UNITED STATES OF AMERICA{PRIVATE }
NATIONAL INSTITUTES OF HEALTH

+ + + + +

SCIENTIFIC MANAGEMENT REVIEW BOARD
(SMRB)

+ + + + +

WEDNESDAY
SEPTEMBER 15, 2010

+ + + + +

The Scientific Management Review Board convened in Conference Room 6 of Building 31 at the NIH Campus, Bethesda, Maryland, Norman Augustine, Chair, presiding.

BOARD MEMBERS PRESENT:

NORMAN R. AUGUSTINE, Chair
JEREMY BERG, Ph.D.
WILLIAM R. BRODY, M.D., Ph.D.
GAIL H. CASSELL, Ph.D.
ANTHONY S. FAUCI, M.D.
HON DANIEL S. GOLDIN
RICHARD J. HODES, M.D.
STEPHEN I. KATZ, M.D., Ph.D.
THOMAS J. KELLY, M.D., Ph.D.
DEBORAH E. POWELL, M.D.
GRIFFIN P. RODGERS, M.D., M.A.C.P.
WILLIAM L. ROPER, M.D., M.P.H.
SUSAN B. SHURIN, M.D.*
LAWRENCE A. TABAK, D.D.S., Ph.D.
HAROLD E. VARMUS, M.D.
A. EUGENE WASHINGTON, M.D.
HUDA Y. ZOGHBI, M.D.

EX-OFFICO MEMBERS PRESENT:
FRANCIS S. COLLINS, M.D., Ph.D.

DESIGNATED FEDERAL OFFICIAL:
AMY PATTERSON, M.D., Executive Secretary

*Present via telephone

ALSO PRESENT:

STEPHEN L. ECK, M.D., Ph.D.; Eli Lilly
CHARLES BAUM, M.D., Ph.D.; Pfizer, Inc.
KEN DUNCAN, Ph.D.; The Bill and Melinda Gates Foundation
BRIAN HALAK, Ph.D.; Domain Associates
THOMAS R. INSEL, M.D., National Institute of Mental Health
JEAN-PIERRE PACCAUD, Ph.D.; Drugs for Neglected Diseases Initiative
ERIC D. PERAKSLIS, Ph.D., Johnson & Johnson
ROBERT CALIFF, Duke University Medical Center
JEFF ALLEN, M.D.; Friends of Cancer Research
STEVEN M. ROWE, M.D., M.S.P.H.; Cystic Fibrosis Foundation
GREGORY C. SIMON, J.D.; Pfizer, Inc.
AMY COMSTOCK RICK, J.D.; Parkinson's Action Network
MARGARET A. ANDERSON, FasterCures
BARBARA McGAREY, J.D.; NIH
BENJAMIN BUTLER, J.D.; NIH

C-O-N-T-E-N-T-S

C-O-N-T-E-N-T-S (CONTINUED)

C-O-N-T-E-N-T-S (CONTINUED)

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

8:08 a.m.

CHAIR AUGUSTINE: (presiding) Good morning everyone. If you would take your seats, we will begin.

All right. Welcome to the second day of the sixth meeting of the full SMRB. I hope everyone had a good evening. We have got a busy day today.

Two major topics. The first is to complete the discussion and data-gathering aspect of the TMAT topic and then we will turn to the report this afternoon of Bill's group and I want to be sure that we have a quorum this afternoon and get as many inputs as we can.

So, we will try to stick pretty close to the schedule, because I know people have airplane commitments, including myself.

Let’s see, I notice in terms of the attendance, the attendance award goes to this side of the table this time. You will all

need to work on your colleagues a little bit here.

Two announcements, just quickly. One is that for the members there is a sign-up sheet that will come around that if you need taxis to the airports and the likes this afternoon, if you will note it on there, that will be arranged.

And secondly, for the members of the public who are here, first of all, welcome and secondly, if you have comments that you would like to make, and we certainly welcome that, there is time allotted this afternoon, albeit rather brief, but there is time, and there is a sign-up sheet out in the hall.

We kind of do it in first-come, first-served, five minutes max, and again, as we said yesterday, we welcome longer inputs by mail or other form.

With that said, let's -- Arthur unfortunately is letting his regular job interfere with this. He had to go back to his

institution today, so I will kind of try to pinch hit for him in this wrap-up of the TMAT data collecting, if you will, information collecting.

And our first speaker this morning, who will kind of lay the groundwork for the next panel discussion, is Dr. Stephen Eck, who is with Eli Lilly, and I am not going to go into biographies, because you have everybody's resume in your book. So let me turn to Dr. Eck.

DR. ECK: Well, it is a pleasure to be here this morning. My apologies for missing yesterday's proceedings. I will try to start by giving you a brief overview of the history of industry-academic collaborations in drug development, provide a little bit of perspective -- I think most of this history is known to you -- and then I will move to where I think there are some constraints and opportunities, and finally five areas that are my favorites for how academic and NIH research

can improve the efficiency, productivity and innovation in drug development.

So, there is a long and rich history of collaboration between industry and academe and it has changed substantially over the years and I think that is worth appreciating. The pharmaceutical industry really flourished with academic collaborations in the middle part of the 1900s and this was certainly evident at Lilly, where work, where we moved from a company that largely sold botanicals for medicinal purposes in the early 1900s, to a research-based company.

And that research was driven by our ability to interact with academic investigators. And I listed some of the major ones, certainly not all of them- our collaboration with the University of Toronto on insulin, the Indianapolis City Hospital, to open a research clinic on pellagra and other related disorders, collaboration with the University of Rochester on pernicious anemia

are some of the very early events.

And there was somewhat of a decline in this process as industry became much more independent and brought more R&D in-house and became more vertically-integrated in this area.

And arguably, I thought, I think the industry thought it could sort of mimic the innovation cycle that had been produced in the electronics industry and in other markets.

Notably, the Bayh-Dole Act and other changes sort of changed that tide and we have now gone to a situation where pharmaceutical research would be essentially impossible without academic collaboration.

And Lilly today -- I don't have a slide of all our collaborations but they are extremely diverse. They vary from our collaborations on discovering new tuberculosis drugs, to very small-scale but detailed investigations of the genetics of schizophrenia drug response.

So, this has not been without some difficulty and I think you are certainly all aware of the attention that has been brought toward conflict of interest of issues. Frankly, this is largely a beast of our own creation. I think we did not do a good job of maintaining a distinction between what was legitimate, scientific research and what were marketing activities.

And although some of these efforts may be well-intentioned, I think it sort of spoiled the fun for lots of people.

So going forward, I think we need to keep this in mind, there are clearly different agendas at stake here, but there needs to be a clear separation between the research activities that we conduct and how we publicize that and our marketing activities. And all of these financial arrangements need to be explicitly transparent and stand up to scrutiny.

So, there are some distinct

cultures and resource differences between academia and industry and I don't want to go through all of these, but I would like to highlight two.

One is the diverse talent pool that exists outside of industry. The industry approach to drug discovery and development has become increasingly narrow. Clinical pharmacology, which is part of my group, is a very good example. We don't embrace the entire field of clinical pharmacology. We embrace essentially that aspect which is needed to get a drug label.

And there is a lot more interesting pharmacology out there that we don't explore. As a result, we tend to employ people who work on the practical matters of developing a drug and getting a label and there is a lot more to drug research in the science around this than we are ever going to pursue.

There is also a lot of talented

people out there who have different ideas and different approaches that aren't ever going to work for a drug company for a variety of reasons. So, I think this alone is a very good basis for a collaboration.

The second topic I want to highlight is that the project has premiered outside of drug companies. We tend to focus on a portfolio. We are trying to drive top-line revenue growth. It is a major problem in the industry right now. So we are somewhat agnostic to how we succeed, how we achieve that goal, and make trade-offs on projects constantly, much to the annoyance of some of our collaborators.

The academic investigator has a vested interest in a particular topic and it may occupy a large portion of their time during their career, and this sustained focus of activity, I think, is very important and provides a certain amount of stick-to-itiveness that we often lose sight of.

Those two elements alone, I think, are plenty good reasons why we need to foster collaborations between academic researchers and commercial drug developers.

This is a graph I made which is not the least bit scientific and it is flawed in a quantitative sense. But, it was an attempt to illustrate sort of the linear thinking that goes into the process of developing and marketing a new drug and who contributes, where.

And the blue roughly illustrates where the contributions come from academia and green, roughly, where the contributions come from the industry side. And most of the early work around the biology of disease and target identification in recent years has occurred on the academic side and not within industry, as industry has moved away from this to a large extent.

And this is in sharp contrast, for example, with our company. When we founded the

Lilly Clinic in 1926, it focused entirely on understanding the disease, and had nothing to do with the process of discovering a drug.

The Lilly Clinic today, which operates in Singapore, focuses entirely on developing drugs and not the least bit on understanding disease, so we have come -- we are 180 degrees from where we were when we built our own clinic.

In the middle part, the lead generation through sort of Phase III is dominated largely by the pharmaceutical industry, in part because we control the assets and we are a little bit secretive and we are pretty particular about what gets done when.

I would argue that that probably needs to change, in that we are -- the period from target identification to a new drug launch has shorted considerably, and science is occurring while you are running your drug development program, and that new science

needs to be incorporated in.

We have gone to disclosing what clinical trials were running. I think we will move even further forward to disclose publicly a lot more details about what those clinical trials are. I think, and I would hope, that more openness in this area would foster collaboration and that we could bring in outside ideas and use outside talent to further this mission.

Finally, on the post-marketing research side, pharmaceutical companies do not do a lot research on the post-marketing side. It is really market extension: how can we maximize the value of the drug? We get a new line indication. An example is fibromyalgia where there are now several drugs marketed, both by Lilly, Pfizer and others.

So, we have done a lot to bring new drugs forward but have not contributed proportionately to understanding the biology of fibromyalgia, just to pick one example.

And of course, the ability of the academic community to contribute here is not largely going to be impossible due to the fact that now everything is public, and they have free access to do the work with or without us.

There are several concerns and benefits to the collaborations that I have not touched upon, and I am going to point to a couple of my favorites. First of all, we need to have a greater willingness to disseminate new discoveries and ideas more quickly.

We tend to be rather conservative in this area. When I was with Pfizer before joining Lilly, we had the distinction of having the least number of publications per R&D dollars spent. We actually looked at our $8 billion budget at the time and the total number of publications produced and we were last among the big pharma, and certainly well behind academics in terms of the number of publications per research dollar, if you look at an investigator with R01 for example.

So, we need to bring the information forward a little more quickly, so that this can be incorporated into practice and I will get to that in a minute.

The other area I would like to highlight is the exchange of scientific reagents, tools, and technologies. We produce a lot of tools that, I think, could be more routinely made available. They are not the subject of value for the company. They are not the basis for revenue generation. We have moved away from patenting everything we think about, to patenting a much more narrow spectrum of what we invent and, largely, it is around the composition-of-matter patents that are valuable.

The tools, reagents, are much less valuable in terms of generating revenue, but are extremely valuable if we could disseminate them and see more broad use.

For example, our group is responsible for developing PET ligands. They

do not have any proprietary interest to us. We use them to study receptor occupancy, so we can, for instance, select a dose of a new CNS drug, but that tool might, if made more broadly available, contribute to understanding of receptor biology or some other area of neuroscience.

So these are the fives areas that I have picked where, I think, industry needs help in advancing innovative medicines, and I will focus on innovative medicines because we have largely made money in the past by incremental improvements that were valued by society.

I think we are running out of room there, in terms of the incremental approach. I think we need some radically new approaches, particularly in diseases such as Alzheimer's and cancer, where there are still large unmet medical needs.

So, I picked these. There are a lot of others that other individuals might

have chosen, but these are the ones that show up on my desk on a routine basis.

Target identification, understanding patient heterogeneity, biomarker development, identifying unique subsets of patients that are responsive to a new drug, so-called personalized medicine or, at Lilly, we call it tailored therapeutics, and providing tools to help physicians manage complex information, and I will give examples of each of these.

So, in target identification and validation, this has been really the strength of the academic community. The industry previously relied on a pharmacology that was known to exist in nature, aspirin was known to the pharaohs, the alkyl agents were discovered as a result of toxic agents used in World War I and so forth and so on.

We have moved away from that to using target-based drug discovery, which is the mainstay of most pharmaceutical company

pipelines. And I listed here a handful of what I would call popular targets, in that two or three or four major pharma companies are chasing these targets as a basis for new therapeutics.

And with the exception of two of them, all of them really came from academic discoveries. And you can make this list much, much longer. These are just some of the popular ones.

The ones which had significant discovery contributions from the pharmaceutical industry, were certainly CTLA4, which Peter Lindsley discovered when he was with BMS up in Seattle, and that contributed to the development of Orencia, the CTLA4-ig fusion protein, and later to MetRx, Pfizer and BMS's separate contributions to developing antibodies against that receptor for cancer.

And then the NAV1.7 for pain, which was largely an academic discovery but was funded substantially, in part, by Pfizer

and Duncan McHale, who used to be in my group when I was at Pfizer and was a major participant in it.

So, there is some work on the industry side, but clearly the bulk of this comes from academia, and that is not likely to change in the near future and that is something that should be certainly encouraged.

The numbers on this slide are less important than the concept, but it illustrates that many of the drugs we use today do not have the intended effect in a lot of the people that take them. That is just the simple fact. There is a huge amount of empiricism in the use of medicines. It is try it and see if you like it.

As my internist says when he has a new patient with hypertension, it is like trying on shoes. Try some on until you find ones that fit.

That type of empiricism is not a very efficient use of resources; it is not

particularly scientific or rewarding for the patients either.

So, we could improve on this and I think this is the second big area where I think academic-NIH collaboration with industry could reap huge benefits.

We need to understand patient heterogeneity at the molecular level with much greater detail than we do now. A broad-based approach to large patient populations such as type 2 diabetes, schizophrenia, depression, are not going to make major advances until we understand that these are really much more complex disorders and that new drugs need to target very specific segments of this market, and I will say more about that in a minute.

This is a slide that I borrowed from our CEO. Again, I think the numbers on the slide are less important than the concept and the numbers will change depending on what particular drug you are talking about or what particular market.

The point is that we do not need to market drugs to the entire therapeutic area or the entire indication to have a good return on investment. Increasingly, segmenting the market is the hallmark of mature industries, whether you are making automobiles or selling soda pop or in the drug development business.

You can do a better job of meeting your customer needs if you segment the market. And that is why markets segment. And, I think, that is true in the pharmaceutical industry.

The current choice of statins, for example, is largely arbitrary. My mother, my brother, and I all have the same inherited form of hyperlipidemia. I take Lipitor because I like Lipitor and actually it has got the best label -- I don't take Lilly's statin but don't tell anybody that.

My brother takes Crestor. Not sure why. He doesn't have hypertriglyceridemia and his HDL is just fine and my mother takes synthostatin because she is basically cheap.

So, the market segments but that is not rational. We need to provide a rational basis for this and, I think, when we bring new medicines forward, we identify the right segment for each patient. This can be very acceptable in terms of revenue for drug developers.

The third area is biomarkers and I will go through this fairly quickly in the interests of time and I think this is an area you all know very well. They have very little proprietary value, as I mentioned, with the PET scanning example.

They become more value when we disseminate them widely, we allow a lot of people to use them, the people using well validated assays and share their information, then the utility of that assay climbs much more quickly than if it is held in a proprietary way.

This is just one example. This is Lilly's support for the biomarker consortium.

I sit on the executive committee of the biomarker consortium. It is a bargain for us. For every dollar we put in, it generates five dollars' worth of investment because four other companies will also put in money on average and so we only have to pay for a fraction of the work, and this is all done and made available to the public.

