U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

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ADVISORY COMMITTEE TO THE DIRECTOR (ACD)

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99th MEETING

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FRIDAY,
DECEMBER 4, 2009

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The Committee met in Conference Room 6 in Building 31, C Wing, of the NIH Campus, Bethesda, Maryland, at 8:30 a.m., Francis Collins, Chair, presiding.

PRESENT:

FRANCIS COLLINS, Chair, M.D., Ph.D.

Director, NIH
CHRISTOPHER AUSTIN, M.D.
MARY BECKERLE, Ph.D.
LINDA BIRNBAUM, Ph.D., DABT, ATS
JEFFREY BOTKIN, M.D., MPH
PENNY BURGOON
COLLEEN CONWAY-WELCH, Ph.D., CNM, FAAN, FACNM

CATHERINE DeANGELIS, M.D., MPH
HAILE DEBAS, M.D.
DAVID DeMETS, Ph.D.
MARIA FREIRE, Ph.D.
ELIZABETH FURLONG, JD, Ph.D., RN
MICHAEL GOTTESMAN
RICHARD HODES, M.D.

KAREN HOLBROOK, Ph.D.
RALPH HORWITZ, M.D.

PRESENT (Continued):

JAMES JACKSON, Ph.D.

THOMAS KELLY, M.D., Ph.D.

RAYNARD KINGTON, M.D., Ph.D.

MARY-CLAIRE KING, Ph.D.

STORY LANDIS, Ph.D.

BEATRIZ LUNA, Ph.D.

JEFFREY MURRAY, M.D.

JOHN NELSON, M.D., MPH, FACOG, FACPM

LANA SKIRBOLL, Ph.D.

JAMES THRALL, M.D.

BARBARA WOLFE, Ph.D.

KEITH YAMAMOTO, Ph.D.

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1 P-R-O-C-E-E-D-I-N-G-S

2 (8:33 a.m.)

3 WELCOME AND NIH DIRECTOR'S REPORT

4 CHAIRMAN COLLINS: Good morning,

5 everybody. Raynard just said that was the

6 best part: Getting to whack the gavel. Well,

7 actually, I think there are going to be a lot

8 of interesting things to talk about during the

9 course of this meeting today. And I want to

10 welcome you to the 99th meeting -- wow -- of

11 the NIH Advisory Committee to the Director,

12 but it's my first in this chair, although I've

13 sat in this room for other meetings in the

14 past, presided over other NIH directorates.

15 But this is my first chance to be here with

16 you as the Director of the NIH.

17 Before we get started, let me

18 remind you of a few items. This meeting is

19 open to the public. That includes members of

20 the press. It is being webcast globally. So

21 be careful about what you say. Lots of people

22 may be listening.

1 We are also transcribing the
2 meeting. So that means you should speak into
3 the microphone, hit the red button there when
4 you are speaking. Otherwise your wise
5 comments might be lost to history. And we
6 wouldn't want that.
7 You have meeting notebooks at your
8 place. And meeting materials and handouts are
9 located in your notebooks. And at the
10 conclusion of the meeting, if you would like
11 to have those mailed to you, just let us know.
12 And we can take care of that.
13 We will take a group photo of the
14 ACD members just before lunch. And we will
15 organize that when we get to that point. So
16 I particularly want to say today is time also
17 to express gratitude to several ACD members,
18 who have ably served on this group because
19 this is not a life sentence but actually an
20 opportunity to contribute your wise advice for
21 a period of three years.
22 And so we want to say thank you to

1 Catherine DeAngelis, to Karen Holbrook, to
2 Mary-Claire King, to John Nelson, and to
3 Barbara Wolfe for their participation as
4 members of the ACD and as representatives of
5 the scientific community and the public.
6 So we appreciate your thoughtful
7 advice over the course of your service here
8 and hope we can continue to contact you in the
9 future for other activities where we may need
10 to depend on your unique expertise. And we
11 will certainly count on your input today as we
12 go through an agenda that has some pretty
13 interesting topics for us to all discuss.
14 I would also like to take this
15 opportunity to thank a new member who has
16 joined us for the first time for his
17 willingness to do so. And that is Haile Debas
18 from the University of California, San
19 Francisco. Haile, most welcome to be here.
20 Haile is the Executive Director for Global
21 Health Sciences at UCSF.
22 We are missing a few members today

1 who had other obligations they could not
2 escape from. And that is Joan Brugge, Alan
3 Leshner, and Susan Hockfield. But we will
4 look forward to seeing them at the next
5 meeting.
6 We are putting together a slate of
7 new members to try to identify expertise in
8 areas that we think NIH is going to be looking
9 particularly closely at. We have the chance
10 in this process of rotation to do so. And we
11 will try to identify some wise, thoughtful
12 individuals to join this group to try to, if
13 possible, replace the expertise that we are
14 losing, although that may be a challenge.
15 Before I go any further, I did
16 want to take a moment here to reflect on a
17 dear colleague and one of the true giants at
18 NIH, who died on October 6th. And that, of
19 course, is Dr. Ruth Kirchstein.
20 Her service to NIH lasted more
21 than 50 years. And she was active right up to
22 her last days. She was on a conference call

1 with me within a week before her death,
2 providing some very helpful advice on a thorny
3 issue that we were wrestling with.
4 She came to NIH in 1956 as a
5 medical office in clinical pathology and led
6 in the development of a test that provided a
7 means for ensuring the safety of viral
8 vaccines, such as those for polio, measles,
9 and rubella.
10 She was instrumental in advocating
11 the use of the Sabin oral vaccine for polio.
12 And in 1974, Ruth was appointed as the first
13 woman director of an NIH institute, NIGMS,
14 where she served for many years. She last
15 served as Principal Deputy Director of the NIH
16 and twice served as Acting NIH Director.
17 Ruth is an absolutely legendary
18 character. Her passion for biomedical
19 research, her care for the people at NIH were
20 hallmarks of her long and illustrative career.
21 We thought it would be appropriate
22 in recognition of her many contributions to

1 NIH to show you a brief video from NLM
2 exemplifying her passion and her commitment to
3 the highest standards of biomedical research
4 and leadership.
5 So if we could, can we run that
6 video, please?
7 (Whereupon, a video was shown.)
8 CHAIRMAN COLLINS: What a leader
9 she was. And I know I speak for all of NIH
10 when I say we lost one of our dearest and most
11 dedicated public servants.
12 In fact, let us stand for a moment
13 just for a reflection of her memory and all
14 that she has done for us. If you would,
15 please stand with me for just a moment of
16 silence.
17 (Pause.)
18 CHAIRMAN COLLINS: Thank you all
19 very much.
20 And I know Ruth would have hated
21 that.
22 (Laughter.)

1 CHAIRMAN COLLINS: Time wasted.
2 And Ruth always was the last person to want
3 anyone to make any special efforts to
4 recognize her, but I hope she will forgive us
5 for just this moment of reflection.
6 And I hope her dear husband, Al
7 Rabson, who also would have hated the fact
8 that we just did this, will also forgive us if
9 he is watching on the video this morning. Al,
10 we love you, too.
11 Okay. Well, there have been some
12 significant changes in terms of leadership at
13 NIH since you all last met here. And I wanted
14 to comment on those and also to thank some
15 people who have done incredible things for NIH
16 over the course of the last year.
17 This past July I was honored to be
18 nominated by President Barack Obama and then
19 was confirmed by the Senate and sworn in on
20 Monday, August 17th. So if you're counting,
21 this is my 115th day, and I do hope it will be
22 a good one.

1 I want to take a moment, though,
2 before going further to say what an incredible
3 privilege it was to step in to building 1, to
4 the Director's office, and find that this
5 organization had been so ably managed during
6 the interim since Elias Zerhouni stepped down
7 back in November by the Acting Director, Dr.
8 Raynard Kington.
9 In fact, I would think we ought to
10 actually applaud this fellow for what he did.
11 (Applause.)
12 DR. KINGTON: I hate that.
13 CHAIRMAN COLLINS: Sorry, Raynard,
14 but we had to I think collectively express the
15 appreciation for the incredibly wonderful
16 service that you performed during those
17 months.
18 And it's certainly been a
19 challenging set of months, particularly with
20 all of the things that you will describe to us
21 in a little bit about the Recovery Act, which
22 needed to be responded to in a very rapid time

1 table.

2 And in that regard, I would also

3 want to thank Larry Tabak. And I don't know

4 -- oh, he's in London? All right. He's

5 actually representing NIH in London at an

6 important meeting.

7 Larry Tabak stepped in during this

8 interim as well to serve as an Acting Deputy

9 Director and focus on the Recovery Act and

10 organize an incredibly challenging set of

11 efforts to put out RFAs and organized reviews

12 involving no less than 15,000 reviewers with

13 much able assistance from Sally Rockey and

14 Tony Scarpa and many others across the entire

15 NIH. This was an amazing outpouring of effort

16 to get things done.

17 But Larry as the field general of

18 this enterprise really put in an incredible

19 effort and continues to play this role in

20 helping to oversee the Recovery Act

21 investments and making sure they're going to

22 the very best science. So I have been very

1 fortunate to be able to walk into an
2 organization that was in such fine shape.
3 I want to mention a couple of new
4 leadership things that have happened since
5 last you met. One of the things that I
6 decided to do was to bring on a new position,
7 a Chief of Staff.
8 The issues that surround NIH are
9 sufficiently complex that with Raynard
10 continuing as Deputy Director, there are still
11 many other issues relating to our
12 relationships to outside organizations that
13 need that kind of senior expertise by someone
14 who both knows science and those policy.
15 And so I am happy to introduce to
16 you Dr. Kathy Hudson, who has joined NIH as
17 the new Chief of Staff, Kathy, known to many
18 of you from the role that she has previously
19 played as the head of the Genetics and Public
20 Policy Center, at Johns Hopkins, supported by
21 the Pew Foundation and prior to that at NIH,
22 where she was an Associate Director at the

1 Genome Institute and before that had an
2 important role in the department. So she is
3 experienced and knowledgeable and has been a
4 wonderful addition to the senior staff.
5 I am also happy to say that in
6 just the last couple of weeks, I was able to
7 bring on board a new institute director, this
8 one for my old institute, the Genome
9 Institute. Dr. Eric Green was appointed as
10 the Director of the National Human Genome
11 Research Institute on December 1st. He is at
12 a retreat at Cold Spring Harbor today, so is
13 not here to receive your smiles.
14 Eric comes to this position with a
15 great deal of experience already as Scientific
16 Director of the Genome Institute, highly
17 regarded in his own work on comparative
18 genomics and a very organized and
19 well-respected leader around here and will
20 step into this, I think, ready to move the
21 institute into a new phase of exciting vision.
22 I want to recognize Alan

1 Guttmacher, who served as Acting Director of
2 the Genome Institute for some 16 months and
3 who I will mention in another regard in a
4 moment.
5 So I also want to thank the Search
6 committee -- in fact, there are many search
7 committees going on right now but thank the
8 search committee for the Genome Institute, who
9 worked hard in coming up with a very exciting
10 list of potential candidates and made this a
11 good experience for me in my first opportunity
12 to do that kind of selection.
13 Two NIH directors have moved on to
14 new opportunities since you all last met. The
15 National Heart, Lung, and Blood Institute,
16 ably led by Dr. Betsy Nabel for the last five
17 years, were I think a bit taken aback, as was
18 I, to learn that Dr. Nabel had accepted a
19 position as the new President and CEO of
20 Brigham and Women's Hospital in Boston, a
21 place where she trained, a place where she had
22 enormous personal and professional connections

1 and a place which offered her an incredible
2 job.
3 We can all understand why this was
4 such, an irresistible force drawing her away
5 from us. Even as we said farewell with a tear
6 in our eye, we celebrate Betsy and all of the
7 things she accomplished as part of her term as
8 the Director of the NHLBI because she has been
9 an incredible leader around here.
10 And so, actually, she will start
11 on January 1st in Boston, but she stepped down
12 from the Heart, Lung, and Blood Institute on
13 November 30th.
14 We have moved quickly to appoint
15 Dr. Susan Shurin, who has previously served as
16 the Deputy Director as the Acting Director of
17 the institute, Susan a highly respected
18 pediatric oncologist and cardiologist who is
19 now serving ably in that role, and a search
20 committee is getting underway, even as we
21 speak, to go out and find the very best person
22 to step in as the permanent leader of this

1 critical part of NIH.

2 Another institute is also engaged

3 in a search for a new leader. And that is the

4 National Institute of Child Health and Human

5 Development.

6 After leading that institute for

7 23 years, Dr. Dwayne Alexander moved over to

8 the Fogarty International Center in September

9 to bring his expertise to that organization in

10 a new initiative on maternal and child health

11 with close connections to the State

12 Department. And this is part of the White

13 House global health initiative.

14 Dwayne has obviously over the

15 course of more than 20 years led many

16 important initiatives. I could mention, for

17 instance, the back to sleep initiative and

18 efforts in various infectious diseases and

19 obviously has brought great distinction to

20 that part of NIH in efforts to try to identify

21 an individual who could step into that role

22 initially.

1 This may seem a little complicated
2 to you. And it was. We asked Dr. Shurin,
3 whom I have just mentioned a moment ago, who
4 is now the Acting Director of Heart, Lung, and
5 Blood, to serve as the Acting Director of
6 NICHD. And she did so most ably for a period
7 of two months.
8 Finding, however, that Dr. Nabel
9 had a surprise for us, we had to regroup a
10 little bit. And in a very happy sort of
11 multi-body solution, Dr. Guttmacher, a
12 pediatrician of considerable renown, a
13 geneticist, and also somebody with
14 considerable experience in the area of
15 reproductive health research, which is another
16 important part of NICHD, agreed to step in as
17 the Acting Director of the Eunice Kennedy
18 Shriver National Institute of Child Health and
19 Human Development, has taken on that role as
20 of December 1st and I'm sure is finding that
21 to be interesting and challenging with many
22 issues that Institute is dealing with, not the

1 least of which is the national children's
2 study, a major flagship initiative of NIH as
3 a whole.
4 So I want to thank those who have
5 been so willing to step in to these leadership
6 roles. As you can tell, we have a lot of
7 searches underway. And we are optimistic we
8 will find fabulous people for each of them.
9 In addition to the ones I have
10 just mentioned in terms of NHLBI and NICHD, we
11 have a search that is very close to conclusion
12 to bring in a new Director of the Office of
13 Legislative Policy and Analysis.
14 That is a critical part of my
15 senior leadership team. Acting Director
16 currently is Roz Gray. And we got a fantastic
17 list of applicants. So I can be quite
18 confident in telling you that we're going to
19 have a super person for this role and may be
20 able to get that wrapped up in the near
21 future.
22 And, by the way, Dr. Shurin has

1 just arrived. I was just talking about you,
2 Susan. If you're wondering who this heroic
3 figure is, there she is --
4 (Laughter.)
5 CHAIRMAN COLLINS: -- now stepped
6 in, as you've heard, as Acting Director of
7 NHLBI.
8 We have a search underway for the
9 directorship of the Office of Behavioral and
10 Social Science Research. Current Acting
11 Director is Dr. Christine Bacharach. We have
12 a search underway of the Office of Extramural
13 Research, which is ably led by Acting Director
14 Dr. Sally Rockey.
15 And, as those of you who have been
16 on this group for a while know, we have been
17 on this Division of Program Coordination
18 Planning and Strategic Initiatives, otherwise
19 known as DPCPSI, a new part of NIH, which was
20 formally established in legislative terms by
21 the NIH Reauthorization Act in 2006 and which
22 has a number of important activities under its

1 particular rubric, especially the common fund.
2 And so Lana Skirboll has been
3 serving as Acting Director, and we are
4 initiating a search for someone to come and
5 run that with great scientific energy and
6 vision.
7 So a lot of activities there.
8 But, just the same, we have such capable
9 people in each of those positions as actings
10 that you should not worry too much that
11 somehow the place is not going to be moving
12 forward.
13 At the same time, for all of
14 those, if you know of terrific candidates for
15 any of the positions just mentioned, we would
16 love to hear about it. We generally have
17 discovered that you don't hire people for
18 these kinds of leadership positions by putting
19 out an ad and hoping someone will apply.
20 Usually the people you most wish
21 to bring on board already have a job. And
22 usually they are actually pretty good at it.

1 And oftentimes they are having fun at what
2 they are doing and haven't thought of
3 themselves as coming to a position within the
4 federal government.
5 So it takes some brainstorming.
6 And if we can tap into your expertise as part
7 of that collective brainstorm for any of these
8 positions, please speak to me or to Raynard
9 about possible candidates that you might want
10 to put forward for us to consider.
11 One more change about to occur,
12 and that is also in the senior leadership of
13 NIH. That is our Associate Director in the
14 Office of the Budget, Mr. John Bartrum, whom
15 I have depended on considerably for many
16 details about the budget. And it is a hot and
17 heavy time for the budget right now with the
18 F.Y. '11 budget being formulated within the
19 administration.
20 John has accepted an opportunity
21 to join the House Majority Appropriations
22 Committee as a senior professional member

1 assisting Mr. David Obey, our Chairman of
2 Appropriations, in many issues related to how
3 to put together a budget for F.Y. '11 and
4 beyond.
5 So I guess, again, as we with a
6 tear in our eye say, "Goodbye" to John -- and
7 today is actually his last day -- we are very
8 much also happy to congratulate him on this
9 new challenge and thank him for his service
10 and say with great joy that we think we have
11 a friend in a very important place in the
12 congressional appropriations process.
13 I would like to give John a few
14 minutes here to give us a final moment to give
15 a budget update on where we are at the moment
16 in a lot of the deliberations because, after
17 all, the budget turns out to be fairly
18 important.
19 So, John, do you want to run us
20 through a few points?
21 MR. BARTRUM: Again, it's been a
22 pleasure to have been a member of the NIH

1 family. Once you are a member of the family,
2 you are always a member.
3 An update on the budget, I think
4 Dr. Kington is going to give an update a
5 little bit later more specifically on the
6 Recovery Act. But, in general, as a reminder,
7 we had $10.4 billion. And we obligated about
8 $4.8 billion. We have committed, meaning the
9 second half of the grants will go out in 2010,
10 of about $7 billion.
11 So we are really about 30 percent
12 of the money that is left to be obligated. A
13 lot of that is in the extramural construction
14 area, shared instrumentation area. There is
15 also some on the research areas.
16 On the F.Y. 2010 budget, we are
17 currently under a continuing resolution that
18 expires on December 18th. I feel very hopeful
19 that by December 18th, we'll have a final
20 budget for 2010. There is some scuttlebutt in
21 some of the newspapers or whatnot that there
22 could be a continuing resolution, but I don't

1 see that as a real player.

2 Our 2010 budget request was

3 roughly $31 billion, $30.9 billion. The House

4 passed a version that is $500 million more

5 than our request. The Senate passed a version

6 that is exactly what our request was. So

7 where we will end up we don't know. It is

8 likely that we will either be at our request

9 level or the 500 or somewhere in between. It

10 depends on how the negotiations end up in the

11 end.

12 Of note, in the 2010 budget, it

13 had a specific initiative for autism and

14 cancer. Both sides, the House and the Senate,

15 express not great support for having earmarked

16 toward specific disease areas.

17 The Senate version of the bill

18 actually has stronger language against that.

19 The House version has softer language. How

20 that will play out, how that will end, what

21 that will mean is yet to be seen, but it

22 should be of note.

1 As far as the 2011 budget, we are
2 in the game that we play. I can't give you a
3 lot of details on it. I can tell you where we
4 are at in the process is that we have
5 submitted our budget to HHS. HHS has
6 submitted it to OMB. OMB has provided some
7 feedback. And the administration is in the
8 final parts of negotiating it. And the budget
9 will roll out in the first Monday in February,
10 and we'll go through the process from there.
11 So unless there are any questions,
12 that's all I have as a budget update.
13 CHAIRMAN COLLINS: Any questions
14 for John? Mary-Claire?
15 DISCUSSION
16 DR. KING: Could you give us a
17 little more analysis on the use of the word
18 "targeting"? I wouldn't have thought that
19 cancer and -- what was the other example?
20 Autism?
21 MR. BARTRUM: Autism.
22 DR. KING: Those are pretty big

1 categories. In what sense was that considered
2 targeting? And what can we do to help
3 Congress realize that there is an awful lot of
4 research that falls under those two general
5 categories.
6 MR. BARTRUM: Well, it was
7 identified as targeting when the
8 administration said they were going to target
9 funds towards this and they were going to
10 ensure that we had a specific amount of the
11 increase be focused on cancer and autism
12 research.
13 Normally when our budget process
14 goes out and we get the execution, Congress
15 allows the science to drive the research. A
16 lot of the money goes into cancer and autism
17 and all of the areas that you described, but,
18 as opposed to picking one or two winners, as
19 it were, or one or two favorites, as it were,
20 over others.
21 And so that was the concern from
22 the committees, that how do you decide that

1 this one or that one is more important than
2 the other, as opposed to letting the science
3 drive the allocations.
4 CHAIRMAN COLLINS: Yes. There's
5 an important difference between highlighting
6 areas of special scientific opportunity. And
7 certainly when I talk about exciting things
8 that are happening right now, cancer is often
9 one of the first things I bring up about the
10 idea of earmarking and trying to pick out
11 particular winners in the research portfolio
12 and saying, "Well, they should get a more
13 rapid growth than other areas that don't
14 happen to be on that list." That disturbs us
15 because we really want the decisions to be
16 made on the basis of scientific opportunity.
17 I think the Congress generally has
18 been quite good about recognizing that for
19 NIH. And we have been largely protected
20 against the kinds of earmarking that have been
21 really quite painful for some other agency.
22 Okay. Thank you, John.

1 Another update -- and I thought it
2 would be fun as part of this Director's report
3 to ask various guest appearances to be made.
4 We at last December's ACD meeting had a
5 discussion led by Sally Rockey on the
6 financial conflict of interest issue,
7 particularly on the area of extramural
8 grantees and the degree to which we are
9 vulnerable and the whole enterprise is
10 vulnerable if conflicts of interest are seen
11 to be happening without proper oversight.
12 And, as you probably know, that
13 has led to some extensive discussions and a
14 process that will lead in the fairly near
15 future to the posting of a notice of proposed
16 rulemaking, where NIH will, in fact, take a
17 more active role in oversight of extramural
18 potential conflicts.
19 So I am going to ask Joe Ellis to
20 give us a brief update on where that all
21 stands.
22 MR. ELLIS: Okay. Good morning,

1 everyone. Of course, this has, of course,
2 gotten quite a bit of interest over the past
3 several years by not only the press but the
4 watchdogs, the Office of Inspector General,
5 and on the Hill.
6 And NIH uses this regulation, put
7 this regulation in place, to assure that our
8 sponsor research is conducted with the highest
9 scientific and ethical standards.
10 Now, the current regulation, which
11 has been in place since 1995 and applies to
12 both contracts and grants, is designed to
13 promote this objectivity in research.
14 The primary player and
15 responsibility with this regulation really
16 rests with the granting institution, who has
17 to promulgate policies consistent with the
18 regulation and provide oversight within their
19 institution, relying on their investigator to
20 disclose their interest and comply with the
21 institution's policies and directives
22 regarding this, again using the policies and

1 oversight they provide; and, finally,
2 reporting to NIH those conflicts of interest.
3 NIH provides the oversight as the
4 grantee agency with this and assures the
5 compliance with these regulations. And this
6 practice is probably something that we are
7 going to continue as we consider a change in
8 regulation because of the fact that the
9 employer of the investigator and the fact is
10 the institution, and they have a mixed
11 knowledge of both the programs they are doing
12 and their other relationships to judge
13 financial interest and whether those
14 constitute a financial conflict of interest.
15 So NIH considered the interest in
16 these areas and some of the interest we had
17 seen in our compliance activities. And we
18 decided to go out for what is called in
19 government parlance the advance notice of
20 proposed rulemaking.
21 Believe it or not, that is
22 considered an informal process. The reason

1 that is considered informal is it does not
2 give an indication of where the agency is
3 going with the final regulation, as you get
4 when you get a notice of proposed rulemaking,
5 which shows our thoughts in that matter.
6 So we drafted this in a very broad
7 manner to ask questions addressed in all
8 aspects of the regulations and how that might
9 be enhanced in the future in six broad areas:
10 first, expanding the scope of the regulation
11 and the disclosure of requirements.
12 The regulation currently doesn't
13 include things like financial interests for
14 folks under a phase one SBIR, which is pretty
15 minor, but we thought we should address that.
16 Also, there is a question about
17 where people get their sources of income from,
18 sometimes from nonprofits, sometimes from
19 public institutions; defining what is a
20 significant financial interest. The current
21 regulation focuses on interests that are
22 particularly relevant to the research to which

1 the investigator is applying for support. And
2 there have been questions raised as to whether
3 that is broad enough to actually capture those
4 interests and have those be properly evaluated
5 by the institution.
6 Also, the identification and
7 management of conflicts by institutions. We
8 asked questions, again, that were very broad,
9 asking, whether certain types of interest
10 that, just by their very nature, would
11 constitute a financial conflict of interest.
12 Perhaps there is some interest
13 that might be tapped in the application of
14 regulation. We focus again on ensuring
15 institutional compliance and requiring
16 institutions to provide additional information
17 where looking at ways that they can enhance
18 their information they provide to NIH. We can
19 really enhance our oversight and assist the
20 institutions in this very difficult area.
21 And probably the most challenging
22 question we ask is defining what is an

1 institutional conflict of interest and how
2 that might be managed.
3 Now, we published this advance
4 notice in May of last year and had the comment
5 period open until July 7th. We received
6 around 70 responses. And that's a little bit
7 misleading because many of those responses
8 came from national organizations, like AAMC,
9 AAU, and Covar. So they represented many
10 parties. We actually got some other
11 responses, saying, "We believe what this
12 organization said."
13 So NIH has been working with those
14 for the past several months. We have convened
15 a committee that is co-chaired by Dr. Insel
16 and Dr. Rockey. And they have included
17 program staff, in particular, from various
18 institutes, who work closely with these
19 issues, particularly in the area of clinical
20 research and clinical trials, so that we have
21 a broad spectrum of input on this and have
22 had, really, very vigorous discussions.

1 So we are going to the final stage
2 of getting that input and developing what will
3 actually be a more formal thing of a notice of
4 proposed rulemaking that would actually result
5 in a change in the rules over the next few
6 months. And we expect that this will be
7 published after it is approved by internal NIH
8 leadership; HHS; and, of course, the Office of
9 Management and Budget. So we are trying to
10 push this out as soon as we can.
11 The goal for this ultimately is to
12 have a final rule published in the summer and
13 fall of this calendar year. So that is
14 basically our status.
15 CHAIRMAN COLLINS: Thanks, Joe.
16 Are there any questions? Yes,
17 Tom?
18 DR. KELLY: So once you have
19 finished your internal process and you have a
20 set of rules, is there going to be an
21 opportunity for public comment after that
22 point?

1 MR. ELLIS: Yes, that's a very
2 good point. The notice of proposed rulemaking
3 by the process used in the federal government
4 provides four public opportunities for input
5 and comment on that.
6 So that will be published. We
7 will probably do a summary of the changes that
8 we are anticipating, giving some feedback on
9 the initial comments we received from the
10 advance notice of proposed rulemaking and
11 providing a draft of what the final regulation
12 probably would look like. So there is ample
13 opportunity for input and comment and
14 consideration.
15 We have gotten quite a few points
16 from the advance notice and also from other
17 points of input driving this process. So we
18 very much need and appreciate the input from
19 folks who really understand the issues and
20 some of the complexities that we are facing in
21 balancing this.
22 CHAIRMAN COLLINS: Yes?

1 DR. BECKERLE: Do you have any
2 external consultants or members of the
3 committee or group that are really working to
4 develop the proposed guidelines at this point?
5 It's all internal.
6 MR. ELLIS: Well, right now this
7 is pretty much held within the NIH because
8 it's a federal function.
9 DR. BECKERLE: Yes.
10 MR. ELLIS: We have gotten some
11 advice from outside parties to help us address
12 and think about how we might approach some
13 other questions, but they are not part of the
14 committee.
15 DR. BECKERLE: Thank you.
16 CHAIRMAN COLLINS: Well, thank
17 you, Joe. I appreciate this. Let me just say
18 from my perspective this is a matter of
19 extremely high importance to get right, that
20 the credibility of the biomedical research
21 enterprise has been placed at some risk by
22 specific examples, fortunately, I think rare,

1 but still quite disturbing, when they come to
2 public attention, where individuals who are
3 the recipient of NIH grants are seen to be
4 involved in activities that, at the minimum,
5 represent the appearance of a conflict of
6 interest and in some instances appear to go
7 well beyond that.
8 If we want the public to trust
9 what we do and to support it, we have to be
10 sure our house is in order. And so I
11 appreciate all of the efforts that have gone
12 into preparing for this new version of
13 oversight, which may; in fact, undoubtedly
14 will, create a sense of burden upon extramural
15 grantee institutions but seems highly
16 warranted because of the seriousness of the
17 issue.
18 Joe, thank you for your leadership
19 on this.
20 DR. DeANGELIS: If I may, Francis,
21 I would never beg to disagree with you, but
22 from where you sit, it's rare. From where I

1 sit, it is not rare. And I think that this
2 issue of conflict of interest in medical
3 research is from my perspective one of the
4 biggest, if not the biggest, issues right now
5 because we have lost the public trust and with
6 good reason.
7 And, as I said, I wish you were so
8 right, Francis, that it was rare. It is not.
9 I can give you dozens and dozens -- and I
10 won't, but I can give you dozens and dozens of
11 examples of this is rampant right now, just
12 from my seat.
13 We keep clamping further and
14 further down. And I can tell you right now
15 that I finally have the attention of the
16 International Committee of Medical Journal
17 Editors, which are the editors of JAMA, New
18 England Journal of Medicine, Lancet, The
19 Annals, the big journals, internationally to
20 finally -- we are going to come out with
21 something that is going to be very, very, very
22 -- that addresses this in a very strict way.

1 It is a big problem. And I am so
2 happy that NIH is really looking at this very
3 closely. Thank you.
4 DR. WOLFE: If I could just add to
5 that? I agree with you entirely. I mean, the
6 headlines with the people writing for -- well,
7 putting their names on articles that have been
8 written for them by various drug companies,
9 for example. I mean, the issues just go on
10 and on.
11 Everyone I think is really
12 focusing on it. And this just has to be
13 handled. It is a problem that is growing. I
14 think that we don't have any real sense of the
15 size and how it creeps in to all kinds of
16 publishing and other kinds of issues.
17 I guess I wonder, too, whether
18 it's -- how broad the look is. I mean, when
19 we fill in forms, we include not just our own
20 interest but that of our family members. And
21 so I have always thought at the university
22 level are the questions that are asked broad

1 enough? So I just encourage you to look very
2 broadly. This is incredibly important.
3 CHAIRMAN COLLINS: Beatriz?
4 DR. LUNA: Yes. I think I
5 mentioned this at the last meeting I was here.
6 So I am reporting as a young investigator from
7 the trenches. And I think this is great that
8 there is great transparency and that we are
9 going towards, I mean, obviously this has to
10 be done.
11 I think it is also important to
12 consider that being this extreme in trying to
13 be careful might also be giving the perception
14 to the public that the minute that you do any
15 work with pharmaceuticals or something of that
16 sort, you turn out to be an unethical
17 scientist.
18 I think that I am not sure the
19 provisions are being done to actually clarify
20 that to the public. I have been accused in
21 the past. I have never done any
22 pharmaceutical-funded research because the

1 public may not have agreed with my results.
2 And I realize that they are using that to be
3 equivalent to unethical behavior. I think
4 efforts should be made to clarify that to the
5 public.
6 CHAIRMAN COLLINS: So I appreciate
7 all of those comments. Cathy, certainly you
8 do sit in a chair where you see aspects of
9 this in ways that perhaps the rest of us are
10 not fully aware of in your role as JAMA
11 editor. This is a place where we must get our
12 house in order.
13 But, Beatrix, I appreciate your
14 pointing out that what we don't want to do
15 here is to come up with a system that
16 discourages scientifically worthy
17 collaborative efforts between the public and
18 the private sector.
19 What we need to be sure is that
20 they are done in a way where there is full
21 disclosure about what the arrangements are and
22 that there is not the appearance or the

1 reality of a financial conflict of interest in
2 the investigators who are NIH grantees who are
3 involved in those.
4 I think that can be achieved, but
5 you're right to point out the danger of going
6 too far and causing people to think that no
7 such relationships can be pursued without
8 ethical questions.
9 DR. DeANGELIS: If I may say, I
10 absolutely agree with this. I give this talk
11 called "Conflict of Interest" that I could
12 give someplace in the world every day, no
13 exaggeration because I have done it in five
14 countries in the last four months, in addition
15 to the United States. And, Beatrix, you are
16 right on target. And that is the danger.
17 The last slide I show is two
18 porcupines hugging and dancing. It's a card
19 my husband gave to me a long time ago. And I
20 can't imagine why.
21 CHAIRMAN COLLINS: Yes. What was
22 that about?

1 (Laughter.)

2 DR. DeANGELIS: Anyway, I show

3 that and say if these porcupines can obviously

4 work together so beautifully, certainly,

5 certainly scientists and clinicians can work

6 very closely with pharmaceutical companies and

7 certainly the NIH because without the

8 pharmaceutical companies and the for-profit

9 device companies, we would be still taking my

10 grandmother's brioche instead of something

11 good. So thank you.

12 CHAIRMAN COLLINS: Thank you.

13 So obviously very strong and

14 important feelings on this topic. And we will

15 continue to keep you apprised. But I do think

16 we're on the right path here towards a system

17 that is going to tighten this up in a way that

18 brings back the integrity and the credibility

19 of our system in a way that is desperately

20 needed right now.

21 I realize that so early in this

22 meeting I have already screwed up the agenda

1 by skipping over the legislative update.
2 Excuse me. So Roz Gray has a few minutes to
3 tell you what is going on in the legislative
4 arena, Roz being the Acting Director of OLPA.
5 And, by the way, these particular
6 handouts are to be found under tab 6, but you
7 will notice that they are now out of order
8 because of my having skipped over Roz. So
9 we'll come back to that. It's the first thing
10 under tab 6.
11 MS. GRAY: Good morning. I would
12 like to just give you a brief snapshot of what
13 congressional interest has been in NIH and
14 what our interactions have been with the
15 Congress over the past year.
16 This has been a really active
17 session for us, despite health care reform and
18 all of the focus on that. We have had 18
19 hearings in which NIH institute directors or
20 program people have participated.
21 There have been 21 courtesy
22 visits. I think Dr. Collins has done about

1 half of those just since August, 27 briefings
2 on various topics.
3 There have been three member
4 visits to NIH, the last of which was held in
5 early October, and there were 16 members and
6 19 staff, which is the largest contingent in
7 probably the last 25 or 30 years that any of
8 us can remember.
9 There have been 154 bills
10 introduced that either mandate something for
11 NIH or authorize us to do something, talk
12 about NIH being on a task force, or our
13 research informing various issues.
14 So it has been an active season,
15 which is pretty typical of what we see during
16 the first session of a congress. So this
17 isn't unusual.
18 Regarding health care reform,
19 which seems to be the focus over the last six
20 months, these are just topics that we are
21 watching that are of interest to NIH.
22 There is only one set that is

1 really research-specific regarding autism. It
2 would have the interagency task force working
3 with the Secretary on some training grants for
4 services. But, as you know, the Interagency
5 Autism Committee is chaired by an NIH
6 institute director.
7 I am going to skip over
8 comparative effectiveness. Emergency
9 medicine, pediatric and other age groups,
10 basic research to inform better outcomes. NIH
11 would be appointed to a health care quality
12 task force. Our pain management research
13 would be used to inform decisions about the
14 best way to treat people for pain.
15 Postpartum depression, there is a
16 continuation of certain kinds of research in
17 NIMH and also authorizing NIMH to do a study
18 on mental health issues resulting from a woman
19 resolving a pregnancy. And then there is a
20 large emphasis on prevention and wellness.
21 Regarding comparative
22 effectiveness, there are two models. You

1 probably know that there have been multiple
2 bills that have gone through multiple
3 committees. And now there is a House model
4 and a Senate model.
5 The House model would have the
6 center within AHRQ, with the trust fund funded
7 from caps on Medicare health insurance
8 premiums, some from the general fund, and a
9 variety of other sources.
10 It would establish a commission
11 outside that would provide oversight. It
12 would authorize AHRQ to conduct and support
13 CER research, develop research methodologies
14 and data resources, and establish some
15 advisory panels that would provide them with
16 some advice on the types of research that
17 would be done. And it would have them set
18 research priorities and an agenda.
19 Now, the Senate model has a
20 nonprofit institute that would be outside of
21 government with a similarly funded trust fund.
22 It has a governing board, probably similar to

1 the commission.

2 NIH would have a seat on both of

3 these, but on the governing board, there would

4 be a rather sizeable contingent of people

5 representing the drug industry.

6 It would also have some of the

7 similar authorities about conducting and

8 supporting research, et cetera. Agreements

9 with federal agencies, what the initial

10 legislation said was that this institute could

11 contract with federal agencies, which is

12 something that NIH doesn't have authority to

13 do. So that would have been a problem.

14 The new language says agreements

15 with federal agencies. So that opens up a

16 little broader avenue for funding, but it

17 would also set research priorities and

18 agendas. And there are a number of provisions

19 in there that are a little bit concerning to

20 the research community.

