.

We also had some of those Catalyst Awards those new entrants come back for their Phase 2s so that was another reason why we saw an increase.

(Slide.)

So how do we review these applications? As I said, we use our same standard review process. This shows you the due dates. When--if we receive an application a due date is April 5th. It usually goes to scientific review in July. It has council review in October and the award date at the earliest is December. So this is the typical six to nine month period that we use on our other awards.

One of the issues for the community is they’re small businesses often with lacking financial backing and if they don't get a small business it's a difficulty for them. So waiting this long time period, which we think is necessary in order to review them, often can be a financial difficulty for the institution--for those organizations. So one of the things that we always think about is whether or not there are things to do

with this review process in order to expedite these particular types of awards. That's why the fast track or that combination Phase 1 and 2 are very important because if you can imagine a person--a small business that gets a Phase 1 traditionally and comes back in for a Phase 2 has to go through that review process yet again. So that fast track, which is a combination, a combo, allows you to just go through that review process once.

(Slide.)

So here is really again our gap funding. We do have Phase 2 competing renewals but I want to talk to you about a couple of other ways that we provide technical assistance for our grantees in order to help them with commercialization; try to bridge this gap and get to commercialization more quickly.

(Slide.)

So first of all we have a technical assistance program within the SBIR program. This is authority to conduct discretionary technical assistance. We--what we do is pool about $5,000 per award centrally into central NIH. We have a program both for Phase 1 recipients and Phase 2. And it’s really trying to help those organizations, those

small businesses, make better technical decisions and solve technical problems that arise during their project. So what is it about their markets, their potential for commercialization that might be hindering them? So we want to give them some assistance on this.

(Slide.)

So our first program is the Niche Assessment Program. We can fund up to 100 Phase 1s per year. We have a vendor who helps with this. What this person does is if you're one of these hundred recipients the vendor goes away and does a market analysis for the company that has received this assistance. And they identify alternative uses for the technologies, where those companies might have a competitive advantage, and a market entry strategy. Remember this is in Phase 1. This is very early in the process. And we really think that helping them at that point identify the markets upfront sets them on the right stage as they go forward into the R&D development or in the R&D research and development phases.

The second program is for our Phase 2 recipients. We fund about 40 or 80 of these companies a year. This is a very hands-on technical

assistance program. What we do is we have again a vendor who actually works and has meetings with the SBIR Phase 2 recipient to set up a business strategy and planning process to help build their alliances to find investors to help market their product. So right here we are helping them at the beginning or during their Phase 2 to go on to that commercial stage.

(Slide.)

We have also what's called PODs. I like these acronyms that we can say. PODs is a web-based tool to track SBIR/STTR outcomes by award and company. Currently this program is only accessible to NIH staff but we are hoping that we will expand this so that it will be available to the public. The people that receive the commercialization assistance outcome data are tracked and there's a company based module that's going to go online to allow companies to update their commercialization data regularly.

You're going to see in a moment that a couple of studies we've had have tried to determine what is the rate of commercialization for our small business programs. And we have some differences in outcome of this. So we think that by

tracking commercialization in a centralized database we'll have a better way to do the analysis and to see how successful our programs are.

(Slide.)

We also have a Pipeline to Partnership Program, which is a web showcase of SBIR/STTR and NIH licensed technologies. This is really like a match making service where we have our recipients and potential strategic partners and investors come online and take a look at each other. It searches by application category so if you are working on diagnostics, if you're working on tools, therapeutics, et cetera, you can do your matches through there. And you can also search by disease and see what kind of technologies are out there. And it's used by both our small business concerns and by outside parties. So we are seeing that this is a fun and important match making program.

(Slide.)

Now, let's talk about the--some unique features of our program. First of all, we have the ability to since we implemented fast track to try to accelerate how quickly we award grants. We are 95 percent grants. We also use contracts so that flexibility to use either a grant or contract

mechanism is good. For example, Department of Defense uses almost entirely contracts. Some might debate this mix and that's something you can certainly look at. We have a distributed and centralized approach to the program where we have the—my office which does the centralized policy development but really allow the institutions, each IC here, to develop a program in a way they see fit. And so we have a very team approach to the SBIR program.

(Slide.)

There are some special programs within the SBIR program. I just want to point out a couple of them.

About 30 percent of all of our awards--most of them are company-initiated. In other words we have a parent funding announcement, the companies with their grand ideas come in, like our other programs they are sent to the appropriate study sections,
they are reviewed and then the Institutes and Centers decide whether or not to fund them. However, about 30 percent of all of our awards result from funding opportunity announcements that are targeted. We're asking for specific types of

technologies or services that we want developed and we solicit those and the companies come in and response. The NCI actually uses more--25 percent of their funds towards contracts. They also have a Regulatory Assistance Program which really helps the small businesses get through the FDA process. And they also have a Phase 2 Bridge Program which helps those Phase 2s do the longer term approach. They also have an investor forum where they bring in investors to take a look at their small business awardees to help them to find investors and venture capital for their programs.

(Slide.)

We also have just embarked on the SBIR Technology Transfer Program. This is where small businesses that we have supported are working with our intramural program. We have some contracts on specific topics where we want this relationship to develop. And we are--in our Office of Tech Transfer we are developing a new exclusive license agreements for startup companies. So to really help these startup companies collaborate with us here at NIH. So if you want to look at that you can go and look at that particular website there.

(Slide.)

So, we have been evaluated quite extensively and we went through a national survey to evaluate the SBIR program that we did back in 2002 and then again in 2008. We did find that we were meeting our congressional goals for the program and 75 percent of the 2008 study cohort commercialization has at least been initiated and that the companies grew under the program. So the number of permanent hires in the community was going up.

We've had multiple GAO reports on the SBIR program. The National Academy did a whole federal SBIR study in 2008 and one in 2009. They did one specifically to NIH.

(Slide.)

Now when it comes to commercialization we've had a bit of--we generally say that we--about 40 to 50 percent of our companies, based on these studies that have gone on, actually commercialized products.