This is a larger list of collaborations that Lilly has had through the FNIH. I think the FNIH is a great vehicle for doing this. It provides openness, transparency, and also can keep the research at arm's length, which helps with managing conflicts of interest.

One very good example of this was the GAIN Initiative, which Patrice Milos at Pfizer started with Francis Collins's folks. This was -- the cost of that was roughly $55 million to Pfizer. That was not in the round-off area of my budget at the time. In fact, it was less than what was left over in the

external collaboration budget at the end of the year that went unspent. These are very manageable sums of money and can produce a huge amount of public good.

Identifying unique subsets of patients I have already alluded to. This is another example where, what I would describe as a relatively poor CNET inhibitor, PF-02341066 as it is affectionately known -- it probably has a new name now -- was rescued by the background work on the EML4-ALK fusion gene and its relationship to lung cancer progression in a subset of individuals.

Now that academic work, if not for that backdrop, there would not be a path forward for this drug, and I think there are going to be many, many more examples of this where the academic community can help identify better subsets of patients and so use drugs appropriately.

The last topic I will address is information overload. This is a slide from

Steve Friend. The amount of information that clinicians have at their disposal is virtually unmanageable today. It is not reading the literature. It is understanding the literature and it is being able to incorporate that into your clinical practice.

There are lots of -- I think we can address this by developing better tools that are well validated, that help clinicians in everyday practice manage the information and use it effectively.

I will point to just the last bullet-point, because I think this is very important to us as drug developers. We are going to launch medicines that are going to have a very narrow use. And that narrow use is going to have to incorporate lots of specific information, and it is well beyond age plus BUN equals Lasix dose. It is way more complex than that and it is not going to be a little mnemonic that you can keep in your head.

There is going to need to be a

tool, and a validated tool, and frankly, if it is our drug, I would like to have that tool on our label, and I would like to have it FDA-reviewed and approved and have it squeaky clean, not some back-of-the-envelope calculation.

If that is going to happen, that is going to require a lot of input from people outside the pharmaceutical industry to guide how those tools are built and how they are used so they are truly useful.

So, I will give you an example. Well, this is just some areas where you might think about how this could be used. You are all familiar with the genetics of warfarin dosing and I will say a little bit more about that, HLA B5701 genotype, the risk of hypersensitivity for abacavir and fluvoxacillin and many other types of information to become available that affect drug use. But, this is going to be way more complex than just this test for this drug.

So, this is from the Coumadin label. I actually had my check-up on Monday and I shared this with my internist. It was kind of interesting. First of all, he could not interpret the chart. So it is not likely that he is going to read the drug label and know what *1/*2 CYP2C9 mean, let alone what Coumadin dose I should get, based on this table, okay?

Secondly, I didn't even know that VCORC or CYP2C19 had anything to do with Coumadin and that the genetics might be interesting, the background for the table. This is an academic internist at a major, academic medical center who has got 30-some years of practice under his belt, okay?

So, you know, we have to reduce this to something that is intelligible and immediately useful.

So, I picked this not because I have studied this and know this to be a good tool. It is just illustrative of the idea, and

you can go to the website and play with the tool. It is kind of fun.

But, it is sort of idiot-proof, quite frankly, not that physicians are idiots, but it is simple. So, you know, it just asks you for information and you put the information in and there is a lot of -- you put the indication in and whether they smoke and have liver disease and their genotype and all this stuff -- and it estimates the dose for you. And in fact, with electronic medical records, this could run in the background. It does not necessarily have to be manually inputed by the physician before he picks up the prescription pad. By the way, he is not going to have a prescription pad. He is going to write electronic prescription and he is probably going to go to Medco or some other provider who can look over this and actually do the genotyping for you.

So, I think partnerships between academia and industry, between academia and

NIH and companies like Medco, who are very interested in applying these tools, is a very important area for us.

It gets even more complex than this. This is a model for -- a mechanistic model for clopidogrel dosing, which is quite complex. It is a very interesting drug and it certainly has a lot to offer the public, but it does not offer the same thing to everyone equally.

There are lots of things that influence your ability to get mileage from this, including your CYP2C19 status, your ABCB1 genetics, whether you can metabolize the drug, whether you can absorb the drug, whether you are taking a proton pump inhibitor, whether you have had a prior stroke or MI, whether you are old and decrepit, whether you are of low body mass -- all these things we have data around that influence the use of this class of drugs in general.

And so, these can be modeled

effectively and we can build good decision-making tools that can people can reduce clinical information to dosing strategies.

I have a couple of more slides then I will conclude. So, I think the areas of collaboration on the preclinical side are clearly target identification and validation. If we are going to drive innovation, this has to be at the forefront, and we need to understand patient subgroups that are going to benefit from a particular target. Unquestioningly, these are areas of tremendous interest.

On the clinical research side, there is the biomarker research, comparative effectiveness research, which I really did not talk about in any detail, pharmacoeconomic research, particularly what is value? What constitutes value? And what are we going to be compensated for as drug developers? We don't want to work on something that nobody is actually that interested in.

We need to advance regulatory science, how we review drugs, how we get drugs approved and how we manage this data. It is relatively unchanged in the last 20 years. I think this is the time for reform of drug regulation.

And finally, we need to be able to implement personalized medicine in a regulated environment by having robust decision-making tools.

There are several key aspects to the collaboration, which I think deserve attention. I have mentioned most of these. But, I think the bottom one is the most important. We need to be absolutely transparent in all aspects of the collaboration. Everyone needs to play with their cards on the table face up.

I think we have some very good examples in the past. I think the GAIN Initiative, which I have already alluded to, is a great example where public good can be

generated from close collaborations.

Nobody had any leg-up on anybody else in the process. There was no proprietary interest in this. So let me stop there and I will be happy to answer questions. Thank you very much.

CHAIR AUGUSTINE: Dr. Eck, thank you very much. The floor is open to questions from the panel. Please.

MEMBER KELLY: Thank you very much. That was a very useful, interesting presentation. So, you sort of focused on the role of academia and probably by extension in NIH really in the early stages of the process, mostly, I would say -- discovery phase, tool development, patient stratification.

But, we heard yesterday that NIH is actually fairly heavily involved in later stages of the process, high-throughput screening, optimization, that sort of thing, and some academic institutions are as well.

And I would be curious as to

whether you think NIH and academic institutions have a use for there. Are there particular niches, like rare disease for example, that industry will not cover, and academe and NIH might have a role to play?

DR. ECK: I think it is hard to be overly prescriptive on what that is. I think everything is going to become a rare disease as we segments markets more and more. So rare diseases in and of themselves could be -- fall into that category.

But, the rareness of the disorder is not really a good determinant of whether the pharmaceutical industry is going to be interested. It is really the product of probability of technical success and the prevalence of the disorder.

I would argue that if there was a path to approval of a drug, that had no reimbursement, that would never be paid, it was a small indication, but we had absolute certainty that every dollar invested would

lead to that product being launched, there probably isn't a drug company around that wouldn't do it, because it can be done.

The problem is the probability of technical success, when put against rareness, makes for a very risky business. We are more likely to take risks on something that is more prevalent just for financial reasons, so --

MEMBER KELLY: I was just sort of using that as an example. I was more interested in the kind of the general idea of what is the most efficient and best role for academe and NIH in drug development?

DR. ECK: It depends where your expertise is. I don't think there is any one formula or recipe. For example, some very useful and profitable new medicines have come from academic research.

Alimta, which had 48 percent growth in the first half of this year, one of our products for lung cancer, was discovered by researchers at Princeton, who basically

developed the platform, and it was refined somewhat by Lilly before being taken into clinical testing.

Similarly, Lyrica at Pfizer came out of Northwestern, so there are many examples where that initial process can flourish well in either -- whether it's an NIH lab or an academic lab and I think that, you know, if there is interest, if there is a sustained focus, that certainly could be quite rewarding.

CHAIR AUGUSTINE: Gail.

MEMBER CASSELL: Tom, what I would say is, based on my observations with the Lilly TB drug discovery effort, which I lead, and as I mentioned yesterday, we are partnered with NIAID and infectious drug -- or the infectious disease research institute in Seattle.

I would agree totally with what Steve has said, and that is there is no -- should be no compartmentalization. I think it

depends on the individuals and the individuals' skills in terms of the role academia can play.

And I have seen them be very efficient and helpful in almost every phase. For example, we have a compound that we are -- that is pre-clinical and living very well along, but it is IV-only, right?

So, we want to explore all possibilities, and one of the best aerosol biologists in this country that works with drug discovery/drug delivery, one is at Harvard, David Edwards, the other is Tony Hickey at the University of North Carolina.

So, working together with them, writing an NIH grant, being successful in getting the grant. Now, we are poised to explore this. So, I am really optimistic, looking forward, that the more you have this iterative process, free process of going back and forth between the academic investigators, NIH, that you are going to get much better at

this.

It's the freedom of having those kinds of interactions that make it work. And I was thinking about why this is working so well, and I think it is because everybody is committed to the same goal -- it is TB drug discovery. Everybody realizes the urgency as they do for rare disease and any disease, really.

And it is the glue money to pay for the project managers, the unattractive daily operations, that bring all this together, and I don't know if Ken Duncan, I can put him on the spot, we were chatting about this on the way over this morning. So, it really is the glue money that, I think, helps make all this happen, and that is where perhaps NIH and their foundations and industry can help. But, I think that you have got to use all the talent, that is the bottom line.

MEMBER ZOGHBI: So, repurposing drugs is really a very efficient way to

advance translational research, and there are many new discoveries in academia that could benefit from using some of the existing drugs in pharma.

I always find this very difficult to actually accomplish. I am actually, in this situation, when I am ready for very many pre-clinical trials, but the pharma is very hesitant to share the compounds I need from them, and this is a major roadblock.

How can we get over this? Their fear apparently is that something happens in this other disease we are testing drugs in, that now might prompt the FDA to put a warning or something on a drug, and we can't live like this, I mean, there are so many opportunities so how do you propose --

DR. ECK: Yes. This is not a rare occurrence, where a company is developing a drug for an indication and someone in academia, could be the NIH, or any place, looks at this and says, you know, this drug

should be applied here and then we get antsy, saying well, you know, but if we give it to them and they have an adverse event, then we have to report it, and then that might slow our progress.

There have been some examples where this has been done well, you know, where pharma has actually allowed the academic investigators to file their own IND, to cross-reference the master IND that the drug company owns, and do this collaboratively.

But, it requires a lot of intestinal fortitude, and frankly we often don't have that. There is no pat answer as to how to make people do it, because we don't have a way to make people do these things. But, I think, increasingly this will become more approachable, because we need a greater diversity of approaches to some of these ideas.

Many of the mechanisms we have, we don't actually know the indication. I mean,

neuroscience is a great example where we have drugs that are exquisitely focused on some process in the brain and we think, well, is it good for depression, is it good for schizophrenia?

We are not very clear because the animal models are not very forthcoming. A very good example is our mGlu2/3 agonist, which we are developing for schizophrenia. The biology of that pathway was largely unexplored in man prior to us bringing the drug forward for schizophrenia.

And I would argue that we are still a little bit handicapped by the fact that it is very novel treatment -- experimental treatment right now -- for schizophrenia. Hopefully, it will get approved.

But, we don't really understand those pathways very well and to use anyplace else, is speculative on our part because we have not pursued that and it is not part of

our current game plan. So, there are many opportunities like this and there are probably many more than are apparent because we don't actively seek this out.

I think, similarly, we have well-behaved pharmacologic tools that we have abandoned in developing as drugs. They have good oral bioavailability, they have good time on target, they have reproducible biology, but they fail in early development because they don't -- in the study we ran, and then we lose interest, and so they get put aside and they are not explored elsewhere.

Many of these drugs, or putative drugs, could be made available, I think, for exploratory drug to understand biology, if not to find a different indication. There is not an efficient mechanism for doing it. It is largely personal advocacy.

I think as the companies become more transparent, in terms of what we do and why we do it and how we do it, that will

create a little more pressure to seek these opportunities, but I don't have a pat answer.

But, we are aware of this issue.

CHAIR AUGUSTINE: Dr. Eck, thank you very much. I think the pressures of time require we proceed but your comments have been most helpful. We now want to turn to the panel discussion. You have the biographies of the panelists. Once again, as yesterday, these folks have gone to a huge amount of trouble changing their personal schedules to be here, and we thank you for doing that.

Our two moderators for this session are right here at the head of the table, Richard and Eugene, and I turn the agenda to you.

MEMBER WASHINGTON: We decided to launch this session by having Richard provide an overview or a few examples of public-private partnerships that involve NIH.

MEMBER HODES: Thank you. As Gene noted, Amy and I thought it might be useful to

provide a little background about the framework in which NIH in its current activities sees public-private partnerships and provide a couple of examples just to then trigger discussion by the panel.

The aims will be -- for this whole session will be to explore some of the features which define successful partnerships. You have heard a good bit about metrics and defining goals -- they will be important -- focusing on what we have learned from past experience.

So we will look at a range of differing scales or scopes of public-private partnerships in which NIH has been involved, provide you briefly with three examples of them and then we will talk about the challenges, considerations, outcomes, deliverables of the studies.

This slide is just meant to indicate that there is quite a scope of public-private partnerships, which can be very

useful, valuable from small ones on a scale that may involve dollars, times, number of collaborating entities, data, et cetera.

Could be a single institute or a center, single investigator with a single partner and one project, or it can scale up to some very complex interactions, and we have seen some examples of those, which involve multiple institutes, foundations and companies.

The first example that I will touch upon briefly here, is the Osteoarthritis Initiative. It began a number of years ago in conversations with Steve Katz, director of NIAMS, with myself, recognizing this among the many areas in which there is a large need for interventions, for therapies, very little known about pathophysiology, therefore very little in the way of targets.

And so, we determined to set out and look for the interest in pursuing a search for biomarkers, in this case largely imaging.

A couple of points I would mention. Number 1, first, relates to the comments from Francis and Harold yesterday about the fact that we can indeed engage with the private sector, so there was no problem with Steve Katz and I having conversations about the scientific interest and strategies with leaders in industry.

When it got to a point where those conversations had to do with actual potential financial support, we turned to the Foundation of NIH and backed away and that formula, that distinction, has worked very well.

I will just point out one other anecdote that is very much in mind here and I think is illustrative of what we have learned in past years. As Steve and I and some of our staff entertained what the scope and plans and ground rules would be for this collaboration, I remember being uncomfortable with the notion that collaboration would involve undue, inappropriate, or apparently even unseemly

preference given to a given entity, private sector, in exchange for financial contribution, and so suggested that the basis for the starting point in these conversations ought to be one in which there was no special advantage given to the partners, that the advantage would be one which was global and involved common interests.

And admittedly, in the examples we are looking at, in a pre-clinical or pre-competitive scope, this was easy to do. So we set out, with some trepidation I must say, but the results were enormously gratifying and resulted in participation in this study with a budget of $50 million, nearly $20 million of which came from private sector and is ongoing now, looking at imaging techniques to try to develop ways in which the biomarkers might be used to better support ultimate tests of intervention.

Now, a second study which had a similar background followed thereafter. This

is the Alzheimer's Disease Neuroimaging Initiative. And based on some of the lessons learned in planning the Osteoarthritis Initiative, we set out in a similar partnership here.

It involved contacting now a much broader scope of private sector, and I will illustrate how broad that was. It also importantly involved -- including the FDA at a very early stage -- and again, just as a paradigm for a meeting I remember I think in this very room, we brought together representatives, the senior research side of many of the private sector entities that were interested, as well as NIH folk, and we had at that time Mark McClellan here, along with staff, indicating how receptive the FDA would be, should there be successful determination of potential biomarkers for considering those, at least, and authenticating them for use in clinical trials and studies.