21 So what is the status of these?

22 Just to let you know how long this is going to

1 take, the House bill passed on November 7th.
2 The Senate bill is currently under
3 consideration, but they are working on
4 amendments to the legislation.
5 Then there has to be a conference
6 since the two bills are not similar. Then the
7 House and Senate will then pass their
8 conference bill or whatever comes out of
9 conference.
10 The President will have to sign
11 it. And the effective date, that is a moving
12 target because if you have got to set new
13 systems, new institutes, whether they are
14 inside or outside of government, it takes a
15 while. It may take six months. It may take
16 a year. So these things will not be
17 immediate.
18 What is the outlook? Unless there
19 is a miracle, there will not be a bill this
20 session. While we are concerned about the
21 research provisions, in the grand scheme of
22 health care reform, these provisions are just

1 a small piece. But there is no likelihood
2 that this will get enacted this session.
3 CHAIRMAN COLLINS: Tom?
4 DR. KELLY: So is this at the
5 point where there is some model being
6 discussed about how comparative effectiveness
7 research will be funded? Is this going to
8 come out of existing resources or is this
9 going to be new money or what is the thing?
10 MS. GRAY: It would be trust fund
11 money. They would be funded through trust
12 fund. Now, this wouldn't stop NIH from doing
13 its own CER the way we have been all along.
14 That comes out of our budget.
15 CHAIRMAN COLLINS: Yes. It's a
16 great question, Tom. As you know, the
17 Recovery Act gave NIH $400 million to do
18 comparative effectiveness research, which we
19 are using, I think, in interesting and
20 appropriate ways following up on the IOM
21 report about where the gaps are that most need
22 to be filled. But we do wonder about the

1 future.

2 Obviously the worst thing for NIH

3 would be an unfunded mandate, where we are

4 expected to continue to do this without any

5 additional streams of support.

6 The trust fund that Roz mentioned

7 is a potential new source, which would come

8 out of something other than appropriation.

9 This is a tap on health insurance plans and

10 which might, therefore, make it possible to

11 continue to do a lot of this effort without

12 taking money away from other meritorious

13 biomedical research.

14 Our greatest concern would be that

15 they would come up with this mechanism in such

16 a way that it was difficult or impossible for

17 those trust funds to actually find their way

18 to NIH research projects, hence the illusion

19 that Roz made about the initial version of the

20 Senate bill, where they talk about having this

21 nonprofit institute contract with NIH, which,

22 actually, we could not do. That would be

1 illegal.

2 So there has been some attention

3 paid to that concern. And we remain

4 optimistic that something will get worked out

5 here, although it is not exactly clear what is

6 going to happen.

7 And, again, this is a tiny little

8 piece in the view of the people in the

9 Congress of this huge health care reform bill.

10 And there has always been some concern about

11 whether it would just sort of get done without

12 paying attention to the details in order to

13 get the rest of this critical piece of

14 legislation through and signed by the

15 President.

16 And, of course, we are all in

17 agreement that health care reform is critical.

18 And, yet, this is turning into such a

19 complicated array of issues.

20 Ralph?

21 DR. HORWITZ: I want to reinforce

22 Tom's point as well, the question that he

1 asked. It does strike me that there is a
2 tremendous amount of work that needs yet to be
3 done around the fundamental methods that will
4 be used to effectively promote the kind of
5 research under comparative effectiveness
6 studies that would advance the health and
7 health care people.
8 And much of that expertise lies
9 within the NIH --
10 CHAIRMAN COLLINS: Sure does.
11 DR. HORWITZ: -- and its grantees.
12 And finding a way to ensure that NIH has a
13 prominent role there I think is an essential
14 part of the development.
15 CHAIRMAN COLLINS: Thanks. Agree.
16 And, of course, we have been working closely
17 with AHRQ as a partner. In fact, we have
18 weekly intense conversations with Carolyn
19 Clancy and her staff about comparative
20 effectiveness research.
21 And those who understand the
22 missions of our two organizations can

1 appreciate the synergy here between NIH, which
2 does primary research, and AHRQ, which has as
3 its major area of expertise doing secondary
4 analyses, particularly when there are multiple
5 studies that can be meta-analyzed together.
6 But not everybody on the Hill
7 seems to understand those different roles.
8 And I think if we are going to have an
9 effective output here of CER, it is going to
10 need to be sure that there is a recognition of
11 where the strengths are of both of these
12 agencies.
13 Yes? Colleen?
14 DR. CONWAY-WELCH: I just wanted
15 to point out the recent media disaster on --
16 CHAIRMAN COLLINS: I don't know
17 what you are talking about.
18 (Laughter.)
19 DR. CONWAY-WELCH: And when I
20 initially read about comparative effectiveness
21 research, I was very pleased because it makes
22 such logical sense. But it is not being

1 well-translated to the public.

2 And I hope that the media folks at

3 NIH and AHRQ work together to figure out how

4 to craft this message because right now it is

5 not going in the right direction.

6 CHAIRMAN COLLINS: Well, we

7 certainly would agree that the mammogram

8 controversy over the last couple of weeks has

9 not been a good model of how to take what is

10 supposed to be scientific, objective

11 conclusions and translate them into

12 recommendations that the public could embrace.

13 And the amount of contentiousness this has

14 raised has really been quite distressing to

15 watch.

16 NIH as the research organization,

17 not the standard-setting organization, has

18 largely been in the role of trying to provide

19 information about what the facts are. But

20 obviously it has been a difficult interval, to

21 be sure.

22 I think in ability on the part of

1 the task force to perceive just what a hand
2 grenade they were flinging into the
3 circumstances around this issue has not been
4 a helpful model of where we should go the next
5 time.
6 Well, thank you. Oh, I'm sorry.
7 One more. Barbara?
8 DR. WOLFE: The point that I
9 wanted to make is not this, but it is a good
10 opportunity for a teaching moment. So someone
11 who has used this in the classroom, it is not
12 all the negative.
13 The question I wanted to raise,
14 which maybe I can answer myself, is that we
15 talk about comparative effectiveness. But as
16 an economist, that is really sort of step one.
17 And one would think that we would want to look
18 at cost-effectiveness.
19 I know it gets more controversial,
20 but, nevertheless, I would like you to say
21 something about the process and whether you
22 see any potential for going that way.

1 I mean, we have two parts of the
2 conversation. We talk about ways to reduce
3 the cost or the increasing costs of health
4 care. And then we turn and we say, "But we
5 can't do cost-effectiveness research," which
6 seems like we are quite inconsistent.
7 CHAIRMAN COLLINS: Well, there's a
8 political component to this, where
9 cost-effectiveness is clearly a third rail
10 that a lot of people don't want to touch.
11 And there is, frankly, a
12 scientific research question about, are there
13 models for assessing health care delivery
14 incentives that might actually be worth
15 knowing about?
16 The first meeting I convened as
17 the NIH Director was a small brainstorming
18 meeting of health economists, Alan Garber,
19 David Cutler, Mark McClellan, Eric Lander. We
20 had two or three hours. Well, he's
21 everything, you know.
22 (Laughter.)

1 CHAIRMAN COLLINS: We had a two or
2 three-hour pretty interesting discussion. And
3 we will follow up on that with a larger
4 conversation because I do think there is an
5 opportunity here for NIH to consider funding
6 some interesting research about even things
7 such as how do you model incentives for
8 providers in order to result in good outcomes
9 but also cost-effective models that would
10 reduce the likelihood of focusing all of the
11 attention on what tests you order and focus,
12 instead, on the outcome for the patient. So
13 we are going to be involved in this in
14 whatever way we think scientifically makes the
15 most sense.
16 Okay. Thanks, Roz. Well, yes,
17 James?
18 DR. THRALL: I think there's a
19 fundamental issue related to how we
20 conceptualize evidence-based medicine. If we
21 think it is a scientific endeavor, we are
22 going to be disappointed. It is really where

1 science and social utility come together. I
2 think part of the problem with the mammography
3 screening issue is the failure of
4 understanding of that interface.
5 CHAIRMAN COLLINS: I think that's
6 very well-put.
7 Okay. I know we are falling a
8 little behind on our agenda. I am not too
9 surprised. These are topics everybody has a
10 lot of interest in.
11 I am going to ask Raynard Kington
12 now to tell us all where we stand with the
13 funding through the Recovery Act, an important
14 part of what NIH has been up to for the last
15 several months.
16 DR. KINGTON: Thank you.
17 I'll try to go quickly. As all of
18 you know, ARRA appropriated $10 billion
19 directly to NIH. This diagram just
20 illustrates the various components, 300
21 million for extramural scientific equipment,
22 shared instrumentation, another $500 million

1 that went to NIH for construction on our
2 campus, another $1 billion for extramural
3 constructions and improvements on your
4 campuses, and then $8.2 billion for extramural
5 science.
6 Of that, about $800 million went
7 to the Office of the Director. $7.4 billion
8 was spread proportional to base budgets, to
9 the institutes and centers and the common
10 fund.
11 In addition, as was just alluded
12 to, $400 million went to NIH via AHRQ for
13 comparative effectiveness research. There are
14 two broad approaches to allocation of these
15 dollars: one, to support new mechanisms; and,
16 two, to accelerate existing science. For
17 supporting new mechanisms, we funded existing
18 applications that had been peer-reviewed and
19 found to be meritorious by councils and were
20 amenable to two-year funding.
21 We also allowed selectively
22 competitive supplements where applications

1 were submitted to extend existing grants
2 beyond the current specific aims. And then
3 there were NIH-wide and a smaller number of
4 ISE-specific solicitations.
5 And, finally, for acceleration of
6 existing programs, we used our existing
7 administrative supplements program, including
8 a summer program geared toward hiring students
9 during the Summers of '09 and '10. I will
10 talk a little bit more about that later.
11 This slide just illustrates the
12 breakdown across those various sources, uses
13 of funds, for the grant component of the '09
14 funding commitments. Of course, almost all of
15 these commitments were for two years.
16 So this, although it was
17 technically just an obligation for '09, there
18 was a commitment to an almost comparable
19 number for '10. About 26 percent of the funds
20 went to new, competing applications through
21 solicitations; 32 percent went to pay line
22 extensions; a small percentage, 5 percent, for

1 competitive, so-called competitive, revisions,
2 where you could submit a competitive,
3 peer-reviewed application to go beyond
4 specific aims.
5 CHAIRMAN COLLINS: By the way,
6 there's a typo. That should be billion, not
7 million, at the top of the slide, just in case
8 you're worried about what we were doing here.
9 DR. KINGTON: Yes.
10 Billion/million.
11 (Laughter.)
12 DR. KINGTON: It was billion, as
13 the President noted when he was here.
14 Administrative supplements, about 35 percent.
15 And then summer supplements of one percent.
16 This was a program that was geared toward
17 hiring ultimately about 5,000 summer students
18 from high school through college during '09
19 and '10.
20 This gives you just a broad
21 breakdown of the number of applications and
22 the success rate across some of the road

1 map-specific solicitations, Challenge Grants
2 Program, which generated a huge response, a
3 little over 20,000 applications.
4 Ultimately we substantially
5 increased the commitment of funds, but even
6 with that commitment, we were only able to
7 fund about four percent of applications. And
8 we anticipate that some percentage of the
9 unfunded applications will be resubmitted at
10 some point.
11 For the grant challenges, a
12 somewhat similar number of applications.
13 These were more targeted in that they were for
14 broader, bigger projects. And also while
15 there were topics that were identified, they
16 could also be on topics that were not
17 specifically solicited by institutes, centers,
18 success rate of about 19 percent.
19 There was a targeted solicitation
20 to encourage recruitment of new faculty.
21 About 25 percent of the 141 applications were
22 funded. And the Administrative Supplements

1 Program specifically targeted towards summer
2 research experiences received about 1,300
3 applications and overall about 4,900 slots.
4 It was hard to calculate a real success rate
5 there, but 4,900 slots were committed to for
6 '09 and '10.
7 In terms of CER, this just breaks
8 down across those mechanisms how many grants
9 were funded for comparative effectiveness
10 research. These funds came from the $400
11 million that were funneled through AHRQ.
12 With regard to common fund, again,
13 this was in the Office of the Director. It
14 received a proportionate amount of the dollars
15 and spread across these various mechanisms as
16 well to existing programs or opportunities
17 that were consistent with the mission of the
18 common fund.
19 There are a number of F.Y. '10
20 solicitations that are in the various stages
21 of being awarded. The first two, the RC3 and
22 R43, are both efforts to try to explore new

1 models for supporting small businesses.

2 The R15 is an existing program for

3 area program that targets dollars to

4 institutions that historically have not

5 received a lot of NIH funding.

6 There is a new solicitation

7 specifically geared toward building

8 infrastructure, linking academic health

9 centers and communities, particularly with

10 resources that are already funded by the

11 Department, such as community health centers

12 and senior centers.

13 There are a number of other

14 institute-specific solicitations. This just

15 lists NCRR, NIAID, and a few others as well.

16 And, if you would like to have alerts for

17 those, you can go to grants.nih.gov/recovery.

18 Obviously these dollars have

19 broader intended impact, perhaps broader than

20 we usually have. The prominent goal is to

21 stimulate the economy in the short run, to

22 create and preserve jobs but also to be a

1 smart, long-term investment for the American
2 people in the biomedical research enterprise.
3 There has been unprecedented
4 reporting. And several Web pages provide
5 pretty ready access to the first stages for
6 reporting from the institutions that receive
7 these dollars.
8 In many ways, our institutions
9 were better prepared because there was already
10 a fair amount of reporting. It was perhaps
11 more painful reporting, but they knew how to
12 report.
13 And we had, I think, among the
14 highest success rates in terms of institutions
15 that needed to report how actually reported
16 data. You go to recovery.gov. You can also
17 go to NIH's Web page for
18 report.nih.gov/recovery.
19 And we have a number of tools
20 there which allow you to look across states
21 and congressional districts, institutes, and
22 centers, and see exactly which grants were

1 funded under ARRA dollars. This has been used
2 widely. And we encourage you to go there to
3 track if you would like information about what
4 dollars are going to your state or to your
5 institution.
6 You can also drill down to the
7 precisely grants that were funded. In many
8 ways, we were well-prepared for this increased
9 transparency because the Office of Extramural
10 Research had already made substantial
11 investments in tools that would allow the
12 extramural community to see in more detail
13 what grants we were supporting.
14 Finally, I want to thank both the
15 broader scientific community, who without a
16 doubt sort of rose to the occasion with these
17 solicitations, but also NIH staff, who
18 postponed vacations and travel and really put
19 in heroic amounts of work to make sure that
20 these dollars were obligated wisely and
21 efficiently. And they deserve an
22 extraordinary amount of credit for really

1 heroic work. And I'll stop there.

2 CHAIRMAN COLLINS: Thanks,

3 Raynard.

4 Questions for Raynard?

5 (No response.)

6 CHAIRMAN COLLINS: All clear?

7 You're still resting from writing all of those

8 applications? That was quite a year. All

9 right. Thank you. Thank you.

10 Well, it really was an amazing

11 amount of work done by NIH staff to make it

12 possible for that kind of volume of grant

13 applications and decisions to be made.

14 I spent a lot of my first six

15 weeks as NIH Director reading a lot of these

16 grants because I wanted to see just how had

17 this worked out having this opportunity for

18 pent-up innovative ideas to come forward

19 because, of course, we had gone through a

20 five-year period of flat budgets with

21 declining success rates.

22 And it was clear the community was

1 anxious for the chance to show their stuff.
2 And to read through those was indeed quite
3 exhilarating, fantastic ideas from
4 investigators through many different
5 disciplines.
6 And so I think we will be able to
7 say what we got with the Recovery Act dollars
8 is really exceptionally wonderful science and
9 also creation of some economic stimulation
10 since each NIH grant on the average creates
11 about seven jobs.
12 DIRECTOR'S VISION FOR THE NIH
13 CHAIRMAN COLLINS: Well, I want to
14 spend a little time with all of you this
15 morning outlining some areas that I think are
16 particularly exciting right now for NIH going
17 forward and to see your reaction to some of
18 these ideas. And so I was going to outline
19 for you a few areas, themes, if you will, that
20 seem ripe for further exploration.
21 You will see that they are rather
22 broad and touch upon virtually all diseases

1 and all institutes but perhaps represent
2 circumstances that we have arrived at special
3 opportunities.
4 So let me begin, though, by saying
5 that this has been a pretty wild ride, this
6 first 115 days. In trying to figure out what
7 the right metaphor is, well, it is sort of
8 like this. That would be the kid drinking
9 from the fire hose except I don't think it
10 quite does justice because it really feels
11 like drinking from a fire hose while riding a
12 roller coaster because there are so many
13 things coming at you every day.
14 The staff here is phenomenal. And
15 the science is truly exciting. And we have
16 had some very exciting moments during the
17 course of these 115 days, one of which was on
18 September 30th, when President Obama, whom I
19 serve with great honor and delight because he
20 is somebody who really cares about science,
21 came out to NIH and spent some time. You see
22 him here in the laboratory. At that

1 particular moment, Tony Fauci is telling him
2 about new developments in HIV/AIDS research.
3 Secretary Sebelius, who came along
4 and actually then spent several hours with us,
5 including going to the clinical center and
6 seeing a patient and then talking with the
7 institute directors about areas of
8 particularly high scientific interest, also
9 was present for this.
10 I had the chance to teach the
11 President some things about cancer genomics
12 and to find out just what an amazingly sharp
13 intellect we have in the White House in terms
14 of the questions he asked, the way in which he
15 could perceive immediately the consequences of
16 some of these developments.
17 It was a very good day. He came
18 and gave a speech in Masur Auditorium, which
19 I hope maybe some of you had a chance to see
20 on the Web.
21 It was a well-crafted,
22 exhilarating, inspiring presentation about the

1 value of science for the future of our nation
2 and our world and certainly electrified the
3 people who were able to be there filling that
4 auditorium with about as much energy as I have
5 ever seen.
6 So let me just say in terms of
7 what NIH aims to try to do, we need to reflect
8 back upon our dual role here. We are science
9 in pursuit of fundamental knowledge about the
10 nature and behavior of living systems and also
11 about the application of that knowledge to
12 extend healthy life and reduce the burdens of
13 illness and disability. It is a pretty broad
14 but I think pretty appropriate mission
15 statement for what this organization has done
16 and will do.
17 I know many people hearing that
18 the Genome Institute Director was coming to
19 the helm worried that that might mean that
20 this was all going to turn into top-down big
21 science at NIH.
22 I want to reassure all of you, as

1 I have been doing in various public
2 presentations, as I will do tomorrow in San
3 Diego at the cell biology meetings, that, in
4 fact, I do believe that the foundation of NIH
5 in terms of its success, in terms of its
6 contributions and amazing advances in science
7 comes from the ideas from individual
8 investigators driven by a hypothesis that they
9 have come up with in pursuing their creativity
10 and the energy in the best possible way to
11 learn new things about how life works and how
12 disease comes about.
13 We will not stray away from that.
14 At the same time, I think it has been true
15 that there are circumstances where organized
16 projects that no single investigator could
17 accomplish can empower all of the RO1
18 investigators.
19 And we should not be shy to
20 identify such opportunities and then do so in
21 a fashion that produces data of very high
22 quality and make it immediately accessible to

1 those who need access to it. So getting the
2 balance right is always an important issue.
3 And I'm sure it will continue to be.
4 As I talk about five
5 opportunities, then, I would not want you to
6 think that these are intended to be areas
7 where big science is the answers. Although
8 there are some big science projects in here,
9 a lot of what really needs to happen is
10 individual investigator-driven.
11 So let me go through these five
12 themes fairly quickly. And then I will be
13 glad to hear your thoughts. The first of
14 these is to take the unprecedented
15 opportunities that have arrived recently with
16 various types of high-throughput approaches to
17 understand fundamental biology and to uncover
18 the causes of specific diseases.
19 What am I talking about?
20 Obviously a bunch of this now is coming from
21 genomics and particularly from the remarkable
22 advances in sequencing technology, so-called

1 next generation or next gen DNA sequencers,
2 which allow you to collect truly prodigious
3 amounts of data, not only by genome sequence,
4 but in many ways, this kind of sequencing
5 technology is threatening to take over what we
6 previously used hybridization platforms for
7 and replaced that with the kind of digital
8 data that one can obtain from these high
9 throughput sequencers.
10 That's, however, not the only
11 technology that is in this circumstance of
12 great opportunities. Nano technology, we have
13 a nano medicine component in the road map
14 right now that is looking interesting; small
15 molecule screening, about which I will say a
16 little bit more in minute; new imaging
17 modalities, going all the way from single
18 cells to organs or organisms.
19 And the opportunity that this
20 presents to work on comprehensive approaches
21 that ask questions that have the word "all" in
22 them, what are all of the proteins in the

1 cell? What are all of the components of the
2 immune system? What are all of the variations
3 in the genome that are associated with a
4 particular disease risk?
5 And for all of these things,
6 computational biology is going to be
7 absolutely critical. And if I have an anxiety
8 about where we are going, it's that I still
9 don't think we have nearly the kind of
10 capabilities, both in terms of trainees and
11 increasingly even in hardware, that are going
12 to be necessary to handle the very large data
13 sets that are coming out of many of these
14 projects and that have great nuggets of truth
15 to be mined from them but only if you have the
16 approach to do so.
17 There are many examples I could
18 point to that are ripe for this kind of
19 expanded effort with this particular theme.
20 And two of them were mentioned as actually
21 priorities of the administration: cancer.
22 The Cancer Genome Atlas, which is

1 now ramping up to derive the variations that
2 occur, somatic mutations in the 20 most common
3 cancers, is going to totally change our
4 understanding of the landscape of cancer.
5 Autism I think also if we could,
6 in fact, derive complete genome sequences on
7 a significant number of autistic kids and
8 their parents, we might begin to understand
9 what the genetic contributions really are
10 here, recognizing there is a lot of
11 heterogeneity here at the DNA level and, of
12 course, not implying that this is a genetic
13 disease because clearly there is an
14 environmental component that is critical as
15 well.
16 The microbiome, which is a project
17 already underway learning about all of the
18 microbes that live on us and in us and using
19 these same tools to identify organisms that we
20 can't culture but they have nucleic acid and
21 we could learn about them in this way, this is
22 going to be fascinating.

1 There are more microbes on us and
2 in us if you count up their cells than our own
3 cells. They have got us outnumbered. So we
4 had better learn more about them than we
5 currently know.
6 Second opportunity, moving now
7 more into the translational arena, is how to
8 take all the amazing basic science discoveries
9 in virtually all diseases that are pouring out
10 of laboratories and making sure we are doing
11 the best job of building a bridge from that
12 basic research effort into drug development or
13 therapeutics of other sorts.
14 This photograph probably doesn't
15 look too familiar, but it looks a little
16 different today than when this picture was
17 taken because that is how you now get across
18 from the left to the right on a bridge. And
19 we need to build that kind of bridge as
20 effectively as we can for diseases.
21 Now, many people would say that is
22 the business of the pharmaceutical and biotech

1 industry. And that is certainly true in
2 circumstances where there is a sufficient
3 economic incentive to build such a bridge.
4 But if you want to talk about rare
5 diseases or diseases of the developing world,
6 where the market may be relatively small, then
7 maybe NIH investigators could be empowered to
8 play a more significant role in helping to
9 build that bridge, feeding the pipeline, if
10 you will.
11 You will hear more about that from
12 Chris Austin this afternoon, but, just
13 briefly, I think the stage is set for NIH to
14 play an expanded role in this kind of
15 translational activity.
16 There are all these new
17 discoveries about fundamental basis of
18 disease. New drug targets are turning up in
19 great numbers from genome-wide association
20 studies and other sources.
21 I think the idea here would be to
22 empower academic investigators to at least

1 start down that pathway using small molecules
2 or biologics or stem cells to develop lead
3 compounds or lead approaches and effectively
4 de-risk projects to the point where they
5 become attractive for the private sector to
6 license. And so there is a real opportunity
7 here for public-private partnerships.
8 Small molecules is certainly an
9 area that NIH is increasingly invested in. We
10 have now these four large-scale screening
11 centers, one of which is here in Rockville and
12 has the capacity of a mid-sized pharmaceutical
13 company.
14 And out of that have come a whole
15 variety of really fascinating findings in the
16 research arena but some of which could go
17 further into the so-called valley of death,
18 the preclinical phase.
19 As common diseases increasingly
20 are seen as a collection of rare diseases, the
21 importance of doing this is only growing by
22 the day.

1 Here, of course, I must also point
2 out -- and we're going to be talking about it
3 in a very important session at this meeting in
4 the near future -- the value of pushing
5 forward the stem cell research arena with the
6 new information that is likely to come out of
7 research with the policy that is now being
8 implemented, allowing federal funds to be used
9 for approved human embryonic stem cell lines.
10 And with all of the advances that
11 are coming out on induced pluripotent stem
12 cells practically every week, I think we are
13 all very excited about seeing where this goes
14 and still not sure what the therapeutic
15 implications are going to be.
16 And the degree to which that can
17 be pushed forward in both extramural and
18 intramural environments it seems to me should
19 be a very high priority to really find out
20 what the potential is here so that in a few
21 years, we won't still be saying, "Well, we
22 can't tell you for sure what the promise may

1 be.

2 Maybe in a few years we will

3 actually have some data on clinical

4 applications and what exactly the problems and

5 the potential there might be.

6 The third opportunity of my five

7 is actually to put science to work on health

8 care reform given the importance of this to

9 our nation and the way in which NIH is being

10 looked to to provide the kind of evidence that

11 would guide decision-making. We embrace that.

12 And I think we should pick carefully the kinds

13 of areas that are most in need of attention

14 and go after them.

15 Comparative effectiveness research

16 is a part of this. And we have already talked

17 about that in an earlier conversation. Some

18 of that also ought to be devoted not just to

19 comparing therapeutics for people with illness

20 but also comparing approaches to prevention

21 and trying to understand whether the

22 personalized approach to prevention does, in

1 fact, provide benefits, as opposed to one size
2 fits all. And you can't do this effectively
3 without getting deeply engaged in behavioral
4 research and trying to understand what it is
5 that motivates health behavior changes.
6 If we want to be effective in
7 designing the health care system of the
8 future, then it has to take account of this
9 terribly important issue of health
10 disparities. And so this is certainly a
11 significant part of this third theme, to
12 figure out how to design research projects
13 that will both identify and provide potential
14 solutions for health disparities, studying
15 both the environment, genetics, whatever role
16 each one plays.
17 Pharmacogenomics is in here as
18 well and a very exciting area at the present
19 time. Large-scale prospective studies, like
20 the national children's study and perhaps
21 whether we should consider engaging in a study
22 like the U.K. has, their biobank study, which

1 is on the path towards collecting clinical
2 information, DNA samples, and lots of
3 laboratory tests on half a million people,
4 should we consider initiating something of
5 that sort in the U.S. de novo or at least
6 cobbling together some of the prospective
7 studies that are underway for specific
8 diseases to try to achieve something along
9 this line?
10 I have a personal view that this
11 could be one of the greatest discovery engines
12 for the future. Although it would be an
13 expensive undertaking, it might well be worth
14 it in terms of what we would learn and the way
15 in which it could stimulate a whole host of
16 case cohort studies that would flow forth from
17 it.
18 Health IT, an area where, again, I
19 think some research efforts, particularly to
20 guide the way in which health IT is going to
21 be implemented in this country, would be
22 valuable. And I have mentioned already health

1 research economics and the importance that we
2 attach to studying the health care delivery
3 and including things like payment incentives
4 to look at ways to reduce costs and improve
5 outcomes.
6 The fourth of the five themes is
7 to encourage a greater focus on global health.
8 I think many of us who have increasingly
9 perceived the opportunities, particularly in
10 this administration, for the U.S. to play a
11 role in the propagation of soft power, or, as
12 Secretary Clinton calls it, smart power, would
13 like, I think, to embrace the idea of using
14 some of our resources to study diseases and to
15 provide possible solutions in terms of
16 prevention diagnostics and treatments for
17 conditions that affect primarily people
18 outside our own borders.
19 It has certainly been a personal
20 passion of mine for some time. And I think
21 the science here is going in the direction of
22 providing some real opportunities.

1 The scientific advances make an
2 attack possible in diseases that have
3 previously not had much work done on them
4 because we are learning a lot about pathogens.
5 We have genomic sequences on lots
6 of these. We have the opportunity for small
7 molecule screening from some of the faculties
8 I have previously mentioned, RNAi screens to
9 identify good targets, and vaccine
10 development.
11 This could allow us to go beyond
12 AIDS, malaria, and tuberculosis, although we
13 need to do more work there as well to also
14 begin to approach in a more intentional way
15 some of the other neglected tropical diseases,
16 like schistosomiasis or trypanosomiasis, that
17 affect hundreds of millions of people
18 worldwide.
19 And let me say this is not
20 something that should be limited to infectious
21 diseases because obviously the greatest area
22 of growth, unfortunately, in terms of disease

1 in the developing world is in noncommunicable
2 diseases, such as tobacco-related disease,
3 heart disease, and so on.
4 So I think while this is something
5 that we are currently trying to figure out
6 where the gaps are and make sure we make wise
7 investments, I would like to see NIH and its
8 investments in global health increase in the
9 coming years.
10 We are having a meeting on January
11 6th, inviting to that high-level leadership in
12 the global health arena from the Gates
13 Foundation, from the Wellcome Trust, from a
14 variety of other philanthropies, from the
15 State Department, U.S. AID, and WHO. And we
16 hope to in the process sort of lay out a
17 pretty good landscape of what currently is
18 being invested in and try to see what
19 opportunities have not received the attention
20 that they might.
21 And, finally, none of this is
22 going to happen unless we have a vigorous and

1 energetic and innovative biomedical research
2 community.
3 Many of you I know would share the
4 concerns that have been expressed by a lot of
5 people about whether our system of peer
6 review, though it is the envy of the world in
7 terms of the way in which we identify
8 meritorious research, can sometimes tend to be
9 too conservative.
10 And people with out of the box
11 ideas may find that without having already
12 done the research, they aren't going to get as
13 well-received by a study section as they
14 should be.
15 We have over the course of the
16 last few years and led by Dr. Zerhouni, come
17 up with a number of mechanisms to try to
18 encourage that sort of innovation.
19 The Pioneer Award you see here is
20 one of them. There are others; the new
21 innovator awards and the transformative R01s,
22 which we have now funded each of these, at

1 least in the first cycles.

2 And, again, these were grants that

3 I spent a fair amount of time reading in the

4 course of my first few weeks. They are really

5 interesting. And they are high-risk

6 enterprises, but that is just the kind of

7 thing that we should be spending a significant

8 chunk of our portfolio on.

9 I should tell you these three

10 award types now have swollen in a good way to

11 occupy one-third of the common fund. So the

12 common fund, which is a significant part of

13 NIH's ability to invest in things that no

14 single institute might be able to do, supports

15 a number of large projects but now at this

16 point also is very heavily invested in these

17 high-risk, high-reward grant mechanisms for

18 individual investigators.

19 The first bullet here, though, I

20 just want to linger on for a moment. You all

21 are no doubt aware of what we are facing in

22 terms of the F.Y. '11 budget situation. The

1 Recovery Act dollars, which we were required
2 to spend in a two-year period with a few
3 exceptions, where we were able to get
4 permission for multi-year funding, but the
5 vast majority of the $10 billion given to NIH
6 has to be spent in F.Y. '09 and F.Y. '10.
7 Of course, we have revved up a
8 wonderful engine of discovery; as a
9 consequence of that, all of the challenge
10 grants and all the grand opportunity grants
11 that got funded, wonderful science, but just
12 for two years.
13 And those who have made real
14 progress are going to come back hoping to
15 continue their work. Those who applied and
16 didn't quite make the cut are going to come
17 back with revised grant applications.
18 So we expect in F.Y. '11 we are
19 going to have an exceptionally large number of
20 grants coming to us. What will be the ability
21 to support those? That is not currently
22 known.

1 The F.Y. '11 budget is currently
2 under the deliberative process. And the
3 administration will be announced by the
4 President in early February. And then the
5 Congress will need to deliberate upon it.
6 But there seems no question that
7 the likelihood of being able to have the same
8 annual budget that we have had in '09 and '10
9 with that extra money from Recovery Act is not
10 high at all. In fact, it is unlikely that
11 that will be possible.
12 So how, then, will the community
13 adjust to this? And how can NIH try to soften
14 what is otherwise going to be a very difficult
15 year with success rates that might fall to
16 historic lows? There are no easy answers to
17 this.
18 And, again, this is the thing that
19 keeps me awake at night more than anything
20 else is how do we take all of these scientific
21 opportunities that I have been talking about,
22 which are breathtaking in their scope?

1 And all of these investigators who
2 are pursuing those ideas, many of whom came on
3 board because of the opportunities of the
4 Recovery Act, keep the community going.
5 In addition to that, I think we do
6 need to pay attention to our peer review
7 process and whether the current innovations
8 have been put together to try to be sure we
9 are focused on appropriate criteria for review
10 are working.
11 The common fund, which I have
12 mentioned, I am paying a fair amount of
13 attention to in terms of how we identify
14 projects that should get onto the on ramp and
15 get included in this very important part of
16 the NIH portfolio.
17 And training programs, like all of
18 you, I continue to worry about the way in
19 which our training efforts, while we are
20 bringing on board talented young scientists,
21 we are not doing a terribly good job of giving
22 them a chance to become independent as quickly

1 as possible.

2 The average age at first grant

3 award of an independent sort, R01 or

4 R01-equivalent, stands at age 42. That cannot

5 be the right answer.

6 Do we need more programs; for

7 instance, like that pioneered at the Whitehead

8 and I think now implemented at several other

9 places, where we take particularly promising

10 graduate students and move them directly into

11 independent positions, giving them good

12 mentorship and some resources and allowing

13 them to begin to pursue their own ideas

14 without going through a period of four to

15 sometimes seven or eight years as postdoctoral

16 fellows, which is not in every instance the

17 right thing.

18 What do we think is the right

19 number of graduate students and postdocs and

20 tenure track faculty? And are we making a

21 mistake -- I think we probably are -- by

22 focusing so much of our attention on that as

1 the only successful pathway for scientific
2 trainees and perhaps undervaluing all of the
3 other ways in which well-trained scientists
4 can contribute to future discoveries? I think
5 this is a very tough question about how to
6 come up with such an analysis that could be
7 justified, but we are somewhat vulnerable by
8 not having a good answer to that question.
9 If we are suggesting that we need
10 more trainees, okay. Well, how many more? If
11 we are suggesting that we need more faculty
12 recruits -- and we have just stimulated some
13 of that with the Recovery Act. And I believe
14 that is right, but what is the trajectory we
15 are aiming for. What would be the landscape
16 of a healthy research community?
17 So let me finish by just saying a
18 few words to all of you, my Advisory
19 Committee. And a very critical Committee this
20 is indeed, one that I am going to be counting
21 on a lot in the coming months and years to
22 provide wise advice about a host of complex

1 issues that come across the Director's desk.
2 Certainly the focus during the
3 last now some 44 years that this particular
4 organization has been in place is program
5 development, resource allocation,
6 administrative regulation and policy, and
7 almost everything else.
8 As I have been here now for three
9 months, when a complicated issue comes up
10 where I think I need advice, oftentimes the
11 question is, well, maybe the ACD ought to get
12 engaged in this. And, of course, the stem
13 cell conversation we are going to have shortly
14 is a concrete example of that in this
15 particular meeting cycle.
16 The ACD has over the course of
17 time provided perspective, feedback, expert
18 advice, and you represent a critical link
19 between NIH and the biomedical research
20 community.
21 Some of the areas of discussion
22 and deliberation we have already talked about.

1 And some of these no doubt will come back
2 again at other times. But you can read the
3 list here of issues that have been
4 deliberated.
5 I expect over the course of the
6 coming months that there will be several
7 others that we will need your help on. And I
8 think we will follow the tack that has been
9 done in the past when those happen to try to
10 set up a subcommittee of the ACD to identify
11 one or two members of the ACD to serve on that
12 subcommittee.
13 And I hope you will be willing to
14 do that when asked, to deliberate more
15 intensively than the ACD as a whole can do
16 about that issue and then bring back findings
17 to the group to deliberate upon and to make
18 recommendations to me.
19 Because this is a Committee that
20 is chartered through the Federal Advisory
21 Committee Act, you are required to hold your
22 meetings in public, as we are doing today.

1 And we strongly agree with that.
2 But we also are able to set up working groups
3 or subcommittees that can deal with specific
4 topics and then can come and present their
5 findings to the group as a whole, as we will
6 do today with stem cells. And that has turned
7 out to be a pretty effective way to get work
8 done.
9 So I don't think I could tell you
10 at this very moment what the next list of
11 tasks will be, but there will be tasks. I do
12 appreciate because you are not jumping up and
13 running from the room your willingness to
14 consider being involved in some of those
15 subgroups as those needs come along.
16 I hope that you would agree with
17 me that this is a time for boldness, that this
18 is a time where medical research has great
19 promise to help the human condition in our
20 nation and in the world, that we will have
21 many stresses upon us, perhaps most visibly
22 the budget but many others as well, but that

1 collectively as people with passion and belief
2 in the value of what we do, we have a lot to
3 offer.
4 And we are fortunate at the
5 present time to be in an administration that
6 believes in science, believes in the ability
7 of science to address and even solve pressing
8 problems of the world. And we shouldn't be
9 shy to step forward and say we are ready to
10 take those on when we have the tools to do so,
11 even if it means at times that we have to take
12 something on that we're not sure we can
13 succeed at.
14 And so I will finish with my
15 favorite quotation from poet James Russell
16 Lowell, "Not failure but low aim is a crime."
17 We don't intend to aim low at NIH in the
18 coming months and years. And I hope you will
19 help me with the aiming high part.
20 Thank you very much.
21 (Applause.)
22 CHAIRMAN COLLINS: I am going to

1 come back and sit down and then listen to your
2 comments and discussion. So questions,
3 comments? John?
4 DISCUSSION
5 DR. NELSON: Thank you very much
6 for that report, outstanding. And you bring
7 an amazing amount of energy and perspective.
8 I appreciate that.
9 I want to ask this question
10 carefully because I am trying to put it
11 together in my own mind. You did a good job
12 of speaking broadly. I would like to speak
13 broadlier.
14 I would like to know how NIH
15 should, might, or could deal with issues that
16 are larger, such as the public health issues,
17 clean air, clean water, toxic waste, et
18 cetera. And at the same time, as part of that
19 question, ask, how do you intend or might it
20 be appropriate to consider reaching out to
21 other agencies within the federal government
22 and private groups to partner so we get bigger

1 bang for the buck?