(Slide.)

So in this case when the NRC did the study on NIH's program, as I said, 40 percent reached commercialization. They thought there was effective mission alignment with the NIH and SBIR. They

thought that the SBIR awards had positive effects on healthcare. The companies grew and retained two FTEs per project. That doesn't sound like much but when you consider that most of our companies are about ten people, two FTEs is 20 percent so that’s pretty big. And we maintain the distributed management structure and program flexibility which they found was good.

(Slide.)

Now, let me give you a couple of examples--I’m almost done here--of some of our successes. I won't go through all of these but the Biopsy Sciences did a water containing ultrasound visible marker in breast cancer imaging.

DeltaNu had small Raman spectroscopic instrumentation for medical devices. They’ve had $11 million in sales.

(Slide.)

You probably know IntraLase, which has done laser in corneal surgery on the market.

Martek Global Services is the Omega 3fatty acids that you find in infant formula. That company was recently acquired for $1.5 billion.

And the Sonicare Toothbrush was developed through our program. They have $1.5 billion in

sales and over 500 jobs created from this program.

So and there's many more. I would love for you when you embark on this study to go on to the website and see. On our website we have all of our awards. There is some really fascinating work that is going on.

(Slide.)

So what are some of the challenges for our program? Well, the attributes--I'm going to talk both sides of some of these attributes. First of all our pros are that our grants and contracts, we have multiple funding announcements so we do it throughout the year and multiple due dates and budget times and fast track and Phase 2. So we do all these flexibilities. And--but we don't have much--we don't have anything in the way of administrative funds to support this program. In other words, we cannot set aside a piece of this SBIR program to manage this centrally. Also, it gives flexibility to the ICs to manage the program in the ways they see fit and align the programs with their mission. So one might—one of the things you might want to look is how well that's being done in the ICs.

The application and review—it follows our

standard procedures. They are getting very rigorous review. However, that is a six to nine month process. Is that too long for small businesses? SBA has pushed us to shorten this--so because we put it into our very time tested process we have-—it's been difficult for us to shorten this. We do have SBA oversight, which really helps us because we can have joint agency funding opportunity announcements. We do this often. We just did our robotics with the National Science Foundation for small businesses. We can also implement best practices and learn from each other. So having SBA oversight is good. However, it's oftentimes difficult. We have to educate the SBA about our program. Sometimes they don't agree with us in the flexibility that we want to implement and sometimes there's delays when there's new policies arise and we have to implement those new policies. And then, of course, the reauthorization. It is great that we're under an authorization. I it gives us stability but the problem is if we don't have the reauthorization then there's instability. So it's a pro and a con.

(Slide.)

So here's some things to think about. You can think about our processes for SBIR program to

implementation and management. I think there's always ways to tweak programs to make them most effective and there's certainly things to think about. But we also want to think about what our role should be because right now our role pretty much is at Phase 1 and Phase 2 but in this entire continuum are there ways that NIH could engage in other aspects of the continuum, bridging the gap, the commercialization aspects, et cetera. Is there ways we want to do that?

And then, also, in what ways are we using SBIR to meet our mission? When you think about the stand up of NCATS it might be an ideal opportunity to bring small business in the private sector through the small business community into the program. Now, I will tell you BIO is very, very engaged in the small business program because many of the bio companies are small businesses. So they are very interested in the small business program and oftentimes will engage us and support the small business program up on the hill and other places. So when NCATS stands up, and as well as how the other ICs use the small business program, it is something that you might want to weigh in on.

(Slide.)

I'll just say there's much more information and let me just introduce Matt Portnoy, who is our director of SBIR here. This is Lenka Fedorkova, who is our assistant here, a program analyst. And this is Sherry Mills who oversees the Office of Extramural Programs, which is one of my divisions under which the SBIR program resides.

(Slide.)

Okay. And I just wanted to--that's just an appendices of the contracts. This just shows you the diversity of the contracts under SBIR. These are all the NCI contracts and the kinds of areas, the topics that the NCI solicited under the SBIR program. So you can see how very targeted these are.

Thank you very much.

I'll answer or our team will answer any questions you might have.

CHAIRMAN AUGUSTINE: Alright, thank you very much.

I saw a couple of hands up. I saw Gail and then I saw Steve and Sol.

DR. CASSELL: Sally, that was a very good presentation.

I was a member of the 2009 NAS committee

in terms of the SBIR program and I think it's safe to say that the report was a congressionally requested report but they were very pleased with it.

And I think it did help in terms of reauthorization and everything.

As you know or may know, in fact they've now requested yet another review and the Department of Defense, NASA, and NSF have all signed up for that but NIH hasn't to my knowledge.

And I wonder why because it seems to me--I understand, you've you know really undergone your own review and that's one thing but since this is an independent review and it is a congressionally mandated review I'm wondering wouldn't it maybe be a reasonable thing to be a part of that review.

DR. ROCKEY: So, yes, and we've been approached a number of times. As you said, the last review was 2009. What we and--what we were waiting for was one of the things that's going to happen is with the reauthorization there's quite a bit of change in the program with the reauthorization. And we thought that the 2009 study would serve as a baseline for any changes that we might implement and we felt that it was actually more timely should the group come forward and assess us after the

reauthorization and after we have implemented the programs to see what the impact of that reauthorization was. And that's the main reason why at this point we just thought it was a timing issue. Now, of course we thought the reauthorization might happen back in 2009 but it still has not happened so things have been delayed. But we did feel it was important to get that reauthorization in there because there's a lot of changes that are in the reauthorization that we are going to have to implement immediately.

CHAIRMAN AUGUSTINE: Steve?

DR. KATZ: So my question related to exactly that--that point. That 2009 report was specifically geared toward NIH. It came out a very positive--a very positive report. So what more do we need? In other words, how often do we need such a report?

DR. ROCKEY: Right. I mean that was part of the reason but I do think it's critical as we implement the reauthorization that we that a look at the impact of this reauthorization and whatever flexibility different agencies are going to do to implement the new pieces of legislation.