And so, we went forward in this

study, which in its first five years, was a $40 million contribution from NIH and I think in the end nearly $27 million from private sector.

And the complexity is illustrated here. There were some 19 companies and two non-profits. This was biotech, major pharma, imaging companies, all of whom worked extraordinarily well together.

A number of products came from this immediately that were hard to envision beforehand. Rather than having a small number of dedicated centers, realizing we needed to be prepared for large-scale application, ended up with some 60-plus centers in Canada and in the U.S., all different hardware and software platforms.

It led to the development of technologies which allowed these all to be harmonized and deposited in a single database. The data were made available in essentially real time to the research community,

nationally and internationally, and has already produced, I think, in terms of validating the ability of imaging techniques as well as recently some CSF protein markers, a phospho-tau and an amyloid peptide, to show very strong predictive value in tracking the course of apparently early-stage Alzheimer's disease in this case.

Global was mentioned. This has been successful enough to spawn these, now nascent, in some cases already existent, parallel enterprises in Europe, in Japan, in Australia, and others being developed, which will harmonize again these techniques, allow great power for quickly identifying the relative usefulness of various biomarkers.

And I show you just one outcome to illustrate how quickly this can in fact translate further downstream, the real aim of this study, providing potential markers for use in testing drugs, some of these methodologies are already being embraced in

ongoing studies by Pharma.

But, this illustrates imaging technique that you can see here in estimating the number of patients who would be needed to achieve in a 12-month, multi-center, randomized clinical trial, detecting a 25 percent effect with 80 percent power.

By standard use of changes in cognitive function, the numbers are in the hundreds for even smaller effect size in the thousands, where the ability of imaging -- and this will be even more true with some of the biomarkers developed -- cuts down by an order of magnitude potentially the number of individuals needed in these studies, already potentially very valuable as we, the FDA and private sector work together to try to apply some of these techniques.

The third example I don't need to go into, it was mentioned in the talk you just heard. In contrast to the first two, which arose from a commitment from NIH in a

particular area, then looking for partnership -- broad, but in that defined area -- another style of public-private partnership is illustrated by GAIN here, Biomarkers Consortium another, which have set aside to provide a broad context or matrix in which private sector and NIH might come together to explore any of a variety of issues.

Here some of the studies initially have focused on ADHD, bipolar disease, diabetes, nephropathy, major depressive disorders, psoriasis, schizophrenia. So, it is a somewhat different style, not targeted to a particular area, but providing a framework that will serve many.

So, there are a number of public-private partnership outcomes and deliverables that are illustrated here. Again, I stress the examples I mentioned so far, in a sense are some of the easier, because they are pre-competitive.

But, these, broadly, can be

identified as purposed to foster basic research, which can be pre-competitive, but certainly have intellectual property attached to it, to enhance clinical trials themselves, to expand the pre-competitive space or develop products and technologies. And these are clearly non-exclusive and much-overlapping categories, but this is the frame that NIH's office of public-private partnerships has in mind for categories of such enterprise.

The challenges -- development of appreciating of the similarities and differences among partners, different aims, sometimes they converge, sometimes they complement, developing common goals -- we certainly heard a good bit about transparency -- long-term commitments are important just as NIH leadership changed, and we found the leadership at pharma, and many of you will be well-aware of changes as well.

When the goals appear to be of broad appeal, the support by both NIH and

private sector, happy to say, have persisted now over multiple years.

So, shortages of funding, identifying the expenses needed, what exchange there will be of non-monetary resources, the desired products of partnership, importantly, intellectual property rights, how NIH review and management function.

In all of these examples that I have cited and in many of the others, NIH has generally carried out peer review in an attempt to ensure its objectivity and making sure that this is compatible with the needs of our partners, is important to these partnerships.

And then privacy and integrity of data as it affects human subjects, greatly important as well.

So this last slide, which I will leave up, describes the questions which you have for discussion for the panel and I will now turn to the panel with these topics and,

Gene, would you like to take it away?

MEMBER WASHINGTON: Okay. Just to further frame this session, I would remind us that the overall emphasis on how we in fact cultivate partnerships with an eye toward developing successful projects that can be measured in terms of whether or not they deliver on the goals being outlined originally by the partners.

And those of us who are involved in development, in particular, know that when you hear about a big gift, as in the case of the development of a big hit with a drug, there have been years of cultivation that has taken place.

So, I would like to start by asking the panelists, from your perspective, just in terms of cultivating the relationship, before you even get to the specific project, what would you see as most important attributes of that cultivation process? And why don't we start with Dr. Baum?

DR. BAUM: Sure. I think if -- on the big picture?

MEMBER WASHINGTON: Yes.

DR. BAUM: Probably the first point would be sort of an overall view that that is welcomed or desired on both parties, certainly from our part, we can tell you that there is a number of areas where we think that this sort of external innovation work, where we need help, we are seeking help, we can make that pretty obvious, what those areas are.

And then, if there is some response on your side of general interest or specific interest in some of those areas, then that is a good place to start, those places where we have shared goals and mutual interests, I think you have to have that or it doesn't go anywhere.

And then making the connection between the scientists at both institutions is really critical to making this work, and that they have a mutual interest in working

together and goals that are compatible.

I think that really is the basis for a good collaboration, for any good collaboration, and particularly here. Since there are challenges, I think you need that strong shared goal to start with.

DR. DUNCAN: So, the Gates Foundation doesn't really have that many partnerships directly with industry, but we do work through our grantees. So, I will talk from some experience that we have had through a number of our grantees who have gotten together and who have worked together quite a lot to try and look at best practices.

And one thing I would say is from the very beginning, it's establishing mutual trust and confidence at a pretty senior level. That has been really, really critical, establishing credibility and the commitment from both sides, both from the public side and from our pharma partner, then establishing contacts at all levels.

And so, starting off at a certain level, but then making sure that the right scientists are talking to one another, again becomes really critical, so that when the details start to emerge, that the right person with their hands on the detail is able to have the discussion and the negotiation.

Understanding mutual objectives and constraints is just as important. Getting to a situation where everybody is in a win-win situation is really critical. Another point that we have found quite helpful is a sort of staged relationship, where we start off with a project with a very specific endpoint and then people can then decide whether to build on that relationship or whether we have done what we actually wanted to do together.

That has been really important, so that from the beginning, you are not saying to a potential partner, you know, we have got this early discovery program but we actually want you to supply 10 million tablets to x

number of patients in 10 years' time.

That just puts everybody off, because nobody knows how things are going to move. Lines of communication become really critical, making sure that we have the appropriate points of contact and at the right times.

And then the final point I would make, really, is oversight, establishing whatever oversight is actually going to be in place. Do you have the right groups of people who can make decisions? Can a group from each side of a partnership actually get together and decide whether to start a project or to end a project, or does everybody have to go back to some other committee and always have to be referring back and forth? And I think establishing that up front is actually very important for moving forward.

One thing that our product development partnerships, like the Medicines for Malaria Venture or the Global Alliance for

TB Drug Development have done very successfully with pharma is establish what they call mini portfolio agreements where they take a number of different targets and then can move them forward through the pipeline.

And they have groups which work jointly and can take decisions on whether something has been declared a lead, whether it is declared a candidate, and that has been a very successful way of moving resources between different projects at different stages in a pipeline.

And those sorts of agreements are things which really could be modeled anywhere, and I would say that bringing together some of the public efforts with pharma companies, with others, is a question of trying to structure the right sorts of agreements.

And to come back to something that Gail mentioned earlier, we have found that sometimes it is not about where the money is coming from: it is about just getting the

right people with the right skills together, and some money, to make it happen, whether that is just people in lab coats who can actually get the work done, or the money that allows people to meet and takes people away from their day jobs to actually focus on what they need to do. I'll stop there.

MEMBER WASHINGTON: Dr. Halak.

DR. HALAK: Well, the further down the row you go, I guess it's harder to come up with something original. I think they captured most of it. I would emphasize the aspect of shared -- of determining what the goals are up front and making sure, before anything gets started, that people are aligned.

And, I think, that is easier probably when you are talking about some of these pre-competitive, more discovery-based projects, because it seems to me that that is more congruent with how an academic researcher usually thinks. It is more open-ended.

As you get to driving a specific

scientific discovery or project forward into something that is a product, I think it gets a little more challenging because then the -- as someone stated -- I think it was Steve in the beginning, the academic researcher is often focused on very open-ended questions where any answer is positive, whereas the private enterprise is looking for a specific answer.

I think that is where the NIH needs to begin to foster and sort of encourage the academic side that it is okay to drive for those specific goals, because that is, I think, where there is often a conflict between private and public.

DR. INSEL: Well, from the NIH side, you have already heard from Richard, who gave, I think, a really good summary of the kinds of things we think of.

I think it is important for the committee to realize, we do a lot of this and I think we do it pretty well. We have also had a number of failures and so it might be

helpful to actually talk a little bit about what has not worked at times in the past.

In terms of your question, Gene, about making it happen, the key things right now are having the fora where people get together to begin to do this. FNIH, through the Biomarkers Consortium, which Steve is part of down here, and Larry Tabak has been on the executive committee, has been one place to do that. The Institute of Medicine has fora for drug discovery and for neuroscience and other areas where there are opportunities for different partners to come together and talk about possibilities.

So, there are a number of those. I suppose the lesson we have learned best perhaps from the Biomarkers Consortium, if you think about what worked and what didn't work, was, as Dr. Duncan mentioned, having the right people at the table, and the right people means, for us, having the FDA involved was really important, maybe more important for

pharma partners than for us, but important for the whole group.

The second was having people at a particular level who could speak on behalf of whoever they represented. One of the problems we had in the early days was having people who would come to the meeting and really could not represent who it was that we thought they were representing.

And the third, for us at least within the neuroscience sector, is having multiple pharmas involved. The optics are problematic, still for us, I think, when we work with a single company on a particular project and it becomes easier if there are many different companies, as in the Biomarkers Consortium; it becomes really a safe haven for us, too, both to explore ideas and then to implement them as well.

MEMBER WASHINGTON: Thank you.

DR. PACCAUD: Well, definitely there is not much left on the list of answers

that I tried to provide on that question.

One aspect for a PDP-like Drugs for Neglected Diseases Initiative is that we realize now, after seven years of existence, that we have been working much more with the private sector and are leveraging much more good partnerships with the private sector than with academia.

And this is probably bound to the remarks that have been done before. Academics have a very clear and understandable goal when they are starting a project. They look at us as a financing body, which we are not, or we don't consider ourselves as a financing body. We are an R&D organization that puts assets into where we think we can provide -- we can have the most successful results out of that.

So, one of the difficulties is to really align the objectives of the few academic groups we still have, we still are working with, with ours, which are delivering as soon as possible an answer or treatment or

drug.

Whereas with the private sector, we are definitely trying to leverage their assets and we try to understand -- and it is easier to understand why they want to work with the NDI or MMV or TB alliance and we will not elaborate on that.

But, we have found by experience that, besides all the good things that have been said about the commitments of everyone, we need to really get the top people in the private sector to be behind us, and then we have found that if that is happening, everything else is quite simple.

And the last point, maybe, that has not been mentioned, within the way that we have found partnerships, the most efficient is that even if we are dealing with colleagues, Pfizer, or GSK or Sanofi-Aventis, we try to build a relationship of equals.

We are small organizations. They are huge. It works well when we are each other

respecting the way we are working and trying to communicate on that.

MEMBER WASHINGTON: Thank you. Okay, just -- go ahead, thank you.

DR. PERAKSLIS: So, just a couple of things to add to that. First, yesterday something came up that I think is important in this kind of pre-negotiation space, and that is this really optimizing the basic biology. This is the thing that pharma -- we are least good at doing and, more and more, we are looking to access it, so you have got a product or an area of opportunity that is going to lead -- so that is really, really important.

I fully agree with having the best people and the best science ready for this. It is like anything else. It is somewhat of a courting or a dating process, so it should be low energy, it should be easy, it should go well, it should build momentum, when you are talking about these things.

I think the team size and structure should really be optimal when you are looking at this and quite frankly, though, I think what I have not heard here is it should be done against a framework of governance.

An example I will give is, at J&J, I know for a fact, I can confirm twice and I think I have a third case where separate CTSAs have brought me the same proposal, that you are trying to do something that is very, very, very similar, and I know it has happened twice because I have done enough meetings where I know they are talking about the same proposal, and the third time I am not sure yet.

But, what it has led me to think of is it is kind of -- when I ask them well, you know, so and so is doing this too, have you considered -- what I got was criticisms of the other party. So, just being honest, as a partner here of what we see sometimes, not day in and day out but the reality of it, that

doing these partnerships against a framework, a strategy in governance, I think, is real important.

MEMBER HODES: I would just like to -- it has been touched upon some, but Tom in particular mentioned the usefulness of looking at examples of failure. Taking advantage of having the group of you here, can you comment on -- not necessarily failure -- but areas in which perhaps there has been a particular difficulty in interactions with NIH. Obviously, the reason for the question is to look for those areas where we can modify or improve the ways in which we try to deal with our partners.

DR. ECK: Let me try to address that. I think the rules of operation with the federal government are substantially different than operating with other parts of the private sector and we don't have a harmonized set of rules for clinical practice around use of patient samples, around privacy issues, around

informed consent.

And this is, in some ways, problematic. I was at the clinic for Special Children, meeting with Dr. Morton, their director, and there is work that we can do with him that we couldn't do with the NIH, just because of the requirements for reporting and -- that are non-standard.

And so, there are currently types of research that we wouldn't bring to the NIH, because they are frankly too difficult to negotiate and the disclosure requirements are too complex, and it is much easier to go to an academic investigator or a private research institution to do that work. And that is, I think, sometimes unfortunate.

MEMBER WASHINGTON: Others?

DR. BAUM: I am not sure I can think of a particular instance with the NIH, but I think the most common problem is that the goals need to be shared and need to be mutually beneficial. I think that is when you

have a real collaboration that is good for both sides so you both have skin in the game, basically.

So, if you share funding for a project, or the outcome of the project is good for both parties, that really drives it forward. If that is not the case, then generally they run out. Things don't happen. That has been the majority of cases where it has not worked out.

The other is, where in the past we have made just uncommitted grants of funds to groups without clear goals or expectations and that often just has not worked out at all for either side really, because there were expectations. It just wasn't made clear up front and that has often not gone well. So we have really gotten away from that sort of funding.

DR. INSEL: Richard, you said it, but we probably should emphasize that to some extent this is an asymmetric partnership. So

we go into these things interested in making sure that an NIH project that has been peer-reviewed and will be in some ways NIH-managed could get joint funding or support for some part of it, like an ADNI or for many other projects that you talked about.

GAIN maybe is an exception, because there, what we were bringing was something in kind. We were putting samples in, whereas Pfizer was supporting the genotyping.

But, in general, we don't -- if someone else comes with an idea, we cannot just throw money on the table the way we are asking other partners to do, and that is a somewhat different relationship than others may be used to. And I just think we need to be clear about that, that we don't have a simple way of funding something that hasn't gone through the peer review system, and I am not saying we should, but I think it needs to be understood up front, that that is one of the things that has often been a problem, at least

in the Biomarkers Consortium.

I would say the other where we have failed the most in the beginning, and Larry may want to chime in on this, is we did this as a kind of broad solicitation. We asked the community, you know, send us your best ideas, and most of what we got, I think Larry would agree, were the projects that could not get funded through peer review.