2 CHAIRMAN COLLINS: It's a great

3 question, John. And it is actually one of my

4 own personal passions and priorities as well,

5 to be sure that we are reaching out and

6 building strong relationships with other parts

7 of the government.

8 Yesterday, for instance, I met

9 with Roger Beachy, who is the new Director of

10 the National Institute for Food and

11 Agriculture. We had a very interesting

12 conversation about ways we could work together

13 on food and nutrition and on global health

14 issues that are also part of his agenda.

15 Earlier this week I met with Steve

16 Koonin, who is the Under Secretary in the

17 Department of Energy. And we had a really

18 interesting conversation there about areas

19 where we could work together on biofuels and

20 on certainly our common interests that relate

21 to things like beam lines for doing structural

22 biology, which is a critical part of our

1 relationship, and on genomics, so lots of
2 things going on there that we could build on.
3 This global health meeting that I
4 mentioned in January will involve several
5 other parts of the government, especially the
6 State Department, which has such a critical
7 role now in the global health initiative, very
8 large and multibillion-dollar, $63 billion,
9 going into this over the course of the next 5
10 years. And we want to be sure that we
11 understand all of the ways in which that can
12 be coordinated.
13 Even within the Department, we
14 could strengthen our relationships with other
15 agencies. Tom Frieden, the head of the CDC,
16 brought no less than about eight or nine of
17 his senior staff to NIH. And we had a
18 half-day, a very interesting meeting just two
19 weeks ago, with him and cooked up a bunch of
20 new ways that we could work together on things
21 like tobacco and obesity and comparative
22 effectiveness research and cardiovascular

1 disease and a whole host of other things as
2 well.
3 And with Peggy Hamburg now as our
4 Commissioner of FDA, Kathy Hudson and I have
5 been meeting regularly with her on issues like
6 genetic testing oversight and the opportunity
7 to come up with a research agenda for
8 regulatory science, which also could use some
9 interesting new ideas about how do you design
10 clinical trials in new ways for things like
11 combination therapies for cancer or rare
12 diseases, where you have only a few patients
13 that can actually be signed up.
14 So I think you are quite right to
15 point this out. And I think it hasn't always
16 been the case that parts of the government
17 have taken advantage of opportunities that
18 they might have done together and everything
19 we could do, especially if budgets are going
20 to be tight, to try to make the most of those
21 synergisms we will be doing. Thanks.
22 Yes, Karen?

1 DR. HOLBROOK: Well, thank you
2 very much for your ideas and your thoughts.
3 One of the things I have seen NIH do
4 repeatedly over the years is be very timely
5 and pick up issues that are very important
6 with time.
7 I think there is one issue that I
8 would love to see something major happen with.
9 And it is very timely right now with all of
10 our returning veterans.
11 There is an enormous issue of
12 returning veterans with disabilities,
13 physical/mental disabilities. And if you
14 think of the broad interdisciplinary kinds of
15 programs that you can put together in
16 rehabilitation, engineering, science, and
17 medicine collectively, you can put together
18 all kinds of things that advance people in
19 virtually every single area in terms of
20 medical devices, in terms of assistive
21 devices, in terms of drug development, in
22 terms of treating drug disabilities, mental

1 disabilities, PTSD, TBI. Your Stem Cell
2 Program fits into it. And you can just think
3 how broadly you can go with this.
4 That I think has just enormous
5 opportunities for partnerships with the VA,
6 partnerships with the public-private sector in
7 terms of working with laboratories like
8 Draper, like SRI, in terms of developing
9 devices and sensors. I mean, it just can go
10 on and on.
11 This is a real thrust for us
12 because we sit next to the largest VA in the
13 nation in terms of returning veterans. So we
14 see this on a daily basis, but we see it in
15 our universities everywhere.
16 I think this is an enormous
17 opportunity for interagency collaboration as
18 well as across all of the institutes of the
19 NIH from the bioengineering to the cognitive
20 areas to the neurosciences.
21 CHAIRMAN COLLINS: So I agree that
22 is another very important area for

1 collaboration. There is a major initiative
2 that has gotten underway with the Department
3 of Defense working with NIMH, Tom Insel, on
4 traumatic brain injury and ways in which this
5 kind of needs of returning veterans, both in
6 terms of PTSD and other areas that relate to
7 consequences of service, could be worked on
8 together.
9 And Rod Pettigrew, who is here,
10 I'm sure could tell you about some of the
11 efforts that we are collaborating with in
12 terms of coming up with sophisticated
13 technologies to assist those who have been
14 wounded in battle.
15 I think you are right, though.
16 This is an area that we ought to continue to
17 push as hard as we can with the VA, with DOD
18 because national needs are great. And we have
19 things we can bring to the table.
20 DR. HOLBROOK: Well, the other
21 thing -- let me just finish one other quick
22 comment -- you might say, well, what about --

1 this is just trendy. This is something for
2 now. Well, it isn't. It's forever because
3 these folks are forever.
4 But even if you look beyond the
5 veterans, you have an aging population that
6 all of this relates to just as well.
7 CHAIRMAN COLLINS: Yes. Point
8 well-taken. Thank you.
9 Ralph?
10 DR. HORWITZ: Something to pick up
11 on John Nelson's point is, well, you made a
12 very I thought compelling presentation that
13 has an extraordinary vision but that also
14 outlines difficulties both in the short term
15 and long term for funding that vision.
16 One of the frustrations for so
17 many of us in biomedical research but also in
18 practice is the way in which technology seems
19 so often to add to cost of care, rather than
20 reduce cost of care, as it seems to be able to
21 do in other industries.
22 I wonder if NIH has thought about

1 or could think about ways of partnering with
2 CMS or other agencies within the government in
3 which new technologies could be engineered
4 with a specific focus on reducing costs,
5 rather than the sort of additive supplementary
6 costs that seem to be so much embedded in the
7 current model.
8 CHAIRMAN COLLINS: Yes. We would
9 love to do that. CMS still does not have an
10 administrator. And we are looking very much
11 forward to having that particular leadership
12 position filled. There has been in the past
13 certainly interest in that kind of
14 partnership, although it's always a bit
15 complicated in terms of what is possible with
16 regard to access to record information.
17 I think in many ways, the way in
18 which technology has raised costs is not just
19 a comment upon the technology itself but
20 obviously on the way in which it is utilized.
21 And here again we come back to
22 that issue of what are the incentives that

1 providers are driven by in terms of what kinds
2 of decisions are made. I mean, you can point
3 to the CTs and the MRIs as the easiest example
4 where we are probably over-utilizing some
5 pretty good technology that you could
6 certainly say has been a great boon but in the
7 current circumstance is getting brought into
8 diagnostic situations that are probably a bit
9 overdone.
10 I think we need to keep pointing
11 out, though, that -- because I hear this a
12 lot, "Oh, NIH, you are going to develop more
13 technology. Well, that is just going to make
14 everything more expensive." But that is not
15 necessarily the way it has to be.
16 If you look at some of the things
17 that have happened, well, one of the examples
18 you could take is the ability to use genomic
19 technology to assess which women who have had
20 breast cancer with negative nodes may not need
21 adjuvant chemotherapy because they have a very
22 low likelihood of recurrence.

1 The estimates I have seen are that
2 50,000 women this year will go through that
3 kind of analysis and a substantial number of
4 them will, therefore, make decisions not to go
5 through chemotherapy because the benefit is
6 likely to be quite small. And ultimately that
7 will save us this year $100 million in health
8 care costs because chemotherapy is expensive.
9 And there are obviously consequences that
10 occur. So, even though the test is not cheap,
11 the overall benefits to the health care system
12 are substantial.
13 We I think, though, need to
14 continue to look for examples like that and be
15 sure that we are mentioning them when people
16 are drawing conclusions that technology is
17 always going to be a cost increase or not, a
18 cost decrease or --
19 DR. HORWITZ: If I can just follow
20 up --
21 CHAIRMAN COLLINS: Yes?
22 DR. HORWITZ: -- quickly? And

1 that is that financial incentives certainly
2 play a role here. But so is the way in which
3 information is structured and analyzed and
4 presented. And many of the ways in which it
5 is currently presented lead to actions and
6 behaviors that are not always in the best
7 interest either of the patient or of the
8 system more broadly.
9 So I think, again, NIH through its
10 leadership and research around cognitive
11 strategies, behavioral strategies really play
12 a major role in helping to reshape the way in
13 which technology issues.
14 CHAIRMAN COLLINS: So Tom and then
15 Barbara and then Mary-Claire.
16 DR. KELLY: That was a great
17 presentation, Francis. And clearly you have
18 given a lot of thought to these issues. I
19 think it is an incredible time for science, in
20 spite of the fact that you are going to face
21 a lot of difficult challenges over the next
22 couple of years.

1 One part of your talk that
2 resonated a lot with me has to do with
3 training and making some decisions about what
4 the future workforce should look like. And
5 this is something I have talked about before
6 in this group.
7 If you look at the demographics of
8 American science, it has been changing very
9 dramatically over the last couple of decades.
10 To just take one sample, the age at which an
11 early investigator gets his first NIH grant
12 has been going up and up.
13 Now, we do things to try to
14 improve training and to provide support for
15 early investigators, but we really don't have
16 any idea whether those programs have much of
17 an effort and what their effect will be in the
18 long term.
19 So I believe that we need to
20 really, in spite of the fact that it is
21 difficult to think about workforce issues, I
22 think we need to really think about these in

1 a deeper and more quantitative way and try to
2 do some modeling and make some decisions about
3 what science ought to look like in this
4 country 20 years from now.
5 CHAIRMAN COLLINS: I totally agree
6 with you. It's not going to be easy.
7 Barbara?
8 DR. WOLFE: I also wanted to
9 congratulate you on this kind of broad
10 breadth. I think maybe what I am going to
11 raise is implied, but you had limited time.
12 I am so excited to hear your talk
13 about the tie between science and health care
14 reform and your focus on health disparities.
15 I wonder if there are larger opportunities
16 that ought to be sort of pushed right now
17 because as we do health care reform, we really
18 have an opportunity to learn much more about
19 what prevention strategies work, what kinds of
20 delivery models would reduce disparities.
21 We have a period now of high
22 unemployment and a great deal of poverty. And

1 so, again, these are all targeted
2 opportunities. For some it takes planning
3 right now because once some of these reforms
4 take place and we have coverage, you sort of
5 want to design some of the experiments or the
6 research designs early on before some of this
7 takes place.
8 It is a very unique time, a unique
9 opportunity to take advantage of the changes
10 that we hope are coming.
11 CHAIRMAN COLLINS: So I totally
12 agree with you. And I do think we have a
13 window here that is not going to remain open
14 indefinitely. Once we have a system that gets
15 in place, it is going to be much harder to
16 change it than to get it right to begin with.
17 Again, this is something I think
18 all the institutes perceive as a high
19 priority. And particularly those that are
20 already invested in those kinds of research
21 programs related to health disparities are
22 attempting to craft the kinds of protocols

1 that will help provide the answers in this
2 regard.
3 But we need to work hard to be
4 sure that we have got that landscape attended
5 to. It is a complicated landscape, as you
6 well know. The point is very well-taken.
7 Mary-Claire?
8 DR. KING: I would like to return
9 to the point that both you and Ralph Horwitz
10 were making, which I think is an excellent
11 one. It seems to me that NIH has been at the
12 forefront of developing technology in a
13 variety of ways.
14 We are good at it. We know how to
15 use it. It is fun. We attract brilliant
16 young people into it. Us old people learn to
17 love it, too. It is a great thing.
18 Ralph's point that technology adds
19 to the cost of care, rather than decreasing
20 it, is, of course, the direct opposite of our
21 experience within the NIH of having technology
22 work for us and rapidly decreasing the cost of

1 getting to the next step in research results.
2 So I wonder if you would give us a
3 little of your analysis of how NIH as a
4 fundamental biomedical research institution
5 can use our collective experience to help in
6 this other area because the problem that Ralph
7 raises is a problem of health care, of actual
8 application of boots on the ground and how do
9 you actually deliver the goods to the patient.
10 What our experience has been as an
11 institute is in basic research. How can we
12 help? How do you see the NIH taking a role?
13 CHAIRMAN COLLINS: Well, it's a
14 complicated pathway, isn't it, because the
15 technologies that we develop -- and I agree
16 with you -- apply with great benefit in terms
17 of reducing the cost of getting to the next
18 really big breakthrough and understanding are
19 obvious to all of us who do research. And we
20 count on them. And they are in many ways
21 responsible for advances in ways that we taken
22 for granted. In fact, technology doesn't

1 always get the credit it ought to for having
2 stimulated a lot of our really new insights.
3 I think what we have to do is to
4 identify the way in this those sample
5 technologies are, in fact, ripe for
6 translation into the health care system.
7 Take the example of DNA
8 sequencing, near and dear to my heart and
9 yours. If we were to get to the $1,000 genome
10 -- and probably that's within 3 to 5 years --
11 being a reality and if we were able to set up
12 a system where that could be offered to
13 individuals and become part of their medical
14 record, then you could imagine how this would
15 empower pharmacogenomics in ways that are
16 otherwise going to be limited just by the
17 logistics of trying to get the NDA test
18 results back in time for the provide to be
19 able to use the information.
20 When you consider that a drug,
21 adverse drug reactions are the fifth leading
22 cause of death in this country. Not all of

1 those are going to be preventible via this
2 method. But some of them will.
3 That would be a pretty powerful
4 cost-effective and life-saving approach that
5 would I think be a cardinal example that we
6 could put forward of how this very marvelous
7 revolution of research, could move access into
8 practice.
9 We have to think carefully about
10 which are the good fit for that and make sure
11 that we are not advocating on a general basis
12 that that will always be true.
13 And, here again, of course, this
14 points out just what a big problem we have in
15 this country taking evidence that has been
16 generated for research studies and actually
17 implementing those in the standard practice of
18 medicine without many years going by and lots
19 of mistakes along the way.
20 So it's a good point. It's
21 challenging to figure out how to do this.
22 Probably my usual reaction is let's pick some

1 really good examples and try to do those
2 right. And then maybe the rest will start to
3 follow.
4 DR. MURRAY: So one of the really
5 great legacies of you and the Genome Project
6 was to foster the ethic that information
7 generated as part of public funding would be
8 held in public trust and be very rapidly
9 available for use and so on, maybe even the
10 most important legacy, even beyond the
11 sequencing in some ways. So it is wonderful
12 to hear that you are going to be having these
13 partnerships with Burroughs Wellcome and Gates
14 and working with people like that.
15 I wondered if you have thoughts
16 about how the NIH can help that ethic sort of
17 work down the steps to the individual
18 investigator to clinical trials to
19 partnerships with these other nonprofits and
20 so on to make that kind of information more
21 universally available, at the same time
22 protecting the needs of the individual

1 investigator to have their intellectual
2 property to get out there in protecting
3 patient privacy.
4 CHAIRMAN COLLINS: Another great
5 question, Jeff. And, of course, you have been
6 deeply engaged in many of these debates about
7 what is the right balance between not wanting
8 to provide a circumstance where individual
9 investigators get scooped with their own data
10 before they have a chance to draw their own
11 conclusions but making sure that information
12 that could be highly valuable doesn't stay
13 squirreled away for long periods of time.
14 I think the idea that community
15 resource projects has sort of matured into a
16 pretty good concept here if what you are
17 engaged in and what NIH is supporting is a
18 project that has substantial value as a
19 community resource. Whether it is a genome
20 sequence or a database of genome associations
21 with particular common diseases, then that is
22 the kind of project that really should get out

1 there immediately, even before publication,
2 with appropriate attention to embargoes so
3 that the people generating the data don't get
4 scooped on their own data but making it
5 available for those who want to go to the next
6 step in their own research to get started
7 right away.
8 When it comes to individual
9 investigators who are pursuing their own
10 specific target that you can't really think of
11 as a community resource in the same way, then
12 I do think we have to be sensitive to the
13 usual rule that at publication, that data
14 should all be made available, but maybe we
15 don't require people to put it out there ahead
16 of time unless they are so motivated to do so.
17 Obviously when it gets into
18 interactions with the private sector or around
19 things for which intellectual property becomes
20 an issue, it gets more complicated.
21 The sense that I think the
22 community has had that we need to be more

1 thoughtful -- and this has been a good
2 evolutionary process -- about what fits into
3 pre-competitive and what is competitive -- and
4 I think some of the excesses of the 1990s in
5 terms of claiming everything for intellectual
6 property that you could have now I think been
7 balanced out by a realization that a lot of
8 those claims didn't accomplish very much other
9 than kind of getting in the way of research.
10 So certainly from my perspective,
11 NIH has a lot of tools to enable this issue of
12 open access to be pursued, to be made
13 available for public attention.
14 We, after all, make grants. And
15 we can have conditions on those grants awards.
16 And we do that when it is a community resource
17 project that we want to be sure is accessible.
18 The Cancer Genome Atlas is a good
19 example, for instance. And for me personally,
20 having seen the benefits of that kind of open
21 access for rapid progress and relatively few
22 examples where it has actually done harm to

1 any investigator to have their data made
2 available sooner, rather than later, we are
3 going to be pushing as hard as we can in this
4 area.
5 I think the community ethic has
6 very much moved in this direction in the last
7 few years. And that is something we should
8 encourage and celebrate.
9 Keith Yamamoto?
10 DR. YAMAMOTO: I want to return to
11 the points that you raised about training and
12 the comment that Tom Kelly made a little while
13 ago and look at it in a slightly different
14 framework.
15 I think we are all concerned about
16 those scary statistics about the age of the
17 first shot and the first R01. And I think NIH
18 should be congratulated on the new grant
19 mechanisms, other kinds of efforts that have
20 been made for new investigators.
21 CHAIRMAN COLLINS: You have helped
22 us a lot with those, Keith. Thank you.

1 DR. YAMAMOTO: The point that you
2 made about Whitehead Fellows Programs that
3 many of us have copied I think is good. But
4 I wonder if the NIH may be coming out of a
5 working group of this Committee but whether
6 the NIH should think about going back to first
7 principles and reexamining what it is the
8 goals of graduate training should be.
9 What is the product? What is the
10 intellectual product in a way, the creative
11 product, that graduate training should be
12 endeavoring to produce as its endpoint and how
13 much of what it is that we are putting to our
14 programs now really moves toward that product?
15 Furthermore, as you pointed out,
16 postdoctoral work is now extending four, five,
17 six more years. I would submit that at least
18 academia has never looked at postdoctoral
19 training as an educational imperative. It
20 should never examine what should go into that,
21 I think probably initially because of the
22 artifact that when many of us trained, it was

1 a linear pathway from beginning graduate
2 school to becoming an assistant professor.
3 And so there was no real need to
4 put much attention individually on what is a
5 product of graduate education and what is a
6 product of postdoctoral education, which right
7 now is sort of an oxymoron should be.
8 I wonder if it would be worth the
9 NIH doing that. I think that if they did or
10 if we did, it might be we might discover that
11 much of what we are doing does not really
12 point in that direction. A lot of the years
13 that get spent in these "training periods" are
14 not really focused in this way.
15 There will be many potential
16 outcomes of a finding of that sort, but
17 certainly two of them are that we would
18 reattract into this endeavor a set of students
19 right now that I think look at what it is that
20 we are doing in the period of time that it
21 takes. And they simply stay out, and they go
22 somewhere else and do something else. So we

1 are losing human capital.

2 The other, of course, is

3 economics. Graduate training periods in

4 average in this country are now well over six

5 years, maybe over six and a half, way by far

6 the longest in the world, and postdoctoral

7 training periods similarly.

8 Those are NIH training grants

9 through NIH R01 grants. A huge number of

10 dollars is going into that. So economic and

11 human capital would be the outcome of being

12 able to look at this.

13 We know of some examples of

14 training periods that are much shorter. I'm

15 involved in one at Cold Spring Harbor. Their

16 program is just over four years. They are

17 coming out with magnificent products in terms

18 of the quality of their trainees.

19 So we know that it can be done.

20 And it might be worth putting some real

21 directed effort in this direction.

22 CHAIRMAN COLLINS: Okay. I

1 appreciate that. And this is connected in a
2 certain way to the workforce analysis that we
3 were talking about a little bit earlier
4 because you need to figure out what are your
5 needs and how do you get there.
6 I know we are running a bit late,
7 but these are really interesting questions.
8 We will take three more. And then I think we
9 will take out break a little bit later than we
10 were supposed to.
11 So Mary Beckerle is next on my
12 list here.
13 DR. BECKERLE: Thanks. I want to
14 start out by saying that I think the way you
15 framed the opportunities for the NIH is very,
16 very compelling. And I think it is going to
17 be compelling to scientists who care very
18 deeply and passionately about seeing their
19 work have impact on human health.
20 I also think it is going to be
21 very compelling to our elected officials in
22 the public. And so that sort of trio is a

1 very nice combination.
2 One thing that I think is really
3 appropriate for this time in our history is
4 the emphasis that you placed on the
5 application of our strong foundation of
6 knowledge to impact understanding the human
7 disease and to really move forward in clinical
8 translation to try and improve detection,
9 diagnosis, therapy, and prevention.
10 I think that one thing we want to
11 be really careful not to lose in all of that,
12 however, is that all of the foundation that
13 really is enabling us to be in that position
14 really has come from I think an incredibly
15 remarkably in my lifetime history of
16 fundamental discovery and basic science and
17 also the emergence of what I would say is just
18 really unimaginable technologies that have
19 really also facilitated these advances.
20 I mean, I reflect back on when I
21 was an undergraduate and I read a textbook and
22 thought we knew everything and that as a

1 graduate student, I thought we knew
2 everything. And then as a postdoc, I thought
3 we knew everything. And now I completely know
4 we don't know everything.
5 Maybe I knew that as a postdoc.
6 By that time, I hope I did.
7 (Laughter.)
8 DR. BECKERLE: Otherwise there was
9 a problem with our training. But I guess my
10 point is I think we have to be very careful
11 that we don't sort of grow complacent in a
12 sense because of all of the tremendous
13 advances that have been made and begin to
14 think in any way that we are done with
15 discovery and all we need is application at
16 this point in time.
17 This concerns me really greatly
18 because I think there is a -- I guess I am
19 sort of struggling with how the NIH can both
20 sort of simultaneously emphasize the
21 tremendous opportunity that we have right now
22 without discouraging in any way the

1 development of more trainees and the continued
2 emphasis on the fundamental discovery that is
3 really going to be driving the next level ten
4 years from now.
5 I think when we look back at some
6 of the great advances over the past two
7 decades that are really now beginning to have
8 tremendous impact and are fueling this
9 tremendously exciting translation, many of
10 those came from discoveries that had nothing
11 to do with human health or disease focus.
12 I think it is going to be really
13 important for the NIH leadership and all of us
14 as scientists to think about creative ways to
15 really frame the opportunities so that we
16 don't foreclose on the opportunities for the
17 future.
18 CHAIRMAN COLLINS: That is very
19 articulately stated. Just look at the Nobel
20 Prizes from the last couple of months being
21 awarded next week, in fact, for telomeres and
22 for ribosomal structure. You can't help but

1 see the wisdom of what you are saying. And I
2 think we do.
3 Even as we emphasize the
4 opportunities now for translation, which is
5 what the public is very much hoping to see,
6 that we don't impact that we're any further
7 along in understanding the real basics of what
8 is going on than just a tiny bit.
9 As Edison once said, we don't know
10 one-millionth of one percent about anything.
11 I think that is probably still true when it
12 comes to understanding how life works. But
13 yes, it is a pretty tough problem.
14 Maria Freire?
15 DR. FREIRE: So I could have just
16 passed and let you say what you said because
17 it was exactly what I thought we needed to
18 emphasize. But, Francis, to your point, the
19 public is excited about the piece of
20 translational research. We need to make them
21 as excited about the importance of basic
22 research. That is what we need to do.

1 What I wanted to address, though,
2 is this smart diplomacy and the issue of
3 neglected diseases, which, of course, are near
4 and dear to my heart, and the changing
5 epidemiology of the chronic diseases and the
6 double burden of disease.
7 It strikes me that the world is
8 changing, that we have new players in the
9 world scene. It is not only the north, but we
10 are having an enormous amount of science and
11 research being done in China and India and
12 South Africa.
13 And if we are going to continue to
14 have an important biomedical enterprise, I
15 think our leadership and our interactions with
16 some of these nascent forces would be
17 important. And this is a good opportunity for
18 --
19 CHAIRMAN COLLINS: Yes. I totally
20 agree. And we will have some of those
21 representatives at this January 6 meeting. I
22 certainly think if we are going to make real

1 headway in global health, a big part of it has
2 to be about capacity building in countries
3 where these problems are most prevalent and
4 where the opportunity for training and
5 building that capacity has not been fully
6 realized.
7 Cathy DeAngelis?
8 DR. DeANGELIS: Thank you,
9 Francis. I am so encouraged listening to your
10 view of the translational research, really
11 truly from, well, the genes, all the way to
12 the patient bedside. I think that is so
13 exciting.
14 I would like to specifically go
15 back just a bit to what Ralph and Mary-Claire
16 has said and before Beatrix. Why is it that
17 the new technologies that are so marvelous,
18 that have come out of discovery, much of it,
19 funded by NIH, why have all of these things
20 that should be cost-saving end up costing so
21 much?
22 And I think it is primarily

1 because of misapplication. And I think that
2 the promise of the genetic screening is so
3 great on the one hand. On the other hand, I
4 have a fear, sort of a niggle in the back of
5 my head that we're going to get into the same
6 problem there because I think I had at least
7 100 submissions and manuscript studies on
8 snips. And to try and say these are the
9 people that will help when you screen.
10 The problem is -- and it's very
11 much showed its ugly head in how the mammogram
12 issue was misperceived, I think, tremendously
13 by the public, by the press -- that we will
14 have more information about on whom we should
15 use these expensive technologies, but I think
16 they will continue to be misapplied because I
17 think a lot of clinicians either don't know
18 that they shouldn't be using them so broadly
19 or are afraid that if they don't use them,
20 they're going to get sued or they're going to
21 feel bad because they miss something.
22 So I wonder if you have any place

1 in your plans to study this in a way to say,
2 "Look, if you can come up with some
3 information, you say, 'Here. Here is
4 something. We know how this screening is
5 going to help. We know that this is the
6 technology that can be used to further it.
7 But look at this. Only ten percent of the
8 people who actually ended up having this
9 expensive stuff really needed it.'"
10 Now, what will happen to the other
11 90 percent? Do you have any idea or any
12 thoughts about maybe that would be some -- it
13 wouldn't be that costly, but I wonder if you
14 thought about that.
15 CHAIRMAN COLLINS: It's a very
16 tough problem. And it's certainly getting
17 into the territory of health delivery, which
18 can be pretty complicated to set up as far as
19 a controlled study, but it is one of the
20 things that maybe could be factored into the
21 kinds of studies we were briefly talking about
22 earlier to test what are the right incentives

1 for health providers.

2 One of the things we are

3 interested in doing is now with these HMO

4 networks, which have been funded by a number

5 of the institutes, particularly NHLBI and NCI,

6 could we begin to carry out some of these

7 experiments, where you actually offer the

8 opportunity for that kind of preventive

9 information to be obtained on individuals and

10 made available to their providers and you set

11 up different incentive systems for how those

12 would be acted upon and different educational

13 modules for both the patients and the

14 providers and try to see what actually

15 motivates good decision-making that is both

16 benevolent and leads to a good outcome and

17 that is cost-effective.

18 You can kind of imagine how that

19 might go. And, again, we are planning to

20 bring together the leaders of a bunch of these

21 HMO networks that have a lot of capacity that

22 hasn't really been tapped into for this kind

1 of question and see what kind of research
2 model could be put forward. I agree that
3 there is a lot we could learn that way in the
4 real world, not in some small-scale but in a
5 fairly large-scale fashion.
6 Well, this has been a great
7 conversation. And I, as usual, have failed to
8 pay attention to the timetable. And we are
9 well over the time where we should have moved
10 into the stem cell discussion. Mindful that
11 this is a biomedical research institution and,
12 therefore, we are aware of biological
13 imperatives, it might be a good idea, even
14 though Raynard is urging me to just go
15 straight on, --
16 (Laughter.)
17 CHAIRMAN COLLINS: -- for us to
18 take a five-minute but not a second longer
19 than that break for people to refresh
20 themselves in various ways.
21 So five minutes only, please. And
22 then we will come back and get into a very

1 important discussion about stem cells.
2 (Whereupon, the foregoing matter
3 went off the record at 10:42 a.m. and resumed
4 at 10:49 a.m.)
5 CHAIRMAN COLLINS: So we are going
6 to now move into a very important discussion,
7 which involves decision-making by the ACD, on
8 the topic of human embryonic stem cells.
9 And we are going to begin with the
10 presentation by Lana Skirboll to provide the
11 background for this important issue, which, of
12 course, has been the subject of a lot of
13 deliberations. And then we will hear from the
14 hardworking chair of the working group, Jeff
15 Botkin, who is going to present their findings
16 to you about specific decisions we are asking
17 you to make.
18 Lana?
19 DR. SKIRBOLL: Thank you, Francis.
20 STEM CELL POLICY AND ACD STEM CELL
21 WORKING GROUP REPORT
22 DR. SKIRBOLL: So what I want to

1 do today is to give you the background, the
2 NIH policy, the basis upon which you will be
3 considering the presentation and the
4 discussion and findings by Dr. Botkin and
5 point out also that Dr. Landis is here as
6 chair of the stem cell task force if we have
7 discussion and that Jeff Murray also is
8 serving as the ACD representative on the
9 working group.
10 So basically we are going to walk
11 through the NIH guidelines for stem cell
12 research. I think many of you were involved
13 with and participated in a brief phone call,
14 a brief phone call briefing at the time of the
15 release. But I want to remind you of them
16 because they're very important for the
17 decision today.
18 And then the ACD working group,
19 Jeff Botkin, who is here -- where are you?
20 There you are, Jeff -- will get up and tell
21 you about the findings.
22 Executive order 135-05, very

1 important to NIH, titled "Removing Barriers to
2 Responsible Research Involving Human Stem
3 Cells," on March 9th of 2009. You can see
4 many of the Hill advocates and others who were
5 there to watch the President Obama sign the
6 executive order. Among them former NIH
7 Director Harold Varmus you can see there in
8 the corner.
9 The executive order calls for the
10 Secretary of HHS through the Director of NIH
11 to support and conduct responsible
12 scientifically worthy human stem cell
13 research, including human embryonic stem cell
14 research to the extent permitted by law.
15 It told us that within 120 days --
16 and this is warp speed for government to
17 create guidelines and get them out, draft, and
18 get them out in final. Within 120 days of the
19 order, the Secretary through the Director
20 shall review existing NIH guidance and other
21 widely recognized guidelines on human stem
22 research, including provisions establishing

1 appropriate safeguards and issue new NIH
2 guidance on such research. And the Secretary
3 shall review and update such guidance
4 periodically and as appropriate.
5 We released the draft guidelines
6 in April, April 23rd of 2009. Over 49,000
7 comments were received. And those were all
8 read and examined. We looked at them
9 carefully. They were substantive. This was
10 a system that really worked because in the
11 end, there were many changes that were made to
12 the guidelines.
13 There were, however, no changes to
14 the basic eligibility criteria. But what we
15 did change was we did not provide exact
16 wording for consent forms but required a
17 robust informed consent process and that there
18 must be a written consent as part of the final
19 guidelines.
20 The final guidelines were
21 effective on July 7th of 2009. And the
22 guidelines set forth that all human embryonic

1 stem cells must be all human embryonic stem
2 cells funded with NIH research using human
3 embryonic stem cells, must be derived from
4 embryos created by IVF for reproductive
5 purposes and no longer needed for that
6 purpose, and donated by individual or
7 individuals who sought reproductive treatment
8 and who gave voluntary written consent for
9 human embryos to be used for research
10 purposes. That was a must.
11 So now we get into what appears to
12 be a rather complicated flow chart, but let me
13 walk you through it because it is really
14 important to understand what role you play
15 vis-a-vis the announcement earlier this week
16 that NIH had approved 13 lines that had gone
17 through administrative review.
18 When was an embryo donated? You
19 notice I'm not talking about when the line was
20 derived. I'm talking about when the embryo
21 was donated. If it was donated prior to July
22 7th to the final date of the guidelines and it

1 meets so-called section 2(a), what is section
2 2(a)? That is the section of the guideline
3 that lays out very specifically the
4 requirements for the informed consent process.
5 If it meets that section, then it
6 goes to administrative review. It is the
7 submitter that makes that decision. A
8 submitter submits the lines and says, "We
9 believe our lines meet section 2(a)."
10 The 13 lines that Dr. Collins
11 approved earlier this week were submitted by
12 George Daly's lab and Rockefeller University.
13 And those submitters chose to go this route.
14 And they reviewed. Each of the elements of
15 section 2(a) was reviewed. It met section
16 2(a). And those were approved for funding.
17 If it does not meet section 2(a)
18 and it was derived prior to that date, it has
19 the opportunity to go to the ACD working group
20 for review and ultimately on to you. The ACD
21 working group provides a set of findings. But
22 please note what Jeff is about to talk to you

1 about is the findings from their review. It
2 is you who will make the recommendations to
3 the NIH Director regarding eligibility for NIH
4 funding.
5 If a set of lines, however, were
6 derived after -- sorry. If the embryo was
7 donated after the July 7th date -- I caught
8 myself -- and it meets section 2(a), yes, the
9 same is true. It goes through section 2(a)
10 but if after July 7th derived here in the U.S.
11 and it does not meet section 2(a), there is no
12 opportunity to go to the working group. In
13 other words, after the date of the guidelines,
14 all newly derived lines, the embryo must have
15 been donated according to the requirements of
16 section 2(a) if they were donated in the U.S.
17 The guidelines when we developed
18 them, we understood that it was okay and
19 appropriate for NIH to be setting specific
20 requirements for what is U.S.-donated embryos.
21 Given the fact that many countries
22 have developed their own rules and regulations

1 and that we were not in a position nor should
2 we be in a position to necessarily dictate to
3 them the specific requirements of that
4 donation, we allowed a second route for
5 embryos that were donated outside the U.S.
6 And in that case, after July 7th,
7 in the U.S. must meet the requirements.
8 Donated outside of the U.S., they also have
9 the opportunity to come to the ACD.
10 Why does this matter to you?
11 Well, there is a limited -- hopefully there is
12 some subset of lines that were donated prior
13 to July 7th that may be submitted to us for
14 review. And you would think that your work
15 will have a limit to it.
16 But, in fact, because of this
17 allowance of lines that are donated outside
18 the U.S. from now into the future to come to
19 the ACD, your work may continue for a long
20 time. And I just wanted to give you a fair
21 notice on that.
22 So what are the section 2(a)

1 requirements? The institution must assure
2 that all options available in the facility
3 pertaining to the embryos no longer needed for
4 reproductive purposes was explained. Please
5 note these words. It doesn't say, "All
6 options are necessarily presented to the
7 couple" but all options that are available in
8 that IVF clinic.
9 No payments were offered for the
10 embryos. And policies and procedures were in
11 place that neither consenting nor refusing to
12 donate embryos would affect the quality of
13 care for the donors.
14 Institutions must assure a clear
15 separation between the decision by the donor
16 to create embryos for reproduction and
17 decision to donate embryos for research.
18 That is, the decision to create
19 the embryo for reproduction must be free from
20 the influence of researchers. The physician
21 and researcher, where practical, should not be
22 the same person.

1 Consent for donation must be
2 obtained at the time of donation. And donors
3 must be informed that they have the right to
4 withdraw, of course, until the derivation
5 occurs; i.e., the embryo is destroyed, or
6 until identifiable information has been
7 removed where you can't reach back and find
8 the, connect the embryo, the donated embryo,
9 with the donors. So you couldn't withdraw.
10 Section 2(a) also says that during
11 the consent process, the donors must be
12 informed that the embryos would be used to
13 derived HESCs for research. What would happen
14 to the embryos in the derivation, that the
15 cells may be kept for many years, that there
16 is no restriction or direction regarding the
17 individuals who may receive medical benefit.
18 This was future-looking on our
19 part. I think embryos that are being donated
20 now, as Dr. Collins said earlier, we are
21 hopeful for future medical benefit. It's not
22 an issue now, but we wanted to make sure it

1 was in the guidelines.

2 Research is not intended to derive

3 medical benefit to the donors. And research

4 results may have a commercial potential. And

5 the donors would not receive those benefits;

6 finally, whether information identifying the

7 donors would be available to researchers.

8 Please note it doesn't say that

9 they will be de-identified or they will be

10 anonymized but whether information identifying

11 the donors would be available to researchers.

12 So, again, those are the specific

13 requirements set up by which embryos that were

14 donated in the U.S. before and must adhere to

15 after the July 7th date.