So I would think that we would be willing

to engage once the reauthorization goes forward and then put it on a time scale where we can have some--see what the impact of those changes are.

CHAIRMAN AUGUSTINE: So Sol and then Bill.

DR. SNYDER: Of the--Amy had indicated and Francis indicated also that one concern was try to increase the excellence of the grant applications. So I was wondering about a couple of ideas. So one was that from what you described it sounds like the Small Business Administration is behind this rule that venture funded companies can't apply but since the great majority of small biotech companies are venture funded, including a lot of good ones, if that rule just vanished then you'd of course have more people applying and that would be better.

The other question about increasing the excellence is that biotech--the major funders of the biotech nowadays are not interested in what biotech originally was, which was to take the most avant-garde discoveries at universities and then try and create commercialized things. Nowadays the timeline--the horizon of imagination is very tiny. And so biotechs aren't doing what they're supposed to be doing. They're just doing little gimmicks because nobody will give you money unless you're in

Phase 2.

You start a brand new company with $50,000 and you're supposed to already be in Phase 2. Anyhow, but one thing that’s trying to change all that is a lot of universities are having drug discovery units which are doing what the original biotech companies used to be doing and then interacting with companies.

I gather SBIR takes care of some of those kinds of things. And that, of course, will fit also with the NCATS approach. And I wonder whether you considered any of these things in terms of enhancing excellence.

DR. ROCKEY: Right, I think you're exactly right.

For the second point, I think that's one of the things that you all as a group can take a look at to see how the structure of the whole sector has changed and how that might be impacting any policies or processes that we put in place now--we have in place or are going to put in place.

For the venture capital piece of it I do want to point out that you can still have venture capital but it’s--backing but it's complicated and you can't have as much and in the same structure as

you had had prior to 2003. Both the House and the Senate give some relief to venture capital. The reauthorization in both the House and the Senate give some relief to venture capital and--so that we could have more companies with venture capital backing participate in our program. And for NIH I think that's particularly important.

I also think that's important because as economy has changed venture capitalists are—some of the venture capital money has dried up as well and they are really going for those really highly innovative projects that they think could lead to potential profit and they're backing them and I think those are good ones for us to back as well because they've been something that has generated interest across the sector.

So it's a little odd that we would say that a company that has venture backing is one that we don't want to bet on either. You know, it seems like the opposite would be true.

However, I want to remind people that even when there's venture capital backing, in general, those are the projects that are further down the line. The company, one of the problems with the venture capital issue is that the company becomes

ineligible. Even though they're coming back for Phase 1s on projects and ideas that have not themselves had venture capital backing so because it's in that very early initial stage. So it seems a little odd to exclude a company that has venture capital backing for projects farther down on the pipeline and then exclude the company from being able to come back in and have extraordinary creative initial stage ideas.

But I think both of your points are very important and I think that's something that the group can take a look at. And we do, too, and we're looking at the structure, too, as things change over time.

CHAIRMAN AUGUSTINE: Bill?

DR. BRODY: Yes. In fact, I'm going to start a biotech company. I'm going to call it Groupon Biotech. That's really the only way to get funding these days.

(Laughter.)

But one of the problems--and I agree with Sol that it's great to have venture capital be able to invest and you outlined exactly the problem. You put the seed money in and then you can't get Phase 1. So the counter argument, of course, is, well,

why should the government pay to make the venture capitalists rich.

But one question I have, which would obviate that problem, was could--let’s say you fund Phase 1 at--I forget which phase, the beginning phase is Phase 1, and then you come back for Phase 2, and now you have got three venture capital firms. Could we put our money in and get the government's money in and get equity?

DR. ROCKEY: Well, there are some—I mean, in general, because of the way that we support these, like everything under Bayh-Dole, there is a--all the rights that associate with Bayh-Dole also associate to the grantee.

DR. BRODY: But I mean equity for the--for the dollars we put in.

DR. ROCKEY: I mean there's things you could think about and we don’t do it now but there are--

DR. BRODY: Because--because I know one university-- universities have struggled in the past with, you know, should their endowment invest in faculty started companies. And one university that’s doing this, I think, fairly successfully, says, okay, we’ll only do this--the problem is how

do you vet the idea?

DR. ROCKEY: Right.

Dr. BRODY: We'll only do it if we have a named venture capital in the lead in--

DR. ROCKEY: Right.

DR. BRODY: So this is--this would be

DR. ROCKEY: I don't think currently under our current authorization we'd be able to do that or our legislation we'd be able to do that or even under our current IP or our current investment policies or our regulations. But nonetheless, you know, there's something to think about.

I mean, I think one of the great joys about what this committee can do is sort of start with a clean slate and think about things that.

Now remember that we do have to--this is an authorized program and the program is very specific in its authorization about many things. So it's driven--

DR. BRODY: You mean specific to NIH.

DR. ROCKEY: The whole authorization.

So it's a very, very detailed authorization that in part drives and then, of course, we have the SBA piece of that over top.

So whenever we want to make changes they

also—they have to fit legally under the authorization and then also under the SBA policy. So that is a complication of the program but nonetheless we've been very aggressive in pursuing some of the flexibility that we have today. And usually we have made a cogent argument that's won the day when we go to the SBA.

So as long as you have, you know, the justification behind it and the facts behind you, you usually can make the argument.

CHAIRMAN AUGUSTINE: Others? Alright. Please? Susan?

DR. SHURIN: There's another aspect, which is this is the sort of going out aspect. At the NHLBI we've been concerned about the quality of what we're supporting for quite some time. And so we have an internal process that has been going on for about the last year-and-a-half now to really identify the things that we want to see develop. And so we're putting out an increasing number of RFAs and RFPs to address the gaps that we see at our end. And so it's designed to do two things.

One is it says this is a high priority and so it actually--I don't say it gets around this but

I think it’s a motivator plus if it’s something that we really want we’ll invest more heavily in it. It implies a higher level of commitment on our part to see things all the way through to the end. And we think that it--we're beginning to see some real signs in some of the conversations that we have that this is impacting the way that the small businesses are thinking about these applications.