And so, all of a sudden we had the B- and C+ efforts instead of what we were looking for, which were the A+ efforts. This got fixed when NIH said we will bring you our best efforts and ask for our partners here to support pieces of them and grow them out in a way that made them even better projects, ADNI being a superb example of that, or ISPI-2, which is another one that you mentioned in your slideshow.

So, I think that is probably a lesson learned that took us about, what, Larry, 18 months to figure out, before we

began to realize that we could do this but not in the way that we thought going in.

DR. ECK: If I could just add to that, I think the expectations around funding need to be reexamined. I will give you a specific example. We are currently involved in a negotiation where another large pharma, right here, has samples, well-genotyped, well-curated, that they are going to contribute and that Lilly has samples that are well-genotyped and curated and we are going to offer these to an academic investigator to study the basic biology of a disease.

And what we ran up against is while Lilly and Pfizer had no trouble getting their attorneys to agree that we are going to submit these samples and the data, and the academic person can do the research and publish this, we ran into trouble with the academic institution who wanted us to pay them to do the research and that is just not realistic.

I mean, it is a very large donation on our part, to make -- not only make the resources available, but we invested to get the data to where it was and we cannot always be the funder of that work. It's a very interesting area of biology but it is not mainstream to what we need done so we cannot always be expected to fund that.

And, I think, there is often the expectation that we have very deep pockets and money for everything that could be done. If that persists, many good ideas will not survive. I think in-kind donations from industry, in terms of data sets, are valuable but they cannot always be accompanied by the cash needed to prosecute the work. All parties need to contribute something.

And I don't think we have a really good way of doing that with our academic partners. In some cases, we have done it well with NIH.

MEMBER WASHINGTON: Dr. Duncan and

then Gail.

DR. DUNCAN: So, thinking about the pre-clinical space, we have had fairly mixed interactions. I would say we had very, very good interactions with the intramural program, with several projects through our grantees. We have had a little bit less success on some of the contract work that really helps to support a lot of the extramural researchers.

I can think of things, but they are pretty anecdotal, of researchers who have said, you know, I have said to them you can go to an NIH contract and get a particular piece of work done, sometimes they have said well, you know, it just takes forever, or the processes are so difficult that to try and get it prioritized and get the data back is going to be six months or a year.

And for us, it is then often, we are just left saying well, we just have to pay to get the work done, because it is just not realistic for us in any sort of turn-around

time to actually get things moving, or to get the right sorts of studies, and it is something that I mentioned yesterday.

Sometimes, giving people a bit more flexibility to actually be part of the team, to help to determine what is the right study to do, and then just get on and take a decision and do that study as opposed to saying, well, it is on my list that you have to do these ones or else you have to go back for another iteration and you have to wait for another prioritization of a certain set of experiments.

And yet, these contracts are really perfectly suited for getting just the really critical little pieces of information that can often mean the difference between a project sitting on the shelf until somebody writes another full grant proposal, or it just moving on with another partner.

And so, a little bit more flexibility is certainly one thing I would

like to see, and somebody to take a hard look at some of the metrics around how that is certainly helping to support our projects.

MEMBER WASHINGTON: Gail?

MEMBER CASSELL: Thank you, Gene. I would like to just second what Dr. Duncan has mentioned as being something that someone needs to pay close attention to, but also this concept of flexibility to add to what Steven Eck has said. It seems to me if there were even a smaller pot of money available through NIH, that that investigator or Pfizer, Lilly and the investigator could approach and get the short turn-around in terms of peer review or review, it could facilitate the beginnings of the work that in the meantime that investigator could go through the normal channels in terms of applying for a substantial R01 or whatever.

And getting back to the question that you asked, Steve, about access to compounds and everything, what I find is that

one of the biggest challenges for the academic scientist is finding the right person. It all goes back to the right person within the company that would be sympathetic, interested if you will, in working with you.

So Steven, one thought that I had, and I realize it would be a committed resource, but if in fact each of the companies had a single point of contact, and Ken and I have been talking about this too, Duncan, so that you knew, if you went to that person, then it would be up to that person to track down who, within the company, and then to get back to you.

As it is now, I must admit it, I know within Lilly, it is a rather hit or miss process, so a lot of time can be wasted and also you don't always get to the right person.

And so, maybe this is something that the companies can think about in terms of how we could do it better, or you may have some suggestions.

But, I think this is an area that one might -- well, it could be very profitable and before I lose my opportunity, I just would say that one of the initiatives that Lilly has that is somewhat the reverse, I think, of what are you saying, Huda, we launched an initiative last year called PD-squared, where from throughout the world, we were encouraging investigators to submit compounds, no structures of those compounds, just the compounds, that would be screened in highly validated assays in different therapeutic areas.

And, if in fact, there are valid hits, then the investigator can take the data, because all the data will be turned back to the investigator, go work with another company and/or work themselves, just in their own laboratory using that data, and/or choose to work with Lilly to further develop those compounds, if in fact the investigator so chooses.

So, what is -- I think that whole process now is very automatic, mostly electronic and seamless in terms of the confidentiality agreement, the tech transfer agreement, and we are learning a lot from that process and will soon apply it to the TB drug discovery effort as well.

So, that might be taking some learnings from that, but trying to reverse that might also help address the concern that you have raised.

MEMBER ZOGHBI: Maybe I can just make one brief comment. I think the problem is not finding -- I found the right person at a very big pharma, a fantastic person who really was enthusiastic. It ended up the lawyers and the marketing people who are dealing with drugs in already clinical work. Therefore, their sisters and brothers of these drugs, they are very --

And I think this is really a problem. This requires a cultural change at

the FDA, at the companies, to begin to -- it is much cheaper to repurpose drugs than to really start *de novo* every time we have a new medical problem. So, it is a serious problem.

DR. HALAK: So, just to comment on that, because, I think, one of the biggest things that I know is not directly the topic here, because we are talking about what can NIH do, but I think perhaps NIH can force this issue.

I think the most important partnership is the one between the NIH and the FDA and then I think I would also loop in CMS and the PTO, because if the goal is to get a product out to patients, you can't really look at just the scientific process of getting something proven.

You have to look at the whole process. I mean, never -- I invest in early stage companies -- never once do we just look at the science. We look at what is the regulatory path and one of the biggest

problems, for instance, is -- take an area like diabetes. We were a founding investor of Amylin, which had two products approved, first in class, for diabetes, that are helping a lot of patients right now.

We would never invest in that company again, because getting a diabetes drug approved is so difficult now. It is difficult for good reason. There has been some worry about cardiovascular side effects. However, the answer may not be if the FDA would talk to constituents like basic researchers, the industry, et cetera, maybe they would realize the hurdles that that imposes, and maybe the answer would be something like a conditional approval, where -- now I am getting into specifics -- but just by way of an example, where something could be approved only to be used with patient registries and then only after a certain number of patients have been analyzed for long-term outcomes, then you could get full approval.

But, my point is, is not to delve into a specific idea, but to say that really, I think the FDA, NIH, CMS, PTO and industry, if the goal is to push products forward, need to be talking together about what an action at one organization is doing to another organization in terms of achieving that hopefully common goal of getting products to the market.

I think too often, from the outside looking in, it feels like they are operating in silos. The best example of that was even within the FDA, when there was a proposal by -- I guess it was mainly driven by Congress -- but there was a proposal to separate evaluation of safety and efficacy. I don't know how you do that.

So, I think they need to come together and all start working together.

MEMBER WASHINGTON: Okay, Richard? He passed. Any other comments? On the original question from Richard regarding what NIH could

do to improve access, development of partnerships and if not, we are going to turn to the question of metrics. And Dr. Duncan mentioned metrics. We have a specific question. In the context of -- yes, Larry.

MEMBER TABAK: Amy reminds me that NIH is going to be having a meeting or perhaps a series of meetings, specifically on the issue of drug rescue or drug repurposing. I think it was mentioned yesterday as well.

So, this opens up a new dimension of NIH-industry partnership, so --

MEMBER WASHINGTON: Okay. Great. Thank you. Turning to metrics, specifically in reference to NIH, but even more generally, as you have developed public-private partnerships either with NIH or with academia, or if you are in government, with private partners, what have been the metrics for success and what should they be? And why don't we start on this end with Dr. Perakslis?

DR. PERAKSLIS: Thanks. So for me,

we have got a lot of them, and I think the ones that are most meaningful, tend to come down to time, where there are frequent milestones that showed incremental value, that built momentum, built success, built confidence, and built good relationships in the team, or not.

How quick was it to sign the deal? Did you end up in a protracted legal process, which then, again, you are dating, it starts to cause other problems. So, I think time is very, very important.

And the fact that patients are waiting in some of these cases, it is not just early stage, sometimes it is late stage. And some of the most interesting things I see done are on the Phase IV side, or on the late-stage acquisition side, and usually there is a lot of money put into these, but success can come very rapidly when they are done as well.

But, we are not at that point doing the type of science that I think we need

NIH to be involved in, and what I will give is the great news we had with abiraterone in the last couple of weeks for prostate cancer. There is still a lot of science to be done around that. We have got a great drug, it looks like, but you know, a lot of questions that will come up now.

MEMBER WASHINGTON: Please.

DR. PACCAUD: On our side, I think it is similar, I mean, we do have patients on the one side that are expecting drugs that are not existing so far. We are not going into projects at a very early stage, again because of this urgency, so we try to be quite pragmatic.

And that means that we are measuring our success by also the time it takes to kill a project on various series we have been looking at. And we can't do that probably in an easier way because the ultimate goal is to identify a couple of molecules that will proceed successfully into the next steps

of the clinical development without having to hold on a pet molecule which you could certainly have seen many times in academia. So, that's a big measurement of success.

We have very clear milestones to all our development processes and we have checkpoints at committees that are joint committees between our partners and that ensures at least that we are hopefully trying to use the money as efficiently as possible.

So, it's time -- time to kill would actually be the summary of how DNDi is trying to operate.

DR. INSEL: The only thing I would add is that whatever this is going to be needs to be shared and you can imagine the problem of having two different sets of how you measure success. So, that is something that needs to be up front.

DR. HALAK: Yes. I would agree. I think the key -- the metrics are going to be different for every project, but I would pick

up on two points that have already been made. Number 1, they need to be shared, number 2, I think they should be frequent. I think people respond to goals that are relatively near-term and importantly, as they are hit, the partnership can really gain some momentum because people get excited about that.

So, I would take the project and chop it up into a lot of goals and hopefully in hitting the first few, you actually build momentum and people realize that and get excited about the partnership.

DR. DUNCAN: It's difficult to add very much beyond that, beyond all the comments that have been made and one thing I would maybe say is that if things are not going well, and it is really critical that teams recognize that and deal with issues and don't let them fester.

Because the worst thing that can happen is for a milestone to be missed and then somebody to say well we will revise this

at the next six-monthly meeting, nothing much has happened. It just goes on for a long time and then the relationship breaks down. I think that's where the honesty between and the trust between partners becomes really critical, that people can be really open and honest about what is working and what is not working and address the things that are not working, because if you don't, you won't be successful.

DR. BAUM: So a lot -- I agree with the comments made previously. I think, one from the very beginning that has come up before is contract turn-around. So, I think, on both sides that's an issue that we have to be cognizant of and work together so both of us can push it: we can push it on our side but also we need advocates on the NIH or in academia to help when things get stuck, finding out why and helping push it along and an internal advocate always helps with that.

And then, I think, what others have said, that you have to have measurable

goals with a common understanding so it is on the table, everybody knows what they are, and if you have the budget for it, a project manager to be in place for the project, so that somebody is there to keep an eye on it so that you don't get completely out of whack.

Once that happens it is very difficult to come back so, I think, it is really critical to keep that up and then to come to -- if it's a revised plan, that's fine -- but to do that rather than let things go so far off that it's difficult to recover. I think that's when the relationships usually go bad.

MEMBER WASHINGTON: Okay. Dr. Eck?

DR. ECK: I think really all the important ones have been mentioned. I don't have much to add to any of that. But, I agree, I think the conflict resolution is key. If we do 50 percent of our work on the outside, we could manage a lot of partnerships in conflict resolution, whether it is with a corporate

partner or whether it is a CRO or an academic investigator, it's key to the success of the project and timeliness.

If the project cannot be done, maybe it shouldn't be done.

MEMBER WASHINGTON: Yes, I am going to open it up for questions from others, but I would like for the panelists to be thinking about the question of, in departing this broad topic, what would be the one message that you would want to convey to us, SMRB, but also to our colleagues at NIH, regarding what you would like to see done to ensure that we accelerate the development of drugs, whether it is through the partnership or whether it is through some policy. But, I would like to have you thinking about that while we open this up to others.

DR. CALIFF: I just want to make one comment relevant, I think, to yesterday and to today, and it was really taking off on Brian's comment. I take it a little

personally, since we are doing the outcome trial with the Amylin drug, which is a 14,000-patient trial in 40 countries. It's going to cost about $300 million to do it. I guess that's a significant investment to --

DR. HALAK: Yes, that's a little more than we have to spend.

DR. CALIFF: -- private partnership, but I think an issue that really struck me yesterday and today is the role of the NIH as a communicator, where I think in the old days that did not need to be a focus of the NIH. That is because science happened in the little areas where people worked in their laboratories and then eventually things boiled up to the top.

Now, there is a need for such coordination, you often have one side of the equation battling the other side of the equation. So I mean, in the course of the day yesterday and today I heard this, we have got to get more drugs on the market. I was

involved in discussions with the FDA about we have got to shut these people down because all this stuff is dangerous and there's significant things may happen in the next month that are going to retard people who think we need to get drugs on the market more quickly because of concerns about safety.

So, the NIH is actually attached to all the elements here in one way or another and somehow I really agree with Brian, that if these things are left sort of competing, you end up with a stalemate in a lot of ways, a sort of Brownian motion, and somehow the NIH, I think, needs to play a more effective role in coordinating communications to bring the sides into a common forum where things can move forward.

I don't know how that is going to happen. Yesterday, it was striking how many things within the NIH other people in the NIH didn't know about, much less those of us who are on the outside. Not an easy task, but it

seemed to me a striking feature of the discussion.

MEMBER WASHINGTON: Thank you. A very important point.

MEMBER HODES: Just to follow Rob's comments, you have heard mention of some initiatives such as biomarkers and the forum through IOM. Have any of these begun to serve the kind of purpose that Rob is talking about?

Certainly, we found that a number of these initiatives that having the FDA specifically there has been important, but I don't know that we have addressed all the issues, surely not those that Rob has mentioned, the competing issues of effectiveness and risk.

Gail.

MEMBER CASSELL: Well, I am pleased that the Forum has been mentioned. I actually co-chair the IOM Drug Forum and started the drug forum in 2005. But, we don't serve this purpose. We haven't even thought about it.

But, I have been sitting here thinking -- Amy came and presented a lot of the initiatives that have been discussed, the CAN and so forth, to the Forum, and I have been thinking all this time that we should be doing more and could be doing more to try to bring about some of the things that people are suggesting and recommending and maybe even setting up some interactive tools, which actually probably could be done and that's something that we should explore.

But, it is obviously, I think, a void that needs to be filled, maybe by all of us, but in particular I think the Forum could do a much better job of it than we have in the past.

MEMBER HODES: I suspect, if Francis were here, he would comment again on the new partnership, the strengthening partnership between FDA and NIH. Last night at a dinner, Peggy and Francis jointly received the essential partnership award for what they

are doing, and I think that is a forum too -- not mutually exclusive -- where this kind of conversation, I am sure, will take high focus.

MEMBER CASSELL: Well, you know, the Forum has I think also helped to play a role to bring about the recommendation for this kind of joint effort between NIH and FDA, and we will continue to try to push that. Our report that dealt somewhat with that earlier this spring will be released in the next few weeks.