16 But suppose there were lines and

17 many of them were derived decades ago, where

18 the embryo was donated decades ago. And we

19 did not have the privilege and opportunity of

20 looking at any number of guidelines that have

21 been created over the years, I think starting

22 with the NIH guidelines in 2000 and the NAS

1 guidelines, several issues of the NAS
2 guidelines, and the ISSCR guidelines.
3 We created this second route. And
4 this second route is the one that involves
5 you. So for embryos donated anywhere before
6 July 7th, the working group will take into
7 account the principles of section 2(a), not
8 the precise wording but the principles of
9 section 2(a).
10 45 CFR 46, subpart A, which is the
11 common rule on informed consent, and several
12 points to consider, points to consider, not
13 requirements, that during the consent process,
14 whether the donors were informed of other
15 available options pertaining to the use of the
16 embryos, offered any inducements for the
17 donation, and informed about what would happen
18 to the embryos.
19 It is important to understand when
20 the working group was given its charge to look
21 at this 2(b), there was a tendency, of course,
22 to go back and follow those specific

1 requirements of 2(a). But that was not the
2 intent here.
3 We make our intent on 2(b) very
4 clearly in the preamble to the guidelines.
5 And if you will bear with me, I want to read
6 this because it will be very important in your
7 understanding the findings and the review that
8 the working group worked on.
9 We were cognizant that there had
10 been more than a decade of discovery. And
11 many lines were derived consistent with
12 ethical standards and our guidelines that were
13 developed by states and countries and other
14 entities, all that were informed over time.
15 These various policies and
16 guidelines we found when we did our analysis
17 of them had many common features, rely on a
18 consistent ethical base, and required an
19 informed consent process, but they differ.
20 Importantly, they differ in the details of
21 implementation.
22 So it is important to recognize

1 that the principles of ethical research; i.e.,
2 voluntary informed consent to participation,
3 have not varied in this time frame, but the
4 requirements for implementation and procedural
5 safeguards employed to demonstrate compliance
6 have evolved.
7 What this all means is that when
8 you're looking at the materials that come
9 forth to you, it is not a requirement -- I am
10 stressing this again -- that they meet every
11 checkpoint of 2(a) but essentially that they
12 meet the principles of ethical research.
13 The ACD again from the preamble
14 will advise the NIH on whether these core
15 ethical principles and procedures used in the
16 process for obtaining informed consent for the
17 donation of the embryo were such that the cell
18 line should be eligible for NIH funding.
19 The working group is not charged
20 with undertaking a de novo evaluation of
21 ethical standards but considers the materials
22 in light of the principles and points to

1 consider in the guidelines as well as the
2 common rule and, rather than grandfathering
3 the ACD working group, will enable preexisting
4 human embryonic stem cells derived in a
5 responsible manner to be eligible for use in
6 NIH-funded research.
7 Just as a reminder, at the full
8 extent of the guidelines, there was section 2þ
9 of the guidelines, which had to do with the
10 use of embryonic stem cells. Sorry. This has
11 to do, section 2(a) had to do, with that
12 foreign condition that I described earlier.
13 So, again, donated in the U.S.,
14 they must adhere to 2(a). Donated in a
15 foreign country, they could go to the ACD
16 working group, both before and after the date
17 of the release of the guidelines.
18 This is the area that I was just
19 mentioning about ineligible research. So this
20 is about use. This is not about whether they
21 are eligible for funding, for use in
22 NIH-funded research, but what research using

1 embryonic stem cells and in this case
2 pluripotent stem cells for NIH funding.
3 That would be research in which
4 HESCs, even if the lines are eligible or IPSCs
5 are introduced into a non-human primate
6 blastosis, research involving the breeding of
7 animals where the introduction of an HESC,
8 even if the lines are eligible, or IPSCs may
9 have contributed to the germ line.
10 Other research not eligible for
11 NIH funding I think you are all well-aware of,
12 we cannot, NIH cannot, fund the derivation of
13 stem cells from human embryos. And NIH is not
14 using funding research using HESCs derived
15 from sources, including SCNT, parthenogenesis,
16 or embryos created by IVF solely for research
17 purposes.
18 The review process. So NIH staff,
19 as I mentioned before, conducts the
20 administrative reviews for section 2(a)
21 compliance. The ACD working group reviews
22 other submissions under section 2(b) and

1 section 2þ.

2 The working group findings, what

3 was happening today, are presented to the ACD.

4 And the ACD makes the recommendations to the

5 NIH Director. Francis will make the final

6 decisions about eligibility of human embryonic

7 stem cells.

8 Finally, eligible stem cells go up

9 on the registry. And they will become a

10 one-stop shopping source, if you will, for

11 researchers who are putting together

12 applications or even have ongoing grants who

13 wish to use eligible lines. Those first 13

14 lines went up on the registry the day before

15 yesterday.

16 The working group Jeff is going to

17 talk a little bit more about them, but let me

18 just say we work very hard to get a balance

19 here between all really talented and

20 thoughtful people, ethicists, scientists,

21 public members, and IVF physicians, so that

22 all perspectives could be brought to bear on

1 this 2(b) discussion.

2 Over 100 HES lines have been

3 submitted for review. And that includes for

4 ACD an administrative review. Review is

5 ongoing for many of these. As I said before,

6 Dr. Collins approved 13 lines the day before

7 yesterday. They were lines from Children's

8 Hospital in Boston, 11 lines, and 2 lines from

9 Rockefeller.

10 The working group findings for 28

11 lines are being presented to the ACD today for

12 consideration. They were a single submission.

13 I think that is a good thing for your first

14 round at this, meaning you were looking at one

15 set of documentation. It would have been much

16 more complicated if it had been 28 lines and

17 28 different sets of submissions. But what

18 you have before you is the documentation for

19 the 2(b) consideration.

20 So your turn. The goal today is

21 to try to get to a recommendation to the NIH

22 Director regarding the eligibility of these 28

1 lines for use in NIH-funded research.
2 I am happy to take questions. And
3 if not, I will turn this over to Dr. Botkin,
4 my working group chair.
5 CHAIRMAN COLLINS: Any questions
6 about the process? Tom?
7 DR. KELLY: Yes. Could you say a
8 little bit more or whether there is any
9 guidance in these guidelines about the issue
10 if the consent specified a particular use of
11 the cells, under what circumstances that
12 restriction could be broadened or could be
13 considered to be broadened, number one.
14 And, number two, I am gathering
15 from looking at what we are supposed to be
16 doing that we may not have to comment or we
17 may not have to comment on that, I suppose,
18 because you said eligible and eligible for
19 funding are two different things.
20 So could you give us a little more
21 guidance in that area?
22 DR. SKIRBOLL: Well, that's good.

1 You sort of answered your own question. The
2 discussion today absolutely is about eligible
3 for use. But yes, we do take note that this
4 is the first set of lines that will come
5 before you that do have a restriction in the
6 informed consent.
7 This is an implementation issue
8 for NIH. It is certainly open for discussion
9 here. But ultimately NIH will have to create
10 a policy. I can tell you now it is not the
11 first set of lines that have come in that will
12 have restrictions.
13 Certainly the lines that were
14 created prior to the July 7th date were
15 created, all created, in the private sector
16 for many purposes and many different kinds of
17 experiments. So I suspect that we will face
18 this, maybe not frequently, but we certainly
19 expect to face it.
20 NIH absolutely will have to come
21 up with a policy about how to handle it. We
22 do have the registry capable of taking note of

1 that so that if scientists choose a line, they
2 will know if there is a restriction associated
3 with it.
4 Ultimately when an application
5 comes in on a case-by-case basis, NIH will
6 have to make decisions about whether the
7 application adheres to a particular
8 restriction or not.
9 DR. KELLY: So do I take that to
10 mean we here do not have to worry about that
11 issue?
12 CHAIRMAN COLLINS: I think it may
13 come up in the specifics of this conversation,
14 but I think what Lana is saying is that it is
15 ultimately going to be NIH's problem to figure
16 out whether particular applications are
17 consistent with restriction or not.
18 I think Beth Furlong was actually
19 next and then Mary-Claire.
20 DR. FURLONG: On page 5 of the
21 PowerPoint that I have, the second slide.
22 It's your third slide on section 2(a)

1 requirements.

2 One of the criteria is research

3 results may have commercial potential. The

4 donors would not receive benefits. Would you

5 speak to the ethical arguments that were used

6 on both sides for that indicator?

7 DR. SKIRBOLL: Right. Well, this

8 was a deliberation but also had been broadly

9 discussed in the ethical community. I think

10 the NAS guidelines, the original NIH

11 guidelines, and the ISSCR guidelines made this

12 very clear.

13 This is a statement of

14 understanding. There had been a long and, you

15 know, somewhat complex issue on this. The

16 important thing is to inform people that

17 commercial potential, some of which would be

18 very far down the pike, they would not be

19 expected to have that benefit.

20 It would be up to the donor to

21 decide whether that was unacceptable to them

22 from a donating point of view and would,

1 therefore, choose not to donate.

2 DR. FURLONG: Would you speak to

3 the ethical arguments that were used on both

4 sides of coming to that?

5 DR. SKIRBOLL: Do you mean

6 donating, meaning getting benefit versus not

7 getting benefit? I am not sure if I am the

8 one to speak to those ethical issues in

9 specific. Maybe Jeff would get to them. But

10 I think the debate has been over the years

11 that that appears to be an inducement.

12 The commercial benefit, gaining

13 commercial benefit, from this is an inducement

14 to donate and, therefore, is part of the

15 ethical consideration of not offering

16 inducements.

17 CHAIRMAN COLLINS: Mary-Claire?

18 DR. KING: First, Dr. Skirboll, I

19 really wanted to congratulate you on the

20 conference call that you held a week or so

21 ago. It was excellent. Those things are not

22 easy to do well, and you were great. Thank

1 you very much.

2 I would like to ask a question

3 about how general the availability will be for

4 lines that are approved. Will NIH put in a

5 place a requirement that a line that is

6 approved be made available not only to the

7 researchers who are specifically requesting

8 that it be approved but to researchers

9 generally?

10 DR. SKIRBOLL: That's a great

11 question. The first answer to that question

12 is that these lines are not held by NIH. NIH

13 doesn't own the lines. The intellectual

14 property is held elsewhere. And, as you know,

15 the intellectual property issues related to

16 human embryonic stem cells is complex.

17 With Dr. Collins at the helm here,

18 I can assure you that the sharing of those

19 research materials we will strongly encourage

20 the sharing of those by moral suasion. We

21 cannot by rule, but we will be pressing

22 investigators to do that.

1 Now, we also recognize that some
2 investigators may be more or less able to
3 scale up and to provide them to researchers.
4 And that is another question that will come to
5 NIH.
6 This would seem to me to be
7 reminiscent of the issue that arose with the
8 development of mice during Harold's time here
9 and that there are various forms of suasion,
10 not all of them simply moral that can be used.
11 CHAIRMAN COLLINS: We will use the
12 means available. And I think the other
13 question is whether there needs to be a
14 repository like the Jackson Labs, equivalent
15 for approved stem cell lines. And that is
16 also something that is under consideration.
17 We would not want to put
18 taxpayers' money into that if it is not
19 necessary because many of the people who have
20 derived these lines are, in fact, highly
21 motivated to distribute them, as is George
22 Daly, who is the person who is now sending

1 probably a lot of these out in the near future
2 since 11 of his lines were approved 2 days
3 ago. But if it turns out that this is a real
4 barrier that we could help with, we are
5 prepared to try to help.
6 Barbara was next.
7 DR. WOLFE: Well, I wanted to just
8 raise a question in terms of a principle here.
9 I'm trying to get the right way to phrase it.
10 These orders or the changes all
11 come from an executive order. And we in this
12 case are all pleased because it opened up
13 research opportunities.
14 But people are now applying and
15 starting to use these lines. Is there a
16 precedent here where there could be a new
17 executive order?
18 And so then the researchers who
19 are using some that have some restrictions,
20 that in the future, it could be decided that
21 those lines would not be viable? And so that
22 the science that is going on would then be

1 stopped because of potential changes?
2 I am just concerned a little with
3 the principle that we will have science going
4 on. And by establishing this principle this
5 time, is there the potential that the science
6 could be interrupted in the future?
7 CHAIRMAN COLLINS: Yes. Let me
8 address that. I think that is unlikely
9 because of the broad support now in a
10 bipartisan way for stem cells, but it is not
11 impossible.
12 I noticed with interest the press
13 release that Congressman Degette put out on
14 Wednesday, after the approval of the first 13
15 lines, again highlighting this as a concern of
16 herself and of Representative Castle, the
17 Republican who has worked with Diana on this
18 issue and again highlighting their intention
19 to try to seal a congressional remedy to avoid
20 that kind of flip-flop in the future with an
21 executive order that might go the other way.
22 So, even though I think, at least

1 in the current climate, that would be hard to
2 imagine, one can't, of course, in Washington
3 ever rule out anything. So it is probably an
4 appropriate question to raise.
5 Let me just make one comment for
6 the record. It was mentioned we had a
7 conference call a week ago just because we are
8 so careful about these things. That was an
9 information conference call, which is entirely
10 something we do all the time with ACD. But
11 decisions on this topic of stem cells are
12 relegated for open sessions, like the one we
13 are having right now.
14 So should we hear from Jeff?
15 DR. SKIRBOLL: Yes. Thank you.
16 DR. BOTKIN: Thank you, Dr.
17 Skirboll and Dr. Francis. It is my privilege
18 to represent our working group today. And I
19 do want to thank Dr. Skirboll and Dr. Gebwah,
20 and Betsy Dean for the administrative support
21 that we have received. We were promised
22 outstanding administrative support. And we

1 really have received this. So thanks so much
2 for that.
3 My presentation is going to be I
4 think relatively concise. On the one line
5 that we have up for consideration today, Dr.
6 Skirboll mentioned our working group,
7 relatively small in number but just an
8 outstanding group of folks with a wide variety
9 of perspectives to bring to the table.
10 And I have been most impressed
11 with people's dedication to the task at hand
12 and the vigorous nature of the conversations
13 that we have around the lines that have been
14 submitted to us so far.
15 We have got two Dr. Davises from
16 Cleveland and two Jeffs, which is an
17 administrative challenge in and of itself.
18 (Laughter.)
19 DR. BOTKIN: Dr. Grainger from
20 University of Kansas provides outstanding
21 expertise for us from his background from the
22 Center for Reproductive Medicine; Rick Lifton,

1 background in genetics; Bernie Lo, a premier
2 bioethicist here in our country; Terry
3 Magnuson, probably well-known to most of you
4 from University of North Carolina; and then
5 Jeff Murray and Carlos Pavao, who also
6 participate with us.
7 So a few comments about our
8 specific process for the working group. First
9 of all, all conflicts of interest are
10 disclosed up front.
11 And, consistent with the previous
12 conversation, we think this is a big issue
13 nationally right now. We take this element
14 quite seriously.
15 And we will make a firm commitment
16 to you to avoid any appearance of conflict of
17 interest, much less actual conflict of
18 interest.
19 All of our working group members
20 read each of the applications. And then each
21 application is assigned by me to a member of
22 the working group as a primary reviewer.

1 I am pleased to say Jeff Murray is
2 the primary reviewer for today's application.
3 So my plan is to defer all of the tough
4 questions to him.
5 Three potential outcomes of our
6 deliberations: positive finding, negative
7 finding, or table. And tabling means
8 additional information from the applicant is
9 being requested through the NIH. And this has
10 been a common action to date so far for the
11 few that we have seen.
12 Our findings to you will include
13 majority and minority opinions, as
14 appropriate. We want to give you a flavor of
15 how that conversation went.
16 And I would say for today's
17 presentation, for the line under consideration
18 today, they were not substantive disagreements
19 on the findings that we will present today.
20 Material submitted by the
21 applicants, of course, treated as
22 confidential, at least up until meetings of

1 this kind.

2 So the working group is reviewing

3 materials from a number of submissions right

4 now and is scheduled to conduct reviews on a

5 rolling basis.

6 We can't anticipate at this point,

7 as Dr. Skirboll mentioned, exactly how many

8 lines will be submitted over time. But we

9 shall see.

10 Clarifying information has been

11 requested from a number of the submitters so

12 far. We may find that this process becomes a

13 little more streamlined over time as we and

14 submitters began to anticipate what the

15 information is that we like to have in order

16 to conduct a thorough review.

17 We have had a couple of challenges

18 that we have recognized so far with several

19 submissions that we have had the chance to

20 review.

21 Number one is the fact that the

22 consent for clinical services that couples

1 undergo as part the in vitro fertilization
2 process is distinct from the consent from the
3 research process.
4 And it may be that we want to look
5 at those clinical consent forms as well to try
6 to get an understanding of what the process
7 was for the couples from the clinical service
8 through to the consent for research donation.
9 Documentation of the options is
10 particularly relevant in the clinical consent
11 form, what options were mentioned to couples
12 at that time. And those options, of course,
13 may not be covered with the research consent
14 form.
15 Information on the timing of the
16 consent relative to the treatment is
17 important. I would say -- and I will probably
18 make this comment again -- the ethics here
19 really revolve around the informed consent of
20 the couples and that they're making an
21 informed, uncoerced, unmanipulated choice.
22 And so we will be focusing on the

1 process to a great extent of what the couples
2 went through as they considered this
3 possibility for donation for research
4 purposes.
5 Having said that, the
6 anonymization process limits the ability to
7 obtain full documentation, at least from
8 specific.
9 As we will see with this
10 particular application, we may not know what
11 clinic they came from, much less what couple
12 certain lines came from. And so that limits
13 in some circumstances our ability to review
14 these materials.
15 So the submission today is from
16 Harvard, 28 lines submitted. And the working
17 group thanks Harvard for a very thorough
18 submission. It was excellent documentation
19 they provided.
20 And Dr. David Korn, Vice Provost
21 for Research there, is assigning official.
22 And he was very responsive to our requests for

1 additional information. So thanks to Harvard
2 in that respect.
3 It covers 28 lines from embryos
4 donated in U.S. prior to July 2009 under a
5 single IRB-approved protocol and informed
6 consent form. So we will be dealing with
7 these as a group with one exception that we
8 will focus on in a minute.
9 Protocol designed fairly early in
10 this process. And I think that is important
11 for us to keep in mind. I think, as Dr.
12 Skirboll had mentioned as part of her
13 presentation, it is our obligation to look at
14 the era in which lines were donated and
15 created.
16 In other words, the ethical
17 conversation as well as a lot of the issues
18 around these lines has evolved substantially
19 in just the last ten years or so. So there is
20 certain unfairness if we were to apply today's
21 contemporary standards about the expectations
22 for donation and derivation to lines that were

1 created in earlier eras. So we are trying to
2 look at them under the standards that were
3 appropriate to today.
4 They were following 2000 NIH
5 guidelines. And they make a point of this,
6 those being existing guidelines that were
7 appropriate for them to follow at the time
8 this protocol was developed.
9 This is the process that Harvard
10 used to acquire embryos and to create the
11 embryonic stem cell lines. They originated in
12 multiple clinics around the United States.
13 They were providing clinical services to
14 couples, reproductive services. And there is
15 a collaborating IVF clinic.
16 Now, this is a term that in used
17 in the documentation. This is a regional
18 clinic that, of course, not a formal name, but
19 that is what it is being referred to, that
20 provided important services for the procedures
21 that we are going on here.
22 Basically what happened was many

1 of the lines, an unknown number, many lines
2 originated at this collaborating clinic
3 itself. Many embryos originated at the
4 collaborating IVF clinic.
5 In addition, there were a variety
6 of other clinics around the country that had
7 embryos that were no longer being used for
8 clinical reproductive services. And couples
9 became interested in donating those for
10 research purposes.
11 So the process was the couples
12 contacted the collaborating clinic. The
13 collaborating clinic discussed with the
14 couples over the phone the nature of the
15 research process and what they would be
16 getting into should they decide to donate
17 embryos for the purposes of research. And
18 then a consent form was sent to couples that
19 they signed and sent back.
20 At that point the embryos were
21 transferred frozen to the collaborating clinic
22 and then subsequently on to Harvard. And in

1 that process, there was a careful process of
2 anonymization. And this was an era, in
3 particular, in which there was a great deal of
4 controversy around the conduct of this work.
5 Some folks felt there were threats
6 to their welfare and health based on public
7 knowledge of activities. And so Harvard,
8 appropriately so, as well as the collaborating
9 clinic went through a process of anonymization
10 for these lines.
11 And so we don't have the ability
12 to identify the clinics that were the
13 originating clinics for these lines, much
14 less, of course, any of the specific
15 individuals that may have made donations. So
16 I think this is important to understand how
17 process worked for this particular submission.
18 Now, for our purposes, the working
19 group, we wanted clarifying information about
20 several aspects with the submission. And what
21 was the timing of the consent process? We
22 want to understand, as best we could, what the

1 sequence of events was.

2 What options were made available

3 to patients as they were considering the

4 possibility of donating embryos? What was the

5 financial and academic relationship of

6 individuals at the collaborating IVF clinic

7 with Harvard?

8 I want to speak specifically to

9 line 25 for a second. This is the only

10 individual line that will get attention from

11 the working group.

12 The consent from the donating

13 couples was obtained during a lapse in the IRB

14 approval of the consent and the protocol. As

15 folks are aware, IRB protocols need to be

16 renewed at least on an annual basis. This is

17 a big deal for investigators and IRBs.

18 But for a variety of

19 administrative reasons, there was a lapse in

20 the IRB approval of this protocol for a period

21 of time that was about seven or eight months

22 in length. They realized that was the case

1 subsequently and renewed the approval of the
2 project at that time.
3 Now, several lines were derived
4 during that period of time from embryos that
5 had been consented during the appropriate IRB
6 coverage. This was the only line in which the
7 consent itself was obtained during the lapse
8 in the IRB approval.
9 Now, Harvard proceeded to evaluate
10 carefully this issue. And they approved
11 continued use of line 25 based on a variety of
12 considerations. Donors had signed the consent
13 form. And, in fact, it was the same consent
14 form that was in use before and after the
15 lapse occurred.
16 No changes in the protocol had
17 occurred during the period of the lapse. And,
18 of course, there was no ability to reconsent
19 the embryo donor.
20 Now, it is important to emphasize
21 the last point here. The human subject
22 regulations don't specify what should happen

1 in this situation. It is up to the IRB to
2 make a determination given the circumstances
3 of the individual protocol what is ethically
4 appropriate, what is most appropriate for the
5 protection of human subjects involved.
6 So Harvard's IRB did carefully
7 evaluate this and decided it was appropriate
8 to continue to use that line. And that is
9 entirely appropriate given the regulations and
10 Harvard's careful deliberation.
11 Now, our finding is going to come
12 to a different recommendation here that I will
13 present in a minute. But there should be no
14 implication that Harvard was not acting in
15 full accord with regulations and research
16 ethics as commonly practiced.
17 All right. So here, then, are the
18 2(b) requirements Dr. Skirboll outlined for
19 you. And I am going to just walk through
20 these very quickly, as our working group does,
21 to indicate whether our findings are
22 consistent with the criteria.

1 Embryonic stem cells must have
2 been derived from human embryos, ones that
3 were created using in vitro fertilization for
4 reproductive purposes, so no question that
5 that criterion is fulfilled; two, that were
6 donated by donors who gave voluntary written
7 consent for the human embryos to be used for
8 research purposes.
9 And, again, we have consistent
10 consent documents that are thorough, document
11 that the couples provided voluntary written
12 consent. So we believe both of these criteria
13 are plainly met by the Harvard application.
14 Principles articulated in section
15 2(a). The Harvard application does not
16 fulfill all of the criteria by 2(a), but the
17 two criteria that are not entirely met we did
18 not feel raised any significant ethical
19 concerns with the application. I can talk
20 about those in a little bit more detail here
21 in a second.
22 We also have the obligation to

1 look at the Code of Federal Regulations, 45
2 CFR 46, subpart A, which is common rule. And
3 our review of the application and the consent
4 form, the protocol was consistent in our view
5 with the common rule. So we did not identify
6 any concerns that were raised by that review.
7 And then there are several points
8 to consider during the informed consent
9 process, including written or oral
10 communications, whether the donors were
11 informed of other available options pertaining
12 to the use of the embryos.
13 Now, this is a challenging one on
14 which we spent a fair amount of time because
15 the clinical consent forms were not available
16 to us given the nature of the protocol and the
17 referral end of these embryos from a variety
18 of different clinics.
19 So we had made a request back to
20 Harvard to say, is there any possibility of
21 obtaining specific consent forms that might at
22 least illustrate the nature of the consent

1 process for the clinical purposes? And,
2 again, we have the consent form that we
3 reviewed, of course, for the research
4 purposes. These were not available to us.
5 We felt, nevertheless, comfortable
6 that this criterion was adequately met for
7 several reasons. First of all, the consent
8 form itself, the research consent form,
9 clearly provides the alternative of destroying
10 the embryos as an alternative to donation of
11 research; secondly, part of the protocol that
12 explicitly states that the embryos are only
13 considered when couples have completed use of
14 the embryos for their reproductive purposes.
15 We did receive assurances from the
16 collaborating IVF clinic that, indeed, all
17 options were offered on a regular basis, not
18 illustrated to us in a consent form but
19 illustrated to us through an assurance that
20 all options were offered to couples at that
21 time other than the option of donating the
22 embryos for use by other couples for their

1 reproductive services.

2 That was not a routine option that

3 is or was offered to couples during that

4 period of time but other options in terms of

5 continuing to store them, transferring them to

6 another clinic, destroying them, using them

7 for research purposes. All of these other

8 options were presented at the collaborating

9 clinic.

10 So collaborating clinic staff feel

11 that this is quite consistent with what was

12 the standard at other referring clinics around

13 the country who provided the embryos. We

14 don't have actual physical documentation that

15 that is the case.

16 We feel given the sequence of

17 events and the fact that the couples were

18 contacting collaborating clinic if they were

19 interested in research purposes, that from an

20 ethical perspective, we are not concerned that

21 couples were coerced or manipulated or

22 uninformed about the nature of the choice they

1 were making when they agreed to donate their
2 embryos for research purposes; offered any
3 inducements for the donation of the embryos,
4 that is clearly stipulated in the consent
5 form; and, three, informed about what would
6 happen to the embryos after the donation for
7 research. And, again, we think that the
8 research consent form adequately covers what
9 would be done with those embryos.
10 Here is an additional
11 consideration relevant to some of the
12 discussion just a little bit earlier that we
13 wanted to raise.
14 So this is not on the working
15 group's plate to decide. Nevertheless, here
16 is what the consent form language says. These
17 sales will be used to study the embryonic
18 development of endoderm with a focus on
19 pancreatic formation.
20 The long-term goal is to create
21 human pancreatic islets that contain beta
22 cells, cells that produce insulin for

1 transplantation into diabetics.

2 Now, the Harvard IRB was asked to

3 look at this issue when a question was raised

4 about whether these lines could be put in a

5 general biobank for use beyond this initial

6 stipulated use.

7 The Harvard IRB determined that it

8 was acceptable to use sales more broadly based

9 on an interpretation of the common rule

10 regarding use of anonymized tissue.

11 And probably the point I want to

12 make here at the end is this is an active area

13 of debate right now nationally about how this

14 situation should be managed. And let me just

15 describe the situation in general terms.

16 You as an investigator say we are

17 going to use your tissues for research on X.

18 Tissues are donated. Research on X is done.

19 Now those samples are anonymized. They cannot

20 be traced back to you. And other

21 investigators want to use them for research Y.

22 Is that ethically appropriate? Is

1 that consistent with the regulations? And I
2 will just say that this is an active area of
3 debate right now nationally, both on the
4 ethics as well as on the regulatory aspect.
5 So an important point here is that
6 Harvard decided that they could be used more
7 broadly. That is quite consistent with common
8 practice and consistent I think with the
9 regulations, certainly at the time, again
10 understanding that there is an evolving
11 discussion about this particular issue. So
12 this is a thorny issue that will need to be
13 addressed at one level or another beyond the
14 working group.
15 So here are our findings for you.
16 CHAIRMAN COLLINS: Can we ask a
17 question?
18 DR. BOTKIN: Yes?
19 DR. WOLFE: Is that for just this
20 one line, 25, or is that for all of these
21 lines?
22 DR. BOTKIN: No. That's for all

1 of the lines. All lines were obtained under
2 that same consent language.
3 So the ACD should consider
4 recommending that 27 of the 28 lines submitted
5 by Harvard be eligible for use in
6 NIH-supported research.
7 We are finding that line 25 should
8 not be approved for this purpose. And I
9 think, consistent with the guidelines and
10 consistent with the standards that have been
11 articulated, we want the approval, we
12 encourage the approval, to be beyond reproach.
13 And we think while the approval of line 25 by
14 Harvard was entirely consistent with the
15 regulations, that we have different standards
16 to live by at this level. And so our finding
17 is that line 25 should not be eligible for
18 thorough finding.
19 Question?
20 CHAIRMAN COLLINS: Let's say a
21 word about how we are going to proceed. At
22 this point we want to hear the discussion very

1 much from the ACD members.

2 Clearly the decision that you need

3 to make -- and we will take a vote on this --

4 is whether any or all or some subset of this

5 set of 28 lines should be considered eligible

6 for use in NIH-supported research.

7 I would also like to hear your

8 thoughts about the way in which there might

9 need to be a restriction based upon the

10 language of the consent form in terms of what

11 kinds of research these lines could be used

12 for given the focus that you have heard from

13 Jeff already about the endoderm, as mentioned

14 in the consent form.

15 The decision we are asking you to

16 make is whether they can or cannot be approved

17 for eligibility for some kind of NIH-funded

18 research. And in terms of the eligibility

19 question, that is going to fall to NIH to try

20 to figure out how best to do that. But we

21 would like to hear your guidance on that.

22 Again, the decision that we would

1 hope that you would be willing to make in a
2 formal way is whether any or all of these
3 lines could be considered for eligibility for
4 research of some sort through NIH funding.
5 I hope that was a clear sort of
6 distinction between the two issues. Now let's
7 hear some discussion.
8 DR. HORWITZ: Point of
9 information.
10 CHAIRMAN COLLINS: A point of
11 information first.
12 DR. HORWITZ: Did the working
13 group take a vote? And if so, can we know
14 what it was?
15 CHAIRMAN COLLINS: Working group
16 gives findings. They don't make
17 recommendations.
18 DR. HORWITZ: Okay.
19 CHAIRMAN COLLINS: So I guess they
20 probably don't take votes, but you did say
21 earlier that there was no substantive
22 disagreement about what you are putting here

1 on this slide. Is that fair, Jeff?

2 DR. BOTKIN: That is correct.

3 CHAIRMAN COLLINS: Thank you.

4 So Cathy?

5 DISCUSSION

6 DR. DeANGELIS: Well, Francis, as

7 far as the first part, the use for the cells

8 that produce insulin for transplantation, I

9 have no concern about that, but I have great

10 concern about the next step: the use of

11 anonymized biospecimens for research not

12 addressed, et cetera, et cetera.

13 I am trying now to get, I e-mailed

14 my office to get, the citation. We recently

15 published an article showing that -- now, this

16 was a sperm donor who didn't realize that he

17 had the genes that carry very substantial

18 cardiomyopathy. And they discovered, I

19 believe it was, five infants who were born

20 were this. Some were stillbirth.

21 And we found it by accident

22 because we got this one article submitted,

1 which was a study. Simultaneously we had an
2 article submitted that was a piece in my mind
3 from I'll call it the mother who had been
4 impregnated. Actually, she wasn't. She was
5 the partner of the mother.
6 And she was writing to present how
7 heartbreaking it was -- and I didn't mean
8 that, believe me, as a pun -- of she and her
9 partner to have this infant born with this
10 cardiomyopathy. And we sort of put two and
11 two together and discovered it was this
12 father.
13 And so I think without knowing as
14 much as possible about the donors, to use
15 these stem cells for any purpose that might
16 lead to that sort of thing would be extremely
17 dangerous or perhaps will leave to untoward
18 events that could backfire on what should be
19 wonderful research and should lead to great
20 things.
21 I am just a clinician speaking.
22 CHAIRMAN COLLINS: Lana, why don't

1 you come to the table for this discussion
2 because I think a lot of issues may get
3 raised. This one I wasn't quite expecting.
4 I think when it comes to
5 therapeutic applications, which is what you
6 are concerned about, --
7 DR. DeANGELIS: Yes.
8 CHAIRMAN COLLINS: -- nobody
9 really knows where this field may go or may
10 not go. I think certainly the vast majority
11 of applications in the short term are going to
12 be of the basic science sort, --
13 DR. DeANGELIS: That's terrific.
14 CHAIRMAN COLLINS: -- although
15 obviously clinical implications are
16 downstream. And certainly because these lines
17 if they are approved can be used for a variety
18 of different explorations, the full genome
19 sequence will probably emerge from these along
20 the way.
21 So that if there were an easily or
22 not so easily even discernible serious genetic

1 flaw, that would be ascertained prior to
2 contemplating a clinical utilization.
3 John, did you want to --
4 DR. SKIRBOLL: I think in the end,
5 it is important to remember that there are
6 very few cases we are talking about using
7 human embryonic stem cells themselves in a
8 clinical situation.
9 But the somatic cells that are
10 derived from them, any use of them, would be
11 subject to FDA regulation and all of the
12 safety issues ensuing.
13 CHAIRMAN COLLINS: John?
14 DR. NELSON: I assume the motion
15 is on the floor. If not, I make the motion.
16 But to discuss it, I think that what we are
17 doing today is historic and believe that it
18 should be done so terribly carefully. We
19 shouldn't use the microscope. It should be an
20 electron microscope.
21 And I commend Harvard for being
22 forthcoming about the lapse in something that

1 was a technicality. And, to be fair, there
2 isn't a bit different way that this is treated
3 than any other. But because of that lapse and
4 because of making sure every "I" is dotted,
5 every "t" crossed, I believe that the working
6 group has done us a favor by pointing out how
7 carefully they and this group will scrutinize
8 these kinds of decisions.
9 And, for those reasons, I support
10 the recommendation of the working group.
11 DR. LUNA: I know that we are
12 going to vote. And that is separate from what
13 you said, maybe some insight as to the future.
14 I am thinking a little bit about the consent
15 process that is very specific.
16 But you do want to support
17 innovation. You do want this to be available
18 to people we don't even know where they could
19 take this research to.
20 So maybe provide NIH with guidance
21 as to having a uniform way, uniform phrasing
22 to put into the IRB that specifies that it

1 could be used for general purposes and, more
2 than anything, delineate what it will not be
3 used for so that it can really be available
4 and support innovative work.
5 CHAIRMAN COLLINS: Oh, yes. That
6 would be fantastic for future prospective
7 opportunities of this sort. We are, of
8 course, dealing now with a consent form that
9 was written seven or eight years ago. And it
10 is what it is.
11 Unfortunately, we are asking you,
12 therefore, to try to interpret what is the
13 best circumstance and the best way to try to
14 honor the intentions of that time. But
15 certainly going forward, we would agree with
16 what you have just said.
17 Mary?
18 DR. BECKERLE: I have a comment
19 and then a question. So my comment is I think
20 I would endorse the exclusion of that line 25
21 from further consideration, as your group
22 recommended, given the lapse in the IRB.