DR. ROCKEY: So that is a, that I think, is a really critical issue. As I have pointed out, NCI--and if we put NHLBI you’d probably see similar type things. To the degree the Institutes and Centers use it as a targeted program versus a company initiated idea. I mean, I don't think you want to ever lose the idea that these companies with their grand--their really spectacular ideas come forth and find a place. But, you know, one might--might ask the question of what’s the proper mix of targeted type research versus that that’s initiated by the company. And again we struggle with that obviously in our--just our base programs at each and every Institute and Center. So that's something, you know, for the SBIR program to think about as well.

DR. SHURIN: One other comment on that,

which is it sort of plays into the fact that we're also sort of simultaneously building a global health program. This enables us to make investments in U.S. companies, which then potentially will have a very wide—a very broad worldwide market.

DR. ROCKEY: Right

DR. SHURIN: So that this has again significant potential impact--

DR. ROCKEY: Well, I--

DR. SHURIN: --again much more broadly.

DR. ROCKEY: Yes, and they can have global markets certainly in the actual--in the commercialization phase and their market can span across borders. But there are rules about whether or not research can happen internationally in the SBIR program because it really is targeted towards domestic organizations. But nonetheless there are some ways that you can have foreign research actually done under the program.

CHAIRMAN. AUGUSTINE: Alright. If no one else had anything else?

As the day has gone on, Francis, I have been thinking several times there's an organization called IN-Q-TEL here that's funded by the government; supports the intelligence community. And

I thought a number of times they're doing some things that might just relate to what you're doing. And Bill really brought it to mind that they award--they deal with small startups and they can award contracts and grants. They can also take equity positions. And one of the first companies they took an equity position with was a little startup that's now known as Google. And--unfortunately, they also took positions with a dozen companies you've never heard of.

(Laughter.)

But, you know, in that world you go for a batting average. You don't expect to hit on all of them.

But anyway they do take equity positions and--because a lot of these little outfits would rather have equity than--

DR. ROCKEY: Yes. I wanted to point out there was a program last year, too, called QTDP, which is the Qualifying Therapeutic Development Program, which the IRS ran. They got a billion dollars through healthcare reform. And what this was for--it was almost like a--it was a grant or a tax credit to small businesses that had actually participated in therapeutic research. And we funded

a lot of them. It was a billion dollars and they were able to receive I think it was 200--

(Simultaneous discussion.)

DR. COLLINS: We reviewed them but we didn't have to pay for them.

DR. ROCKEY: We reviewed them. Yes, the IRS paid for them but it was an interesting--we reviewed them but it was an interesting way to reward those companies that were in the therapeutic arena and they--many of our small businesses that we support through the Small Business Program are also recipients of those awards.

CHAIRMAN AUGUSTINE: I'd encourage you to make a contact with IN-Q-TEL. I could help you if you want. Not just on this issue but just in general. They've got some ideas that might be useful and.

DR. FAUCI: [not at microphone] It relates to what Norman was saying. The IN-Q-TEL model has been incorporated into the medical countermeasure approach of the BARDA, the Biomedical Advance Research and Development Association at the Department. So the IN-Q-TEL model is already being embraced at HHS level. So it would be easier than you think. We could actually connect with downtown

and find out what's going on there.

CHAIRMAN AUGUSTINE: Great. Terrific.

I have one other question. You mentioned six to nine months processing time. Why does that take so long?

DR. ROCKEY: Well, that’s our typical--in fact, six months is short in our process. Part of it is driven by when our councils meet because everything takes--is necessary for second level review.

So you have to have--first of all, you have to give enough time for the community to respond and then enough time for the review and then to get it to council. And oftentimes--as I can maybe find that slide or maybe not--that takes six to nine months. So because we use our study section system to support or to review the small business program that's the time it takes for our--and on average sometimes we get it out in six months which is shorter than our standard programs. So, but, yes, it is an issue. The length of time is an issue.

CHAIRMAN AUGUSTINE: Now, for little companies like that that’s pretty tough. Also--to be probably less polite than I should be--in this day and age of communications it would seem that the

councils ought to be able to find a way to meet on some of these things other than everybody flying to Washington.

DR. ROCKEY: Well, they actually--as we know, we do have some electronic agreement on reviews. They can do it outside of the actual meetings. But, yes, that is an issue. However, I will say that having three deadlines a year--companies are coming in and timing things so that they sometimes put in three grants--three applications so, you know, they're getting one thing after another funded and there really isn't gaps in their timeframe. But, yes, particularly for new start ups that are trying--buying out.

CHAIRMAN AUGUSTINE: That's a killer.

DR. ROCKEY: Yes.

CHAIRMAN AUGUSTINE: Anybody else want to ask any questions?

I guess that does it.

Thank you very much.

DR. ROCKEY: Great. And will it be--we're on hand to help you in whatever way you need as you embark on this and we'll certainly be--provide you data, provide you information, whatever you need.

CHAIRMAN AUGUSTINE: Thank you. We

appreciate it.

Francis, I think that it’s your turn.

CHARGE TO THE SMRB

DR. COLLINS: Well, I appreciate Sally's very articulate summary of the program.

And as you can see it has a number of remarkable successes--you only heard about a few of them but I think we also feel at NIH that there may be ways the to make this program even more effective, and that's why we bring it to your attention.

After all, there have been seismic changes in the community in terms of biotechnology and small businesses and their need to keep going. And even a study that was done three years ago may now seem a little out of date considering how things have changed as far as access to venture capital and all the things that were just mentioned in terms of the very limited patience that venture capital has for anything that has longer than a two or three year horizon to become profitable.

And so all the more reason why we think our SBIR and STTR programs ought to be really fine tuned to try to capture the very best and most promising science.

And I think this is also something that we could do in terms of looking at this with great scrutiny that would be very well received by people who are concerned about the economy. After all, Kaufman Foundation recently points out if you want to see where are jobs actually being created, it's in small businesses. And if we're trying to create jobs we should be doing everything we can to nurture that sector and perhaps there are ways to make this program even more effective in that regard.