So again, I think we can do a better job of that. We have great representation actually both from FDA, with Janet Woodcock, and Mark McClellan, Peggy certainly comes and speaks fairly often and Amy and others.

So, we can work on this as well I think, Richard, that is a great suggestion, yes.

MEMBER WASHINGTON: Okay, we are going to wrap up, starting on the end with Dr.

Perakslis.

DR. PERAKSLIS: The one thing that we didn't touch on, that I would like to, is yesterday we talked about training, and you know we have talked about the need for good project managers. We should really consider a phenotype of a good scientist, high energy, highly emotionally intelligent, highly extroverted, the type of folks you may want to incent to run some of these translational projects, both across your institutes and with the private sector.

MEMBER WASHINGTON: Thank you. Yes, please.

DR. PACCAUD: Okay, well just jumping on the question you ask, what could the NIH do for an organization like DNDi. Clearly, we are seeking to better understand the assets that were particularly presented yesterday between the different institutes having different projects on translational medicine for example, and the way to access

those resources, not only in the terms of being able to access to part of the financing, but probably even more, in terms of competence and networking and bringing the people that have the knowledge and that can provide this knowledge and the infrastructure to actually -- for us to be using this infrastructure.

And I guess, us, from the other side of the Atlantic, we don't have a clear picture of all these different assets within NIH. So maybe working a little bit on the clarity, on the visibility of everything that you have there.

And the second point, back to pre-competitive intelligence somehow, I am just wondering what else could NIH try to do in terms of -- we talk about information a lot, and the overwhelming amount of information we have to deal with with these small organizations like us.

We talked about these repurposing drugs -- drugs that could be repurposed, where

this is located. Probably the NIH can play a role there to try to extract this information from where it is, and to some extent put it in the public domain in a pre-competitive mode.

MEMBER WASHINGTON: Tom, you could have passed.

DR. INSEL: I am going to.

DR. HALAK: Well, If I had to -- you had asked to sort of -- a closing comment, if I had to express one message, I will make two points. The first is the one that I spoke about and then Dr. Califf spoke about. And that is the NIH doing its part to increase collaboration, and not just the FDA.

I talked to the -- particularly on drug repurposing, I would get the PTO involved, because one of the big challenges with repurposing, if you want to depend on industry to take those products over the finish line, is what is the market protection for some of those products that have dated composition-of-matter IP.

CMS is very important, because again, if you want to have companies take things forward, you need to figure out how reimbursement decisions impact decisions by industry.

So that is Point 1, is to have a collaboration between NIH, PTO, CMS, industry etcetera. I guess Point 2 is something we talked more about yesterday, which is changing the culture amongst many academic researchers such that it is celebrated, it is exciting, there is an enthusiasm around, not just basic science, but taking that science into projects.

And then once you have done that, you have to offer the tools and the resources for those people to get that done. It sounds to me like most of those resources already exist. I mean, there's a ton of resources, it sounds like, here.

I think the program managers is probably what is lacking and that is what I

would work on, is training people like that to -- that can really drive a project forward in the most efficient way. So, those are the two things I would leave with.

DR. DUNCAN: So, I think from the Foundation's perspective, the thing that would really help us is if NIH were to support the grantees that we have, especially for development partnerships and one of them is represented here, DNDi, and the others as well, in drug development, to try and move projects forward.

And I think that is a question of bringing the right resources, which we heard about yesterday, these resources really do exist. And how can we try and focus that in a way that maybe tries to help move some projects further along, with a lot of ownership of the project from whoever at the NIH side is actually running these things.

What the PDPs actually bring is a lot of the disease expertise, and a lot of

drug discovery expertise. And one final thing I would add into that is that we have been having a lot of discussions with a group of representatives of the pharma companies, particularly in this area, and there is a lot of expertise in pharma that can be accessed if we can do it the right way.

So, advocacy with the pharma companies to talk at the highest level, to say how important it is to actually work in these diseases would also help to free up some resources internally that would really help to manage projects and move them forward and bring the right expertise to bear with the right project management to ensure that things are done in both a professional way and at the standard that is absolutely required, that things will not fail when they move further forward.

MEMBER WASHINGTON: Thank you. Dr. Baum.

DR. BAUM: So, one of the obvious

ones, I think, overall is in this pre-competitive area, to get pharma companies together with academics, with the NIH and with the FDA, to advance some of these initiatives and around biomarkers, if we are really going to get to a place where we can use more of them as surrogate endpoints to get drug development going more quickly on some kind of conditional approval basis, something like that would certainly be of value in moving drug development faster.

An area of specific interest is also immunogenicity. We have a lot of biologics going into the clinic. There are a number of issues with immunogenicity which we don't understand well at all. Nobody does.

But, I think that is a combined effort with the NIH, with FDA and the pharma companies bringing in a lot of biologics now, could be an interesting research question, actually, of predictive immunogenicity and questions like that. So, I think that is

another area that would be of great interest, and the information exchange that was mentioned before of common areas where you could get information about some of these pre-competitive areas would be very useful, I think, to everyone.

And then, in terms of specific areas, I think for us specifically, efforts in regenerative medicine around stem cells would be of great interest, of specific projects. Rare diseases we mentioned before. RNAI and antisense kinds of approaches and in particular delivery, which is a big problem for everyone in this area, I think would also be of interest.

And we are developing, as I mentioned before, the external innovation network, and that could be an area where drug repurposing could be -- we could definitely make a contribution as being one of many who could probably help you with that and that's a specific effort which we have set up now, so I

think that would be something we could do in the near term.

MEMBER WASHINGTON: Thank you. Dr. Eck, you have the last word.

DR. ECK: I would mention just two topics. One is I think that the NIH has a great opportunity to be the neutral convener in many of these and that there are very few other bodies that can do that.

To address some of these issues like access to experimental drugs for other purposes or repurposing of drugs that are not going to be taken forward, I think if the NIH has a relationship with the leadership of these companies, it goes a long ways to greasing the skids for individual collaborations.

Companies work from the top down for the most past, but the senior executives of the companies are not always aligned with NIH interests, and I think that gap needs to be closed if we are going to make this work a

lot more smoothly.

I think the other areas are areas that cut across the interests of many pharmaceutical companies, and across a big chunk of drug use. Rheumatoid arthritis is a great example. We don't really know how best to use anti-TNFs. We can't even define what an anti-TNF non-responder is.

These are -- we spend a lot of money in this area in prescription drugs, yet we don't get full value as a society. This is not a problem that one drug company is going to solve, but just to take that one disease, that is a great opportunity to bring together a diverse group of scientists to solve that.

Because I don't think that will be tackled within a pharmaceutical company. As much as we might want to, we won't figure it out on our own.

MEMBER WASHINGTON: Thanks. Thank you for all your comments and for your participation.

CHAIR AUGUSTINE: Okay. Again I would add our thanks, and our thanks, Gene, to you and Richard for your serving as the moderators for this session. I think we are right on time. We will pick up at exactly 10 o'clock. We will take a little break here.

(Whereupon the above-entitled matter went off the record at 9:39 a.m. and back on the record at 10:04 a.m.)

CHAIR AUGUSTINE: Okay, we will turn to our next panel and we will begin by thanking each of you, and some of the members, I notice, are doing double duty today. We particularly appreciate that.

The plan for the panel, in terms of moderators, is that Tony and I are to be the moderators, and that is a little distressing because I don't see him right now, but we had this great plan. I will stall.

In any event, you have got the biographies of the panel, so we will dispense with formal introductions of the various

members. As I said, a couple of them we have met from prior sessions -- and does anybody know a joke or something?

The man of the hour. Tony, I have just said that you and I are going to do this together and you are going to kind of start out and then I will try to follow and back up.

MEMBER FAUCI: Norm, are we going to have the first presentation, Jeff Allen?

CHAIR AUGUSTINE: Yes, do you want him to --?

MEMBER FAUCI: Yes, why don't we do that. So just as a very brief introduction -- as you see from the title of the session -- that this is engaging in a dialogue with the public, and that may seem sort of like the curving off of all the important things that we are talking about but, as far as I am concerned, this may be the most important thing, because if we are going to engage in a dialogue with the public, we have to understand what it is that we want to dialogue

with them with, and as you know from the discussions over the last day and a half, it has not exactly been crispy clear about what it is that we really need.

So, I think that this could be a session where we might accomplish two things, maybe crystallize a little bit more our thoughts and what we have been discussing, and then figure out what the best way to dialogue with the public.

So, in this regard we have asked Jeff Allen, who is the executive director of Friends of Cancer Research, to start us off with a presentation on engaging in a dialogue, and then we will move to the panel, ask them to give very brief statements concerning some of the questions that we have posed and then hopefully have a good discussion thereafter. So it's yours.

DR. ALLEN: Thank you. I am actually glad to hear you say that there has been a little bit of vagueness over the last

couple of days because -- I guess when I got the call about my assignment from Amy, I was left thinking: a dialogue about what? And this wasn't due by any means to her explanation of what the questions were, but I think it was noted yesterday by Dr. Rubinstein early on, as we heard about all of these exciting projects, why are we not seeing more things come to fruition?

So I thought this was difficult -- to really put a thumb down on what clear communications strategies look like. So I thought we would step back very quickly and just say, how are we doing at addressing the problem as a whole? And are people really understanding why things aren't coming to fruition?

So, a number of general studies have cited things like -- that have been talked about already yesterday and today -- about what goes into the length of time, the people, the money that it requires to bring a

single drug to market, and are we summarizing this too much as far as details versus simplification, and what are the tradeoffs?

We have heard a number of kind of catch phrases to engage the public and describe the concept of translational research, like bench-to-bedside, microscope-to-marketplace. Is that really getting caught up a little bit too much into what actually that "to" is and how big the "to" is, as compared to the challenges?

Have other terms like "Valley of Death" helped describe, really, what the challenges are, and the pitfalls to the topics that we are trying to address today?

So, certainly the challenges have been acknowledged -- and I don't know if this is true for the public's standpoint -- but roughly 20 percent of new drugs that enter clinical testing ever actually make it to market.

In oncology, drugs that are even

just starting being looked at, only eight percent of those make it. So, we have our challenges ahead of us, with a 92 percent failure rate. I don't know how to positively communicate that. But, it is certainly one that I don't think is widely understood and is one that is going to have to be dealt with head-on as we embark into new models of translational research and trying to engage the public around the importance of this type of research.

So, where is the current understanding from the public? And I know there was a lot of kind of excitement when this article came out, and I thought it was very interesting because people focused on the promises that were made very early on, particularly by President Clinton in introducing Dr. Collins's efforts around the Human Genome Project that -- I think it was something to the effect of -- this may allow us to prevent all diseases.

And so an article like this comes out and basically the headline is the headline. Now if you actually do read the article, it continues on to conclude with the inherent uncertainty in science, but the headline is the headline, and the public oftentimes doesn't make it to the end of the article.

But, at the same time it is not wrong to wonder why it has taken so long, and that is why we are here. It is really time to revise the models that are focused on directed translation of the biological findings to new medicine.

But, it is equally as important to make sure that we bring the public along on this journey, to make sure that it is like the snowball rolling down the mountain and gathering steam, as hopefully we start seeing early signs of success.

But, this is far more than a communication issue. There needs to be

fundamental changes. I think the public is looking for fundamental changes, wants to understand what goes on at research institutions, and I think that defining the problems and the road forward for progress is one that is incredibly important to lay out at the outset, and then that can be communicated.

The challenge of course is how to do this for the many different audiences that need to hear about complex topics like translational research and drug development, and it of course needs to be tailored to specific outreach.

So, I would say it is even worth taking a look in some of these. You might note, even, that we separated here general public, patients, advocacy. Many times those get clumped together, but the messaging to those individuals that represent those groups are of course always very different.

I was struck that several -- now maybe more than several -- years ago, when I

first moved to Washington D.C. to work at Georgetown University -- I am from Ohio -- and telling people I am going to work at Georgetown University didn't really require much of an explanation.

And, I just Googled this, when I was thinking about this, the operating budget for Georgetown is a little bit less than a billion dollars. When I went from Georgetown to come work at the NIH, I don't think anyone knew what that was, and it is not to say that the 30 plus billion dollars at the National Institutes of Health is responsible for a communication plan.

But, people certainly didn't know where I was going or even what I was doing there. Even in Washington, D.C., I think people knew where I was going and what I was doing, but they didn't even know what was here as far as the operations that go on and the really expert science that is housed right here.

So, there has to be a strategy with the goal of communication as far as mobilizing the support from all of these different components in order for it to be successful. No one is fundamentally against the concepts of translational research, but I suspect most don't know what role they can actually play.

So, as far as the advocacy community, I think it is very important to equip the advocates with information. Now, it is hard for federal agencies at times to kind of make the case. There is a delicate balance of providing information without lobbying per se.

And, oftentimes, government officials can't give information directly to Congress without first being asked.

But, I think this is a pretty good example of why a mobilized and educated advocacy community is needed. Engaged advocates are seen now by the emergence of new

philanthropic efforts that we have heard a lot about yesterday afternoon and this morning, where impatience for progress is evident for these changing paradigms in translational research.

One example, I think where the advocacy community is frequently fractured on these issues is just the idea around research in general. You know, every year -- I don't know if this is readily known -- but every year the advocacy community spends about three months waffling back and forth about what the "ask" for the NIH budget should be.

You know, should it be the rate of inflation, should it be BIRDPI, should it be BIRDPI plus three percent, should it be how to maintain the ARRA funding base?

So, after about three months -- I don't know how the decisions are actually made -- but you either decide to all go along or you decide to split into your different camps and carry different messages on the Hill and

really confuse everybody. And what is the result?

Well, I would say, that at least since the age of the doubling, it is always less than whatever the end "ask" is, so maybe this is evident of ineffective communication amongst the community as a whole.

But, it is an important one, I think, to take a look at how historically research communication has happened, because certainly the question, when trying to mobilize elected officials, is always what is the return of investment?

Now, this is not without its challenges as well. You certainly want to create excitement around research. There's been plenty of studies that go around this, but it is not always known, things like the return on investment for research. Over two dollars per dollar invested in research comes back to the economy. Does that help build a case?

Well, discussing what that money is going to is often difficult, and now we are left with one of those kind of footballs to pass around of how we are going to describe it with the Cures Acceleration Network.

And, I mentioned earlier, it takes a billion dollars approximately to bring a new drug to market. So we have 50 million now and what are going to do with that to create a so-called cure, let alone the Acceleration Network to then compound that into additional cures?

And is this an example of another underestimation of the challenge in order to create an important talking point to kind of galvanize and mobilize the forces necessary to result in progress.

So how are we doing? Well, at three percent and slow growth rates since the doubling as far as the research budget as a whole is concerned, it is a little disheartening to hear some of these comments

that were made when Dr. Collins was testifying with regard to the House Appropriations, where the Chairman of the Committee responsible for funding said, "I am disappointed by the lack of aggressive activism on the part of the professionals in the biomedical research field."

So, I guess, we are not doing very well. I think it is really important, you know, I mentioned there is a fine line here, but it is critical for all the components that have been discussed, whether they be as part of public-private partnerships that were described earlier today, specific roles that different government agencies can play to really find ways to creatively talk about what it is that you are doing. Whether it is the successes or the failures, there needs to be a better communications strategy.

I can tell you personally there have been times when I have been on the Hill talking about the activities or the

initiatives that leadership of different agencies have had, where I have been greeted with things like say, "I have heard more about this topic from you than I have heard from agency x."

And that is a challenge, because that is directly followed with, "That makes it very hard for me to sell to my boss when I don't have any information about the program that you are telling me from the people who are supposed to be conducting it."