1 I just want to say that I have
2 some very deep concern about any action that
3 would suggest that it is okay to sort of
4 rethink and retrospectively consider what was
5 in somebody's mind when they or what they
6 might be open to when you have an informed
7 consent.
8 So I think we really have to take
9 very literally in a sense what is written in
10 that informed consent. And I think we would,
11 especially at this very historic moment when
12 we are in the very early stages of moving
13 forward with this type of work, I think it
14 would really risk the public trust if there
15 were any sense that anyone sitting around a
16 room could, for any reason, kind of go too far
17 beyond what was clearly articulated in the
18 consent form. And so that makes me extremely
19 anxious.
20 I appreciate that it is beyond the
21 specific issue that we have been asked to
22 address today. But, actually, it makes me a

1 little anxious to move on that proposal
2 without knowing what the next level outcome is
3 going to be in terms of that debate.
4 And then my question is, can you
5 say a little bit more about how you are
6 verifying the authenticity of the informed
7 consent and everything else when everything
8 has been anonymized?
9 DR. BOTKIN: Well, the
10 authenticity of the research informed consent
11 is not under question. We do know that
12 everybody signed that consent form and that
13 there is a tight link between the donation of
14 those lines and that research consent form or
15 at least we don't have any reason to believe
16 there are any problems there.
17 What we don't have information
18 about is exactly what the nature of the
19 clinical consent was when the couples
20 underwent clinical services for fertility.
21 DR. BECKERLE: I guess my question
22 is, how do we know that? I mean, if you can't

1 look at the informed -- is there some
2 mechanism by which there is an informed
3 consent and four people sign off saying they
4 saw it and then it was anonymized or is -- I
5 don't know.
6 DR. SKIRBOLL: So I think it is
7 important to -- this mode of functioning for
8 NIH of assurances signed off by an
9 institutional official, there are negative --
10 how can I say it? What? Legal, civil and
11 criminal penalties associated with lying to
12 the federal government.
13 We take quite seriously we do this
14 through a number of other aspects of applying
15 for grants. You may be aware that your
16 institutional official signs off on a number
17 of things, including adhering to the
18 recombinant DNA guidelines, those sorts of
19 things.
20 So we consulted with our lawyers.
21 And we feel that, although we certainly
22 wouldn't want a single letter that simply

1 assures, "Yes, we did this. See those
2 guidelines?" Yes. But where we have a lot of
3 documentation and then seek assurance in
4 places where the Committee felt comfortable
5 with it, we are comfortable with the
6 assurance.
7 DR. BOTKIN: I think one other
8 feature here is that the derivation process is
9 not highly efficient. In other words, quite
10 a few embryos are required in order to create
11 one stem cell line.
12 And so once they have been
13 anonymized, then it may be difficult to take
14 the line and try to track back to who an
15 individual donor was. And that is certainly
16 relevant for any question about whether
17 questions arise about whether those folks
18 should be reconsented or ask their opinion
19 about various aspects of this process.
20 CHAIRMAN COLLINS: Dr. Murray is
21 next.
22 DR. MURRAY: So I want to speak to

1 a couple of the points that were just raised
2 and then also to reinforce what Jeff said
3 earlier about the guidance and support that we
4 received from Lana and from Ellen and from
5 Jeff himself and the Committee makeup.
6 All of us have been on lots of
7 committees. I have never been on a committee
8 that sort of came together, I think, as
9 quickly as this one. There was really good
10 discussion and a lot of back and forth.
11 But I think, as Jeff said, there
12 was really very good consensus, at least on
13 these particular cell lines that we are
14 talking about today, on all of the issues that
15 are being presented.
16 The fact that we are able to go
17 back to Dr. Korn in this iterative fashion and
18 just sort of ask this question again about
19 your concern about how the consenting was
20 taking place and what was present in the
21 clinical sense I think also reassured us that
22 this was done at least as properly as we are

1 able to assess from the documents that we
2 received from them.
3 We did have some other concerns
4 that also came up. And I think again in
5 response to sort of John's comment earlier on,
6 we did take this really seriously. So we also
7 asked them to ensure that there were no
8 financial arrangements that were beneficial to
9 the collaborating clinics that they would have
10 been under any motivation to supply embryos.
11 And, again, they reassured us that all of the
12 financial arrangements were solely for the
13 cost that would take place as part of the
14 consenting process and the shipping of the
15 embryos.
16 So I think we did as good a job as
17 we could and that this iterative process of
18 being able to go back to them and get more
19 documentation and having them to respond
20 really assured us as well as we could be that
21 things were being done properly.
22 And, again, the final point is,

1 was this somewhat unusual arrangement, at
2 least for some of the lines, coming from not
3 the collaborating clinic, which was anonymized
4 to us, but, rather, from the sort of secondary
5 feeder clinics? And, again, they responded to
6 that in the process.
7 Jeff made the point that I will
8 just reinforce, that they really went to, I
9 think, quite extraordinary lengths to make
10 sure that these lines really were anonymized
11 because of the concerns about publicity and
12 threats and so on. So they were taking,
13 really, extra steps at the time.
14 DR. WOLFE: Well, I want to pick
15 up, I think, on the first point that Mary
16 raised. My concern, really, is not with the
17 general approval but, really, with it going
18 beyond the development of endoderm.
19 I mean, I can sort of see the
20 rationale, actually, for why line 25 might be
21 approved because what you are seeing is a
22 lapse, but everything was done the same.

1 This seems like it was very
2 carefully stated, what the purpose was. And
3 so if this sort of said that the ACD should
4 consider recommending that these lines should
5 be used for this purpose, I think there would
6 be no question whatsoever because that is what
7 the consent form stated.
8 This says that the topic is being
9 discussed, but we are being asked to sort of
10 vote on something before there has been a
11 decision made about whether you can go from
12 some specific consent form of this sort to
13 using these lines more generally.
14 Given the need for care at this
15 stage to really be able to move forward on
16 this, I guess I would like to hear a little
17 bit more about what the justification is to
18 really go beyond this, beyond the endoderm.
19 CHAIRMAN COLLINS: Let me suggest
20 a path forward because I hear very much the
21 concern about the restriction in the consent,
22 and I share that.

1 I think one thing we could do just
2 in order to try to move the discussion forward
3 to decisions would be to consider perhaps not
4 one but two votes, two motions. And obviously
5 it is up to you all to make the motions.
6 One would be to decide whether or
7 not these 28 lines or perhaps 27 if you agree
8 with the working group findings that line 25
9 should be excluded have actually met the
10 standards that were put forward in section
11 2(b) of the NIH guidelines.
12 Those section 2(b) guidelines do
13 not reflect on this issue of restriction of
14 the consent form for specific purposes. So
15 you could decide just on the basis of those
16 guidelines. Are you comfortable that we have
17 met that standard, as the working group has
18 recommended?
19 And then as a second discussion,
20 hopefully then leading to a second motion, you
21 could decide, if you wish, also, then, to
22 charge the NIH in whatever way you see fit to

1 adhere or not to the stipulations that consent
2 about endoderm.
3 And I hear a fair amount of
4 concern around the room if we don't do that,
5 that we are perhaps treading into territory
6 that is not respectful of the original
7 process.
8 But if we tried to keep it in
9 those two separate but related conversations,
10 that would help me as the Director in terms of
11 how to go forward to the next step. Again, I
12 don't mean to lead the witnesses here, but
13 that might be a way to try to make progress.
14 I see nodding heads. Well, are
15 there other questions or is it time for a
16 motion?
17 DR. NELSON: I move to divide the
18 question formally into those two courses.
19 CHAIRMAN COLLINS: Okay. I don't
20 know. Do we need a motion to divide it or do
21 we need motion to put forward?
22 DR. HORWITZ: I would make a

1 motion that we approve the working group
2 findings as stated here, recommending that 27
3 to 28 lines be eligible in NIH-supported
4 research --
5 CHAIRMAN COLLINS: Second.
6 DR. HORWITZ: -- and that line 25
7 should not be approved.
8 CHAIRMAN COLLINS: Second. Is
9 there further discussion? It's essentially
10 what is on the slide.
11 DR. KING: But just for
12 clarification, then, does this mean
13 NIH-supported research generally or only as
14 defined by the consent form?
15 CHAIRMAN COLLINS: Do you want to
16 clarify? That's the second question, but --
17 DR. KING: I know. I know.
18 CHAIRMAN COLLINS: -- do you want
19 to clarify the wording of yours? If you want
20 to add something about at least that these
21 meet the guidelines of section 2(b), I suppose
22 you could straighten that out.

1 DR. HORWITZ: So I will accept
2 that amendment to the motion that it meets the
3 guidelines of section 2(b).
4 CHAIRMAN COLLINS: Is there any
5 further discussion?
6 (No response.)
7 CHAIRMAN COLLINS: Then let me
8 call for a vote, please. All in favor, please
9 -- Ralph, do you want to --
10 DR. BECKERLE: I would appreciate
11 a repeat of the final wording on this one.
12 DR. HORWITZ: The Advisory
13 Committee to the Director accepts the working
14 group findings and recommends the 27 to 28
15 lines submitted be eligible for use in
16 NIH-supported research, having met the
17 guidelines of section 2(b). And then line 25
18 should not be approved for this purpose.
19 DR. BECKERLE: I guess I will just
20 say that I thought where we were going is that
21 we were going to say something more along the
22 lines of the ACD recommends, accepts the

1 finding that the 27 of the 28 lines submitted
2 by Harvard adhere to the provisions in 2(b) or
3 2(a) or whatever it is and that 25 did not
4 meet the provisions.
5 But I think if we put into that
6 first motion that they are eligible for
7 funding without the exception of consistent
8 with the consent form, that we still have the
9 concern.
10 DR. KINGTON: The problem is that
11 section 2(b) determines what is eligible for
12 funding. So it is the same thing. So you
13 have to -- but if you have this second motion,
14 then you can express the opinion of the ACD
15 about what type of research should be
16 eligible.
17 DR. KELLY: It seems to me one
18 alternative way to go is to use the language
19 down to research, NIH-supported research, in
20 the areas that were specified in the consent.
21 Okay? And then we could consider a second
22 motion as to whether to expand that.

1 DR. BECKERLE: I like that.
2 DR. HORWITZ: Well, I specifically
3 did not do that because I understood that the
4 goal was actually to address the issue of
5 extension according to consent in a separate
6 motion so that there is some flexibility
7 provided to the Director of the NIH to address
8 that issue.
9 CHAIRMAN COLLINS: I believe that
10 as long as --
11 DR. WOLFE: If we did this first
12 --
13 CHAIRMAN COLLINS: As long as you
14 have two motions that are passed at the same
15 session, you can't take one of them out of
16 context and say you can ignore the second.
17 So if there is a concern about the
18 way Ralph phrased the original motion as being
19 taken too broadly, we certainly would not ever
20 contemplate doing so.
21 DR. NELSON: Dr. Collins, I made a
22 lifetime study of parliamentary procedure.

1 CHAIRMAN COLLINS: Oh, good. We
2 could use that right now.
3 (Laughter.)
4 DR. NELSON: To be fair, sir, to
5 be fair, sir, we should do it in the opposite
6 way. If, in fact, we give consent to do the
7 research and don't specify what the research
8 is, it is hard to do that. So the purpose of
9 the amendment is to restrict it.
10 So the correct way to do this, Dr.
11 Collins, would be to discuss the issue of
12 making sure that we do only what the informed
13 consent says. And then if that is approved,
14 say this will be approved pending that. That
15 is the way to do it.
16 CHAIRMAN COLLINS: That's an
17 excellent suggestion. So may we table the
18 original motion and entertain the one that was
19 going to be second, which was now moved
20 forward?
21 DR. NELSON: That being the case,
22 I move that the research referred to here be

1 restricted to that which is specifically
2 stated in the consent form.
3 CHAIRMAN COLLINS: Is there a
4 second?
5 PARTICIPANT: Second.
6 CHAIRMAN COLLINS: Is there
7 discussion?
8 DR. THRALL: I would like to speak
9 against that motion from two standpoints.
10 First, it is unclear how the so-called
11 specific language interacts with the common
12 rule. So it is not clear that any use was
13 interdicted by the original consent.
14 And, secondly, this is a broader
15 question. And if we were to consider this as
16 an Advisory Committee, I would favor bringing
17 it for more than ad hoc discussion before this
18 group.
19 CHAIRMAN COLLINS: Jeff?
20 DR. MURRAY: So this topic was a
21 point of relatively lively discussion in the
22 working group. And although our remit was not

1 to make recommendations of it, we certainly
2 went back and forth.
3 I think in response to James'
4 point that there was a lot of discussion about
5 what would be the appropriate process, I think
6 that is up to us and up to Francis but that
7 there would be a number of options for the way
8 to go forward on this and whether we should
9 decide that now or whether that should be some
10 formal committee of NIH or some other group as
11 I think something we need to consider.
12 We did not come to conclusions
13 ourselves.
14 DR. THRALL: If I could just
15 comment again? I think it is very dangerous
16 to make this kind of policy in an ad hoc
17 manner like this.
18 CHAIRMAN COLLINS: Well, one
19 option would be for you as the ACD to charge
20 NIH to develop a process for defining a policy
21 about how to handle restrictions in a consent
22 in this particular arena. We would be happy

1 to receive that recommendation.
2 Yes?
3 DR. DeANGELIS: That
4 recommendation will follow whatever we do with
5 this.
6 CHAIRMAN COLLINS: I think, given
7 John's recommendation, that we should first
8 enunciate clearly what the sense of the ACD is
9 about how to handle the restriction on the
10 consent. And then we will come back to decide
11 about section 2(b).
12 Mary-Claire?
13 DR. KING: Yes. If I have
14 understood the discussion correctly, the lines
15 in question do follow under the purview of the
16 common rule.
17 CHAIRMAN COLLINS: Everything
18 does.
19 DR. KING: Everything does. And
20 the common rule does indicate that anonymized
21 samples may be used generally, truly
22 anonymized samples. And from everything we

1 have heard from the Jeffs, these samples are
2 truly anonymized.
3 Therefore, I wonder why we would
4 be asking NIH to revisit this entire issue.
5 I think this is very much what Dr. Thrall has
6 been saying.
7 I am very concerned that if NIH
8 takes the position that somehow the common
9 rule should be abrogated and the truly
10 anonymized samples cannot be used in the way
11 that the common rule previously has specified,
12 that all of genetic research, well, since the
13 development of the common rule, would no
14 longer be valid. And that would be a shame.
15 CHAIRMAN COLLINS: Jeff Botkin
16 appears to have a comment.
17 DR. BOTKIN: Yes. Well, the
18 Secretary's Advisory Committee on Human
19 Research Protection, SACHRP, is actively
20 discussing this issue right now. So it is in
21 process. And that is advisory to the
22 Secretary of Health and Human Services, of

1 course. And OHRP is the governing agency
2 there.
3 And so it has been a very active
4 discussion because it is common practice to
5 anonymize clinical samples, anonymize research
6 samples. And once they are anonymized; in
7 other words, actually, it's broader than that.
8 If the samples cannot be readily identified,
9 the source of the samples can't be readily
10 identified, by the investigators, then it's
11 not human subjects research. So it's outside
12 the common rule at that point.
13 And so this does have implications
14 for a wide variety of research. But I guess
15 one comment I would make in that regard is I
16 would not want to see a precedent set here
17 that would articulate what the standards are
18 more broadly for the conduct of research but
19 really articulate a specific set of
20 considerations around the stem cell lines
21 given the fact that they are set up, this
22 whole process is set up, to be a higher level

1 of scrutiny and ethical standard than is
2 commonly undertaken with the common rule.
3 And so if a decision is made about
4 this, my suggestion would be to make it clear
5 that you are not trying to set standards, NIH
6 standards, for how tissues are managed in
7 general because I think this is a very active
8 problem.
9 CHAIRMAN COLLINS: Yes. There's
10 an example, just to expand on that, that this
11 group has dealt with, which is what to do
12 about genome-wide association study data,
13 where, again, samples that have been stripped
14 of all identifiers are submitted to the DBGAP
15 database, where it was felt because of the
16 potential downstream by some connection
17 depending on DNA sequence that individuals
18 might, although following the standards of
19 anonymization that were true in the past might
20 not necessarily still be anonymous in the
21 future, that there still ought to be an
22 adherence in that circumstance to certain

1 standards of privacy.

2 And also in those circumstances if

3 there were samples that were donated by

4 individuals for specific purposes, like "We

5 want these samples to be used to study

6 diabetes," that that restriction should be

7 honored because it was given in good faith by

8 the participants. And, even if their

9 materials were stripped of identifiers before

10 ending up in DBGAP, that restriction should be

11 honored.

12 In that sense, the common rule was

13 considered as a floor but not a ceiling in a

14 special circumstance of particular sensitivity

15 and high visibility. I think that is the same

16 thing we are talking about here, and I

17 completely agree with what was just said about

18 not extrapolating from this very special

19 situation with all of the very high level of

20 concern and scrutiny that attaches to it in

21 saying that that would apply in other

22 circumstances.

1 But we have to deal about this one
2 right now. I think it probably is the case.
3 I mean, I will speak personally for a moment.
4 If a couple signed that consent form in good
5 faith to donate an embryo for this kind of
6 purpose and later found out that the
7 restriction that they had agreed to had been
8 ignored because subsequently the sample was
9 anonymized.
10 That somehow doesn't seem quite
11 like that is honoring their intentions. And
12 it would be hard for me as the NIH Director I
13 think to feel comfortable defending that in
14 this very visible situation.
15 John and Maria. Yes, John?
16 DR. NELSON: Dr. Collins, as a
17 surgeon, when I get a consent form for a
18 procedure, there is a statement on the consent
19 form that says, "and other necessary
20 procedures."
21 So if I were going to go in to
22 take care of a ruptured ectopic pregnancy, I

1 would try to save the tube. If I couldn't do
2 that, I would have permission to take the
3 tube. But I wouldn't do a cholecystectomy
4 because I didn't have -- no, I am not trying
5 to make fun of it.
6 CHAIRMAN COLLINS: I hear you.
7 DR. NELSON: I have permission to
8 do what I need to do. I believe -- I can't
9 say this well enough -- this is an amazingly
10 important decision we are making today. It is
11 the first of a series of decisions that will
12 have to be made by the ACD. To defer this
13 decision, which is going to take you another
14 six months, I think we need to act today.
15 I believe in this case and this
16 case only, we need to make sure that we do
17 exactly what the consent form said. I
18 recommend, therefore, that as we vote, we vote
19 on this case and this case only.
20 It has nothing to do with the
21 common rule. That is going to be at a
22 different time. I think we would be doing

1 ourselves and, more importantly, the public a
2 disservice, which would make them not be able
3 to trust us.
4 The scrutiny on this decision is
5 going to be significant, Dr. Collins.
6 Therefore, I move that we do it in the order
7 we have talked about. I recommend that we
8 specifically state with the endoderm for beta
9 cells in this particular case only and in the
10 future can take it on a case-by-case basis.
11 CHAIRMAN COLLINS: I think Maria
12 was next.
13 DR. FREIRE: I guess I am sorry I
14 have lost a little bit of my way in this
15 discussion. I just want --
16 CHAIRMAN COLLINS: I can't
17 understand how that could be.
18 DR. FREIRE: So I just want to
19 make sure that what you had originally asked
20 us to consider was whether or not these met
21 the guidelines, correct?
22 CHAIRMAN COLLINS: Right.

1 DR. FREIRE: Not whether the
2 restriction was --
3 CHAIRMAN COLLINS: Because the
4 guidelines actually don't --
5 DR. FREIRE: Don't address that?
6 CHAIRMAN COLLINS: Right.
7 DR. FREIRE: So there are two
8 separate --
9 CHAIRMAN COLLINS: That's why we
10 were sort of separating these into two issues.
11 DR. FREIRE: Just to make sure
12 that I am not losing my way, so what you need
13 to move forward from us, first and foremost,
14 is, do these mete the guidelines? And then we
15 need to separately think about this
16 restriction. Do I have this clear in my mind?
17 CHAIRMAN COLLINS: Right, although
18 I think John's point was because of
19 parliamentary procedure, not wanting to decide
20 about eligibility for research before you had
21 established your views about what that means,
22 that he would prefer -- and I think there was

1 some nodding of heads -- that we first decide
2 what that means in this specific case.
3 DR. FREIRE: Yes. I just don't
4 want to lose my way again. I just want to
5 know what it is we need to accomplish.
6 CHAIRMAN COLLINS: I appreciate
7 your thoughtful clarification. We need this.
8 There is a motion on the table.
9 Do you want to state it again because time has
10 passed and other points have been made?
11 DR. NELSON: I move that the
12 research referred to here be used to study the
13 embryonic development of endoderm with a focus
14 on pancreatic formation to create human
15 endoderm for beta cells only.
16 CHAIRMAN COLLINS: In other words,
17 following the precise wording of the consent.
18 That is what you were just reading?
19 DR. NELSON: Yes, sir. But I for
20 the record read it.
21 CHAIRMAN COLLINS: And is there a
22 second?

1 DR. KINGTON: Maybe we should
2 clarify that the motion is that for any of the
3 lines approved today and subsequent to today
4 --
5 DR. NELSON: For these 27 only,
6 specific and only to this case today.
7 DR. KINGTON: -- that restriction
8 would be followed.
9 CHAIRMAN COLLINS: Okay.
10 DR. KINGTON: You would recommend
11 to the Director of NIH that the agency honor
12 that restriction.
13 DR. THRALL: I don't know if this
14 was -- is this open for discussion now?
15 CHAIRMAN COLLINS: I was waiting
16 for a second because I -- okay. We have a
17 second. Now we are open for discussion.
18 DR. THRALL: So I don't think the
19 motion as stated does reflect what was in the
20 consent form because if I am reading the
21 report of the working group correctly, it says
22 to study embryonic development of endoderm

1 with a focus on pancreatic formation. The
2 long-term goal is to create human pancreatic
3 islets that contain beta cells, the cells that
4 produce insulin for transplantation into --
5 and this may be a typo -- diabetes, rather
6 than diabetics.
7 But if you deconstruct that, it
8 doesn't say that that is the only thing that
9 is going to be done.
10 CHAIRMAN COLLINS: Again, I think
11 John's motion was that NIH should honor the
12 consent form as written. And you basically
13 then read us what was written.
14 DR. NELSON: Raise concerns if we
15 go beyond the consent form in this instance.
16 I think this sets the precedent. And what Dr.
17 Thrall is talking about, if we were to follow
18 logically, the next time something like this
19 happens, we will not have this proscription in
20 here, I would assume.
21 But in this case, Dr. Collins, I
22 couldn't say more strongly if the public felt

that we are gerrymandering artificially what is certainly in the mind of the people who gave the consent, I think we are in a very, very difficult place.

DR. THRALL: Well, but that's a general statement. And if we are going to have specificity in the motion, then it needs to link to that consent form.

And, frankly, that is then going to be a matter of judgment on other people's part down the road.

CHAIRMAN COLLINS: So I guess I don't hear substantive disagreement about that.

DR. KING: I have a question. Question, Francis?

CHAIRMAN COLLINS: Maria?

DR. FREIRE: So how about something like NIH fund research that is consistent with the consent form, you know, in the --

PARTICIPANT: I second that.

1 CHAIRMAN COLLINS: That was the
2 intention.
3 Mary-Claire?
4 DR. FREIRE: -- in using these
5 lines.
6 CHAIRMAN COLLINS: Yes?
7 DR. KING: I would like to quote
8 to us from the working group document that we
9 received for discussion for this meeting. It
10 says, "The Harvard IRB later determined that
11 it was acceptable to use the cells more
12 broadly. And they are now used for all kinds
13 of diseases and tissues."
14 If we pass this motion, as John
15 has suggested, John's motion, are we putting
16 Harvard in an untenable position?
17 CHAIRMAN COLLINS: No.
18 DR. NELSON: No. They're entitled
19 to their view --
20 DR. KING: Okay.
21 DR. NELSON: -- reaching a
22 different conclusion.

1 DR. KING: They can't use --
2 DR. JACKSON: The consent form
3 says use of embryonic cells with a focus on.
4 So yes, this is totally appropriate for them
5 to do this.
6 DR. LUNA: I think we're in
7 agreement, then. It is not for us to
8 interpret the consent form. I think that is
9 the point. It is not for us to interpret it
10 but to say to follow the consent form.
11 DR. KING: But Harvard is doing
12 fine. I mean, it is something --
13 DR. THRALL: The issue is the NIH
14 funding. They don't have NIH funding for
15 this.
16 DR. HORWITZ: But can I be clear
17 if I understand, then, that we were to endorse
18 that motion, that research done with these
19 cell lines would not be eligible for NIH
20 funding; is that correct, except under the
21 conditions of the consent form?
22 CHAIRMAN COLLINS: So we have a

1 motion on the table, which has been, I think,
2 clarified and which we will be sure to capture
3 the intention of the conversation that has
4 just happened that is basically John's motion
5 says that these lines should honor, the use of
6 these lines should honor, the consent form as
7 stated for this particular decision without an
8 implication that this has broader extensions
9 to other circumstances.
10 And that has been seconded, and we
11 have had some discussion. I think it is time
12 to call for a vote. So can I ask all in favor
13 of the motion to raise your hands and say aye?
14 (Chorus of ayes.)
15 CHAIRMAN COLLINS: Okay.
16 DR. JACKSON: The asterisked
17 people can't vote.
18 CHAIRMAN COLLINS: What?
19 DR. JACKSON: The asteroid people,
20 you know.
21 (Laughter.)
22 DR. KINGTON: There are people

here who are not technically members of the Committee yet. They have asterisks by their names. You can vote, but it just won't count.

CHAIRMAN COLLINS: Asterisk, not asteroid. So okay. So yes. Is Lana or somebody keeping track of a vote? Can we have a show of hands one more time, please, in favor of the motion?

(Show of hands.)

CHAIRMAN COLLINS: Okay. Have you got it? And all those opposed?

(Show of hands.)

CHAIRMAN COLLINS: And were there any abstentions?

(Show of hands.)

CHAIRMAN COLLINS: Very good. Okay. Thank you.

Now to the second motion. Ralph, you had --

DR. HORWITZ: Which was the first motion.

(Laughter.)

1 DR. HORWITZ: Thank you, John, for
2 that parliamentary direction. But to move to
3 accept the recommendations of the working
4 group to approve 27 of the 28 lines, not to
5 approve line 25, according to the guidelines
6 of section 2(b).
7 PARTICIPANT: Second.
8 CHAIRMAN COLLINS: Any discussion
9 on this?
10 (No response.)
11 CHAIRMAN COLLINS: Then all in
12 favor, please raise your hands and say aye.
13 What the heck.
14 (Chorus of ayes.)
15 CHAIRMAN COLLINS: Anyone opposed?
16 (Show of hands.)
17 CHAIRMAN COLLINS: And were there
18 any abstentions?
19 (Show of hands.)
20 CHAIRMAN COLLINS: Bravo. That
21 was extremely helpful. So I will take your
22 recommendations under consideration, believe

1 me, and expect to make an expeditious decision
2 in the very near future.
3 I think you have pointed out a
4 critical need for NIH to establish a policy
5 about how to handle restrictions that may
6 appear in future consents that come forward
7 from the working group and to you. And we
8 will do that and develop such a policy and
9 bring it back to you for your consideration.
10 And we will try to be consistent
11 and fair in every way and also to have a
12 process here that is above reproach,
13 recognizing that this is an extremely critical
14 set of decisions with a great deal of public
15 interest and that we would never want to do
16 anything that would compromise the highest
17 ethical standards. We worked very hard in
18 this process to achieve that high goal.
19 And, of course, with regard to
20 what you have suggested, once I have made a
21 decision, if we put these up on the registry,
22 we will make sure that if there are

1 restrictions in the use of certain stem cell
2 lines, that those are immediately obvious on
3 the registry so that nobody gets surprised
4 later on by discovering that. That will need
5 to be communicated most clearly.
6 Again, I would expect to make a
7 decision in the very near future, but I am not
8 prepared to make it right here at this very
9 moment.
10 So, with that, bravo. Thank you.
11 And are we ready to move on?
12 DR. KINGTON: We will break for
13 lunch. And we will do the photo when we
14 reconvene, when we reconvene. Sorry.
15 CHAIRMAN COLLINS: When we
16 reconvene. Okay. So you can go. And we will
17 reconvene at what time?
18 DR. KINGTON: At 1:00 o'clock.
19 CHAIRMAN COLLINS: Yes. Let's try
20 to come back at 1:00 o'clock.
21 DR. KINGTON: We are going to try
22 to come back at 1:00 o'clock.

1 CHAIRMAN COLLINS: Forty-five
2 minutes hopefully will be enough to nourish
3 yourselves.
4 (Whereupon, at 12:17 p.m., the
5 above- entitled matter went off the record to
6 resume for the afternoon session at 1:12 p.m.)
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1 A-F-T-E-R-N-O-O-N S-E-S-S-I-O-N

2 (1:12 p.m.)

3 CHAIRMAN COLLINS: Well, welcome

4 back from lunch. We will hear about

5 comparative effectiveness research in just a

6 moment from Dr. Hodes.

7 A number of us thought that it

8 would be really important to be sure that the

9 motions that were passed before we went to

10 lunch were properly recorded.

11 And, of course, there was a great

12 deal of discussion going on at the same time.

13 So I am just putting these up for you. And

14 let me read them and then see if anybody

15 thinks that is not what we said.

16 So, first of all, recommendation

17 one, the ACD recommends that the use of the

18 Harvard lines discussed today in NIH-funded

19 research be restricted to projects that are

20 consistent with the wording of the consent

21 form. This recommendation is specific to

22 these lines. And, again, that was the vote.

1 Recommendation number two, the ACD
2 recommends that consistent with section 2(b),
3 27 of the 28 lines be eligible for use in
4 NIH-funded research. They recommend that line
5 number 25 not be eligible. There again is the
6 vote.
7 Is there any concern about this
8 recording of your wishes? Okay. And, just to
9 be absolutely sure, I am going to ask,
10 although this is gilding the lily, that we
11 take a vote that you approve these particular
12 renditions of what you have already said. I
13 don't want anybody to think that there was
14 anything here that was not complete.
15 Jeff? Jeff?
16 DR. MURRAY: Can I just make two
17 small suggestions?
18 CHAIRMAN COLLINS: Oh, no.
19 DR. MURRAY: They are totally
20 trivial. So "today," use the date, instead of
21 "today," since that makes it kind of
22 open-ended. And for the 27 of 28 lines, just

say what they are.

CHAIRMAN COLLINS: Okay.

PARTICIPANT: They are Harvard lines.

DR. MURRAY: Yes, they are.

PARTICIPANT: Identify it as the Harvard lines.

DR. MURRAY: Identify it as the -- you can find the numbers, I can.

PARTICIPANT: There is no such thing as a Harvard --

DR. MURRAY: They are HUES 1 through 28.

PARTICIPANT: That's right. That's right.

PARTICIPANT: HU?

DR. MURRAY: HUES 1 through 28.

CHAIRMAN COLLINS: So right here?

PARTICIPANT: The second one, the 28 lines.

CHAIRMAN COLLINS: Oh, okay. Got you. Got you. Got you. Okay.

PARTICIPANT: Parentheses.

DR. MURRAY: Yes, parentheses, capital H, capital U, capital E, capital S.

CHAIRMAN COLLINS: Is that right?

DR. MURRAY: Yes.

CHAIRMAN COLLINS: That wasn't too painful. Okay. May I ask, then, for a show of hands to approve this wording just so we have done this properly?

(Show of hands.)

PARTICIPANT: For both?

CHAIRMAN COLLINS: Thank you. For both, yes, both at once. This is one vote for both recommendations. Thank you.

Any opposed?

(Show of hands.)

CHAIRMAN COLLINS: Okay. We're done. Save. Done. And be sure let's get this version loaded back onto somebody's flash drive. All right. I am happy now. I can't tell you how happy I am --

(Laughter.)

1 CHAIRMAN COLLINS: -- to introduce
2 Dr. Richard Hodes, who has worked long and
3 hard on the Comparative Effectiveness Research
4 Program at NIH. He is going to tell you where
5 that all stands.
6 Richard is the Director of the
7 National Institute on Aging and a wonderful
8 corporate citizen of NIH. So welcome.
9 DR. HODES: Thank you, Francis.
10 COMPARATIVE EFFECTIVENESS RESEARCH
11 DR. HODES: I am happy to have the
12 chance to talk to you about another
13 interesting topic, that being comparative
14 effectiveness research.
15 It is an area of research that has
16 certainly occupied a great deal of interest
17 and time at NIH, nationally, internationally
18 in the context of health care reform. And we
19 welcome the opportunity to discuss with you
20 what CER means, has meant to, and will
21 continue to mean to NIH as we pursue this
22 important area.

1 The first point that we have made
2 repeatedly is that NIH has a long history of
3 investment in CER, long before we knew the
4 initials or the name whatsoever, that
5 patient-centered research in these categories
6 noted, prevention, diagnosis, treatment,
7 behavior change. Held systems in special
8 populations has been an important part of
9 NIH-funded research. The last year when we
10 calculated a full year's worth of portfolio
11 investment was 2008, where some $9.6 billion
12 was in this category.
13 Some other criteria or standard of
14 the breadth of investment are noted here. We
15 will get to the fact that the Institute of
16 Medicine recently in June issued a list of 100
17 priorities for comparative effectiveness
18 research. And it was no coincidence, but I
19 think it was quite telling that some 88 of
20 those 100 are areas in which NIH already had
21 substantial investment.
22 Some of the landmark studies in

1 CER -- and we'll come to the definition of
2 CER, but as we look at these studies, I think
3 you can appreciate that they are the
4 comparisons of two or more potentially
5 effective treatments, interventions,
6 preventive measures, are illustrated here.
7 They warranted headlines in prominent journals
8 as well as in the press. And I will
9 illustrate some of these more specifically for
10 you.
11 As a first example, all-hat, this
12 was a study funded primarily by NHLBI with
13 collaborating institutes and centers, which in
14 this study published in 2002 examined a
15 comparison of 3 different classes of agents
16 for control of blood pressure in some 33,000
17 hypertensive individuals. The comparison was
18 between an inexpensive, low side effect
19 effective thiazide diuretic with an example of
20 an anti-tension-diverting enzyme inhibitor and
21 a calcium channel blocker.
22 I don't have to point out I think

1 here which line is which. The finding
2 dramatically was that there was no difference
3 in effect here.
4 I should go further to data that
5 we won't present. There are actually some
6 interesting differences when one looked at
7 cell population.
8 So in the African American
9 population, in particular, there was actually
10 an increased incidence of some of the events,
11 endpoint cardiovascular events, in the groups
12 where we are seeing some of the non-thiazide
13 diuretics.
14 This is an important demonstration
15 of the kind of the research NIH can do, but
16 perhaps as telling for the presence of the
17 conversation is the incomplete or at least
18 suboptimal degree to which this has been
19 translated into practice.
20 A second example I will cite is
21 the Diabetes Prevention Program. This was a
22 study conducted by NIDDK in collaboration with

1 NIA, National Institute on Aging, which
2 examined individuals who were at high risk for
3 developing of diabetes but not have a chemical
4 or clinical diagnosis of diabetes. They were
5 treated with placebo, which was a standard of
6 care, Health Education Program; or with
7 metformin, an oral hyperglycemic; or with a
8 lifestyle intervention that involved moderate
9 exercise and diet interventions.
10 What you can see here is the
11 cumulative incidence of diabetes that occurred
12 over four years as these individuals were
13 followed. The placebo group showed some 40
14 percent or so of individuals with diabetes
15 over that time, indicating that they were
16 indeed a high-risk group. Metformin decreased
17 the number of conversions to diabetes. And
18 lifestyle was even more effective.
19 In a subpopulation analysis, in
20 this case by age, there were some very
21 interesting additional results. So these are
22 the breakdown by young adult group, 25 to 44;

1 45 to 59; and over 60. And you can see in the
2 25 to 44 group that the lifestyle and
3 metformin were approximately equally effective
4 with about a net 50 percent or so reduction of
5 diabetes over this time.
6 And everyone thinks about the
7 implications of that level of prevention of a
8 disease such as diabetes if it extends, in
9 fact, to their clinical sequelae. This is
10 truly a very exciting finding.
11 If one looks with age, 45 to 59,
12 there is a tendency now for metformin to be
13 less effective while the lifestyle
14 intervention was effective. And by the over
15 60 group -- and I don't know that any of us
16 would have predicted this -- the oral
17 hypoglycemic had no significant effect. And
18 the exercise, diet, lifestyle intervention
19 resulted in a 71 percent decrease in diabetes
20 incidence over those 4 years.
21 So an example of a very important
22 study -- in this case a drug versus a

1 behavioral intervention -- or a breakdown by
2 subgroups was important as well.
3 And, once again, the translation
4 of this remains to be carried out. Some of
5 you may have seen earlier in this year in
6 Lancet a follow-up study that looked several
7 years later and showed there were still
8 important positive events of these studies.
9 So, once again, people can undergo
10 these interventions. They are able to adhere.
11 They are able to persist in their adherence.
12 And there are positive consequences.
13 NIH also has extensive investment
14 in research but also in training
15 infrastructure. Some of the examples here,
16 trial networks, that are amenable to CER
17 research, consensus development programs to
18 evaluate comparative assessments, the National
19 Library of Medicine Center on Health Services
20 Research, the CTSA consortium itself as a
21 resource, integration of CMS and CER
22 databases, and an HMO research network, the

1 latter illustrated here.

2 This is an example of one HMO

3 research network, which has been used to carry

4 out research studies by a number of NIH

5 institutes. It is a consortium of some 16

6 integrated health systems covering 11 million

7 lives with funding from NIH, AHRQ, FDA, and

8 CDC. And it is clearly this kind of

9 infrastructure which is important to future

10 conduct of research in this area.

11 Dissemination is another very

12 critical area. This is an illustration of

13 some of the means that NIH uses to disseminate

14 its research findings, a commitment we have

15 had for a good long time involving public

16 through websites, press, and other programs,

17 patron groups, professional organizations, and

18 presentations to groups such as this.

19 The www.nih.gov alone has half a

20 million to a million visitors a day, which I

21 understand to be the highest level for a

22 federal site other than that just before tax

1 returns are due with IRS.

2 Nonetheless, having talked about

3 the great investment and seriousness which we

4 take with dissemination, it remains an area

5 unquestionably of great challenge with much

6 more to be done.

7 The modern era of emphasis on CER

8 comes with an interest and a realization of

9 the critical juncture we are at in terms of

10 health care or health care delivery in general

11 and is illustrated in this statement by Peter

12 Orszag in 2007, when he was with the

13 Congressional Budget Office, "Only a limited

14 amount of evidence is available about which

15 treatments work and for which patients."