It is interesting because I've been here for 18 years, and we have sat around the table amongst Institute directors on occasion to talk about SBIRs, and the attitude of the different Institutes about this program is really quite diverse.

There are some Institutes that see this as an incredible opportunity. I'm sorry Rod Pettigrew didn't make it here today because apparently he has a significant back injury and is somewhere lying on the floor but if he were here he would tell you how from his perspective in the National Institute of Bioimaging and Bioengineering the SBIR program is an incredible asset because a lot of what they're doing when

it comes to imaging and devices fits very nicely with the small business interests.

You've seen the way that the NCI has tapped into this in a very intentional way. And Susan has talked about doing similar things with NHLBI. And NHGRI, I think, has seen the SBIR program because of things like DNA sequencing technology and other approaches as a real asset.

But there are some Institutes who are like what is this and how does it fit with our mission?

And part of our problem is that at the moment the way that this congressional mandate applies it applies to each of the Institutes. So each Institute has to come up with two-and-a-half percent of their appropriation to spend on this. And some would like to spend more and some would, frankly, like not to spend any. And a--so some horse trading goes on but I'm not sure it's the most efficient way to do things. And maybe that's one of the things I would be interested in a thoughtful group looking at.

Again, you heard already that lots of groups have looked at the program overall across the whole government. And yet I think what we might more be more interested in now is a specific look at

what NIH could do, what levers we have to pull. We can't ask you all to come up with the ways to change the
Congress and their authorization plans. We'll have to see what comes out of their deliberations.

But we can ask you all to look at the flexibilities that we have and advise us about what we might do to focus this program more effectively on the most promising proposals and to be sure that we're actually hearing about them because I think again there may be ideas we never receive because a small business doesn't see us as friendly or the bureaucracy is intimidating or that six to nine month timetable just seems too long for a company that is thinking about its burn rate every day and can't really see how they can wait that long to get an answer.

(Slide.)

So I guess all of those things lead to our request that SMRB would take this on as a group; that you would consider as you see on the screen here this charge that the SMRB recommend strategies for how NIH can optimize its utilization of these programs in keeping with the NIH mission.

So how do we optimize what we've got?

And in regard to how to do that, considering how you could--we could better foster innovation within small businesses that's in alignment with the priorities of the ICs, attract quality proposals yielding the greatest potential for successful commercialization--that is the intent of the program--and leverage resources and expertise to maximize support for ensuring the success of its grantees. What can do to encourage grantees, many of whom are unfamiliar with NIH, to come to us and then to be encouraged to succeed.

This would be, therefore, a different kind of request than what the NRC has taken on, much more focused on our business. But one that I think is quite timely and again considering all of the ways in which we might utilize the considerable expertise of this group this seems to me as a topic that’s ripe for this sort of investigation and could actually do quite a lot of good at a time where we're looking how to be sure we're spending every dollar as wisely as we can.

So I guess that's the charge and I’m hoping that we might, before we all disappear here, even agree about some sort of a subgroup that could take this on and some sort of structure about how to

accumulate the information you might want to have. And we can help with that. And Sally's team is ready and willing to give you all the information you might need to proceed down this path of getting some recommendations in front of us after about five meetings since that is a requirement which we can't get around.

So there we are.

DISCUSSION

CHAIRMAN AUGUSTINE: Thank you, Francis.

And in anticipating the group might want to go ahead with this, we've asked Sol if he would be willing to take on the chair of this group.

DR. COLLINS: A brilliant suggestion.

(Laughter.)

CHAIRMAN AUGUSTINE: He has kindly agreed to do so.

Sol, do you want to make any comments at this point?

DR. SNYDER: Nothing of profundity. I've had just a few hours notice about this great opportunity. And--but I think that some of the items that we have just been discussing indicate that there's ways that this could be done better and use it as a tool to foster the kinds of technology

transfer of the most basic important advances in universities to the marketplace, which is what the whole biotechnology enterprise was supposed to have been done back in the mid-1970's and it has sort of deteriorated. And we could use it as a vehicle to try and reinvigorate what--what we really want to accomplish.

DR. COLLINS: And we would encourage you to be bold about that and suggest things that we could do that might be a bit outside of our ordinary way of doing business. We want to be as innovative as possible here in terms of encouraging these programs.

CHAIRMAN AUGUSTINE: Does anyone else want to comment?

Does anybody have a problem with taking this on as a task? Ok. Good.

DR. CASSELL: We might--I think--I think we--it's a great idea.

And as I--I had no idea this is what you were going to recommend.

DR. COLLINS: Surprise.

DR. CASSELL: You heard my question earlier today so it's perfect timing.

(Laughter.)

CHAIRMAN AUGUSTINE: Okay. Well.

DR. CASSELL: I do think it will be important to pay attention to the NRC committee because Congress pays attention and they're already knocking on our door.

DR. COLLINS: Yes.

DR. CASSELL: So I think it will be important to stay in touch with that committee at a minimum.

CHAIRMAN AUGUSTINE: For sure.

Let's proceed ahead then.

And Sol, thank you.

In terms of populating the committee, a few of us have been giving some thought to people who would have a background that might make them particularly a good candidate to help here. But before we roll out that list maybe we should ask anyone in the group who does have a particular interest in this area if you would communicate that to Amy or to myself rather quickly. That would be terrific. And then the next week or so we will put together a group of volunteers to fill out the committee as required.

And, Sol, we'll obviously get with you to work on that so that you—you're--we've got a

balanced group.

Gail?

DR. CASSELL: Norm, will there be members outside of this committee that will serve on that working group or just members on this committee?

CHAIRMAN AUGUSTINE: We haven't addressed that.

Amy, what's the rule?

DR. PATTERSON: Well that, we do

DR. COLLINS: You're not on. Maybe somebody else will [not at microphone].

DR. PATTERSON: Somebody else has to go off.