And now, of course, this is all more than money. This slide is a little bit outdated, but some kind of recent figures estimate that the total investment in biomedical research is upwards of $90 billion, and this line is still kind of remaining the same as far as if the metric is indeed new drugs and devices.

So, throwing money at the problem isn't exactly just the -- isn't the solution here, so maybe we shouldn't underestimate what

$50 million can do if we are talking about CAN or as far as if we were to parse out the total amount of money that is going towards a translational research effort.

So, the question here is what can the NIH do to help? The current environment is eager for medical advancement, but not exactly supportive of the key players, which makes it very hard. There is an increasing skepticism of government. Certainly, there is zero sympathy towards the industry.

An academic enterprise with reward systems that are not always geared towards start-to-finish drug development and an extremely challenged economic outlook make all of this exceedingly difficult to build momentum behind.

So, I think it is really important to look at the successes and the failures, and why did drug x succeed and why did drug y fail? I think the public is interested in understanding the process, and that will be

important to kind of gain steam as we move ahead.

So, publicize a directed work plan. I think this was talked a bit about in a -- the earlier panel. If you have very incremental goals that can be communicated along the way, it helps to keep people involved, to drive support, get people excited and then of course to also hold people accountable.

In general, there needs to be a new approach to all of this. The current infrastructure for clinical research has been referred to as out-of-date, and, if a new approach is desired, then we need to change some of the old parameters.

I mentioned a couple of things here specifically. The IOM report recently, on cooperative groups in cancer, really highlights the need for fundamental change to clinical research as a whole.

My last bullet point here is not

to insinuate by any means that the peer review process is broken or not efficient. But if we are talking about a new approach to conducting translational research, certainly having the right expertise around drug development -- as a part of the peer review process from the beginning -- is critical to even make sure that we are starting off with the right projects in order to set them up for success.

With regards to the federal government, I think this is a really important point here. I don't want to duplicate anything the was said on public-private partnerships before, but certainly I think we are starting to see some fruition come from that.

But, in order for successful engagement about translational research, the vital role for the other components of the translational research enterprise need to be described. The NIH just simply can't do it alone and we shouldn't expect them to. I think Dr. Fauci made the point yesterday that there

is often a public misnomer of questions, like why aren't more drugs coming out of the NIH?

Well, that is not what they are fundamentally set up to do alone, but they certainly can be a key driver -- if not the major convener -- of many of the other entities that are required for success.

But, I can tell you that the role of other agencies is even less understood. If people in Ohio didn't know that the NIH was in Bethesda or what they were doing, I can promise you that they don't know what role agencies like the FDA can play in the advancement of biomedical research, and that is an increasing challenge.

I understand that the NIH itself is at times a regulated entity, but coordination around activities, with directly the FDA or with other federal agencies, can certainly be improved. I think we saw some mishaps in communications by the activities of some of these agencies, most recently as last

fall with proposed revisions to mammogram guidelines.

I don't think it was necessarily well coordinated by the various different entities that could have worked together to improve that process as a whole. That's a specific example.

But, the need for collaboration goes beyond just explaining how it can work. It actually really needs to happen. Last year, probably really about a year ago, over last summer I had the opportunity to talk to many of you who have been around the table and others about what your understandings or what your direct contact was in working with the FDA.

And I will say it was a very interesting series of conversations that were highly variable as far as how these two agencies should and do work together. I think we have seen some very positive steps in the right direction that have been mentioned

already today through the leadership council, that I know is planning on meeting relatively soon, between the leaders of those two important agencies, to try and increase the open channels of communications and activities that can be coordinated between the two, so as to support both of those agencies' really vital missions for the advancement of public health.

And, in looking at that announcement, it really struck me how important the concept of regulatory science is, and how this actually has begun to create a bit of a public groundswell, without ever once really defining the concept of regulatory science.

Over in Building 10, when the announcement was made, a roomful of advocates came out to pledge their support for this effort. You know people acknowledge that six, seven million dollars isn't exactly going to perhaps change the world here, but there was

such support among the external community that we need to figure out how to keep that going.

Still now, we see the members of the community out there pushing for the importance of this vital collaboration, but not really able to even define what it is going to look like.

And that goes back to arming the advocates. I think having a work plan for the public to rally around, gain support for on the Hill, on the ground, is critically important for these efforts to succeed.

I put one example down here at the bottom. Obviously, by the name on the slide, I am a bit more steeped in the cancer research enterprise, but as a member of the public watching how over the years the debate around the flu vaccines and the challenges haven't necessarily all been communicated.

Essentially, last year we had a challenge with getting the vaccine in time. That was always communicated. Why? It never

quite got out there. The incredible partnership that went into successfully getting it out there? I don't think that was well communicated either.

To try and educate the public around this process of things that are relevant to really all Americans, could be a really great way to explain the challenges associated with translational medicine, and to engage the public.

So let me just conclude by saying that doing this type of work behind closed doors, without public engagement, would really challenge the sustainability for the future of translational medicine. So, I will stop there and we can open for discussion.

MEMBER FAUCI: Thank you very much, Jeff. So, getting back to my opening comments, before I ask the panel to make some brief statements so that we can get into the questions, I think your presentation exemplified somewhat the concern that I have,

and that is that you started off -- and I was -- I don't usually take a lot of notes but I was taking notes on what you were saying -- that you gave a good argument for the public, the need for public understanding in order to garner support for the NIH in general.

What we are talking about in this session is not just the NIH in general, but a very specific initiative that we are trying to launch and we want the people to understand.

And that is why I think this session is so important, because there is absolute, major possibility for misunderstanding what we are talking about. So, you gave an example of something that I have experienced many times, not just me uniquely, but my institute director colleagues, of sitting in front of a committee, a congressional committee, and somebody saying, "What have you done for us lately, where are the cures?"

That was before we had a Cures

Acceleration Network. Can you imagine what the questions are going to be when we have a Cures Acceleration Network, because we are essentially putting ourselves out there?

So I think my own personal -- and also discussing with some of my colleagues -- one of the major issues is to get people to understand something that you said and Tom Insel said and I have said, is that: we are not the ones that are supposed to bring the prize over the goalpost. We are supposed to be participating in a much more effective way in getting concepts that we fund, that we develop with our grantees, into a pipeline that is going to the goal line.

So, we don't do that except with repurposing. I mean, for example, if I could name -- and I don't want to take the time to do it, but some that I have had personal experience with in the last year -- of vaccines that we funded the fundamental concept. We worked with the investigators to

link them up with a biotech company. The biotech company was bought up by a major pharmaceutical. The major pharmaceutical made the vaccine, and when the announcement of the vaccine was made, somehow or other, the NIH got lost in the shuffle.

So, if it wasn't for the -- and that was done -- what we want to do, that was really taking the concept. So that is why I feel really strongly about the need for real, accurate communication about what is the goal of what we are trying to do?

So, with that as the background, we have a bunch of questions that have been put up. How is the public going to interpret and respond to this effort? I think I just explained that very well. How are we going to enhance communication to our stockholders regarding the risk and the benefit of this?

One of our major stockholders are, what I call affectionately the RO1 crew, so whenever there is -- and there is an R01 crew

guy right down at the end of the table, Tom -- when they hear of any initiative that the NIH is going to do, any initiative that is driven by the NIH, there is a considerable anxiety reaction about resources that are going to be taken away from fundamental, basic, undifferentiated research. So, I would like to hear what your thoughts are on that level of communication.

The other is public input -- and these questions are all delineated -- to establish tangible goals and to set priorities. Now to get public input is very important, and we need it because we are a public organization. We are funded by taxpayers' money.

But, that also falls under one of my categories of be-careful-what-you-wish-for, because it may be that the public doesn't really understand well, and that gets to the communication, of what we are supposed to be doing.

So, they are going to wish -- if you give them a wish list, they are ask you for a cure for all of their favorite diseases, and the cure has to come directly from the NIH, which I can tell you today, we can settle that, that is not going to happen. It is going to come from the NIH playing a role in what the pharmaceutical companies do.

And then there are other issues regarding expectations. You know, as I mentioned, after a few years we are going to be asking you to list the several cures that you have. It's like my turning to Gail or to -- who was -- right, right and say can you tell me the list of cures that you have done this past year?

In any event, how are we going to convey the importance of this? So, I will stop with that, unless Norm has any other comments, and could we -- actually why don't we just go from that end first, because this end always gets the short -- if you just make a statement

about some of the things that I mentioned and then we will open for discussion.

DR. PACCAUD: Thank you. Quite an interesting and complex topic. Again, from the perspective of a private partnership organization, the main thing that came to my mind as a danger when you are trying to get into this area, which belongs to some extent largely, we have seen, to the pharma industry, is that you may start blurring the message.

My conception as a European of the NIH is of a basic research funding agency that really actually is the driver of the next development from ideas to product, but that development part has always been taken up by the industry.

Now, you are stepping closer to what the industry knows normally how to do, it is probably essential that the researcher understands the process -- we have heard that yesterday -- so that they know if their research could one day be translated, which

probably to our experience, most of them don't understand at least for our diseases.

So, my first thing would say, be aware of the fact that you will have to be crystal clear about why NIH would start de-risking a part of the job that normally is going to -- should be done by industry, because if they develop a drug, they then, after that, start making some profit. That will be one of the aspects that I think is critical there.

You said it very nicely as well. If you ask the public about what are the diseases that are important, you will get a long list of very interesting diseases and probably most of them rare diseases which are underserved by the industry.

So positioning -- and again, this is probably a statement from DNDi's perspective, well, maybe NIH should position in the diseases where the pharma industry is not going and explain that if you develop

these translational capabilities, this is because you really need to de-risk that for a subset of disease. I wouldn't say that diabetes is a small disease on which there is no profit to be made by the industry. That is their job to do that.

So, to some extent, from our experience, we would warn that the confusion between private and public sector roles there, and I will stop there.

DR. ROWE: Well, thank you for inviting me. I am representing the Cystic Fibrosis Foundation and I think there is a number of parallels to what you are thinking about now to what the CF Foundation went though 10 years ago when they transitioned from primarily funding academic institutions and care centers to doing active venture philanthropy and funding biotech companies and really pushing their therapeutics development pipeline.

So, one point that I would like to

make, which reiterates a point that you have made, which is I think as you are setting up a program that is going to be an active facilitator and partner to pharmaceutical development, I think communication is likely going to be an expectation of your constituents.

And so you might as well consider embracing it now and developing your processes to handle it. It could be a purview, for instance, of your program management group. Certainly, the CF Foundation had that. Once they started funding these biotech companies, it became an expectation of the patients and the families and its stakeholders to report on that progress on how well it is doing.

I think the other point I would like to make in these opening statements is that you are going to need metrics for -- that are easily understandable by a wide variety of people for your progress.

The thing that the CF Foundation

did was develop a therapeutics development pipeline, so on the x-axis is all the various biologics and therapeutics that are in development, on the y-axis is where each one stands in its development path from pre-clinical all the way to available to patients, and that is shown on a regular basis, updated on the website regularly, used by our fundraisers as well as communication with the industry.

And, I think, you are going to want to have that, and it harkens back to a concept that we talked about yesterday, which is that NIH is very complex and has multiple different organizations. Perhaps there is a way to harmonize that in a simple diagram and show that, use it as a communication tool.

When we look back after a decade of working on our therapeutics development pipeline, we developed a program that showed how that therapeutics development pipeline changes over time, and it was very informative

in that while some agents and therapies were moving up the chain and eventually available to patients, there was a lot of activity at the low end of the scale.

They were coming on and coming off the pipeline, and you could show that to patients and constituents, and it was an effective tool to help set the expectations, and you might want to do that now as you start that program to help combat that. So, I will stop there, and I have a few other points on other questions.

MR. SIMON: What does the NIH have in common with the White House, with Pfizer, and Carnegie Hall? They are all defined by how hard it is to get in. And, for instance, I was talking with an executive at Carnegie Hall just the other day, and he said: our walls are what define -- the best acoustics in the world -- but they are also what keep people out.

And, if you have ever seen Carnegie Hall from the outside, it is an

imposing brick edifice. Most people wouldn't think that they have anything to do there. So, when they started a program for Chinese culture, they had -- 40 percent who showed up had never been inside Carnegie Hall before.

When they did a special program on African American music, 30 percent of the people who came had never been in Carnegie Hall before. So their question isn't: how do you get to Carnegie Hall? Their question is: how does Carnegie Hall get to you? And that is the question NIH is asking.

The fence that is now around NIH has actually made explicit what has been implicit for a long time, which is -- it is hard to get here, it takes a lifetime of devotion to science to get here, and the question is: how do you get people in here, out?

In the brief conversation with Dr. Zoghbi, she made it clear to me that Pfizer is a hard place to get into. I have only been at

Pfizer a year and I can tell you that after just a few months, I knew it would be totally possible to spend every waking moment in the building and totally forget the outside world.

In fact, a lot of people who have been there 10 years wonder and ask me why I spend so much time out of the building.

So how does the translational research in particular get out of the building? Well, for one thing -- as you just said, Dr. Fauci -- we need to have the same sort of blue ribbon commissions that look at conflicts of interest, look at congruence of interests.

We are the only country that divides our industry from our government and our academia in the way that we do. We have to have one large brain to get where we want to go, and right now we have divided our hemispheres, and we cannot get there from here.

Other countries will get there a

lot faster than we will, because they are uniting their industry and the academics and the government.

So, we have to start addressing, head-on, that individuals have conflicts of interest, and they should be dealt with firmly. But, as institutions, we cannot continue to demonize different parts of society.

Marcia Angell started with a few criticisms and now, every time she is scratched by a reporter, out comes, "It just shows the corrupting influence of industry in America."

Well, there has been a lot of corruption in academia, there has been a lot of corruption in government. But, we don't need to demonize those institutions because of science misconduct, or political misconduct.

I can tell you that most of the people in the industry -- if not the overwhelming majority of people in the

industry -- are passionate about helping people. But, they have to do it in a way that funds their work, just the way you have to communicate to the public your work to fund your work.

So, my table of contents for today is, what do we do about the R01 gang and the mission? It was the demise of the large-frame computer companies that the large-frame scientists and engineers never wanted any money to go to small computers.

So, what happened wasn't the demise of small computers. It was the demise of large-frame computer companies.

We have to talk about the value of innovation to society from economic terms. We have to define diseases. I mentioned this yesterday. But if the NIH translational program starts dividing diseases into what they really are, based on what we can analyze and attack, and the FDA keeps regulating drugs based on antiquated disease categories, that

won't help. We need the NIH to educate the FDA about the future of medicine.

And finally, one thing I think we need to do with the public is, we need to start thinking of our young people as talent to be drafted out of high school, given scholarships, given the option of employment, the way we do athletes.

It is amazing to me that we can have a draft that stops everybody to watch television for high school football players, and yet when Intel names the top 100 high school scientists, they get a page in the paper, one day.

Those young people should have their careers laid out for them in terms of options, funding, opportunities, and instead we offer them eight years of servitude, debt and ingratitude until they are 40 and can get an NIH grant. So, we have a lot of things we can change. Pick one.

MS. COMSTOCK RICK: Thank you. How

do I follow that?

In terms of communication, I think, the first question you always have to ask is: who is your audience? And quite frankly, patients and public for this purpose I will lump together. Researchers and Congress are all very different audiences with very different needs.

So, I want to talk about each of them very briefly. For the patients and the public, I echo what everyone else has said. I was as dismayed and concerned as everyone in the room yesterday when I heard about the science teacher quotes, that they had never understood before the connection between research and medicine, until they had gone to this conference. Terrifying, to me.