16 As an example of this, more

17 specifically, in this paper published in JAMA

18 in 2009, an analysis of the scientific

19 evidence level or quality underlying the

20 ACC/AHA clinical practice guidelines and,

21 quite strikingly, the evaluation resulted in

22 the conclusion that nearly half of current

1 clinical practice recommendations from the
2 American College of Cardiology and the
3 American Heart Association are not or are not
4 adequately evidence-based.
5 Another perspective that received
6 a good bit of attention earlier this year was
7 this editorial or article from Atul Gawande,
8 who, as you may remember having seen,
9 evaluated practice in a variety of
10 communities; in particular, differences in
11 practice across communities.
12 He, of course, found great
13 variation and found that variations did not
14 correlate in any easy or predictable way with
15 quality of outcome. But, as it reflects to
16 comparative effectiveness research and the
17 need for a strong evidence base, he makes the
18 point that is encapsulated here, "When the
19 right thing to do is well-established,
20 physicians from high and low-cost cities
21 tended to make the same decisions, but in
22 cases where the science is more unclear, some

1 physicians pursue the maximum possible amount
2 of testing and procedures. Some pursue the
3 minimum. And what kind of doctor they are
4 depends on where they come from. In case
5 after uncertain case, more was not necessarily
6 better," an illustration of the reason and the
7 hope that by providing better evidence base
8 and making more clear-cut the relative merits
9 of different interventions, we can overcome
10 some of the problems that were uncovered in
11 this and related research.
12 So in terms of the role NIH has
13 played, the arrow initials are presumably all
14 too familiar to all of you. Under the arrow
15 "Appropriation," CER was allocated a set-aside
16 of $1.1 billion. Of that, $400 million was to
17 NIH; $400 million to the Office of the
18 Secretary, DHHS; and $300 million to AHRQ.
19 There was a federal coordinating
20 council, which initially was responsible for
21 the planning, for use of those funds. There
22 was representation from each of the

1 institutes, and the NIH was represented by its
2 director.
3 More recently, a CER CIT, which is
4 really a senior management team, has been
5 committed to now the future management of CER
6 across the Department. And it basically
7 consists of the leadership of NIH, of AHRQ,
8 and a council representing the Office of the
9 Secretary.
10 The NIH has a CER coordinating
11 committee, which I will talk about further,
12 which coordinates NIH's activities, so far
13 most certainly preoccupied with ERA and making
14 recommendation to the NIH Director that relate
15 to ERA funding of CER.
16 The CER subcommittee in order to
17 better coordinate with other agencies has
18 established at present cooperative workgroups
19 with AHRQ; with VA; with FDA; and, as you will
20 see in a moment, with plans to do so with CDC
21 as well. CMS and other agencies represent
22 equally important partners for the future.

1 Of the $400 million that was
2 allocated to NIH, some $342 million has
3 already been obligated. Here the breakdown is
4 by mechanism, the larger ones being the GO
5 grants or RC2s, again, that many of you are
6 familiar with from a general area, challenge
7 grants, payline expansions, other.
8 The other in some cases referred
9 to the funding for early years of clinical
10 trials, which clearly are going to take more
11 than two years, where the institutes from
12 their normal appropriations are committed to
13 continuing those studies, competitive
14 revisions, and a modest use of administrative
15 supplements.
16 Just a few of the highlights or
17 examples of the kinds of research in CER that
18 have been funded and were possible through ERA
19 funding. The Sprint senior study, Sprint, as
20 you may know, is a study that has been carried
21 out by NHLBI, NIDDK, NIA, and NINDS, that is
22 looking at the merits of more rigorous control

1 of blood pressure than had been the norm.
2 Several years ago some landmark
3 studies, such as Shep, indicated that
4 controlling systolic pressure to a level of
5 140 resulted in very substantial decreases in
6 cardiovascular adverse outcomes, stroke, and
7 ultimately in later years congestive heart
8 failure.
9 Here the question was whether
10 reducing systolic pressure to 120, rather than
11 140, would have still more advantages. So
12 that is the comparative effectiveness:
13 treatment to 140 versus treatment to 120.
14 Sprint senior, in particular, is
15 an indication of the recent realization that
16 it might well be that reducing blood pressure
17 further might have different outcomes
18 dependent upon age and vascular substrate.
19 And so the funding from ERA in this case will
20 allow the expansion of population to include
21 some older adults in a study which will be
22 funded, then, by ERA for the first two years

1 and then revert to a commitment by these four
2 institutes using appropriated funds to
3 continue this important study, very important
4 real world outcomes and a very prevalent
5 condition.
6 Another example of a different
7 kind, the Oregon lottery study. In addition
8 to studying drug versus drug or device versus
9 device, the studies of health care delivery
10 systems and even of health insurance systems
11 is a part of comparative effectiveness
12 research.
13 In this case, some of you may know
14 that Oregon I think a couple of years ago,
15 2007 or so, initiated a health insurance
16 policy plan that was not extended to all
17 members of the population but was extended by
18 lottery to those who were interested in
19 joining the plan. So it became a randomized
20 prospective trial.
21 What will be supported in this
22 case is the analysis of various

1 characteristics of health care delivery and
2 even health care outcomes now for a period for
3 an additional two years beyond initiation, so
4 a very important comparison of in this case
5 health insurance and delivery and interesting
6 complimentation to the studies of individual
7 treatments for individual conditions.
8 The rest you can read and examine
9 at leisure, but they give an example of the
10 spectrum of some of the research that has been
11 supported.
12 This is a list of some additional
13 ones that are addressing some of the most high
14 priority identified needs: comparative
15 effectiveness research in cancer genomics,
16 breast imaging strategies. This has certainly
17 received a good bit of attention recently.
18 Contemporary treatment outcomes
19 for atrial fibrillation in clinical practice,
20 chronic pain management, and so on, a number
21 of areas where current practice is based on
22 clearly incomplete and inadequate information.

1 Some of the key NIH activities are
2 research, of course. This is what we do
3 predominantly to generate evidence that will
4 enable physicians and patients to make optimal
5 health care decisions; research training to
6 develop a workforce that is necessary to
7 understand modern approaches to CER, which is
8 not going to be only randomized prospective
9 clinical trials but needs to take advantage of
10 a much broader set of data and understand
11 better how these can be optimized in their
12 legitimacy and generalizability.
13 Particularly we will say a bit
14 more about personalized medicine because there
15 has been some concern expressed that CER might
16 be the enemy of personalized medicine. That,
17 in fact, would be a real risk if one simply
18 compares intervention A to B and finds that A
19 is better on average for the whole group, that
20 this will ignore or deny the delivery of best
21 care to best individuals.
22 And, really, I think from an NIH

1 perspective, nothing could be further from the
2 truth. This is the reason why we think that
3 NIH, in particular, has a very strong
4 obligation and role to serve.
5 Personalized medicine may in the
6 context of CER involve looking at
7 subpopulations, racial, ethnic, by age,
8 ultimately in an age of genetics and genomics
9 may come down to looking at very
10 individualized risks as well. So we will not
11 be ignoring, rather be emphasizing
12 personalized issues in the context of CER.
13 Establishing centers to provide
14 some long-term support and infrastructure for
15 training and dissemination and behavioral
16 economics, the use now of behavioral
17 techniques that influence decision-making in
18 a modern, if you will, an informed,
19 open-minded strategy, about the best way to
20 increase uptake of CER findings by providers
21 and payers.
22 It simply may not be; in fact,

1 appears to be, that providing information by
2 sending out the facts, even giving good
3 educational format may not be sufficient. And
4 there now are examples of use of defaults or
5 other strategies that will be considered as a
6 part of the overall CER effort.
7 AHRQ and NITSI are spending plans
8 to use the $300 million in areas that broaden
9 their preexisting activities. And they break
10 this down conceptually into horizon scanning,
11 looking for a current or emerging medical
12 inventions that need evaluation, evidence
13 synthesis, and identification of evidence
14 needs and gaps. I think all of these overlap
15 with NIH but also complement very well the NIH
16 efforts.
17 And we have been working extremely
18 closely with Carolyn Clancy and senior staff
19 at AHRQ throughout the period of ERA and would
20 intend to be doing so to the future as well,
21 some further specifics in the areas of program
22 which they intend to approach. And, in

1 addition, they plan to convene a citizens'
2 forum on effective health care, a substantial
3 amount of money put forward to engage
4 stakeholders in the CER enterprise. And we
5 certainly intend to be a partner in those
6 activities.
7 The Office of the Secretary has
8 undergone an interesting process. By
9 direction of legislation, the use of this $400
10 million is guided by a report from the
11 Institute of Medicine, which was in June, as
12 you saw, as well as advice from the federal
13 coordinating committee, also that advice due
14 in June.
15 So since June, there has been an
16 accelerated process by which heads of all
17 agencies, as I have mentioned before, now with
18 lead by NIH, AHRQ, and the Office of
19 Secretary, are examining proposals from
20 individual agencies that fall into categories
21 that are emphasizing data infrastructure,
22 dissemination and translation, research,

1 inventory and evaluation.

2 And, whereas, for NIH perhaps,

3 understandably, research may be the most

4 heavily invested area, the balance is I think

5 appropriately and complementarily different

6 than Office of the Secretary planning.

7 So these are going through a very

8 extensive review process that involves the

9 Department and OMB, but we will take the

10 liberty of offering what we understand are

11 likely to be finally approved initiatives in

12 which NIH will take the lead.

13 To be clear, now in these projects

14 funded by the Office of the Secretary, they

15 were twofold. One is centers for excellence

16 for racial and ethnic minority, focused CER,

17 which is going to be a collaboration between

18 NIH and the Office of Minority Health. They

19 will use the existing NIH centers network.

20 And the second, a behavioral economics and

21 change initiative, in which NIH will take the

22 lead in collaboration with AHRQ.

1 Made mention of personalized
2 medicine but show here, I think well-deserving
3 of the slide in and of itself, to emphasize
4 the fact that CER will be guided by emerging
5 modern science, of helpers to individualize
6 and personalize treatments, both prospectively
7 and retrospectively. And it is an area in
8 which NIH I think is unique in its ability to
9 carry out this kind of investigation.
10 In summary, then, NIH is committed
11 to CER as a research priority. We talked
12 about ERA predominantly because it has been a
13 preoccupation of late, but the challenge I
14 think begins very soon. And we complete the
15 ERA exercises and turning attention to the
16 future and broader areas of CER investment.
17 We think that CER and particularly
18 NIH investment in it will be an effective tool
19 for generating evidence of what works in what
20 populations for informing medical
21 decision-making, therefore, for making it
22 possible for decisions to be made based on the

1 optimal of evidence and potentially to bend
2 the curve on health care costs, probably
3 unavoidable that costs will become an issue.
4 They have been something of a third rail that
5 happily has not diverted public attention
6 excessively from the importance of CER, but
7 CER will among its considerations be looking
8 at health care costs.
9 And we all hope the implications
10 of better intervention and treatment would
11 long term have a positive effect, even if that
12 is not the primary endpoint or subject of
13 study.
14 And all of this, the key challenge
15 is of getting the results of NIH-supported
16 research, including CER, implemented by
17 providers, payers, and the public a challenge
18 they will continue to meet with ever-improving
19 technologies and evidence-based approaches to
20 the communication charge itself.
21 And I thank you for attention
22 through this summary, would be happy to

1 discuss anything of interest to the group.
2 CHAIRMAN COLLINS: Thank you,
3 Richard.
4 Are there comments, questions?
5 Yes, Colleen?
6 DISCUSSION
7 DR. CONWAY-WELCH: Just I don't
8 want to sound like Johnny One-Note. I
9 mentioned earlier today with the problems in
10 how the public was informed about the
11 mammogram issues.
12 And it occurred to me going
13 through your excellent presentation it might
14 be interesting -- well, I guess it would be
15 AHRQ; I'm not sure -- to look at some studies
16 about how to develop strategies to share this
17 information with the public so that we don't
18 have a firestorm every time.
19 And it occurred to me Frank Luntz
20 -- and there are many like him, but he has
21 written words that work. And there are
22 certain ways you frame things that make them

1 much more acceptable. And clearly that did
2 not happen.
3 So I would encourage you all to
4 think about how you're going to translate this
5 to the public because what you have said is
6 excellent. And I think all of us really would
7 agree with it. But how it goes public is a
8 totally different issue.
9 I really think we need some help
10 from wordsmiths.
11 DR. HODES: That's a wonderful and
12 important point that part of the research that
13 would be supported is in the area of
14 dissemination, how to optimize dissemination.
15 But I think we will have to be
16 careful that a part of that research is
17 dealing with the specifics of delivery of
18 message to a diversity of audiences, just as
19 you described. It is a very important point.
20 CHAIRMAN COLLINS: Mary-Claire?
21 DR. KING: Thanks.
22 I would like to bring up a point

1 that I think is an area where NIH specifically
2 has an enormous amount to offer to this area.
3 And that is the field of what came to be known
4 a few years ago as race-based medicine.
5 Race-based medicine was
6 exemplified by a number of medications which
7 were indeed found to be more effective in
8 individuals who were black than individuals
9 who were white or vice versa.
10 And it turned out with some very
11 good underlying pharmacogenetics that it was
12 clear that what superficially appeared to be
13 race-based medicine was, in fact, a difference
14 in easily detectable genetic variation.
15 So there were no bad guys in this
16 story. This was a great story. And it played
17 out very well. And it played out very well
18 because, by happy chance, there were excellent
19 geneticists working with excellent clinicians
20 all along the way.
21 It would seem that this is an
22 opportunity to have more of those studies have

1 similarly good outcomes and that in the Center
2 for Excellence in Racial and Ethic
3 Minority-Focused CER, one might incorporate
4 the kind of pharmacogenetics that proved so
5 satisfactory with the buy bill and other
6 similar experiences.
7 DR. HODES: It is an excellent
8 suggestion. Right now the precise FOAs are
9 being developed. And there certainly is time
10 to address that input to the process.
11 CHAIRMAN COLLINS: I have David
12 next.
13 DR. DeMETS: Yes. Thanks.
14 Well, I am glad that the NIH is
15 prepared to take on leadership here because it
16 is a very challenging area. The two examples
17 you gave are the easy ones: Flat-out no
18 difference and flat-out superiority. I am
19 guessing that most of them will be in between.
20 And, having worked in clinical
21 trials most of my career starting here at NIH,
22 you know, designing trials to show that it is

1 just a little bit worse or a little bit better
2 is challenging.
3 It depends on which population you
4 pick, how well you deliver the standard of the
5 control, et cetera, et cetera. So these
6 issues come up in another arena called
7 non-inferiority design, but they are the same
8 issues.
9 So I think that the experience
10 that NIH has in the NIH community will be key
11 here because some of the players in the game
12 won't have that experience. I think it is
13 really important to step up and step forward
14 on this.
15 DR. HODES: Point well-taken. And
16 apologies, as you know, for having selected
17 the easy examples.
18 (Laughter.)
19 CHAIRMAN COLLINS: John?
20 DR. KELLY: Thank you, Dr.
21 Collins.
22 I am going to ask you to consider

1 reaching out in yet another direction. I will
2 do this as correctly as I can. I love the
3 NIH. And I have learned a ton since I have
4 been here. But in some areas, you are not the
5 household names I wish you were.
6 If I were going to look at
7 something in my specialty, I would not think
8 of your institutes. I would think of the
9 American College of Obstetricians and
10 Gynecologists.
11 Is there a way to consider
12 reaching out to specialty societies,
13 particularly the academic centers, where some
14 research is being done, to get them at the
15 very early stage engaged? If that were the
16 case, dissemination ought to be very easy
17 through the specialty society.
18 The second part of that is you
19 talked early this morning about going to have
20 some behavioral change. I submit there are
21 two kinds of behavioral changes that need to
22 occur: one, the patients; and, one, the

1 clinicians.

2 If we were working together, we

3 might be able to make that happen more

4 rapidly.

5 CHAIRMAN COLLINS: Those points

6 are very-well taken. I don't know if,

7 Richard, you ant to comment. Certainly in

8 terms of dissemination of evidence that is

9 discovered by NIH research, the professional

10 societies are a critical part of that. We can

11 point to examples where that has gone well and

12 examples where it has not and something to

13 learn from that.

14 DR. HODES: And a second point

15 about behavioral issues relating to the

16 providers as well as being provided for is

17 very much in mind and hopefully will be

18 addressed.

19 CHAIRMAN COLLINS: Ralph?

20 DR. HORWITZ: Yes. I want to

21 reinforce points that have already been made.

22 It is wonderful to see just how much good

1 thinking has already been committed to NIH's
2 role in comparative effectiveness research.
3 One of the things that many people
4 worry about is the data from inferior study
5 designs may begin to crowd out data from
6 superior study designs, as we sort of expand
7 to the efforts in this area.
8 This is a place where NIH
9 especially I think in capitalizing in some of
10 the things that Francis was saying earlier
11 today about thinking about whether it is
12 possible as part of this initiative to create
13 cohorts or longitudinal studies or other
14 settings in which we could really get
15 high-quality data from diverse sources that
16 integrate biology with clinical expression of
17 disease and the social and physical
18 environments that shape both the risk of
19 developing disease as well as response to
20 treatment.
21 DR. HODES: Absolutely. And, in
22 part, my allusion to the fact that not all

1 research was going to be in the form of the
2 gold standard, randomized clinical controlled
3 trial, is germane to this.
4 You are absolutely right. We have
5 to make all research of all types and all
6 apparatus as rigorous as it can be, but that
7 has to include development of techniques to
8 best assess the quality of what can be done
9 with existing databases.
10 Some of the broader ones are going
11 to be those where the prospective rigor is
12 least well-developed. And we need to learn a
13 lot as well as to apply what we know now to
14 how to address that whole spectrum of data.
15 The infrastructure of having large
16 populations, this HMO network was just one
17 example. There are a number of emerging
18 opportunities of this kind applying genetic
19 analysis, such as watched these large
20 populations, in a part of ERA funding. And
21 NIH has recently funded, for example, using a
22 Kaiser infrastructure genome-wide assessment

1 of 100,000 individuals.

2 So the numbers will grow and allow

3 the interaction of genetic data with

4 electronic health records to approach as well

5 as we can the points you are making.

6 DR. WOLFE: I'm very excited,

7 enthusiastic about all the support for

8 comparative effectiveness research. But I

9 wonder or I am concerned that there is going

10 to be a lot of this going on, some clearly not

11 funded by NIH in the private sector, which is

12 going to fall into the sort of area in which

13 we are actually going to get misinformation.

14 And so I wonder whether there is

15 an opportunity here to have people come

16 together and establish some basic guidelines

17 on how to do comparative effectiveness

18 research.

19 Maybe NIH is not the right place.

20 Maybe it is an IOM test but whether there

21 should be some group that could be given some

22 oversight that would also be there to answer

1 some questions so when people want to do a
2 good job but they don't really have the
3 background to do it, that there is some
4 expertise that they can turn to because what
5 we don't want to have is a couple of big
6 studies come out with the wrong answer and
7 have people react so negatively that we then
8 no longer really turn to a comparative
9 effectiveness research. It loses its
10 potential because we haven't really guided it
11 very well.
12 DR. HODES: In the more immediate
13 term, NIH is pursuing support through ERA CER
14 funds for at least two infrastructure
15 initiatives that bear relevance here: one for
16 development analysis of methodologies and the
17 other for training,
18 I think our hope is that in each
19 of these areas, once we have funded a cadre of
20 centers and scientists, that these can become
21 networks that may emerge into what you
22 described, a fountain of knowledge and

1 recommendation and best practices. And just
2 how it would be applied would remain to be
3 determined, but I think it is critically
4 important.
5 CHAIRMAN COLLINS: Well, thank
6 you, everybody, for thoughtful comments. We
7 will undoubtedly be talking about this on into
8 the future because, as I described earlier
9 this morning, this is a critical part of what
10 NIH is being asked to contribute to the
11 science of health care reform.
12 And we are not sorry about that.
13 We are actually excited about what we can
14 learn from studies like this. Richard, thank
15 you very much for your willingness to take on
16 so much of the leadership and for the
17 presentation.
18 So we are now going to hear a
19 brief report about COPR. And Beth Furlong, as
20 the COPR liaison for the ACD, is going to give
21 us a snapshot on what COPR has been up to.
22 NIH DIRECTOR'S COUNCIL OF PUBLIC

1 REPRESENTATIVES (COPR) LIAISON REPORT

2 DR. FURLONG: Good afternoon.

3 This morning we heard that the ACD has been in

4 existence for 44 years. And this fall, the

5 Council of Public Representatives celebrated

6 its tenth anniversary.

7 During this week, October 26th to

8 30th, it was jam-packed with activities.

9 Monday and Tuesday of the week was a partners

10 in research investigator workshop.

11 On Wednesday of that week was an

12 internal forum at NIH. This was on staff

13 training on the issue of community engagement.

14 Thursday of this week was the

15 working group of the COPR council.

16 And on Friday of that particular

17 week was our official public meeting. So it

18 was a great week in terms of the tenth

19 anniversary and all kinds of activities.

20 On Wednesday, when there was this

21 internal NIH forum on community engagement,

22 this gives you a list of the various speakers

1 who presented that day.

2 The first two were COPR members.

3 And they reported on a document, a report,

4 that has come out of COPR on community

5 engagement with research.

6 The other speakers were from

7 either NIH or a variety of areas around the

8 country and the kind of community engagement

9 that they are doing.

10 During the Thursday, the workgroup

11 day, these are some of the speakers that we

12 heard from on a variety of issues. The first

13 one I know that we all greatly valued to look

14 at similar issues in another country and how

15 things are being handled; again, a variety of

16 speakers from both within NIH and outside.

17 On that Thursday, during our

18 workgroup day, one of the things that we

19 learned about is a new workgroup within NIH:

20 community engagement in research

21 implementation workgroup. And there are 17

22 members that represent a cross-section of NIH

1 institutes in a variety of key areas.

2 And their charge you can read

3 there in the middle bullet, "To review

4 recommendations, identify NIH programs and

5 processes that can be appropriate for

6 application and incorporation."

7 At Friday's public meeting, these

8 are some of the speakers that we heard: Dr.

9 Briggs, National Center for Complementary and

10 Alternative Medicine; Dr. Glass from the

11 Fogarty International Center. And then he as

12 a speaker certainly ties into one of the five

13 visions that Dr. Collins spoke to this

14 morning. And then we also heard from Dr.

15 Hodes.

16 As I said before, this was the

17 tenth anniversary. And there have been many

18 ways where this has been publicized within

19 NIH.

20 One of the work products coming

21 out of the communications workgroup ties into

22 a major purpose of COPR. And that is to have

1 more communication about NIH to the public for
2 COPR members and the COPR structure to act as
3 a vehicle of information from the public to
4 NIH and then to recommend communication
5 strategies.
6 So an outcome in terms of a work
7 product or a deliverable is going to be this
8 process that is now in existence to elicit
9 more information from individuals throughout
10 the country. And it is to analyze and to get
11 information on what individuals want in terms
12 of health information.
13 So what are their needs? And what
14 are the information-seeking behaviors of the
15 NIH health consumer? This, in turn, will help
16 NIH regive information to the American and the
17 global public.
18 The process that is being used is
19 the RFI, the request for information. There
20 are four shrinks to this process. First, it
21 ties into the presidential directive for
22 transparency.

1 Second, this is a way to reach
2 many diverse individuals and organizations.
3 And this is a process that we are using now
4 but that could be used in the future. And
5 that is part of the ambassador role of COPR.
6 Such input is open through
7 December 30th. And this is the variety of
8 channels that have been used for this RFI. So
9 it varies from the individual current and
10 alumni members of COPR and certainly all of
11 the avenues of NIH, YouTube, Twitter,
12 databases, public bulletin, all of the liaison
13 officers, and all of the NIH institutes, and
14 all kinds of meetings that NIH staff go to.
15 I am going to show two examples of
16 some things that -- what I am showing here are
17 two COPR alumni. But these are some
18 activities that have gone on since our April
19 meeting.
20 This first one is a CBS campaign.
21 And this is an alumnus, Douglas Yee, and how
22 he worked with the National Humane Genome

1 Research Director to speak to two classes in
2 Hawaii. So it is the ongoing interest of COPR
3 members to keep getting the NIH message out.
4 The other one is an alumnus, Val
5 Deford, Omaha, Nebraska, what she has done in
6 terms of spreading a heart message to many
7 women in Omaha and women who are settled,
8 refugees, there.
9 Going forward, again, listening to
10 the vision as we heard Dr. Collins at the
11 October meeting, these are some new topics
12 that COPR will be exploring: the concern with
13 obesity. And certainly the kind of discussion
14 that we heard this morning that COPR shares
15 with the ACD is protection of human subjects.
16 And then, as Dr. Nelson briefly mentioned a
17 few minutes ago, we want to communicate the
18 research stories.
19 And on that note, I will end. If
20 there are any comments or questions?
21 CHAIRMAN COLLINS: Thanks, Beth.
22 Yes?

1 DISCUSSION

2 DR. FREIRE: Excuse me. I think
3 the work you are doing is really fantastic.
4 I just wanted to bring up that, again,
5 reporting from the trenches at the individual
6 level, I find that there is not enough
7 encouragement for us to make our findings
8 translatable in a responsible manner to, for
9 example, the media and so forth.
10 So there are these organized
11 factions, like COPR. But, in fact, we are
12 often asked by the media to tell them what we
13 are actually, what our findings are actually,
14 implying.
15 I wish there was some support and
16 encouragement for us to do this directly
17 because a lot of my colleagues refuse to talk
18 to the media and refuse to make their
19 knowledge public because they are afraid that
20 they would be doing the wrong thing. And
21 those that like it often do cross the line.
22 So it would be nice to have a way

1 of encouraging especially new investigators
2 that it is a responsibility that we find the
3 difficult way to actually translate our
4 findings into a responsible manner.
5 CHAIRMAN COLLINS: Point
6 well-taken. And obviously this is something
7 NIH needs to do in partnership with the
8 institutions where we support research, many
9 of whom have communications officers. But I
10 am not sure that all of the investigators are
11 even aware of the resources they have locally
12 to help them in terms of training to do this
13 kind of communicating.
14 I think the time for scientists to
15 say this is not part of their job has passed.
16 It really falls to all of us.
17 Yes, James?
18 DR. JACKSON: I'm not saying this
19 just because Hodes is in the room, but one of
20 the things that we have found at the institute
21 at Michigan is working with the office, the
22 communications officers, at NIA has been a

1 very, very effective way of really
2 transferring and getting things out, sort of
3 a very, very professional group. And I am
4 sure the other offices are like that.
5 It has been a really effective way
6 of working with them to help disseminate
7 results and findings and so on. And we just
8 over the last 10-15 years found it to be
9 tremendously helpful.
10 We don't have to reinvent a lot of
11 the wheels and other kinds of things that are
12 well-known within just to make that point.
13 And I'm sure that's true at other institutes
14 as well. I don't know them as well, but --
15 CHAIRMAN COLLINS: Yes. I think
16 every institute puts quite a bit of energy
17 into trying to provide that kind of support.
18 John Berklow, who is right here, is the chief
19 communications officer for all of NIH,
20 certainly hopes to make him and his team
21 available for all kinds of interesting
22 purposes when science has made an advance and

1 it is time to tell the world about it.

2 DR. BERKLOW: Dr. Collins? PIO

3 network, we invite the public information

4 officers from all of your institutions to join

5 us on a listserv. And we have periodic

6 conference calls if something big is happening

7 that we want to share information with.

8 So it has been a very effective

9 way to get out news, especially at the local

10 and regional level. So just keep that in

11 mind.

12 CHAIRMAN COLLINS: Well, thank

13 you. Thank you, Beth, for that report. That

14 was very helpful.

15 I mentioned this morning the

16 program called TRND, Therapeutics for Rare and

17 Neglected Diseases, as one of the components

18 of the theme about translating, trying to take

19 basic science and build that bridge. Well,

20 you are about to see that bridge appear again

21 because it seems to be a favorite metaphor.

22 I am happy to introduce to you our

1 Christopher Austin. Chris is the Director of
2 the NIH Chemical Genomics Center, senior
3 adviser to the NHGRI Directorate for
4 Translational Research, and plays a critical
5 leadership role in the coming together of this
6 program, which is aimed to try to build that
7 bridge and even start to push some projects
8 across it.
9 So, Chris, tell us what this is
10 all about.
11 DR. AUSTIN: Well, thanks so much
12 for having me.
13 THERAPEUTICS FOR RARE AND NEGLECTED DISEASES
14 DR. AUSTIN: I am going to give
15 you just a few teeny snippets of science in
16 here, which will probably be nice for many of
17 you, I hope all of you, in order to try to put
18 this in some context and to show you where
19 this came from.
20 So what this slide really is meant
21 to indicate is what this program does. There
22 is technology over here and patients over

1 here.

2 And you may recognize this

3 individual who played for the Yankees. And,

4 if you notice, his fainter eminence is wasted

5 here. That is Lou Gehrig. He was dead about

6 two months after that picture was taken. And

7 this is a little boy with schistosomiasis, two

8 of the diseases that we work on.

9 Okay. So here is the bridge. So

10 I am sure you have been flogged enough with

11 this analogy, but it really is an apt one

12 given what is in the middle of San Francisco

13 Bay, which are sharks and Alcatraz to get

14 stuck on and other things. So this is really

15 what we are trying to do.

16 Francis made mention I used to be

17 in the pharmaceutical industry before I came

18 here, used to be at Merck. And this is a

19 problem that I worked on there. And it is

20 really the problem that I have been working on

21 here since coming here back in 2002, which is

22 to deal with this real paradox which we live

in.

I think this is the critical question for biomedical research for our era, which is we live in the best of times over here knowing more about ourselves through the basic research that NIH has done over the last 40 or 50 years than we have ever known before.

And what has really put the icing on the cake on this is the whole parts list of a number of parts lists that have been put together, one of them, of course, exemplified by the genome. But there are lots of other ones: structural genomics, structural biology initiatives, cell biology initiatives, et cetera.

But at the same time that this work has been done, what many people, including my mother -- and I always think about my mother in this case. I mean, what she really cares about is number of new drug approvals. And that rate has either stayed flat or gone down.

1 And so that is not shown on this
2 slide but is equally relevant is that during
3 this period of the last 12-13 years, spend in
4 the public and private sector has tripled
5 during this time.
6 So spend has tripled.
7 Productivity has gone down by about half,
8 which means that our overall efficiency has
9 gone down by about five-sixths during the era
10 of the genome.
11 Now, sometimes I have been known
12 to blame this on Francis, but I won't do that
13 today. It is not a causal relationship.
14 There are lots of reasons for this. And they
15 are not all scientific. But the degree that
16 they are scientific, the question is, how do
17 we translate this motherload of information
18 into improved treatments?
19 That is what we all want. That is
20 what constituents want. That is what
21 taxpayers want and expect and Congress wants
22 and expects as well.

1 Okay. So I am not going to go
2 through this whole slide. It is in your
3 packet. But, just to lay out the problem
4 here, what we work on particularly and this
5 program works on particularly is rare and
6 neglected diseases, what are rare and
7 neglected diseases, in striking numbers, it is
8 about 7,000 diseases that affect the human
9 family.
10 But of those, if you add up all of
11 the diseases that are worked on by all drug
12 development organizations worldwide, how many
13 diseases are there that are worked on?
14 The number is about 300, which
15 means that if you happen to be one of those
16 6,700 people who happen to get one of these
17 rare diseases, you are just out of luck.
18 And as a neurologist, it is just
19 my medical training I saw a lot of these kinds
20 of patients. And ALS is just one example, but
21 there are many, many, many of them.
22 The reason for this is that

1 traditionally drug development has been done
2 on a return on investment model. So if you
3 are going to do this on a return investment
4 model, the only diseases you can work on high
5 prevalence diseases in the Western world. And
6 it has to be done in a relatively short period
7 of time, which means that you have to work on
8 relatively well-validated so-called
9 precedented targets.
10 So there are two types of
11 neglected diseases. One is low-prevalence or
12 rare, but they tend to be a focus of the
13 Western world. There are about 6,000 rare
14 diseases, as defined by the Orphan Drug Act of
15 200,000 or less.
16 But, even though they are
17 individually rare, because there are 6,000 of
18 them, the cumulative prevalence is about 25 to
19 30 million people in this country that have a
20 rare disease.
21 A lot of them are epidemic
22 diseases that we are all familiar with:

1 Huntington's, Tay-Sachs, sickle cell disease,
2 et cetera.
3 And then there is the
4 high-prevalence disorders but are neglected
5 not because they are rare but because the
6 people who are affected by them can't afford
7 the medicines to treat this diseases. So
8 these tend to occur in the developing world.
9 And most of them are infectious diseases. And
10 they go by all of these names that we are
11 familiar with.
12 So this is really what we work on.
13 In a way that I sort of diagramed this, this
14 is a really striking way to think about this.
15 If you look at this either from the
16 perspective of the human genome or from the
17 perspective of human diseases and you ask,
18 what proportion of each is neglected in
19 therapeutic development, it is about 95
20 percent of each.
21 And the thing is striking about
22 this is that not only -- it is a problem,

1 obviously, and many of you who have had people
2 with these diseases in your family or had one
3 yourself will know that this is a problem.
4 But it is also an unbelievable
5 opportunity because the genetic basis and
6 pathophysiologic basis of many of these
7 disorders has become known in the last ten
8 years, partially through the Genome Project.
9 There are about 2,000 Medelia
10 diseases the genetic basis of which is known.
11 And through GWA studies and other things, we
12 are beginning to understand those things in
13 common diseases as well.
14 So this is really the opportunity.
15 So for a lot of you who don't think about drug
16 development every day, this is drug
17 development in six easy steps. What most of
18 NIH traditionally focuses on in most academic
19 research is way over here to the left.
20 And it's a little bit like one of
21 those old New Yorker cover cartons that most
22 of the world where I was -- I trained in basic

1 genetics. So this was my world for a very
2 long time, too, is doing basic biology.
3 And at some point one identifies a
4 target, which is a lever on which one can push
5 to bring a system back into balance that has
6 gone out of whack, otherwise known as a
7 disease. But all of this system has been,
8 everything distal to this has traditionally,
9 been done in the private sector.
10 But the steps that I am going to
11 talk about just very briefly today are
12 creating an assay testing system that one can
13 then test hundreds of thousands of chemicals
14 on, usually via robots, and then this
15 important step of medicinal chemistry
16 optimization, which is really the heart of
17 drug development.
18 And then what you are doing in
19 that case is adding a progressively more
20 characteristics to the compound, usually
21 starting out with simple potency in a target
22 but then adding about 20 other characteristics

1 that you need to show efficacy and safety in
2 an animal model usually and then safety and
3 efficacy in a human.
4 And so, as you probably know, to
5 go from here to here, the number is quoted all
6 the time, about a billion, billion and a half
7 dollars, takes about 15 years. So this is the
8 problem that we are working on.
9 Okay. So the conventional social
10 contract by which this has been done is this,
11 that if you take this model here, if you just
12 make it a little bit more granular and put the
13 actual scientific steps on the bottom, that's
14 what this is -- this is the drug development
15 pipeline here at the bottom -- and you ask,
16 how has this traditionally been done? It's
17 this basically, that NIH has funded basic
18 research over here. FDA has sat over here.
19 And I am going to use this analogy
20 once, and I will keep using it as a football
21 analogy. We want to start down here. And we
22 want to get down here.

1 Now, NIH has traditionally stopped
2 on about the five-yard line here. And
3 everything in between has been pharma and
4 biotech.
5 And this has traditionally worked
6 for common diseases that affect the Western
7 world. It has never worked for rare diseases
8 or neglected diseases.
9 And, arguably, given what has
10 happened to pharma and biotech in the last
11 five years, it doesn't even work for common
12 diseases very well.
13 So what we have been working on
14 for the last six or seven years -- and TRND is
15 the most recent step in this process -- is to
16 rework this process to make it work better and
17 shift the relative responsibility.
18 So this is the first step in the
19 process you heard about as part of the road
20 map that was championed by Dr. Zerhouni,
21 started in 2003, which was the Molecular
22 Libraries Program.

1 The purpose of this program is
2 just written here. It is to empower the
3 research community to use small molecules in
4 their research, whether it is tools to figure
5 out what genes or pathways do or starting
6 points for new therapeutics.
7 It is a paper that we put in
8 Science now, what, about five years ago. And
9 there is a nice website if you are interested.
10 It is a very well-established program now, has
11 been going on for about five or six years.
12 And so what it has done, in short,
13 is -- and I will get to this at the end -- it
14 works in this space right here from assay
15 development screening, hit the probe chemistry
16 right in here.
17 So what I am going to do now
18 because I really want you to get a -- I want
19 to reduce this to practice for you to give you
20 a sense of how this actually works to go from
21 the theoretical to real because it will
22 indicate what the problem is. And that

1 problem is why we started TRND.
2 Okay. So the ACGC was the first
3 of the big probe development centers started
4 by the road map, what I run now. It is about
5 75 people. We have about 100 collaborations
6 with folks all over the world.
7 Every project we do is a
8 collaboration. We rely very heavily on our
9 usually extramural collaborators for the
10 target or the disease expertise, but we have
11 the assay development screening, informatics,
12 chemistry expertise.
13 So even though we are intramural,
14 we are administratively part of the NHGRI
15 intramural program. But 90 percent of our
16 collaborations are with extramural or
17 foundation folks.
18 We focus on what you might think
19 about as one minus pharma, you know, if you
20 take those big, neglected areas I showed you
21 before.
22 And we produce chemical leads,

1 early stage. They are really research tools
2 meant to validate the targets, these novel,
3 unprecedented targets.
4 And we also spend a lot of time on
5 novel paradigms for assay development,
6 screening, informatics, chemistry, et cetera.
7 I am going to show you this, not because it is
8 important to understand this to get a sense of
9 how trend is going to work. What I want you
10 to take away from this is really orthogonal to
11 the way we are used to thinking about an
12 individual PI lab. And it is done that way on
13 purpose to be complementary to that, to those
14 expertises.
15 So the staff of the center is
16 about a third biologists, about a third
17 medicinal chemists, and the other third
18 informatics and robotics people. And all of
19 these people report to me.
20 So normally these people would be
21 in four different departments, right, biology,
22 chemistry, engineering, computer science, but

1 these people all work within project teams
2 together: biology, chemistry, robotics,
3 informatics. And they have deliverables which
4 require all four to succeed. You can't get
5 there with just one of them.
6 The other thing that is unusual is
7 about 80 percent of the staff come from pharma
8 and biotech. And so we have done this on
9 purpose for reasons you can imagine, but the
10 whole idea was to bring these in, these people
11 in, and say, "We want you to start with the
12 best practices at each of these places, but
13 then tell us how it can be done better." And
14 because we were starting from scratch, we were
15 able to do that.
16 I am not going to go into a huge
17 amount of detail about how we do this. It is
18 a complicated slide. But I just want to give
19 you a sense of how this actually works.
20 Most of the collaborations with
21 molecular libraries in general and the large
22 centers, in particular, start with an

1 investigator who calls me up or one of the
2 people at our center says, "I've got this
3 target. I've got a cellular phenotype. I've
4 got an idea. I've got a rare disease that I
5 want to study. And I would love to have a
6 small molecule compound to manipulate that
7 system. How do I do it?"
8 And so we spend somewhere around
9 three months to three years helping them to
10 develop an assay. This has to go through peer
11 review, this R01-R03 system that this goes
12 through, because within the walls of the
13 center, we optimize the assays into 1536 well
14 plates, which is how we do everything, all of
15 our screening.
16 The compound repository is about
17 400,000 compounds. This is a picture of the
18 robot at the center. And what comes out of
19 this is not a hit list but a candidate probe.
20 That is, we would have sat down
21 with our collaborator before we did this and
22 said, what are the characteristics of the

1 compounds that you need to do the biology that
2 you want to do? What is the potency, the
3 selectivity, the cellular permeability, et
4 cetera, et cetera?
5 If we meet those criteria right
6 out of the screen, we do screening in a little
7 different way that I don't have time to get
8 into. That means we actually hit this at
9 about 50 percent of the time.
10 If we meet those probe criteria,
11 we are done. And we have a lot of secondary
12 assays and a lot of biology to do, generally
13 for another year. But we don't have to do any
14 optimization chemistry. The other half of the
15 time we have to do Med Chem and then go back
16 into the bioassay to improve the properties to
17 meet the probe criteria.
18 So within a biotechnology or a
19 pharma company, this is the first stage of
20 drug development, but it really in our minds
21 is more appropriately considered research tool
22 generation for the purpose of validating the

1 target and may give you a start to Med Chem if
2 you actually wanted to make a drug.
3 This program stops at an in vitro
4 probe; that is, a compound or compounds which
5 are possible which are credentialed for
6 manipulating the target and had demonstrable
7 manipulation of the target to identify a new
8 scientific phenomenon and usually in a
9 cell-based or cell-free system. Sometimes we
10 get in animals, but that is sort of extra
11 credit.
12 One of the reasons that we did
13 that is that all of these data go into the
14 public domain. They all go into Pub Chem.
15 And so there were some IP concerns if we went
16 beyond that.
17 So the center now, the important
18 thing is that it really is completely
19 cross-cutting. So we started out as part of
20 the Molecular Libraries Program. But there
21 are now multiple other institutes, groups of
22 institutes or foundations, who all support us

1 in various ways.