DR. COLLINS: Ok. There you go.

CHAIRMAN AUGUSTINE: [not at microphone].

DR. PATTERSON: Ok. Yes, we have some flexibility in that regard and what we've done on some of the other groups has been brought in ad hoc members or consultants. I think the important thing is we get the expertise that you all feel is important to have at the table.

CHAIRMAN AUGUSTINE: So I should pre-- should probably broaden my request. If you know of other people you think would be good candidates, if you would let us know that, that would be a--that

would be very helpful. And then Francis and Sol and Amy and I will get together to try to put together a group that hopefully everyone will agree upon.

Let's see, the a--in terms of future projects it seems likely, at least to me, that there are other topics that we may want to tackle, particularly in a period of time when we're likely to see some major budget challenges. As Francis said, as somebody said, a crisis is a terrible thing to waste. And so we want to thinking about what else would be opportune to tackle this point in time.

I know, Bill, you have made a proposal and there are a couple of other proposals on the table.

And if there are other people that have thoughts in the public or in the Institutes or--and Centers or from our group as topics that might be areas where we could contribute I hope you'll communicate them to us.

I think we have covered--we're doing an amazing job. We're an hour ahead of time here.

In terms--

DR. COLLINS: You must be a great chair of this group--

(Laughter.)

CHAIRMAN AUGUSTINE: We're being paid by the hour, Francis.

(Laughter.)

Bill?

DR. BRODY: Do we have an agenda for the December meeting.

CHAIRMAN AUGUSTINE: I was just going to comment. We're trying first of all to get everybody's schedules coordinated and set a date for the December meeting. And the December meeting--one of the topics will certainly be what else, if anything, do we want to tackle at this time. And we'll also start getting briefings on--for the group as a whole on the subject of the small business issues. And then we will get brief status reports on the tasks that are underway that we heard about in more depth today.

And Amy, is there anything else that we--that you know of that we want to raise at that point?

DR. PATTERSON: Not at--not at this juncture.

We're also looking at mapping out the other meetings so that you have those on the books.

CHAIRMAN AUGUSTINE: Yes, we'll do that so

that people can make plans.

Let me go around the table and be sure that everybody has had a chance to raise any issues, concerns, comments, complaints, whatever you'd like to raise.

Gail, anything?

We're just going around the table.

DR. CASSELL: [not at the microphone] for a change. I'm not the first one up.

Of course the things that Francis brought up this morning in terms of challenges in our discussions I think are ones that we all should be thinking about. And it seems like we should save some time for the December agenda to talk about some of the issues that were raised in terms of workforce issues, in terms of numbers of grants, grant sizes, not that you'd make recommendations but at least to set aside some time maybe to have some discussions around those topics or maybe to hear--I know that the working group got feedback from the community about the workforce, the size of the workforce. That was due October 7th. I don't know if those results would be--one would be able to hear those by the December meeting but that would be one that I think this group should pay attention to as

soon as possible.

The issue of the minority—underrepresented minorities in science is always a huge one. I know that some people were shocked when the survey request went out that there was no mention of that. Now we see there's another working group but I'm not sure that everybody realized that that was in the works so they were surprised that there were no specific questions when talking about the size of the workforce that that, you know, issue wasn't raised. So I know that's on a lot of people's minds.

But, that's the only thing I can think of right off--off the top of my head.

CHAIRMAN AUGUSTINE: Richard?

DR. HODES: Nothing to add to those great suggestions.

CHAIRMAN AUGUSTINE: Steve?

DR. Katz: Nothing to add.

DR. Briggs : Sorry I was late. I just got relieved from jury duty. I think [not at microphone)

(Laughter.)

CHAIRMAN AUGUSTINE: Guilty or not guilty?

(Laughter.)

DR. Briggs : He was guilty.

CHAIRMAN AUGUSTINE: Sorry. Anything? Amy?

DR. PATTERSON: Just thanks to everyone.

CHAIRMAN AUGUSTINE: Sol?

DR. SNYDER: One question. When we first set up the whole SMRB thing one of the agendas was supposed to be the organization of intramural NIH, Clinical Center being one subdivision of it. Are--is that ever going to be brought up again?

DR. COLLINS: Yes, you're right that that working group basically had a broader charge but zeroed in on the Clinical Center as the component of the intramural program that was clearly the most urgent to try to wrestle with.

So I think if we're having in December some sort of broader conversation of alternative topics to weigh back into that could be on the table.

CHAIRMAN AUGUSTINE: I saw that as kind of a continuing process, too.

Susan?

DR. SHURIN: Nothing to add.

CHAIRMAN AUGUSTINE: All right.

DR. GREEN: Can I just ask--you said there have bubbled up a few topics that might be discussed

in greater detail in December. I mean is it--I mean just like the SBIR sort of was floated at an earlier meeting it was helpful to sort of have it, at least in my brain, so that when we finally came and discussed it I had been sort of cognizant of it. Are any of the topics that have bubbled up worth at least mentioning?

CHAIRMAN AUGUSTINE: Yes, I think they are. Bill, you raised a point--good idea. Would you mind giving a quick summary?

DR. BRODY: (Not at microphone-inaudible).

(Laughter.)

CHAIRMAN AUGUSTINE: Alright, you had raised in an email to Francis and myself an idea for something that the group might look at.

DR. BRODY: Well.

DR. COLLINS: Do you want to turn your microphone on?

DR. BRODY: Oh, I wasn't sure what you were referring to earlier but I think I--anyway, we resolved it in the discussion. I mean we didn't resolve the issue but we discussed it and I think we agreed that it wasn't a structural--something that required structural change so it was sort of outside--organizational change so it was outside the

purview of our group. Is that it?

DR. COLLINS: This is where it does get a little complicated to figure out. Within the congressional authorization for SMRB in the NIH reauthorization act what are the kinds of topics that fit this deliberative body appropriately? And I can tell you, we are always sort of trying to figure out internally as well. When something comes up we have the opportunity to ask SMRB to tackle it or the Advisory Committee to the Director, which is also a very distinguished group of outside experts and to which we've assigned the tasks right now on the diversity issue and on the biomedical workforce issue with working groups that are hard at work. And, again, glad to have their efforts put forward to this group for information but I think we'd want to be careful not to start off in some parallel or even competing track to try to tackle the same problems that are already under study by another group.