Also, I am very active right now on the hot issue of human embryonic stem cell research with the case going on. I am interviewed a fair amount about that. I can't tell you how many science reporters ask me,

"Well, stem cell lines were first derived a little over 10 years ago, and we don't have any cures yet. Doesn't that mean they don't work?" These are science reporters.

There's a huge education opportunity that NIH, I think, would really benefit from taking on in terms of educating the public, not just about translational research, but about research, basic research, the role it plays. Yes, you don't get the ball over the goal line. Explain that to people. Explain the pipeline to people, and I think there will be a lot of benefits, not just from the CAN effort, but for NIH funding as well as recruiting young people. So, I think there would be multiple benefits.

In terms of researchers, they are definitely one of your stakeholders, I don't want to repeat some of what was said yesterday, but just reinforce it. I think there is a huge opportunity with CAN to work on the culture of translational research being

second class research, to work on the culture, to support the outcome, that scientific beneficial outcomes that could lead towards a therapy is just as much to be celebrated, maybe more, as publications.

How NIH does that? There is a lot of opportunity. Do you take some of the CAN money and start a journal for translational research that is willing to publish negative results? NIH is the gold standard for researchers. The R01 crew is envied. Use that cachet and that power and some of that money to promote the culture of translational research.

But, the last audience I want to mention is the one I deal with a great deal, which is Congress. I have had many conversations in Congress about CAN, over many years, actually. We have been talking about this issue long before Senator Specter named it CAN.

And one of the issues that, I

think, hasn't come out in the last day-and-a-half, if you will allow me that, is that Congress didn't expect that NIH had all the answers and knew exactly what to do with $50 million, which if we are on the right track, will far exceed $50 million in a few years.

Congress felt -- in my opinion, based on my conversations -- Congress felt that NIH was the right convener to have this really difficult conversation, and NIH was the right place to house this. But, NIH didn't have a plan in its back pocket for immediate implementation.

And, quite frankly, what hasn't been talked about in the last day and a half is a piece of the statute that creates a board to oversee CAN that has membership from DARPA, membership from industry, membership from VC, membership from patient advocacy organizations.

That was considered a key part of implementing CAN. I work for PAN, a Plan for

CAN. And part -- one of the things that is in the statute that the board is supposed to oversee and work with the director of NIH and the Secretary of HHS on, is identifying hurdles to translational research, and part of NIH's role was to convene that conversation with all the stakeholders and say, this is what some of our problems are. We need to focus on them. Could be conflict of interest. We have talked some about contract issues, could be a lot of things.

And that board is supposed to be powerful, but it is also a huge opportunity for public input and education about the role.

So, I would suggest to you that when you are thinking about how to get started with CAN, it is okay to step back and understand that NIH was slated as the right place to have this tough conversation with significant input.

I have to say it is not lost on me that I am speaking to a board about the

creation of a board, which has the authority to issue a report. That's very, very government. I realize that. But the CAN board, again, was slated in part to identify the hurdles, and in fact if you look at the statute, there is a process created for what they are supposed to do when the hurdles are identified.

MEMBER FAUCI: I just couldn't help but just make one brief comment, because I might forget it as we get into the others. I am, as an institute director, totally, not only in favor of it, but I walk the walk regarding translational research. We do over $1 billion in translational research.

But, you said something that struck me. And that has to do with communication regarding what I was just saying about getting the people who are fundamentally in just the basic research.

You said the CAN number is $50 million and for sure it is going to be much,

much more than that in the next couple of years. The NIH budget is scheduled to be flat for the next couple of years. So if it becomes more, then it is going to come out of the fundamental, basic research and then we are going to have a real problem in communication with a very important part of our constituency.

So, I don't want to get into a discussion, but just so that people know that if that happens, we have a communication problem, a serious one.

MS. COMSTOCK RICK: Yes, I mean I do think -- the focus for new money for CAN has not been dropped entirely and I do think that a lot of this is circular, that if you are able to show that NIH is moving into a truly new space, that it might require new money.

But, education of the importance of basic research is huge.

MEMBER FAUCI: You haven't been to

the meetings with OMB that I have been.

MS. COMSTOCK RICK: I understand. I understand. Congress is not always easy on you either.

MS. ANDERSON: So I want to talk a little bit. I am representing FasterCures. So, we have cures in our name and we deal with the same sort of anxiety that you do in terms of where are my cures?

I think the important thing to talk about here in terms of this communication issue is the context, and I think Jeff pointed it out in his presentation: context is everything.

So, right now we are dealing with a context where the headlines are focusing on where are my cures or what is working in science, what isn't working in science? So I think the public is getting a little bit more sophisticated in terms of understanding, oh, I just read that this big Alzheimer's trial didn't work and it stopped.

I think all of that benefits the greater good in terms of understanding where we are and where we need to go.

I think another piece of context that is important is the aging Baby Boomers. I think everyone is looking around and saying what am I getting, what are my peers getting, the sandwich generation, I mean I am here representing all of these different places, the sandwich generation is looking at their elderly parents who are living much, much longer but with many more chronic diseases and things that have to be managed.

I think all of this is also in the context of safety and risk, so we hear a lot of discussion about patients are willing to accept more risk but then you are talking about a regulatory framework that must ensure safety.

And so, I think, as we speak about what is needed in communications, we have to recognize all of this, and to your point, Dr.

Fauci, about what the NIH does and doesn't do, I think the burden comes back to NIH to be part of that communication process.

I think Rob Califf pointed it out as well. Right now, there is a little bit of a vacuum for how does medical research happen, how do the sectors actually collaborate, how do we pass the baton from one place to the next?

So, I think the basic research community, the R01 crew, needs to get in there. They need to talk about it. It goes back to Greg's point about the next generation of scientists. How are we going to have a next generation of scientists if there is no discussion about it?

I mean, there is a lot more discussion about football than there is about science. So, I think all of these things go together. I think you can't have haves and have-nots in terms of this communication.

Last night, I was flipping on the

internet, saying if I am just Joe Q. Public, Joan Q. Public, how do I get information about the NIH? Well, go to the nih.gov website and play around a little bit. It's not always intuitive.

And, this isn't a bashing session, but it is to say that there are a lot of people out there fishing for information, and they need to have it spoon-fed to them.

Now, can you do it all through websites? Of course not. There are a lot of excellent patient groups, there's coalitions, there are stakeholder bodies that need to be cultivated.

You know, you need to look at it as they are part of your clientele, they are part of your client base. You all need to be a bit of a sales force.

And, I think, part of the challenge is that what would we prefer to have you all doing? We would prefer to have you all searching for cures and doing science. I would

rather have Dr. Fauci out and about within NIH and outside talking about science and translation and how do we get there.

But, I will also say, Dr. Fauci, that I would love to hear you on Diane Rehm every single day of the week, talking about the challenges in infectious disease research, because I think you are an eloquent spokesperson. So is Dr. Collins. He whips his guitar out and suddenly he is a YouTube sensation and the Twitter world is all aflutter.

But, you all need to recognize that there is only 24 hours in the day and there is only so many of you all. So, you have to deploy this communications mission throughout all of the institutes and across the NIH.

And then, I think, you need to start to collectivize the message a little bit, back to Rob Califf's point, we need to bring in academic medicine. We need to bring

in the pharmaceutical companies. We need to bring in the patients.

And I will point out that you can't just say here's our information, come out to this meeting at NIH, go through security, we will give you the information and then go off and do it; you need to meet everyone half way.

And, I think, part of that goes back to the message of leaving the confines of the campus, going to all of these various constituent groups, including Congress.

You know, as Amy pointed out, as Jeff pointed out, when we are on Capitol Hill talking about these programs, we get all of the anxiety, you all get it when you are in front of the witness stand. There just needs to be a constant dialogue about it.

I could give you a list this afternoon of a ton of different vehicles to get those messages out. What is the message? Obviously, that needs to be worked on in terms

of this translational research portfolio.

But, I will say that it needs to go from being one-dimensional to three-dimensional. So, I have witnessed Dr. Collins and his Power Point presentation that he gives out in all of his speeches, evolve over time, as he has started to thread the needle about the translational research package.

But, we need to expand that and it needs to make more sense back to the context of how does basic research fuel all of these engines of discovery, what's the role of NIH, what is the role of TRND?

I mean Chris Austin, who I expected to see here, but he is everywhere. There's -- we need to replicate and duplicate some of this intellectual firepower because I do think that the American public is starting to say what am I getting for my investment?

It's the same thing if they are saying what did I get for my TARP dollar, what did I get for my Gulf Oil spill dollar, what

did get for my auto bailout dollar, what did I get for my medical research investment dollar?

And is it pleasant? No. But, to me, it is the reality that we are in and that I think collectively we need to figure out how do we move forward.

MEMBER FAUCI: Thank you. Ken?

DR. DUNCAN: So, I don't have a huge amount to add to the great discussion that there has been. I represent the Gates Foundation obviously, and working in global health, we are in an interesting paradox here that there is no patient population here in the U.S. that can really voice the need for new drugs for neglected diseases.

And so, we are relying a lot on sort of advocacy and whatnot, and we have put a lot of effort into that area, but trying to get the message across as to why it is important to invest in that area is clearly challenging.

And the Foundation has tried to do

a number of things. One very interesting little side issue here is there is a grant jointly made between the global health program and the U.S. programs which is working in high schools in Washington state to talk about global health issues and to really get schoolchildren engaged in understanding them.

And as they start to understand that, it starts to raise a lot of questions which then makes them very receptive to what the value of science and technology really is and helps them to understand why we need to invest in these sorts of areas.

And I think getting that message across, though, is very difficult. It's challenging. And so one way to approach that is to think about what are you trying to communicate here, and to come back to some of the points that were made earlier, it's not necessarily about a final product, but it's about what steps have come along the way? Have we been successful in moving a project from

the bench into some clinical development pathway?

And tell some of the positive stories, get that message out. And the R01 community is an interesting one for me. We often think about the universities and how people actually communicate their science.

Is it necessary for all R01 recipients to talk about their science and to go out and to show that they have done public engagement? So one thing -- I come from the UK -- one thing that happens there is that basically all scientists who are in academia have to show for their metrics each year that they have had some sort of engagement with the public.

And so, there is a lot of examples of where that might just involve going out to a high school, talking to a group of kids. It might involve bringing people in, teaching them what they do. But actually making sure that it is actually in their -- it is one of

their responsibilities to go beyond just teaching the students that are in their own environment.

And they also, as I understand it, I may not be absolutely correct on this, I think in a lot of the grants that are given in the UK, they actually have to report back on what was the public engagement, how did you communicate this science that goes beyond just the publication in a learned journal, but also some open publication.

It may only just be something on their website, but ensuring that, at each step, there is some engagement, that people see what the value of that research is and they can actually access it.

MEMBER FAUCI: Thank you. Okay so let's open it up for questions, comments or whatever from the board. Gail?

MEMBER CASSELL: So, this is a problem that I have struggled with for a long time. In 2007, I chaired a review of science

and technology at FDA and realized that for 15 years this agency had been woefully underfunded.

And you begin to try to figure out why is that, why is it they have no advocates? Industry can't be their advocates because it would be too self-serving, conflict of interest.

But really, nobody, if we think that people have a poor understanding of the role of NIH, I think the public has a very poor understanding of the magnitude of the responsibilities of FDA.

So, since 2007, we have been, a number of us, Margaret and others of us, have been trying to figure out how can we improve this understanding? We have come to the conclusion in the IOM drug report that was mentioned earlier, we need a massive communication effort.

And then, it became very apparent you can't just talk about one end of the

chain, which is the regulatory authority, but you have to talk about the role of NIH. You have to talk about the role of academia and by the way you have to talk about industry.

The poll that Mary Woolley spoke about yesterday we helped to initiate and the results have been consistent since 2007, that the public expects that these sectors are going to work together to develop new therapies.

So the last time I went in for a meeting we decided that perhaps the Foundation for NIH -- Scott is a member of the forum -- might be a place one could house this educational effort where you could get legitimate financial contributions for this effort, only because you have to have that in order to have the type of massive educational campaign that you need.

And I am only taking up our time to suggest that because I think until we get the message clear and out there, we are still

going to have a really hard time in terms of getting CAN funded as well as it could be or NIH funded as well as it could be or FDA, a strong, scientifically-based agency as we know it, all it has to be, if we are going to succeed in developing new therapies and other healthcare technologies.

MEMBER FAUCI: Dan and then Huda.

MEMBER GOLDIN: I think it is good to have outreach and people in the universities to speak, but the American public wants to see their officials that are in the charge of the program.

And, I know it is very difficult, it is very time consuming, but if NIH wants to undertake this translational activity, you have got to go sell retail. There is no magic, even in the age of the internet.

The leadership of NIH has got to go to every Congressional district, talk to the people there. The local media has to see your presence. You have to meet with advocacy

groups. You have to meet with groups of people that have problems and you have got to listen to the problems, you have to take notes, you have got to come back and you have got to go back and answer them.

The leadership of NIH needs to meet one on one, in the offices, with the members not the staff of the Congress. It is a huge task and there are action items that come from that, and there are expectations that are getting set that are beyond the control, due to the internet, that cause a huge communication failure, and the members and the staff read the blogs, they read the papers, and when there is no response from their government officials, not from the people in the universities -- that's nice -- but that is my suggestion.

The communication problem is really simple. Go to every single congressional district at least every other year. When there, take a day, take a leader,

take some examples, meet with the people, go to high schools, go to colleges, go to the Chamber of Commerce, go to the Rotary Club.

The attendance will be absolutely spectacular, but take a few people. Hold town hall meetings. Have fairs. That is what you are going to have to do, because modern communications demands the actual officials, not their surrogates, to do the job.

And, I hate laying this down, but you could think of seven other approaches. That is the only other answer. Thank you.

MEMBER FAUCI: Thank you Dan. Huda?

MEMBER ZOGHBI: So, I just had a few comments, one to start with the presentation. I was quite upset about the New York Times article and I think it is in part, perhaps, it's our fault.

The genome did accomplish a lot and we just did not know how to sell retail, using Dan's words. We forgot that now we don't expose children to a variety of diagnostic

tests, biopsies, conjunctival biopsies, nerve biopsies, nerve conduction studies. We do the majority of our developmental disorders testing by DNA testing. This is quite helpful.

Many families with terrible, devastating, degenerative dominant diseases, Huntington and many other inherited attacks -- this can now be diagnosed. So, prevention, cancer, breast cancer screens, all of that is really -- prevention is just as important to eliminate a disease as is developing a treatment.

So, I feel we should really capitalize on that. The second thing we don't make a point about is that really what these discoveries do is they have sown the seeds for us to pick up the fruits, 10, 20 years down the line.

We all know the success stories, the statin and Gleevec was mentioned. But, I think it is really important to educate that it was 25 to 30 years from that basic

discovery of a mutation or a translocation to get to a treatment.

And, I think, this is important for two reasons. One, for us to know how much more work has to go in to come to a clinical drug, but more importantly let's go back and review why did it take 30 years? What were the bottlenecks? And, maybe if we can do something about them, this could be very important for translational research.

The last point I want to make is the importance of basic research and what am I getting for it, to follow up on Margaret's point. We can't always get something immediately from basic research, and we have to allow for failures, otherwise nobody will chart a new path.

But, most importantly, sometimes the successes will come 20, 30 years later. Nobody would have thought that bacterial genes imported in DNA repairs would be really important for colon cancers. It took decades

for that.

So somehow, we have to do it and we have to do it without overselling it, we get in trouble, we oversell, the public has high expectations, we fail. So, I just think all these components, we have to figure out how to do it better.