2 We started out making just

3 chemical probes to do research. Now we do

4 profiles, starting culture of drug

5 development. We do a lot of drug repurposing.

6 We do RNAI, GRNAI, and have databases and

7 informatics software and novel chemical

8 syntheses and novel assays and all kinds of

9 things that the center produces.

10 And so we have had from the very

11 beginning, partially from my own interest,

12 partially because of the interest at NIH, an

13 interest in rare, neglected diseases.

14 And this is actually a partial

15 list of some of these diseases that we work

16 on. And you will notice that some of them are

17 rare, like the AT or chordoma. Some of them

18 are neglected, like Leishmania or

19 trypanosomiasis or schisto.

20 There are two apparatus we take to

21 this. One is the conventional drug

22 development paradigm, going from target to

1 screen to hit the lead, the lead opted to
2 preclinical, the preclinical, the clinical
3 trials. And that starts with a collection of
4 three to four hundred thousand compounds. And
5 we expect it to take about ten years, although
6 we are trying to improve that process. And we
7 do projects like this.
8 The other is we put together what
9 is clear. And I can get into this if you are
10 interested. We spent the last three years
11 putting together the gold standard collection
12 of every compound that has been approved for
13 human use worldwide. This is about 3,000
14 small molecule drugs. And the idea here is
15 that you might be able to repurpose them in a
16 shorter period of time.
17 Without going into any details, it
18 is about 3,000 or so compounds. And we have
19 gotten them from these, basically everything,
20 from all the developed countries. This was a
21 huge problem, sounds very simple, but it is
22 actually incredibly hard. But, anyway, it is

1 all done now.

2 Okay. So just three very quick

3 examples. One of them is a rare disease.

4 Again, this is setting up why did we start

5 TRND? You know, there had to be a reason for

6 this.

7 And so this was an early project:

8 Gaucher disease. It is a rare disease that is

9 due to usually often missed sense mutations in

10 this enzyme glucocerebrosidase.

11 It was an assay that we developed

12 with Ellen Sidransky at the Genome Institute.

13 And we were looking for pharmacological

14 chaperons that would allow this mutated

15 protein to fold, localized to the lysosome.

16 I am going to skip through about

17 three years of work to say that we were able

18 to identify chaperons, which correct the

19 defect in patient fibroblasts. So these are

20 fibroblasts from patients who had the most

21 common mutation in Gaucher disease.

22 This is a localization of the

1 glucocerebrosidase protein together with a
2 LysoTracker marker, showing that under normal
3 cases in mutated fibroblasts, there is very
4 little yellow in between. So, in other words,
5 most of the red is not in the green. So most
6 of the glucocerebrosidase protein is not where
7 it is supposed to be.
8 But if you add this compound, you
9 get a lot more yellow. And, even more
10 importantly -- I didn't show it here because
11 it is not as pretty a picture. The important
12 thing is that when you add these compounds,
13 the enzyme activity goes up in the patient
14 fibroblasts. So that is what you are looking
15 for.
16 Okay. So there is a second
17 project that we did with David Williams, who
18 was at Illinois State at the time. As a
19 result of this work, he got tenure at Rush
20 University in Chicago. And so he is now at
21 Rush.
22 This was a project on

1 schistosomiasis, which is a very prevalent
2 parasitic disease, affects about 200 million
3 people worldwide. And, again, to skip through
4 about three years of work, we were able to
5 identify compounds which are curative in a
6 mouse model of schistosomiasis.
7 This is a picture of a normal
8 mouse liver. An infested mouse liver looks
9 like that little bit in the first picture. It
10 is about six times elevated. And each of
11 those white things is worms. These mice live
12 a sensible life span, just like humans so,
13 with this. They are completely debilitated,
14 but they live.
15 So in just a third one, very
16 briefly -- and I put this in here because I
17 knew Keith was going to be here. So I had to
18 throw in something from UCSF, this is, again,
19 one of our early projects. We have been
20 working with Brian Shoichet for years. And he
21 is on our SAB, as a matter of fact.
22 It is a project on

1 trypanosomiasis. And once we found things
2 with Brian, we went to bring Jim into the
3 project as well. This is a project on --
4 trypanosomas cause, among other things, Chagas
5 disease and African sleeping sickness.
6 This is an interesting story for
7 two reasons. One is these are the papers that
8 came out. They are still in the ASAP version
9 of J Med Chem. They just came out a couple of
10 weeks ago. You see there their papers with
11 Brian and Jim.
12 The interesting thing about this
13 is it illustrates both an example of a project
14 where, again, we were able to identify very
15 effective inhibitors of a critical cysteine
16 protease in the one, in the Chagas disease
17 trypanosome.
18 But in the same project, without
19 looking at them, looking for them
20 specifically, we were able to find, actually,
21 better inhibitors of the sleeping sickness
22 trypanosome. And so that is what you might

1 call chemical genomics.

2 Now, just an interesting anecdote.

3 If this had happened at Merck and you are

4 looking for one thing and you find another,

5 you would get penalized for doing that.

6 Right? Incredibly dumb, but that is what

7 happens.

8 And most organizations are like

9 that. If you think about this, whether it is

10 a disease foundation or a company or

11 something, they're working on one thing.

12 But Mother Nature doesn't work

13 that way. Mother Nature works across

14 biologies, across diseases, across organisms,

15 across targets. And we set up a center. And

16 we are setting up a trend to take advantage of

17 those.

18 So that is the good news. This

19 process works incredibly well. I can go over

20 the inefficiencies and the costs, which are

21 much better than where I used to work, but I

22 really don't want to go into that. I just

1 want you to take away that this really works
2 now and it is a really wonderful engine.
3 That is the good news. The bad
4 news is this. The probes, which is what
5 molecular libraries develop, are just the
6 start of drug development.
7 And so here is the bad news.
8 Okay. So here is the cost of drug
9 development. If you go from the beginning
10 down here -- here is basic biology, assay
11 development screening, hit the probe
12 chemistry, the cost is relatively low.
13 However, when you go on to try to
14 -- when you put a dedicated project team
15 together, when you have validated your target
16 and you need to make something that hits all
17 of those 20 characteristics to get into
18 humans, then that becomes a very arduous
19 process, which takes somewhere between 3 to 5
20 years.
21 You have 20 people working on an
22 individual project full-time. Twenty people

1 on one project work for 3 years, 90 percent
2 failure rate. And then frequently, even if
3 you're successful and you get over here, you
4 can't publish it because it's got to be
5 covered with IP, right?
6 So that tells you why this is not
7 done in academic settings. It's just you have
8 to take your entire lab working on a single
9 project.
10 What is also depressing is this,
11 that this is the probability of success. You
12 know that overall drug development is
13 extremely expensive. And it's also very
14 unlikely to succeed.
15 But what you notice is that the
16 probability of success function is an inverse
17 function to the cost. That is, as the cost
18 goes up, the probability of success goes down.
19 One of the reasons that the cost goes up is
20 that the probability of success goes down.
21 So when we realized this back in
22 2003, we realized that NIH science was right

1 here. It was somewhere to the left of assay
2 development. But there was this sweet spot
3 here to the left, where the cost was
4 relatively low. The probability of success
5 was reasonably high. And to fill this space
6 is really what molecular libraries or the NCGC
7 have done.
8 So, to go back to my science and
9 my football analogy, what we have done is what
10 the public sector does is now move from the
11 5-yard line to the 30-yard line. And if you
12 know anything about football, even if you are
13 the Redskins, you know that if you are on the
14 30-yard line, the likelihood of scoring is
15 better than if you are on the 5-yard line.
16 You are not scoring, right? You
17 have still got a long way to go. But you are
18 in better field positions. So hopefully the
19 probability of success will be greater.
20 The problem is for rare diseases
21 and neglected diseases, the biopharmaceutical
22 industry is not dumb. They know this cost and

1 failure function. Nobody in their right mind
2 will work in this area unless you can get a
3 return on investment that will allow you to
4 compensate for this cost and likelihood of
5 failure.
6 So there has been very little work
7 for all of these projects that I just showed
8 you just stopped dead in their tracks. The
9 Gaucher project and the schisto project we
10 finished two years ago. They didn't go
11 anywhere because there was no way to move them
12 forward. And there are lots of other of these
13 things.
14 Okay. So what the TRND program is
15 going to do is fix this problem. So here is
16 basic research over here where it needs to be.
17 And I always say that the reason we can do
18 this is that basic research got us here. So
19 we have got to continue doing this. If we
20 don't, we are eating our seed corn. The point
21 is that it is necessary but not sufficient to
22 score.

1 Okay. So here is FDA down here.
2 Here is an IND in the middle, investigational
3 drug application. That is something you need
4 to get into humans. And then here is the NCGC
5 molecular library. So it has gotten filled
6 this little space.
7 For rare diseases and neglected
8 diseases, there are lots of biotech pharmas
9 and the clinical center in CKSAs, et cetera,
10 that will do the clinical work.
11 The problem is in the middle of
12 this is this space that is affectionately
13 known in pharma as the Valley of Death or at
14 Merck, they called it the Zone of Chaos.
15 There are various other analogies.
16 And this is what TRND is going to
17 do. If you know what the RAID program is, it
18 fits a little bit of the distal end of this
19 process.
20 So TRND is very new. It was just
21 announced in May. But I looked this up.
22 Francis, the first meeting that you and I had

1 about this was exactly four years ago today,
2 where we first started talking about this.
3 The reason we did this, the reason
4 we spent so long thinking about this is not
5 only that we had to build support for this but
6 that we really wanted to make sure that this
7 was not a fools rush in where angels fear to
8 tread problem, right? So we don't want to --
9 this is hard. Nobody has figured out how to
10 do this, right? And so we want to be very
11 careful.
12 Okay. So why is this so hard?
13 And what are the scientific issues? This is
14 extremely difficult science. And so we are
15 going to have to recruit the best people for
16 biotech and pharma. There is going to have to
17 be very close daily coordination among a lot
18 of different disciplines.
19 We have got to have a highly
20 experimental approach, multiple disciplines,
21 multiple approaches taken simultaneously, and
22 rapidly be able to shift priorities if

1 something doesn't work, move into another
2 thing. As I said, these would be 10 to
3 20-person project teams, working an average of
4 2 years with a very high failure rate.
5 Okay. So what is the operational
6 model? And this is still we are still working
7 on this. But we are thinking that this is
8 going to be analogous. What does that mean?
9 That means that these are disease-agnostic, it
10 is a disease-agnostic group that will have
11 in-house expertise, which is able to move very
12 rapidly from one priority to another,
13 multidisciplinary teams. And they will
14 collaborate with disease experts and target
15 experts outside.
16 The whole idea is to take these to
17 a point of external adoption. The point is
18 not to take these through phase three if we
19 can help it but to take them to the point
20 where we have de-risked these enough that an
21 outside organization will pick them up. We
22 will have projects that will inter-trend at

1 various stages.

2 So what are the distinguishing

3 features here? As I said, they are

4 disease-agnostic. We are going to look

5 explicitly for cross-cutting mechanisms, like

6 that Chagas disease example I gave you.

7 Importantly, there is very little

8 process in this space. That is to say there

9 is very little science of preclinical drug

10 development. It is one of the reasons that

11 this field has gone so slowly. And we can get

12 into this if you are interested.

13 One of the things that we are

14 going to be doing here is to develop a science

15 of preclinical developed drug development.

16 When something succeeds, why does it succeed?

17 When something fails, why does it fail?

18 This is virtually never done in

19 the private sector. We can get into that if

20 you are interested. And, importantly, we are

21 going to publish everything. So when things

22 fail, we are going to publish those things,

1 too.

2 What is the science? It is Med

3 Chem. It is in vitro efficacy, pharmacology,

4 tox, and a lot of pharmacokinetics,

5 pharmacodynamics, et cetera, et cetera, et

6 cetera. And then about 20 percent will go to

7 technology and paradigm development, just like

8 NCGC.

9 So we have been interacting with a

10 very large number of outside organizations to

11 make sure that we know the current state of

12 the art, we are able to start from that point,

13 and we can anticipate as many of the problems

14 as possible from here to at least put the

15 concept in humans.

16 So we have been talking not only

17 to the obvious suspects: the institutes and

18 centers and extramural/intramural. We have a

19 Trans-NIH advisory group, which I will mention

20 in a second: FDA, CDC, OSTP, biotech, pharma,

21 VC, rare disease organizations, the WHO,

22 neglected disease organizations, et cetera, et

1 cetera, to advocacy groups that we are already
2 very well-connected with, actually, already.
3 Again, I am not going to go into
4 this in any detail, but to say that we are
5 taking an informatically based approach here,
6 we really are in a unique situation that we
7 are the only organization that I am aware of
8 that is not restricted into what it can work
9 on, right?
10 So most disease foundations, the
11 CF Foundation works on CF. You know, if they
12 find something from Menkes disease, they are
13 not going to work on it. But for us, it
14 doesn't matter. And we can work on
15 everything. Most pharmas and biotechs are
16 limited by the sort of franchises that they
17 are interested in.
18 So we already have developed
19 through the last four or five years a very
20 extensive relational database of chemicals and
21 their activities. And we are adding to this
22 disease information, et cetera.

1 We are going to diversify risk and
2 trend by the stage of the project. Some of
3 these are going to be the lead projects and
4 will be lead-off projects and will be
5 candidate-seeking that will be able to go
6 right into clinical trials.
7 At the beginning, for a variety of
8 reasons, we are actually going to look for
9 some projects that are closest to the clinic
10 that we can get into phase one reasonably
11 quickly.
12 There are actually a lot of
13 compounds out there, failed biotech companies,
14 that are failed that are stalled for business
15 reasons. They are perfectly good compounds,
16 but the company went out of business or
17 couldn't afford to develop it because of the
18 crisis in biotech.
19 A lot of these you can get on the
20 cheap and that have a huge amount of work done
21 on them already. Okay. So the budget at the
22 beginning, the budget that is in the F.Y. '09

1 budget, and assuming we get an F.Y. '10
2 budget, presumably this is the amount that is
3 supposed to be in there, too, $24 million.
4 These projects cost $5 to $10
5 million each a year. They are very expensive.
6 And that is because of the kind of
7 technologies. And none of them are people.
8 You have got to work on these. Average
9 project should take about two years. Some
10 will take three. Some will take one because
11 some will fail. Some will actually succeed
12 not to go longer.
13 Importantly, we are going to need
14 to be and will be because you just have to be
15 ruthless in stopping projects that are not
16 making headway. This is really critical. So
17 it will be multiple things.
18 We can think about this as a horse
19 race. When one horse falls behind
20 sufficiently, you send him back to or think
21 about the majors. You know, you take them out
22 of the majors, send them back to the minor

1 league. And he can come back if he is
2 successful again.
3 So what is anticipated? The time
4 line, F.Y. '09, we got some money at the end
5 of last year that was all spent on
6 infrastructure. This year we are focusing on
7 hiring people, community outreach, and about
8 two to three pilot projects that we are going
9 to use as guinea pigs to establish the
10 operational procedures.
11 Next year we are going to -- maybe
12 the end of this year we will begin to solicit
13 projects for adoption. But, importantly, we
14 don't want to do this until we have something
15 we know we can do. It's just not fair to
16 anybody.
17 And so we want to make sure that
18 we have got something in place. Again, this
19 is really hard. Nobody knows how to do this.
20 It is an interesting example where there are
21 no models of what works. There are lots of
22 models about what doesn't work but no models

1 about what does work. It's an interesting
2 problem.
3 As of F.Y. '11, we think we will
4 have four to five projects ongoing. And then
5 we will probably be fully operational F.Y.
6 '12.
7 The governance, I would say this
8 is working because it is really a work in
9 progress. We actually centered it not at
10 NHGRI but in the ORDR.
11 And we did that for a couple of
12 very specific reasons. One is that we wanted
13 to make it very clear that this is a trans-NIH
14 initiative. And ORDR is inherently trans-IC.
15 It also has very longstanding and
16 good relationships with individuals in a rare
17 disease community, not so much with the
18 neglected disease community. So we're having
19 to build those.
20 There are two groups that we put
21 together. One is this trans-NIH staff
22 advisory group, who advises us on operation.

1 And they integrate what we are doing with the
2 IC-specific initiatives. And they're
3 particularly in places like NIMDS. And NIAD
4 and NCI have ongoing programs that really fit
5 into what we do quite well.
6 There are many others. There is
7 NIDAA, the NIAAA. There are many of them that
8 have these. And then there is an external
9 advisory panel who will be people from
10 academia, mainly from industry, actually,
11 because this is where the expertise lies,
12 patient advocates that will help us select the
13 projects and assess the projects in an ongoing
14 manner. And then there will be a formal, of
15 course, periodic assessment, recommendations
16 about whether they should continue or not.
17 So we plan to solicit projects
18 from an extramural community, intramural
19 community, from foundations, from biotechs,
20 pharmas, et cetera. We have an ongoing
21 discussion, which is a really interesting
22 philosophical discussion about whether this

1 ought to be a bottom-up or a top-down
2 approach.
3 That is to say, should we do this
4 via an RFI, RFA, RFP approach, where you let
5 people suggest projects, which are one-offs,
6 it may not be necessarily related to each
7 other? So it would be hard to take advantage
8 of commonalities or should what we do sort of
9 a top-down approach, where you say, "Okay. We
10 are going to work on a disease that is a
11 chaperon disease."
12 So if we find something, we could
13 work on many of the chaperon diseases or
14 lysosomal storage diseases, or parasitic
15 diseases, all trypanosomal disorder, something
16 like that, or somewhere in between. So that
17 is under conversation.
18 The first level review is going to
19 be performed by this expert panel. And then
20 the second level review sort of, at least our
21 plan is sort of, the thing about it is
22 adequate review will be done by this trans-NIH

1 group. But, really, this is in process. So
2 don't take this too seriously.
3 Okay. So that is it. Be glad to
4 answer any questions if we have time.
5 CHAIRMAN COLLINS: You can see
6 this is a low-energy process led by a
7 low-energy person. So if you got all of that,
8 congratulations.
9 This is an amazing series of
10 advances that are occurring in an area that is
11 unfamiliar to a lot of biologists but
12 enormously promising.
13 So let's take a little time for
14 some discussion. Karen?
15 DISCUSSION
16 DR. HOLBROOK: This is very
17 exciting. What is interesting is you start
18 out with the basic scientists or the
19 researchers in their own institutions. Are
20 there going to be opportunities for them to
21 follow the project along and come in and work
22 with you and --

1 DR. AUSTIN: Oh, absolutely, yes.
2 We are doing this with David now. Actually,
3 we are probably going to adopt him as one of
4 our pilot projects.
5 This is actually a really
6 interesting and important point. One of the
7 things that really is an advantage for us is
8 the deep expertise that lies in the academic
9 collaborator's lap. It is actually very
10 different from what happens in a big pharma.
11 In a big pharma, where I used to
12 be, biologists were itinerants. So you would
13 be a neurobiologist one day and an oncologist
14 the next and a diabetes person the third.
15 And you are really not an expert
16 in your disease. You don't have the models.
17 You don't have the knowledge. You don't have
18 the historical knowledge of the field.
19 But David really knows his worms,
20 as an example. So does Jim McCarroll. So
21 these guys have not only the knowledge of what
22 has worked in the past and what hasn't. You

1 know, chance favors a prepared mind, right?
2 So there is that, but it is also
3 that they have the assays, they have the
4 animal models, all of those things, which are
5 ready to go, which is simply not the case
6 elsewhere.
7 So the problem that we frequently
8 have -- and this is one of the issues we are
9 going to have to deal with in TRND -- is there
10 is an impedance mismatch problem that we may
11 be able to come from the 3 or 4 hundred
12 thousand compounds to 200.
13 You can imagine -- and this
14 happens to us every day, I should say -- we
15 will send 200 compounds that need to be tested
16 in dose response, we'll say, and 10
17 concentrations to an academic lab.
18 And that 2,000 experiments for a
19 graduate student, who may not even be able to
20 not even use the working in '96 well plates in
21 a secondary assay, that is where actually the
22 problem is now. So that is one of our

1 challenges.

2 CHAIRMAN COLLINS: Maria?

3 DR. FREIRE: Well, I think this is

4 actually very exciting for somebody who has

5 been working in this field and can actually

6 understand what you said, actually quite

7 wonderful.

8 Can I borrow your metrics for

9 success?

10 DR. AUSTIN: Oh, boy. What a

11 great question. Well, the proof of concept in

12 humans is really where we want to get. You

13 know, we have had people suggest that it ought

14 to be FDA approval. The problem is that we

15 have to make sure with this project that we

16 don't take on too much, that we put very clear

17 starting points and very clear ending points,

18 and that we own the means of production to get

19 to the endpoint, right?

20 So if we say, "FDA approval," that

21 relies on somebody to pick this up, go through

22 a phase three trial, and get through FDA. So

1 we either control that or it's not going to be
2 our champion endpoint.
3 DR. FREIRE: NIH would be doing
4 drug development? Is that what you are
5 saying?
6 DR. AUSTIN: Well, this is drug
7 development. I mean, it is drug development
8 up to proof of concept in people. But we are
9 hoping because of that, both because NIH may
10 not be the best place to do this. And also
11 the costs of going into late phase two and
12 phase three trials are tenfold higher than
13 they are, even in this space, that to do that
14 would completely bust the budget.
15 So we need to build this in a way
16 where we can market these, if you will, to
17 biotechs or pharmas or VC firms or foundations
18 who will pick these up and complete the
19 transition.
20 CHAIRMAN COLLINS: Which is to say
21 that one of the metrics will be the ability to
22 license out compounds that have reached the

1 point of being attractive --

2 DR. AUSTIN: Right.

3 CHAIRMAN COLLINS: -- to a private

4 sector partner to say, "Okay. We're going to

5 raise our hand now. We would like to take it

6 from there."

7 That is going to be interesting

8 because that means NIH has to be really

9 thoughtful about our IP policy, something you

10 know a lot about, Maria.

11 DR. AUSTIN: Yes, yes.

12 DR. KELLY: So at Sloan-Kettering,

13 we have been doing it for quite a few years

14 now and also tried to put into place some

15 development fund to do the trends, you know,

16 get over the Valley of Doom or Death or

17 whatever you want to call it.

18 I would say the difficulties in an

19 academic environment, which you are, I guess,

20 in a sense, are, first, Med Chem, which is not

21 really an academic discipline. And you have

22 got 100 collaborative projects, and you have

1 got 15 chemists. That is just a drop in the
2 bucket, basically, in terms of doing real and
3 medicinal chemistry on some of these projects.
4 So I think the scale there is that may be a
5 problem for you.
6 Secondly, when you get to these
7 beyond the hits and you are trying to pick
8 projects to bring through the first phase of
9 the development to a point where somebody is
10 actually interested in investing, you can
11 spend an unbelievable amount of money on those
12 things.
13 The probability of success is so
14 low that it is a worrisome situation, I think.
15 DR. AUSTIN: Yes, yes.
16 DR. KELLY: So it is going to
17 depend -- you know, if you are going to be
18 successful, it seems to me it is going to
19 depend a lot on exactly how you go about
20 picking your projects and who you involve in
21 those projects.
22 I assume the IP positions are

1 going to be important in making those
2 decisions.
3 DR. AUSTIN: Yes. So all of those
4 things are absolutely right. I often say to
5 our chemists that our assay development and
6 screening and informatics people actually have
7 a higher throughput than Merck does, but we
8 have 15 chemists. Merck has 1,000.
9 So the way we have gotten around
10 that so far is that we do screening in a
11 different way, which you might remember, but
12 which is just much more efficient. We do
13 screening and dose response in the primary
14 screen, which just takes off about a year of
15 work.
16 Importantly, we have been able to
17 get away with this so far because we are
18 making in vitro probes, which is a much lower
19 threshold.
20 Once we go to this stage, the
21 group is actually going to be about half
22 medicinal chemists. So it will be about 40

1 medicinal chemists. And we are well aware
2 that this is the problem.
3 DR. KELLY: So how do you handle
4 the -- I mean, in an academic environment,
5 that is a very difficult thing to do because
6 --
7 DR. AUSTIN: Right.
8 DR. KELLY: -- these projects
9 don't generally lead to promotion on an
10 academic --
11 DR. AUSTIN: So it is actually --
12 DR. KELLY: How do you manage
13 that?
14 DR. AUSTIN: You know, when I was
15 thinking about coming here from Merck, the
16 only reason why I decided to come here to do
17 this is I thought we could do it in the
18 intramural program, for that reason.
19 It is actually possible to do an
20 intramural program because all the people at
21 our place are staff scientists.
22 So we can pay them pharma

1 salaries. They're not on a tenure track.
2 They're not in the Department. They don't
3 have to deal with the chemistry culture, which
4 I'm obviously aware of, that doesn't reward
5 this kind of work.
6 There needs to be a different
7 model. And we can do this within the
8 intramural program. I think it is impossible,
9 frankly. I have lots of buddies trying to do
10 this in a university setting. And it is
11 really, really hard.
12 DR. KELLY: Given the fact that
13 there are lots of people out in the extramural
14 program that would be interested in this kind
15 of thing and they don't have access to
16 medicinal chemistry, have you given any
17 thought to maybe some kind of a program that
18 would give people in the extramural community
19 access to medicinal chemistry? I guess this
20 is --
21 DR. AUSTIN: That's exactly what
22 it is. That is what this is, exactly. Yes.

1 DR. KELLY: Yes.
2 DR. DeANGELIS: I see this as a --
3 you know, maybe I am too much of an optimist,
4 but if you reach the point where you say,
5 "Okay. We are now at the point where we think
6 we are into the late phase two or phase
7 three," that you then make a deal with the
8 porcupine, the other one, and you say, "All
9 right. Now we are ready to take it to the
10 next step, but, but the only caveat is" -- and
11 this may be the way to initiate what I think
12 would eliminate a lot of the problems in
13 clinical research in the conflict of interest.
14 You say, "Okay. We're going to now send out
15 an RFP. Now, you're going to fund this,
16 Merck. And we're going to now send out an RFP
17 for different groups who would come up with
18 the mechanism to do the research, to do the
19 clinical trial. And we will decide which one
20 is the best, the most cost-effective. Okay?
21 "Now, you, Merck, are going to pay
22 for that, but you will not decide how it is

1 done, when it is done, where it is done, where
2 it gets published, if it gets published," et
3 cetera, et cetera, et cetera.
4 Now, when it is done, the profits
5 are -- I don't know what -- give me a figure
6 -- 90 percent yours. We will take a royalty
7 of ten percent. I mean, I don't know. But,
8 I mean, it seems to me that the potential for
9 this is incredibly. It is extraordinary.
10 CHAIRMAN COLLINS: Yes, an
11 interesting model. Maria just asked if you
12 could sell it for what. I think what we can't
13 do based on past experience -- and Maria will
14 remember just how messy this was -- you can't
15 set a reasonable pricing clause into this kind
16 of deal or Merck will say, "That is a
17 deal-breaker. We are out of here."
18 The royalty stream, on the other
19 hand, is an entirely appropriate --
20 DR. AUSTIN: You could do
21 royalties, right?
22 CHAIRMAN COLLINS: Yes, right.

1 Mary-Claire?

2 DR. KING: So I would like to

3 return to what Tom began. That is how to turn

4 this kind of activity into news you can use

5 for investigators in academic institutions.

6 It is certainly not a surprise to

7 those of us in academic institutions that the

8 level of expertise is far deeper in academic

9 institutions than in pharma. You don't do the

10 same thing we do.

11 To have a library like this that

12 would, in effect, be available as a service,

13 which is what Tom was alluding to and what

14 Francis was alluding to, would, of course, be

15 enormously helpful because we don't do this.

16 So as targets were developed, if

17 individual academic researchers could make use

18 of this without having to put additional NIH

19 money into it; in other words, if it were

20 available as a service in the way a number of

21 other NIH activities were available as a

22 service.

1 And then if there were in some way
2 coupled to that R03 level funding so that the
3 academic researchers could follow up your 200
4 faves because I appreciate that that is going
5 to be very difficult to get R01 funding for.
6 So it needs to be part of the follow-on of
7 this.
8 That means that the idea that
9 somehow there would be some centralized "Gee,
10 shall we go for all the lysosomal storage
11 diseases?" kind of thinking about this doesn't
12 make sense.
13 I mean, it needs to be -- it would
14 need to be driven by the candidates that you
15 receive from 100 or 200 or 300 different
16 investigators nationwide.
17 DR. AUSTIN: What you just
18 described is the Molecular Libraries Program.
19 DR. KING: Good, glad to hear it.
20 DR. AUSTIN: And I am actually
21 depressed you haven't heard about it because
22 you are in a pretty prominent place. But that

is exactly what it is. You really can't think about it as a service because this is really hard. But there are collaborations.

DR. KING: It's a service, right.

DR. AUSTIN: Every single one of them -- this is not put in your quarter, get your Coke. This is --

DR. KING: I didn't say it was an easy service.

(Laughter.)

DR. KING: But you do this --

DR. AUSTIN: It's a collaboration, yes.

DR. KING: Yes, of course, of course.

DR. AUSTIN: Yes.

DR. KING: But you do this component?

DR. AUSTIN: Oh, yes, every. And, actually, it is exactly the same thing. So it's an R03. The investigator, unfortunately, only gets $50,000. Currently that's not much.

1 DR. KING: But that is for
2 follow-up.
3 DR. AUSTIN: Yes.
4 DR. KING: The investigator
5 doesn't have to turn on a --
6 DR. AUSTIN: Yes. But everything
7 else is paid for by road map. And the quid
8 pro quo there is that all the data go into Pub
9 Chem.
10 DR. KING: Sure.
11 DR. AUSTIN: Right. So --
12 DR. KING: That is what you are
13 producing, is that data.
14 DR. AUSTIN: Right, right. But
15 it's important. It's not just the screening.
16 DR. KING: But, then, why is there
17 even a consideration of anything other than an
18 investigator-initiated request?
19 DR. AUSTIN: Right.
20 DR. KING: Why is this --
21 DR. AUSTIN: It's because --
22 DR. KING: -- somehow ambiguous?

1 DR. AUSTIN: Yes. It's because
2 going through this, a brute force approach is
3 going to be extraordinarily difficult.
4 DR. KING: But that is why you are
5 there.
6 DR. AUSTIN: Well, the question
7 is, are we here for the patients or are we
8 here for the investigator community?
9 DR. KING: You are there for the
10 patients because the investigators are there
11 for the patients. And the investigators --
12 DR. AUSTIN: Well, sometimes --
13 DR. KING: There is no point in
14 replicating this everywhere.
15 DR. AUSTIN: Exactly.
16 DR. KING: Memorial has this.
17 DR. AUSTIN: Right.
18 DR. KING: Harvard has this.
19 DR. AUSTIN: Yes.
20 DR. KING: Stanford has this in a
21 way.
22 DR. AUSTIN: Yes. They have --

1 DR. KING: But not every
2 institution should have this.
3 DR. AUSTIN: Exactly. Exactly.
4 But the important issue is -- you know, here
5 is the analogy that I have often used with
6 Francis. If you realize you have a big
7 project, take the Genome Project. Should you
8 do it via bottom up, where people would come
9 to Francis with a linkage so investigators
10 working on bipolar --
11 DR. KING: That is not the Genome
12 Project. This is not the Genome Project.
13 DR. AUSTIN: I actually think it
14 is. And that's why it --
15 DR. KING: Well, then it is not
16 what you said before. I mean, this either is
17 something that is news we can use for
18 individual investigators --
19 DR. AUSTIN: It's both.
20 DR. KING: -- to present targets
21 or it is not. I mean, linkage projects,
22 individual investigators took the results of

1 the Genome Project --

2 DR. AUSTIN: Yes.

3 DR. KING: -- as they were being

4 produced and exploited them.

5 DR. AUSTIN: Yes.

6 DR. KING: But this is done

7 in-house by you, --

8 DR. AUSTIN: Yes.

9 DR. KING: -- if I understand

10 correctly.

11 DR. AUSTIN: Yes. I think it's

12 both.

13 CHAIRMAN COLLINS: I think it's an

14 artificial distinction. So I think

15 investigators will also come with an interest,

16 saying, "We really would like to get

17 attractive compounds for several different

18 diseases that happen to affect ABC

19 transporters."

20 And we are interested in cystic

21 fibrosis, but we are also interested in

22 Pseudoxanthoma elasticum. And maybe we could

1 get a little cabal here of ABC transporter
2 investigators and see whether we could do this
3 in a more cost-effective way by not doing that
4 as a series of one-offs.
5 Of course, this has to be driven
6 by where the scientific community is
7 interested in going. But you can still
8 develop those kinds of economies by doing
9 things in a fashion that makes scientific
10 sense.
11 Ultimately, I mean, it is
12 somewhere out there the goal that this becomes
13 a process that is built on economies of scale
14 that does go after as many of the targets that
15 are possibly there, including the ones that
16 nobody is currently working on by trying to
17 encourage somebody to get interested.
18 DR. KING: And if it is orphans,
19 then it is the opposite of a Genome Project
20 model because the Genome Project was intended
21 at first to be a universal --
22 CHAIRMAN COLLINS: Yes, but all of

1 the genes were orphans until we went after
2 them, right?
3 DR. KING: But it was the
4 universal ascertainment of all base pairs. It
5 wasn't targeted one base pair at a time to one
6 disease at a time.
7 CHAIRMAN COLLINS: Exactly the
8 point that I think Chris was trying to make,
9 that all diseases presumably are important to
10 somebody. And so it ought to be a universal
11 approach when we finally get there and not
12 just focusing on the ones that somebody
13 happens to think is important.
14 DR. KING: But how are you going
15 to know what your targets are if you don't
16 have people who have the knowledge with these
17 targets?
18 CHAIRMAN COLLINS: Then that is
19 where you start for sure.
20 DR. KING: Okay.
21 DR. AUSTIN: Over the last few
22 years, I have had many, many disease

1 foundations come to me directly -- and we have
2 done these projects -- or biotechs that come
3 to us directly. The problem with rare
4 diseases is there are rare investigators.
5 And so I could give you many,
6 many, many, many examples. And frequently it
7 is that the kinds of information that you need
8 are just different.
9 So that is to say that our plan is
10 to have most of these connected to extramural
11 investigators because I showed you that is
12 what NCGC does. Ninety percent of our
13 projects are exactly what you said.
14 And all of these people, whether
15 it is Brian Shoichet or David Williams or all
16 of these people, that is exactly the model.
17 But the question is let's say if a biotech
18 comes to us with a project that they had
19 worked on for the last five years, run out of
20 money, but it has a great potential of having
21 patient benefit. Should we ignore them
22 because they are not an extramural

1 investigator or not?

2 DR. KING: Do they have the data.

3 DR. AUSTIN: Oh, absolutely. They

4 have more data, much more data, than the

5 academics do because this is what they do. So

6 that is the problem.

7 CHAIRMAN COLLINS: So we're

8 running a bit behind here. We've got more

9 questions rather quickly here. So quick

10 questions and quick responses would be

11 wonderful. Mary Beckerle, please.

12 DR. BECKERLE: I think one of the

13 things we are hearing around the table here is

14 a bit of this is an idea that has really

15 caught on around the country also. And a lot

16 of academic labs are starting to do the

17 in-house screening and things.