The whole question of managing science in challenging fiscal times is a little hard to be sure. That sort of is everywhere. And it's certainly from NIH's perspective is a topic that we talk about every time we get together at our

leadership forum, around the table on Thursdays with the steering committee or Institute directors. And now increasingly in conversations with outside constituencies like ARRI, AAU and APLU and AAMC and all those other acronyms that we count on for wise advice and now with maybe consideration about whether an RFI ought to be appropriate.

So when Bill and I talked about this before we agreed that we're facing a major challenge in terms of how we oversee NIH's research abilities to support institutions but it wasn't clear that that was a structural issue given that SMRB is particularly charged with advising NIH about its organization and changes that might improve our ability to carry out the mission.

So I guess while maybe there's a space in there for some component of it to fit that, I think the overall problem is probably less structural than it is kind of a policy decision about how we decide to set priorities and what kind of mechanisms we use to carry them forward.

Tony, you've thought about that issue for a long time so maybe I should ask your input here in terms of that very large question of managing science and challenging fiscal issues and how SMRB

might or might not play a role in that?

DR. FAUCI: Francis, I think the point that you made just a moment ago, you said it's such a large topic, I don't even think that you can address it as the whole topic and maybe pick out one, or two or three of the many things that we put on the list of how we might approach it and say what about this particular issue as opposed to throwing out to the SMRB the whole subject matter. I think we would get drowned by that so that would be my suggestion.

CHAIRMAN AUGUSTINE: So my personal view here having talked to an awful lot of people on the subject lately is that one issue in times of great fiscal austerity that does have some structural implications but it’s certainly not totally a structural issue is how can one more efficiently manage the grants process so that investigators can make better use of their time, better use of the money that’s allocated to them and so on? And that’s a thought.

It doesn't fit the structural definition perfectly; on the other hand neither does the SBIR fit the structural definition perfectly. So I think we're dealing with shades of gray.

And I think with the next meeting we're probably going to want to devote some time to this.

So that certainly the last thing in the world I think this group wants to do is go stomping through the cabbage patch. At the same time we on this committee have a fiduciary responsibility to Congress and to Francis and the NIH, and we want to carry that out. So we'll be able to deal with that.

DR. GREEN: Could I again--in hearing this discussion and seeing that there's not huge numbers of obvious issues to tackle or topics to tackle next, and I'm a little worried that we'll get here in December and we'll sit around this table and there won't be a whole lot of things to chew on except just come out with some ideas.

I mean is there anything we can be doing to try to solicit ideas, either by--here at the NIH or our grantees? I mean what's the right way to sort of collect ideas that are worth discussing that are within the purview of this group because it is more structural and not just everything.

I don't know. I mean I'm trying to think.

I mean some of the topics that were originally chewed on were sort of teed up already. Now is the hard part. And I wonder--I'm just

wondering maybe we have to go outside this committee or maybe we need to have a call for sort of ideas in some way.

I'm just--I'm thinking out of the box here. I'm just worried that we're going to get here in December and just stare at each other across the table.

CHAIRMAN AUGUSTINE: Interesting. That was my view of one of the roles of that first group we set up was to continually--on a continuing basis to look outside, inside and tee up in front of the NIH leadership and the group, including the NIH members, tasks where we could make a contribution.

Richard, you were going to say something?

DR. HODES: No, no. I had forgotten about that. (Not at microphone-inaudible).

CHAIRMAN AUGUSTINE: You remember that was sort of the idea. Maybe we need to reinvigorate it to do exactly what you said. We'll take that under advisement.

DR. CASSELL: Well, Sol raised the question of the intramural program and I wondered--that's a huge topic you could spend a lot of time on. I don't know if you want to say a few more words about what you had in mind. (Not at

microphone-inaudible).

DR. SNYDER: When it came up originally the background in my own personal case was some years ago I chaired a blue ribbon committee to evaluate intramural NIMH. And Elias Zerhouni set it up and he said he wanted that to be a dry run for doing the same thing for the whole NIH because intramural is intramural.

And the concerns were that out there in the extramural world there was an image that intramural is--gets all this money and they are lower quality than extramural. And it's because if after they have been around for two years they have life long tenure and the secretaries have tenure after six months and it should be re-investigated. And so our blue ribbon committee came up with recommendations with sorts of things like utilizing the intramural program as a training device where people could--appointments would be clearly time limited and people would be encouraged after five years or maybe after ten years to go in the external world and they could be further encouraged for universities to want to recruit them, and they would have a reverse dowry. They would be given money to leave town and things like that. And that--some of

the issues are meant to reinvigorate although no one is saying the intramural program isn't of great excellence but to enhance its configuration by whatever.

DR. CASSELL: So I had I guess the privilege--or some might not consider it a privilege to co-chair the committee with Paul Marks to do that intramural or the review of the entire intramural program a little over a decade ago and then we recommended that each Institute be reviewed individually because we--there was no way our committee could do all of them justice.

So when Elias asked me to serve on this committee he said it's time. So I don't maybe disagree that it might be worth thinking about not necessarily the same type of overall review that was done before but maybe certain aspects of it that we could maybe think about that might be worth diving deeper on.

CHAIRMAN AUGUSTINE: A lot of good comments.

We'll take those aboard.

Francis?

DR. COLLINS: Yes, just by way of information, I think those reviews that were done

did, in fact, result in substantial changes in the way the intramural program is reviewed and now every investigator is reviewed rigorously on a quadrennial basis.

My lab just went through this a month ago so I can tell you it indeed rigorous.

(Laughter.)

We're waiting for the written report.

DR. GREEN: I have seen the written report and I was at the exit interview and it was really pretty disgusting.

(Laughter.)