18 I am interested in how your -- I

19 think this is a real opportunity for your

20 center to be, on the one hand, like a research

21 laboratory but with collaborations, but, on

22 the other hand, also bigger than that. And I

1 guess that's in a way what we are hearing,
2 that there could be, really, the potential
3 with so much interest in the extramural
4 community to be really a service, in addition.
5 I just think that that is going to
6 be really important for you as you think about
7 moving forward because I think one of your
8 biggest challenges, I suspect, once people
9 find out that you are out there is going to be
10 demand.
11 If you can run four or five
12 projects a year, you know, you are going to
13 have four or five projects from every
14 institution across the country.
15 DR. AUSTIN: Exactly, exactly.
16 DR. BECKERLE: And how are you
17 going to manage that?
18 DR. AUSTIN: Right.
19 DR. BECKERLE: And not only that.
20 You know, right now you're saying, "Well, I'm
21 focused on rare diseases. And that kind of
22 helps you as somewhat sort of eliminate a lot

1 of issues.

2 DR. AUSTIN: Yes.

3 DR. BECKERLE: But it's not long

4 before nothing will be eliminatable.

5 DR. AUSTIN: Yes, right.

6 DR. BECKERLE: We have been

7 talking about personalized medicine. And I

8 think, you know, pretty darned soon we're

9 going to have 400 types of breast cancer --

10 DR. AUSTIN: Right.

11 DR. BECKERLE: -- that each one is

12 a rare disease.

13 DR. AUSTIN: Yes.

14 DR. BECKERLE: So, anyway, I guess

15 I think it is a real opportunity if you can

16 think about how you can apply the kind of

17 approach that you have been taking with this

18 rare disease sort of umbrella --

19 DR. AUSTIN: Right, right.

20 DR. BECKERLE: -- to the sort of

21 individualized medicine --

22 DR. AUSTIN: Yes. No, you're --

1 DR. BECKERLE: -- and genomic
2 medicine piece.
3 DR. AUSTIN: No. You're
4 absolutely right. And I do about two or three
5 teleconferences or meetings with extramural
6 investigators a week about this. And so what
7 you are saying is absolutely right.
8 Interestingly, the suggestion for
9 the top-down approach, do you know who that
10 came from? Interestingly, it's Halley Deeds.
11 So it's interesting.
12 And so there's something that we
13 can talk about because it is a way to deal
14 with that problem, right? So if we have 100
15 people and 5 of them are lysosomal storage
16 diseases, maybe we should do those. That is
17 the idea.
18 CHAIRMAN COLLINS: We'll go to
19 Keith.
20 DR. YAMAMOTO: As you know, the
21 Golden Gate Bridge up here on the slide is a
22 toll bridge.

1 (Laughter.)

2 DR. YAMAMOTO: So I'm going to

3 talk a little bit about who are the payers

4 here. The $24 million, even for NIH, is a

5 substantial chunk of change. For big pharma,

6 it's not. At least if they were in more of a

7 cooperative mode, it wouldn't be.

8 I'm just wondering if you are

9 thinking of this as a public-private

10 cooperative that goes beyond the kind of

11 intellectual cooperatives that you are clearly

12 building successfully. It would also go in --

13 they would also be paying.

14 That consideration is suggesting

15 from a couple of points of view, but one of

16 them is certainly that it's worth being

17 mindful of the possibility that we will just

18 keep backing this process up until big pharma

19 just keeps saying, "Well, we don't want to

20 take that risk. Why don't you take it? We

21 don't want to take that one either. Why don't

22 you take it?"

1 And so where does that stop?
2 Where do we draw those lines? I think this
3 idea is really exciting and good. I'm not
4 being critical of it at all. But I think it
5 might be worth thinking about that.
6 So what about this public-private
7 sector cooperative idea?
8 DR. AUSTIN: It's a fantastic
9 question. And what is great is that pharma is
10 voting with their feet about what we have done
11 so far, that they call us all the time.
12 I just had a conversation with
13 Johnson and Johnson last week where they want
14 to work with us. The problem is -- I hate to
15 say this -- IP and ethics conflict of
16 interest. So we are very actively -- I just
17 had a meeting last week with OTT and OGC
18 because I think this is absolutely critical to
19 solve, for all of the reasons that you said.
20 So we are trying to work that out,
21 but they are very willing and anxious to work
22 with us and to share risk, and share expenses

1 and everything.

2 CHAIRMAN COLLINS: Haile Debas,

3 last question. And then we --

4 DR. DEBAS: I would have thought

5 pharma would not be interested unless there

6 were a lot of profit at the other end. That's

7 why they would have done it. So it's not the

8 case.

9 So, that being the case, let me

10 suggest a little wrinkle in your Global Health

11 Program.

12 CHAIRMAN COLLINS: Yes, yes. I am

13 listening.

14 DR. DEBAS: I think many of these

15 drugs are, in fact, orphan drugs that are in

16 need in the developing country. And American

17 pharma is not just --

18 CHAIRMAN COLLINS: Yes.

19 DR. DEBAS: So how about in your

20 program, you consider doing some

21 private-public partners or some variation of

22 it with emerging market in Brazil, in India,

1 in South Africa, and Chile because there they
2 need these drugs? And you would be doing
3 something, an incredible contribution.
4 DR. AUSTIN: Having worked in one
5 of those places earlier in my career, this is
6 something of great interest personally to me,
7 too.
8 We are actually working most
9 closely with the WHO about this to try to
10 figure out how to operationalize that. We
11 have also talked to DNDI, the drugs for
12 neglected diseases initiative, about this. We
13 don't know them as well as we know the rare
14 disease organizations. And it creates new
15 complexities.
16 The good thing about it is that
17 there are organizing initiatives. And you may
18 know that there are one of these that just
19 started in Africa.
20 It's a group of African countries
21 that have started a consortium to do clinical
22 trials up to approval in those countries. And

1 so we love this idea.

2 Because we work on many of these

3 disorders, we will work on Leishmania and

4 trypanosomiasis and schisto. That's where

5 these diseases are. So we have to do that.

6 That's a great idea.

7 CHAIRMAN COLLINS: Thank you,

8 Chris. Obviously this has generated a lot of

9 interest. And I'm sure the ACD will be

10 hearing about the progress in this small

11 molecule TRND initiative as we regather over

12 the next year or two because this is a

13 critical moment to see this become a reality.

14 I apologize to Linda Birnbaum that

15 we have held up her presentation, would like

16 now to introduce her. We have a tradition at

17 ACD of asking newly appointed institute and

18 center directors to come and give a

19 presentation about the science that is most

20 hot at the present time in their own

21 institute.

22 Linda is the Director of NIEHS,

1 the National Institute of Environmental Health
2 Sciences, and oversees their very complex
3 portfolio. She came to NIEHS from the EPA,
4 where she had served us for 16 years as the
5 Director of the Experimental Toxicology
6 Division. We are delighted that she is part
7 of NIH and willing to come and talk to us this
8 afternoon.
9 Linda?
10 DR. BIRNBAUM: Well, thank you.
11 INSTITUTE DIRECTOR'S REPORT
12 DR. BIRNBAUM: I am going to try
13 to be as enthusiastic and as energetic as
14 Chris was --
15 CHAIRMAN COLLINS: Good luck with
16 that.
17 DR. BIRNBAUM: -- because it is
18 getting late in the day. But what I really
19 want to do, first of all, thank you for having
20 me here. It is really an honor.
21 And obviously, as I am new to NIH,
22 at this point, I was at the NIH, at the NIEHS,

1 many, many years ago. It is just wonderful to
2 be back.
3 Lots has happened in the years I
4 was away. And I have had lots to learn in the
5 almost ten months that I have been back on the
6 job.
7 So what I really want to do today
8 is kind of introduce you to our institute.
9 And we are kind of unique. We are a different
10 bird in many ways. The first thing, which I
11 think many of you know, is we are not here.
12 We are located in North Carolina. And I
13 invite all of you to come to the southern part
14 of heaven and visit us.
15 This is both an opportunity and a
16 challenge. And, as I go through it, you will
17 understand some of the both sides of the coin
18 that we have.
19 We have a very wide variety of
20 programs supporting our mission of
21 environmental health. We have a National
22 Toxicology Program. And I will talk more

1 about that later since I wear two hats.
2 We have our intramural labs, as
3 all institutes do. And we have our extramural
4 programs as well. Now, what makes this a
5 little unique is that we actually get funding
6 from three different congressional committees,
7 not only the Health and Labor Committee, where
8 we get our regular NIH appropriation, but we
9 also get funding from the Interior and
10 Environment Committee.
11 I will talk a little bit about the
12 Superfund work that we sponsor from that kind
13 of funding because it is important to realize
14 that some of our mission is very programmatic
15 and program-directed, in some ways not all
16 that dissimilar from what you just heard about
17 the TRND program. We are trying to solve
18 certain problems.
19 And then we also have the Worker
20 Training Program, where we get funding through
21 the Energy Committees in terms of providing
22 emergency worker and hazardous worker training

1 throughout the nation.

2 Now, the other thing that makes

3 this a little bit different is that we are

4 really focused on environmental public health.

5 In many ways, our mission, while, yes, we do

6 do bench to bedside and we are involved in

7 some drug development and intervention,

8 clinical intervention, studies, much of our

9 focus is going from bench to public health.

10 Remember, you can't change your

11 genes at this point, but you can change your

12 environment. So as we begin to understand

13 what are the basic biological processes that

14 environmental agents induce to cause disease,

15 we can begin to understand which ones are

16 problematic and which ones exposure needs to

17 be prevented.

18 Just to give you an idea, we are

19 kind of in the middle of the group of NIH

20 institutes and centers. We are not all that

21 big, but we are not that tiny either. I mean,

22 if you look at NIH's budget, which obviously

1 we don't know where we are going to be at in
2 2010, we will be optimistic and maybe
3 realistic and assume we will be somewhere
4 between the House and Senate at about $31
5 billion. But NIEHS from HHS appropriations
6 should be in the neighborhood of close to $700
7 million.
8 Our Superfund program, which has
9 been very, very, very flat for quite a number
10 of years, is in the neighborhood of 80
11 billion.
12 Then we get an additional 10
13 million through the Department of Energy for
14 the Worker Training Program. So that our
15 total budget will be somewhere in the
16 neighborhood of, let's say, $770-$780 million
17 a year.
18 What I should stress and what you
19 will hear is that we have a very, very wide
20 mission. We are not one disease-focused. We
21 are not one age group-focused. We do it all,
22 which, in fact, is, again, the challenge and

1 the opportunity.

2 So I wanted to briefly go a little

3 bit about what some of the exciting things are

4 in the Division of Intramural Research. We

5 conduct both basic applied and epidemiological

6 research, understanding the biological

7 consequences and environmental exposures.

8 Our program is highly interactive

9 and interdisciplinary and involves high-risk

10 and long-term research. We have got at this

11 point in time 12 laboratories and branches.

12 I should mention, actually, up

13 front or maybe we will come back to it later

14 I had the wonderful but daunting opportunity

15 that when I came on board all of my top five

16 are acting. All my leadership of the

17 institute are acting positions.

18 So I am in the process of having

19 the opportunity to recruit the leadership that

20 I really want for the future or the

21 Twenty-First Century of environmental health.

22 Some of the areas that we are

1 focusing on are exploration of the epigenome.
2 This is a major area for us. There is growing
3 evidence and a lot of focus in our institute
4 on the developmental basis of disease and the
5 fact that early lifetime exposure basically
6 sets you up for what happens the rest of your
7 life, both in and of itself and leading to
8 differential susceptibility later on.
9 And, in fact, a lot of the work
10 that we have is looking at how you can have
11 epigenetic changes going on, which, in fact,
12 may offer the potential for reversibility for
13 some of these changes down the road.
14 We have major efforts in the area
15 of respiratory diseases and asthma. Partly
16 that is because one of the best understood
17 environmental insults on human health is air
18 pollution and the different kinds of things
19 that are associated with air pollution.
20 We have a lot of focus on
21 neurodegenerative diseases. And we are going
22 to begin to spend more of our time in an

1 intramural program looking at some
2 neurodevelopmental diseases as oral.
3 We have a world-class program in
4 DNA repair, which has been ongoing for quite
5 a number of years. We have major focus in
6 areas of system biology, the computational
7 approach, to take advantage of the reams of
8 new data that are being developed and to try
9 to put it into a context where it can be all
10 integrated.
11 Chris spoke a little about some of
12 the rare diseases being single gene mutations
13 being associated with single diseases. But,
14 in fact, the complex diseases that are
15 increasing in dramatic incidence in our
16 population, such as obesity, diabetes, asthma,
17 those kinds of things, are complex diseases
18 that have complex ideologies as well.
19 We focus on gene environment
20 interactions. I mentioned the fetal basis for
21 adult disease. And we have a lot of effort in
22 endocrine disruptors. And I will be happy to

1 come back to that topic later as it is kind of
2 near and dear to my heart.
3 And we have a longstanding basis
4 in the study of cancer. So it was at our
5 institute about ten years ago, maybe a little
6 bit more, that the brachy-1 and 2 genes were
7 first identified in collaboration with others.
8 In addition, we have some very
9 exciting work. Thank you, Mary-Claire. We
10 have some very exciting work going on right
11 now in something called a sister study, which
12 is a ten-year perspective, longitudinal
13 cohort. We have recruited 51,000 women who
14 are sisters of women with breast cancer.
15 These women are being followed on
16 a yearly basis. Extensive biospecimens are
17 being taken. Medical examinations and
18 environmental samples are being taken as well
19 from this cohort.
20 We believe that as we go forward,
21 we know this population is at elevated risk
22 for breast cancers, but we know that many

1 other things are going to determine who gets
2 breast cancer and who doesn't. We are hopeful
3 that this will shed a great deal of light for
4 the future.
5 Kind of in an ancillary note, we
6 think that some of the fallout from this
7 study, a lot of the genomic and proteomic work
8 that is being done with accessible fluids may
9 lead to the ability to develop some rapid
10 screening assays for different kinds of breast
11 cancer because we will have these ten years of
12 information that we can look at and understand
13 who went on to get cancer and who didn't, when
14 could we begin to identify things.
15 Another thing I wanted to point
16 out is that for the first time ever we have
17 our own clinical research unit, which we
18 opened at our facility last summer.
19 This was a very exciting
20 opportunity for us. And it is enabling us to
21 actually bring subjects into our own clinic.
22 Because we are 25 minutes at best from the

1 nearest emergency room, at this point we are
2 not going to do anything highly invasive or
3 anything where we really run the risk of
4 having a major problem of very, very dangerous
5 exposure.
6 We have recently set up
7 memorandums of understanding that have
8 actually just been signed with EPA's Office of
9 Research and Development, which does have a
10 clinical unit on the grounds of the University
11 of North Carolina Hospital. So that if we
12 want, for example, to expose mild asthmatics
13 to air pollution, we can do it in a setting
14 where we have the emergency facilities right
15 there.
16 We also have many interactions
17 with different both Duke and Carolina as far
18 as use of their medical facilities. But this
19 enables us to recruit patients.
20 And we have also actually begun to
21 recruit subjects for building 10 in the main
22 clinical center, people who can come in, do

1 some of their basic exams, get the basic
2 information from them down here before they
3 might have to come up to Bethesda.
4 So I wanted to just give another
5 example of another exciting study that we are
6 doing, which is the environmental polymorphism
7 registry, which is a linked DNA biobank. And
8 we have recruited so far 15,000 subjects in
9 central North Carolina.
10 Now, our area is quite diverse.
11 We have a lot of ethnic diversity, SES kind of
12 diversity, well, educational diversity, the
13 whole kit and caboodle. And these 15 subjects
14 represent the diversity of the population. We
15 eventually intend to get up to 20,000
16 subjects.
17 We have all kinds of coding for
18 where these people are from and extensive
19 environmental exposure information as well on
20 these people.
21 We are collecting the DNA and the
22 personal information from all of the subjects,

1 including a lot of their contact information.
2 And some of the exciting things here is that
3 this information is being collected with
4 appropriate consent forms so that as we go
5 forward, we are going to be able to recontact
6 these people for additional analysis later on.
7 Now, we are recruiting by either
8 genotype or phenotype. Kind of both
9 approaches are being used. And we're kind of
10 screening the DNAs to identify subjects with
11 specific genotypes of interest.
12 And then we are recruiting
13 subjects for phenotypic studies based on their
14 genotypes. And we're looking at the gene
15 environment interactions with respect to the
16 phenotypes of interest.
17 And we think that this study may
18 have the potential to be a smaller but adult
19 parallel to the national children's study as
20 it goes forward.
21 We are currently in phase one. We
22 have established a consortium which involves

1 at this point 25 of our intramural
2 investigators as well as this is an
3 interactive process with scientists at the
4 University of North Carolina - Chapel Hill.
5 And we have 110 environmental
6 response genes that have been nominated to
7 look at for the first studies, where
8 genotyping of functional snip is underway.
9 And we expect the phenotyping studies to begin
10 within a month. We are actually pretty
11 excited about that.
12 Now, our extramural program,
13 again, is a collaborative scientific
14 enterprise, as are all of the extramural
15 programs. And we have a number of unique kind
16 of efforts.
17 We co-fund with U.S. EPA the
18 children's environmental health and disease
19 prevention research centers. And we have just
20 gone out for the second round of these
21 centers.
22 And these are, again, large

1 program projects. And one of the unique
2 things is that all of our program kind of
3 projects or program centers require community
4 involvement.
5 And I will come back to that later
6 because it is extremely important when you are
7 talking about environmental issues that you
8 get not only the advocates but the people in
9 the community who are being impacted by
10 exposures involved. And it has got to be a
11 two-way street.
12 We all also have had a
13 longstanding partnership with the National
14 Science Foundation in funding centers for
15 oceans and human health. And this kind of was
16 our first entre into the health impacts of
17 global climate change. And I am going to come
18 back to that whole issue later on.
19 We have a major focus on obesity
20 and the built environment. This is a program
21 that is done in conjunction with CDC. And we
22 are also looking at the early determinants of

1 obesity because it is clear that there are
2 developmental exposures or early life
3 exposures to environmental contaminants,
4 which, in fact, can be predisposed to obesity
5 later on.
6 And then we have a major effort
7 ongoing in terms of autism. I sit on the
8 Interagency Coordinating Committee for Autism
9 Work. And we are currently finalizing the
10 strategic plan for that project.
11 That is a multi-agency partnership
12 with different advocacy organizations as well.
13 And one of our key studies here -- and we have
14 a number of large multi-center studies -- is
15 the early study, the early autism risk
16 longitudinal investigation, in which we are
17 recruiting 1,200 women who are intending to
18 have a second child who already have a child
19 with autism.
20 Again, that ups the genetic risk
21 that these pregnancies have and will enable us
22 to focus on trying to get further definition

1 of what might be the associations that go on
2 to cause autism in a later birth as well.
3 And obviously we have many, many
4 more studies. I am going to just mention a
5 couple of them. One is the GEI program, or
6 the Genes, Environment, and Health Initiative.
7 This is a cross-NIH program that
8 we co-lead with the Human Genome Institute as
9 well. There are two parts of it. The Human
10 Genome Institute is focusing on the Human
11 Genetics Program. And we are focusing on the
12 Exposure Biology Program.
13 This is really a very exciting
14 program. It involves not only NIH's, but it
15 also involves, for example, the Behavioral and
16 Social Sciences Center. It involves NIDA and
17 a number of others looking at a multitude of
18 different kinds of exposures and how they may
19 influence and interact with our genetic
20 materials and I think both on a genomic and an
21 epigenomic paradigm eventually.
22 I think one of the exciting things

1 here is that we are developing very small,
2 often wearable biosensors that can be used to
3 identify individual exposure to a wide range
4 of different types of contaminants.
5 In addition, we are also
6 developing improved diagnostic biomarkers of
7 early response. That can be used to try to
8 understand not only the early pathways but
9 predict and allow for interventions to occur.
10 So, again, some of the widgets and
11 gadgets that have been developed area really
12 quite phenomenal. And they are going into the
13 validation stage right now.
14 Another important program we have
15 is the Breast Cancer and the Environment
16 Program. This is defining how environmental
17 agents affect the lifelong risk of breast
18 cancer.
19 We fund about $35 million a year
20 in breast cancer in the environment research.
21 And we have a co-fund with NCI Breast Cancer
22 and the Environment Research Centers.

1 In fact, that has been a
2 seven-year program. We have recently gone up
3 and requested renewing the project for another
4 potentially five years.
5 And in this project, we are
6 looking at identifying potential windows of
7 susceptibility. One, again, of the unique
8 things about the center, not only is it the
9 community core part of it, but we have in
10 every center both the basic biological studies
11 going on, the cell culture, the animal
12 studies, and we have clinical studies going on
13 and epidemiological studies as well.
14 And so we are applying some of the
15 GEI kind of approaches using direct measures
16 of exposure in diet, looking at polymorphisms,
17 and, again, integrating with the animal in the
18 cell culture models.
19 We are working with the community
20 and the advocates in the research arena. And
21 we are providing education and messages to
22 enable and form lifestyle choices throughout

rejectivities, forms, and mentoring.

Another important thing I will stress as important to community involvement and community in all of our projects is we have recently established an umbrella program called the Partnerships in Environmental Public Health.

This is aimed at strategically coordinating and integrating the various new and existing initiatives. So this includes our environmental justice programs. It includes to has like a dotted line to the community actions that we have in many of our other centers kind of program.

This also involves information on developing communication of risk kinds of strategies so that people can understand what is really important and evaluate what they hear.

We are trying to create and provide materials to increase awareness and literacy about environmental health risks and

1 really evaluate public contributions to
2 advancing public health.
3 Now I want to switch gears to
4 another part of the extramural program and
5 just briefly tell you a little more about the
6 Superfund program, which, as I said before, is
7 a problem-solving program.
8 Its mandate under the Superfund
9 Research Program is to detect hazardous
10 substances in the environment, understand the
11 risk of those hazardous substances to human
12 health, and then to develop basic approaches
13 and methods to reduce the toxicity of
14 hazardous chemicals.
15 So this program actually involves
16 some remediation efforts, developing of
17 microbial degradation processes, developing of
18 biological, for example, different kinds of
19 plants, which may be able to hold down the
20 soil and prevent metal exposure and mining,
21 former mining sites or in former sites with
22 high levels of groundwater contamination.

1 It is a very interactive program
2 between not only NIEHS but with the Superfund
3 program at EPA, both the headquarters EPA and
4 the regional EPA offices, and also works with
5 ATSER, the Agency for Toxic Substances and
6 Disease Registry down in Atlanta, whose
7 mission is to evaluate the effects on people
8 living in conjunction with hazardous waste
9 sites and being exposed to toxic substances.
10 And, as I mentioned, the other
11 part of the Superfund program is the worker
12 training. We have trained over two million
13 workers over the past 20 years across the
14 country in every state, in every territory to
15 do hazardous waste cleanup and emergency
16 response.
17 So, for example, when there was a
18 tsunami that hit Samoa this August, we had
19 actually, one of our grantees had actually,
20 been there in June training the Samoan
21 chieftains in emergency response.
22 And we believe -- and from some of

1 the evaluations that had been done -- that
2 training helped reduce the loss of life that
3 occurred in that area, which is kind of
4 exciting.
5 So now I want to switch and talk a
6 little about the National Toxicology Program.
7 This is an interagency program, which was
8 established, actually, by Joseph Califano in
9 1978 to coordinate toxicology research across
10 the Department of Health and Human Services.
11 And it is headquartered at NIEHS.
12 So when I wear my NTP hat, I
13 actually report to the Assistant Secretary of
14 Health, as opposed directly to Francis, but
15 NIEHS is the largest component of the NTP.
16 And, in fact, the other two components involve
17 NIOSH as part of the CDC and the National
18 Center for Toxicological Research in
19 Jefferson, Arkansas as part of the FDA,
20 although I can tell you that the FDA
21 commitment in interaction is expanding way
22 beyond NCTR as we are doing more testing,

1 toxicity testing, of compounds, for example,
2 that are food additives and herbals and that
3 kind of issue.
4 Now, we get nominations from
5 everyone. Anyone can nominate things we get
6 from our federal partners. We get it from
7 states. We get it from just people. And
8 thousands of agents have been evaluated in
9 comprehensive toxicology studies.
10 And then we communicate all our
11 results through highly peer-reviewed. We have
12 an independent Board of Scientific Councilors
13 that reviews the technical reports,
14 peer-reviewed publications, and the data is
15 all available on the Web.
16 In addition, we have
17 congressionally mandated evaluation
18 activities, such as the report on carcinogens,
19 in which chemicals are listed as to whether
20 they are known to be carcinogenic to humans or
21 anticipated, likely to be carcinogenic to
22 humans.

1 So two weeks ago, we actually had
2 the peer panel that reviewed the listing for
3 formaldehyde. At the conclusion of the peer
4 panel, then we will listen to their advice as
5 well as a lot of public comment.
6 They concluded that formaldehyde
7 is now a known human carcinogen in concert
8 with what the International Agency for
9 Research on Cancer had also agreed upon the
10 previous month.
11 We also do evaluation of the risk
12 to human reproduction. And this is actually
13 the group that focuses on reproductive and
14 developmental effects of a number of
15 compounds.
16 This again is a hazard evaluation
17 report. This is not a risk assessment. But
18 it pulls together all of the information. And
19 one thing that we really were working on hard
20 to do is to put the context of these
21 evaluations into public health.
22 How does the data that exist

1 relate to and what is the impact upon the
2 health of the American and, actually, the
3 public throughout the world?
4 In addition, we are mandated to
5 have a program which is called ICCVATM, which
6 is the Interagency Coordinating Committee for
7 the Validation of Alternative Test Methods.
8 This is a 15-agency committee that
9 we are in charge of that evaluates alternative
10 test methods looking at the three R's: reuse,
11 reduce, and refine.
12 So it's not only to come up with
13 in vitro methodologies. It is to make sure
14 that we have less pain and suffering for our
15 animals and only use the number of animals,
16 for example, that are absolutely necessary in
17 testing.
18 And at this point there had been
19 at least 27 alternative test methods that have
20 been evaluated by this committee. And a
21 number of them have now been accepted by
22 different federal regulatory agencies for

1 alternative use.

2 So since I have come on board, we

3 have kind of renewed some of the areas of

4 emphasis for the NTP. And we are really

5 working to get better coordination across the

6 entire federal government because the mission

7 really is to coordinate tox testing across the

8 entire federal government, not only within

9 HHS.

10 We are working at developing new

11 methods for efficient and thorough

12 toxicological assessments. We are focusing on

13 understanding exposure-response relationships

14 and issues of dosimetry.

15 By that, what I mean is you often

16 hear that toxicology tests are created at high

17 doses. And what does that mean for low-dose

18 environmental exposure?

19 So we are making sure that we are

20 placing the studies in an appropriate context.

21 If you want to compare animals in humans, you

22 have to use a common metric of exposure, not

1 how much is in the drinking water because
2 animals have to have a much higher
3 concentration in their drinking water in order
4 to get the same internal dose.
5 And so what we were doing is
6 making sure that we have appropriate
7 comparable measures. So when we recently
8 released the studies that demonstrated that
9 hexavalent chromium in drinking water caused
10 tumors in both rats and mice following two
11 years' exposure, we also have done the studies
12 now to tell you that the concentrations in the
13 animals are less than ten times higher than
14 the concentrations in people who are living
15 near some contaminated sites in California.
16 So that puts the message in a
17 context that I think will be very helpful for
18 regulatory decision-making.
19 Another thing we are doing is
20 Chris mentioned briefly tox-21. I am going to
21 come back to that, but we are focusing on
22 integrating the results from the new data-rich

1 techniques with traditional tox data to
2 improve the public health context.
3 Again, we have been working with
4 the NCGC and with EPA in the development of
5 tox-21. Francis was one of the leaders that
6 got this whole effort started.
7 I want to kind of make the point
8 that when you are looking for environmental,
9 potential environmental, hazards, you are kind
10 of asking a -- I don't know if the word is
11 inverse or converse question than we are
12 asking with pharmaceuticals.
13 With pharmaceuticals, it doesn't
14 matter if you have, for example, some false
15 negatives. It doesn't make any difference.
16 For environmental screening, it makes a big
17 difference.
18 So some of the beauty of tox-21 is
19 that I believe they are using about 400
20 different assays. They are going to be
21 looking at about 10,000 different chemicals.
22 We are beginning to get the data on about the

first 1,000, I think. I know we have got it on the first 400.

And what we are going to see, I think that is going to be very important for prioritization of further testing of compounds is what really lights up the board.

It is not the chemical that causes. You know, yes, it may have a high affinity for the estrogen receptor. That is not going to be the compound that is going to have the greatest interest. It is going to be the chemicals that really cause multiple kinds of effects.

And I don't think I am talking out of school here. The number two chemical so far in the screening of the environmental chemicals that are lighting up the board is Bisphenol A, BPA, which some of you have heard about. I don't know about you. That says to me maybe some of the data we are hearing about is real.

So overall at the institute, what

1 we are really focusing on is the conceptual
2 shift for environmental health sciences. Kind
3 of the old approach was that chemicals act by
4 overwhelming the bodies' defenses by brute
5 force at very, very high doses.
6 And now we are focusing more and
7 more that a lot of chemicals act like
8 signaling molecules. And, in fact, they act
9 like hormones and drugs disrupting the control
10 of development and function at low doses. And
11 by that, I really mean by low body burdens
12 that are similar to what the average person
13 might be exposed to.
14 We are really focusing on this
15 definition of low dose. Some people, like we
16 just heard a briefing from the CDC this week
17 who are going to be releasing their fourth
18 report on the level of chemicals that they can
19 detect in a statistically based sampling of
20 the American population. It's often called
21 the CDC report card. And I think Raynard is
22 very familiar with that.

1 The exciting thing about it is,
2 instead of "dose," they are actually using the
3 term "levels." Anyway, they are referring to
4 concentrations of, for example, environmental
5 chemicals in biological media. And that is
6 really what, again, as I said before, we have
7 to relate.
8 We are focusing on using low-dose
9 examples, something like BPA, something like
10 phthalates, something like a number of other
11 compounds, which, in fact, when you look at
12 the levels in the population, they're quite
13 low. But we actually find similar levels in
14 some of the studies that have been conducted
15 in animal studies.
16 We are focusing on sensitive
17 windows of exposure. A lot of focus on not
18 only in utero exposures but infantile
19 exposures, pubetal exposures, and realizing
20 that the elderly are also a susceptible
21 population for environmental effects.
22 Then we're, as I said, really

1 looking at the new paradigm for the basis of
2 disease, which is epigenetics, especially
3 developmental changes.
4 Now, I should mention that when
5 you're dealing with environmental exposures,
6 you have got a confounding problem. And that
7 is nobody is exposed to zero. You are always
8 exposed to multiple environmental agents. And
9 that could be both in time and space.
10 It is difficult to decipher how
11 the exposure to one agent will influence the
12 effects of each one. In other words,
13 co-exposure we know, certainly from
14 pharmacology, can also save the metabolism,
15 where you may have competition of compounds
16 going on.
17 Prior exposure may alter the way
18 you handle a chemical or may change the number
19 of receptors, for example, that you have for
20 a chemical.
21 But, again, it is never one
22 chemical at a time. It is a multiplicity of

1 compounds. Linking exposure and disease has
2 to begin to take multiple exposures into
3 account.
4 So just two brief examples of some
5 new high priorities for us. One is evaluating
6 the safety of engineered nano materials. And
7 we have, NIH as a whole has had, a major
8 effort looking at nano medicine. In that
9 effort, there has been a little teeny bit
10 looking at nano safety. Nano medicines and
11 nano technology in general have tremendous
12 potential. However, there is very little
13 known about the safety of these engineered
14 materials.
15 So we have a large extramural
16 research program, which is looking at
17 biological interactions, trying to figure out
18 how do you measure these things, trying to
19 link the physical/chemical properties, and
20 trying to capture all of the results in a
21 searchable base that can be analyzed
22 appropriately.

1 We have an intramural program that
2 is looking at the impact on asthma between
3 carbon nanotubes. And I have to say that not
4 so much from our work yet but from other
5 studies I am seeing, you know, if a carbon
6 nanotube looks -- if it is a long, skinny
7 fiber and it looks like asbestos, we are
8 finding, at least in cultured cells, it is
9 doing the same kind of thing. And so our
10 level of concern is raising.
11 Then we are also trying to
12 understand whether some of these nano
13 materials can penetrate the skin trying to
14 understand the pharmacokinetic behaviors, some
15 of them, and actually engaging in toxicity
16 studies.
17 This is an area that we have
18 actually had congressional language telling us
19 that they want us to focus on the area of nano
20 safety.
21 Many of these projects are
22 coordinated across the federal government.

1 There is a large task force that is involved
2 in working in many different parts of the
3 government at this issue of nano safety.
4 Then the other area I wanted to
5 talk about a moment is climate change in human
6 health. We are providing the Department
7 leadership on this area. With the Fogarty
8 Center, we are heading a trans-NIH group. And
9 we are also working very intensively.
10 We are developing a white paper,
11 which is, again, not only cross-HHS but cross
12 the federal government, white paper on
13 research needs for health effects of climate
14 change. And we hope to release that soon.
15 We organized a White House
16 stakeholder briefing two weeks ago that was
17 very well-intended jointly between HHS and
18 EPA, in which the Secretary and the
19 Administrator both participated.
20 And then we have been partnering
21 with the Wellcome Trust and just released a
22 series of papers that we had sponsored the

1 development in Lancet.

2 The important thing about these

3 papers is that they were the first

4 quantitation or quantification of the dollar

5 cost of global climate change for at least the

6 number of different health endpoints. And it

7 is astounding.

8 Up until 9:00 o'clock this

9 morning, I and the head of global health from

10 the CDC were part of the delegation going to

11 Copenhagen next week.

12 We were cut this morning. So,

13 unfortunately, we still haven't convinced the

14 government that why people really care about

15 climate change is because of what it is going

16 to do to them and their children and the

17 health impacts. But we are going to keep

18 working at it as we go forward.

19 So we also have had a number of

20 challenge grants that we are funding in this

21 area. And, again, this adds onto our work

22 with oceans and human health.

1 So I have talked about a new
2 vision for NIH and NTP. We are partnering
3 much more closely with our sister institutes,
4 with the EPA, with CDC, with FDA, with the
5 Department of Energy, with a number of other
6 groups.
7 Our priority is health and the
8 environment. We are taking advantage of new
9 issues and emerging technologies. We are
10 using both the best individual and the best
11 team science to address complex diseases and
12 complex environmental impacts.
13 We have to improve the integration
14 across research disciplines and with all of
15 our partners. And we are working very hard to
16 improve our translation and communication of
17 basic science findings into human health
18 protection.
19 So thank you. And I am happy to
20 answer any questions.
21 CHAIRMAN COLLINS: Great. Thank
22 you. That was quite a tour de force. And I

1 am mindful of the fact that we have people
2 whose taxis are arriving momentarily. We have
3 an action item we have to actually do
4 something about before we lose a quorum. So
5 if we could do that?
6 DR. BIRNBAUM: Sure.
7 CHAIRMAN COLLINS: And then those
8 who could stay could perhaps would be able to
9 ask Linda some questions. But before you
10 depart, Tom, Raynard?
11 DR. KINGTON: It's that time of
12 meeting when we ask for your approval of
13 pre-approved awards for in action employees.
14 As many of you know, in 2005, when
15 our new ethics rules were promulgated, part of
16 the regulations require that in order for an
17 NIH employee to be eligible to receive a cash
18 award for his or her official duty activities,
19 the award had to be pre-screened by an entity.
20 That responsibility was assigned
21 to the ACD. Karen Holbrook and Barbara Wolfe
22 had been working with our internal lawyers to

1 review a list of awards that we received from
2 organizations so that they can be
3 pre-approved.
4 Under tab 13 of your binders are
5 12 awards from natural organizations that have
6 all been screened and found to have met the
7 legal and regulatory criteria for a bone fide
8 award.
9 This allows NIH employees to be
10 eligible as long as there is no other reason
11 why they shouldn't get the award, to be
12 eligible to receive the cash payment for an
13 award.
14 And we ask for your concurrence
15 and approval of these awards as bona fide NIH
16 awards.
17 DR. FREIRE: In the interest of
18 full disclosure, the Albert and Mary Lasker
19 Medical Research Award is not on the list.
20 DR. KINGTON: So perhaps you
21 should recuse.
22 PARTICIPANT: So moved.

1 PARTICIPANT: Second.
2 DR. KINGTON: Any more discussion?
3 (No response.)
4 DR. KINGTON: All those in favor?
5 (Chorus of ayes.)
6 DR. KINGTON: All those opposed?
7 (No response.)
8 DR. KINGTON: Recuse or abstain?
9 (Show of hands.)
10 CHAIRMAN COLLINS: And recognizing
11 many of you do have to run out the door,
12 perhaps I could suggest if you don't and you
13 have questions for Linda, please approach her
14 and engage in conversation.
15 Linda, our apologies that we ran
16 into this somewhat tight timetable, which
17 tends to happen at the end of the meeting.
18 But we thank you very much.
19 DR. BIRNBAUM: Well, I have to
20 thank everyone because they changed it so I
21 could get here on time. So thank you.
22 CHAIRMAN COLLINS: Thanks a lot.

1 DR. KINGTON: Thank you.

2 CHAIRMAN COLLINS: So, with many

3 thanks to all of you, we are adjourned.

4 (Whereupon, the above-entitled

5 matter was concluded at 3:32 p.m.)

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