DR. COLLINS: Let me point out the reviewers did not have NIH funding. They all came from Europe and Canada just to be sure that there was no kind of conflict of interest.

So I think the whole rigor of the intramural program was substantially tightened up and the Cassell-Marks panel had a lot to do with that. And it is certainly the case that people who do not come through those programs looking as if they're competitive lose resources and are encouraged to move on.

So if there were times in the past where things were allowed to slide, they're not allowed to

slide now.

Just the same, I'm sure there are other aspects of intramural that would be worth having another big look at. I'm again trying to figure out what's the timing and what's the right group but it's probably something we should put on the list to talk about in December.

DR. CASSELL: I'm sorry Michael Gottesman is not here. He was this morning.

I think he's done a superb job as the intramural program in terms of implementing most of those recommendations.

One of the--well, I wrote up the section on training and one of the beasts was broader advertisement of those positions when they became available because they're such prime positions. And almost any week you take a look in *Science* you may see these ads--the positions advertised, which is a big step in the right direction because formally that was not occurring. You know, there was not a broad net cast in terms of recruitment of scientists to the intramural program. And any number of other things that

I could comment on that at least as far as the training aspect that I have certainly observed.

I've participated in two of the individual Institute reviews, NIAID and NIEHS, and I think that--well, again, a lot of changes have been made and good changes at that.

DR. SNYDER: I was just--the comments I made--I wasn't saying what I was thinking. I was saying this is the caricature in the outside world of intramural NIH and I'm fully aware of your valuable committee and how things have been changed and the tenure system is--has lots of rigor now.

CHAIRMAN AUGUSTINE: Continuing around the table. Griff?

DR. RODGERS: Nothing else to add.

CHAIRMAN AUGUSTINE: Bill?

DR. BRODY: Well, in some ways the ultimate question is where is the budget go because that kind of dictates what kind of response is required.

And I think absent--absent that it's hard to make the case--I mean it's one thing if you're in industry and you see the winds of change and you were able to implement some things. I think it's harder in a public organization to make the

CHAIRMAN AUGUSTINE: Absolutely.

DR. BRODY: substantial changes that might

be required--that you or I or somebody here might think or even collectively think unless there is sort of a--well, I guess what I would call a budget crisis, which may, in fact, happen.

I mean it--when people ask me where is the NIH budget I say you just tell me where the Congress is going to go on the federal budget and I can give you some idea, and lacking that it's sort of hard to predict, right.

And so I think that in some sense--but I think I would be happy to have our committee at least discuss some things in consultation with Francis and whoever else you would like because I don't think we want to get out free-wheeling or, as you said, stomping the cabbage patch.

CHAIRMAN AUGUSTINE: It’s a technical term.

DR. BRODY: Yes.

(Laughter.)

CHAIRMAN AUGUSTINE: It is true that, you know, if you’re looking at a 10 percent budget cut, to pick a number, if you can increase your efficiency by 10 percent you're hanging in there. And so it pays to be looking at both sides of that.

Francis, you get the last word as always.

DR. COLLINS: Well, it is interesting to imagine how this conversation might play out on December 21st, which I believe is the day that has been chosen for the next SMRB. There were a couple of dates floating--floated around but that seemed to be the one where we had the strongest list of positives.

Just to sort of put that in context of other things that will be happening, you're probably are aware that the super committee is supposed to put forward their recommendations about how to cut $1.2 trillion by November 23rd, right before Thanksgiving, and then the Congress is supposed to consider those recommendations and they have a up or out vote by December 23rd. So if we're here on the 21st we'll be on the cusp of God knows what kind of tension and crisis atmosphere.

Nobody is really clear what the super committee is going to be able to put forward because obviously finding those numbers of billions and trillions is going to be extremely challenging. And yet most people, I think, are horrified at the concept that they might fail because of the sequestering that would then kick in.

And not to be too gloomy about it but if,

in fact, the super committee fails or the Congress refuses to go along with the recommendation, the consequence of the sequesters for NIH would be truly Draconian. And if we are at that phase on December 21st, we really will have to think very hard about how to manage in not just stressful times but potentially disastrous times.

So that will be fun to sort of plan for and prepare for. Perhaps things will look a little brighter and our system will have actually found a way to achieve some kind of compromise. We all hope so.

But I think this has been a very-- extremely helpful day from my perspective being able to get your feedback on the projects that you've already put in front of us on the Clinical Center, on addiction and drug use and abuse and certainly on NCATS has been very helpful.

And I appreciate your willingness to take on the SBIR/STTR project because I think there's a real potential there to do some good for a component of our portfolio that we really want to be absolutely exceptionally high quality.

And we'll have to see. You have to sort of keep your seatbelts fastened and stay loose on

your feet here in the coming weeks and months because it is so hard to know exactly which trajectory we're on. And who knows. Maybe we'll actually find our way out of the woods in a while but it doesn't look likely that it’s right around the corner.

So, Norm, thank you for your able and expert leadership of this group, and to all the members for putting your time into being here and all the things we ask you to do in the interim.

And, Sol, thank you for agreeing to take on this latest task with those few hours of notification. Appreciate your willingness to do this.

And we will see what we can get done between now and a--well it’s not very far away, a couple of months from now when we all gather to have a holiday or a wake or whatever it turns out to be on December 21st. Thanks.

NEXT STEPS

CHAIRMAN AUGUSTINE: Francis, I was just going to thank you for your leadership of the organization. And you certainly got here in challenging times. I must say that.

And thank all the members of the

SMRB for your good work and thank the members of the public who have been sharing their views with us and spending their time with us.

And a special thanks, Amy, to you and your very able team that puts these things together and organizes them to the point that we can't mess it up too badly.

So anyway, everybody--I guess December 21st apparently is the official date. Does that sound right? So if you'll mark your calendars and everybody have a safe trip home.

Thank you.

DR. COLLINS: Thank you.

CHAIRMAN AUGUSTINE: The meeting is adjourned.

(Whereupon, at 2:00 p.m., the proceedings were adjourned.)