CHAIR AUGUSTINE: I would like to make a few sort of random comments. I promise I will handle the questions from the panel here. But, we have all seen the articles what's wrong with NIH. It didn't produce 70 million units of flu vaccine that we needed, the suggestion as we have heard that the public really doesn't have much of an understanding what NIH does.

We saw the New York Times article and what it refers to and some of you in the last couple of weeks, one of the major news magazines, weekly news magazines, I can't remember which one, had a cover story to the same effect, that what are we getting for our

investment in health research?

And I think there is a problem of understanding the overall issue, but I think we also have a problem way beyond my pay grade, but the culture of the research community itself, which is increasingly, I think, going to be within academe, and that is that the reward structure is set up to reward publishing papers not producing end results.

And I think until that gets addressed to some degree, it is going to be very hard to deal with some of these issues, the broader issues.

We saw the chart that was presented this morning about the budget for therapeutics, R&D budget, versus time. Some years I wrote a little book of laws and I have come up with a new law that shows that if you double the budget for therapeutics you can drive down FDA approvals by 20 percent.

And extrapolating that, if you increased the budget by a factor of 10, you

could drive it by zero, there would be no approvals.

You know, that is a bit troublesome, even though I injected may be a bit of humor here. Clearly, here is a challenge. As we all know, NIH can't lobby, but NIH can inform. And I think there is an important difference.

One of the difficulties I have seen in watching the NIH and the healthcare community as a whole in recent years is how fragmented the message is, and I will give you an example from another world I have been spending some time in -- the broader research community where I have kind been on a one-man campaign for about 20 years to see if we can't get more invested federal money in basic research.

And I have my little spiel. I wandered around Congress, sort of like Dan said, and sometimes I think I made a few points, then I would discover that the next

person after, that came in the door was from the physics community and said boy this research is great, but don't spend it on chemistry, spend it on physics.

The next group that comes in says yes, but don't spend it on solid state physics, spend it on particle physics, and the next group says quarks not bosons. Pretty soon the Congress throws up their hands.

And we have a little bit of that trouble here, where there are a lot of very legitimate needs but somehow we have got to get together and speak with a single voice on behalf of research rather than research for purpose x.

And I must say that physics and chemistry and some of that community has done a really good job in recent years of getting that message.

The conflict of interest issue is one that is immense. I guess I worry about conflicts of ignorance as much as I worry

about conflicts of interest and hopefully -- well let me just say that's a message that I think somebody has got to get the courage to take on.

If not done properly, it sounds like you are in favor of misbehavior. But, I think maybe one way to do it is we live in a competitive world with other countries who are following a totally different rule set and perhaps there is some middle ground where we can behave appropriately, which I think we all want, but also don't handicap ourselves so badly.

And I guess the question I would like to lead to with all of this, for the panel, is that if this afternoon you were appointed to run NIH, what would be the single thing you would do that might have the most impact in terms of dealing with this general category of issues. A tough question, but you are all highly paid.

MR. SIMON: I'll bite. The first

thing I would do is take all the labels off all the buildings and change where everybody is sitting so that every other month they had a different suitemate so that NIH could know that NIH is doing.

I think if there is one thing that we have all learned just yesterday, it was that NIH doesn't even know everything NIH is doing. And it's the labels that keep people apart.

Many of these labels are using antiquated ways of dividing our bodies into parts and then people study those parts and then they discover that's not really the point.

But, as long as people think I am only at NHLBI or I am only at NIAID, and they don't think that they are at NIH, then we are going to have a problem having one mission.

When I was at FasterCures and we did a study of the intramural program, which Dr. Cassell was part of, I went online to look

at the intramural programs at the different institutes.

No two websites were the same, had the same way of describing it, had the same way of navigating it. Anything you learned on one site, you had to start over on the next site and one of the biggest problems was there was no common mission for the total program.

Now, out of $3 billion you need a common mission. I think that is changing, but the first thing I would do is take all the labels off, move everybody around and see how they felt about working at NIH.

MS. COMSTOCK RICK: That is a tough question, the one thing, but I think if you will allow me, my perception of NIH is that there is a little bit of an internal dilemma in NIH, that it sees its role in the larger pipeline in terms of what it offers from the results, discoveries, that come from basic research and what it can lead to, but there is also, internally, a sense that if NIH could be

left alone, and fund the R01 crew and get a budget everything would run smoothly.

And I think if I were running NIH for a day, I might try to truly launch not only

an external communication effort to educate what NIH does, but also within NIH, really have a serious conversation about who are we here for. And the R01 crew is part of what you are here for, but you are spending taxpayer dollars, and you are spending taxpayers dollars for a reason, and I think the stakeholders are the American public, and I am not sure that that is truly internalized.

I think there is too much of a perception that your primary stakeholders are your grantees.

MEMBER FAUCI: Of course, Francis isn't here, so let me -- no, but let me try to at least speak for him. In fact, that is exactly what he did in his very first days of his tenure, when he said there are five areas

that we feel that are important, that we ultimately rely on basic research, which is the core of what we do.

But, he realized and, I think, virtually all of the institute directors realized that there are programmatic issues like what we are discussing today that is critical to our mission.

You know, and Francis articulated five of them, before him Dr. Zerhouni had issues and before him even Harold Varmus did the same thing. So, if there is the perception that the NIH leadership is only wed to undifferentiated research, I think that is a misperception.

Because although we know it is integral to everything we ultimately do, there is a strong feeling that we have other responsibilities.

MS. COMSTOCK RICK: Well, and for many of us in life, our reputation may not be accurate, but I am giving you what I see as

reputation, yes.

MEMBER BERG: So, in addition to NIH's role, I think another big piece, and I would like to hear people's thoughts, and this is my perspective and this comes in large part from having a spouse who is a translational clinical researcher, is that -- and Garret FitzGerald touched on this a little bit yesterday -- the business model for physician scientists at many academic medical centers is, from my perspective completely broken.

It is just impossible or essentially impossible to try to develop a real translational research career without getting sucked back into the clinical business, to the point that it really becomes -- you know my wife used to come home every day saying I can't imagine why anybody would do what I do.

And then she left academia and has now been doing research as a consultant where she is completely outside the system and is

very productive.

You know I think NIH is very -- the number of discussions that I have been involved in about how to better support physician scientists and how to try to facilitate that across NIH is huge. NIH is very interested in trying to support it.

But, it is really hard to do it without getting the academic medical centers to really think about a different model, to really protect people to do research and not have them get drawn back into what is fundamentally just making money for the health system, or keeping the health system above water.

DR. ALLEN: So, in response to the hypothetical about what could be done as a -- again this is hypothetical -- but I think it encompasses some of the thoughts that you just had.

You know, it's very easy for an external panel to come in and point out things

or give a wish list of how they might want to see the NIH work or where public perception has gone awry or what priorities should be.

But, I would ask for a tradeoff and say you know, you want us to knock down the silos and you want us to present a new model of thinking, then I would ask the external community to take steps to do the same.

Those of you who have had the pleasure of working with even the cancer community would know that it can at times be both highly collaborative and highly fragmented and I think that a lot of the problems that haven't been identified are not necessarily inherent to just the NIH. They are often a ramification of the external parties that are involved or deal with the results of NIH research.

And so, how do we address some of those external factors which are an equal impediment to many of the barriers, and I

think that can be an opportunity with the efforts that are under way here, where NIH can act as a bit as a puppet-master to identify those challenges and then call on the external community as well as what the internal forces are to try and address some of those burdens.

So, I know that doesn't answer your question specifically but there may be a role here, rather than just looking at this as an NIH program and I think even with perspective to the CAN initiative, that was the goal.

There were other models that were being looked at that were seen as success and the thought was how can we get government to spur these efforts and coordinate them in an effort to accelerate them?

It's a tall order, but a needed one.

MS. ANDERSON: I think it goes back to the issue of sausage-making that we are talking about here. I mean, the comment that

was made previously about some of the recent press coverage and what it takes to get a drug to market -- it is part of the communications challenge here. We need to talk about all of the effort and all of the discreet pieces and the people who are really toiling and at personal sacrifice in terms of their professional careers, to explain why it is challenging to get from A to Z.

And, I think, that is the piece that is missing. I certainly think in terms of the public awareness, as I have mentioned, as people are hitting the stage where they are starting to get their own diagnosis of who knows what, it starts to beg the question, well, what is going on, why can't we fix this?

I think we need to do a better job explaining we are not making widgets here. It is not a factory. This is not necessarily something that has an easy fix. However, I think in terms of some of the process engineering aspects, and the systems fixes,

that is something at FasterCures that we have heard about since our inception, that whether you are talking about autism or Alzheimer's, or cancer, or diabetes, there are systems problems in terms of how the money is doled out, what are some of the data challenges?

So I think CAN, I think some of the translational research programs at NIH, can address those and I think, it may not be particularly sexy, but you can talk about why fixing that will benefit such a greater good and how that plays a role in the broader, sort of ecosystem.

I use that word ecosystem, because I do think people will welcome NIH having more of a voice in terms of talking about all of the sectors in medical research and I think it will start to chip away at the 50 percent of the American public who have no idea what the NIH is or what this agency is that receives all this money.

I brought with me a report that

FasterCures did a number of years ago. It's called Entrepreneurs for Cures. This focuses on the venture philanthropy sector, which gets a lot of media attention because these are organizations that through patient power and passion have said we are going to collect money, we are going to dole out research dollars, we are going to do it our way, we are going to take what works and leave behind what doesn't.

You know, some of you would say some of that is successful and some isn't. But we did that report because so many of those groups would go out to meet with the scientific community, the funding community, and everybody would say, "Well why would you give you a dollar? NIH is taking care of that problem."

And so, many of these groups were born because they realized, well, NIH can't deal with the entire problem. And so, I think it's part of talking about successes and

failures and how you have to have some failures to get to the successes.

And I go to the point of some of the cancer therapies that we have now, well, the people that are benefitting from those today are benefitting because people participated in clinical trials. So, it goes back to everybody could potentially be in a clinical trial at some point in our life, but we have to have some basis of understanding of why clinical trials matter and why you need that data to get to the end point, for us to consider it on that awful day when the physician says you have this and would you like to join us in this experiment and be part of the greater good?

I think that there is an altruism in terms of the American public and the patient population, but they need to understand what they are hitching their wagon to.

MS. COMSTOCK RICK: There is

another piece, if I can, because it is of personal interest to me. The conflict of interests issues have come up a lot in the last couple of days, and in my prior life, I actually was the director of the U.S. Office of Government Ethics which oversees the conflict rules for the whole Executive Branch, and I ran the ethics program -- the conflicts program -- at the White House before that.

And I have to say that I think these are very connected issues in terms of communication and solving some of the conflicts problems. It is not a good talking point, and you all know that conflicts rules are keeping us from cures; that is not a good talking point.

But I wouldn't -- I am worried sometimes that the conflict rules are used as an explanation for why we can't go forward with certain partnerships, and I have to tell you, I worked in that field for 15 years. Occasionally, I saw something that was

impossible to do, but the vast, vast majority of the time, if you had a specific goal, an outcome you needed, a partnership you needed, it was important and you could communicate -- that is what we are talking about here -- why it was important -- you do have to deal with the lawyers -- you will get the support on the Hill or you will get the support from the lawyers. It can be done.

And I worry -- I think there are opportunities with the communication to even solve some of the problems we are talking about. Make your plan, seek your outcomes, find the partners you need to work with and then if there are hurdles, we will focus on those specific hurdles and you will probably make point son the Hill, because you are coming with a positive plan.

MEMBER GOLDIN: I have a -- someone else wanted to make a comment.

DR. ROWE: I was just going to return to a comment that you made regarding

what the reaction of the R01 crew is going to be as you progress with this.

The Foundation went through this when they started doing the venture philanthropy, where a significant portion of the medical budget went to a, in this case, a single entity, single biopharma entity, instead of what normally would have been going to their R01 crew.

And there was a significant negative backlash and a lot of skepticism about whether this would work at all.

Now, in reflecting about where we are now 10 years from that, a lot of good and basic science has come out of that original collaboration and I think you are going to experience the same thing.

And I don't think it has to be an either/or situation and a way to communicate that would be an important message -- in fact if you look at what is being published by the basic scientists in CF research, many are

using the tool compounds that came out of both successful and failed discovery efforts that were originally funded by the foundation.

And the thing that the foundation did to help facilitate that is to generate tool compounds the have been publicly available to their scientists and clearly communicate which ones were going on, which ones were looking promising, so that the science could follow that in part.

MEMBER FAUCI: That is a good point. Just to make a very brief comment, what we have been trying to do for some time now is to not, as you say, make it an us or them in the sense of the developers and the translators and the basic researchers, but to embrace the basic research community as an important part of the process, which they are, an important part of the process.

And I think the communication, to get them to understand that is something that we really need to do better at. From a

practical standpoint, it is difficult to do that when you have a completely flat budget, which is really functionally a cut.

Because if you even have a modicum of an increase, you can say, we are going to have an initiative in translational research and we need the fundamental, basic researchers to be the source of that ideas and that concept.

But, when it looks like you are taking money away from them, that is where the problem is. So, we are in a particularly different time now, because this is very unusual. Seven years in a row of flat budgets is unprecedented for the NIH. Yes.

DR. PACCAUD: Just -- I was thinking, because of the flat budget, the fixed envelope you are working with, I consider and I assume that NIH has done everything to be sure that it is concentrating on its major mission, for which there must be a clear statement about what it is supposed to

do, and again, my ignorance is there, it's clear there. I haven't read the by-laws or the statement and mission and vision of the NIH.

Can you cut somewhere and what is your capacity of actually killing part of it, because maybe you are moving to some aspects outside of your primary mission, communications aspect as well.

MEMBER FAUCI: That is a very good point, Jean-Pierre. We examine that frequently. We have budget retreats and leadership retreats and we -- this is something that is right up there.

And we have been cutting and cutting and cutting. Remember, seven years of flat is three percent lost per year, when you talk about fat, muscle, flesh, we are down to the synovium. Yes. Okay.

DR. PACCAUD: But, has this been really communicated in a positive way, you know what I mean, in the public? Because you need the support and that is probably -- I

mean, it seems that it is only damaging the collectivity, the scientists are really hurt by that. The general public, do they understand that, and how this is conveyed as a message?

MEMBER FAUCI: you know, again, I don't want to take much time on this, but a lot of activity is put into doing that. It is not easy to get the general public to understand things. I mean, you know, in surveys, would you be interested in this? Of course. Would you be interested in this if you took money away from that? No.

So, the general public is a big, heterogenous group. Fundamentally, with all due respect to them, I don't think they fully understand a lot of what we are talking about.

MS. ANDERSON: I was just going to comment though, I do think the American public understands cost-cutting right now. I think every one of us has probably been impacted by our economic situation in this country.

So, I guess as I listen to this conversation, I think it -- yes this is really challenging and difficult, but it is the reality and I think we are going to have to figure out how do you marry this basic research engine that has to be sort of held sacred whilst looking at NIH's other role.

And I think, you know, I spoke yesterday to a group of university representatives about CAN and the conversation was really about their anxiety and we talked about how we all have to hold hands together on this and be anxious together, but it's not going to go away. We are going to have to figure out what the metrics for CAN are, what the messages are.

As I spoke earlier, we are going to have to talk constantly about it and I think that is the only thing I feel like we can offer, is the ability to communicate and keep the lines of communication open.

I think we have all the faith in

the world that NIH is going to be able to construct this in an effective way, but as I mentioned, meeting all of these groups half way will be part of the challenge and part of the solution.

MEMBER FAUCI: Dan, do you have something to say?

MEMBER GOLDIN: Well, I have a question that I will probably ask you each to email an answer in, because we are running out of time and our chairman is very tough on time. But, I would like to at least frame it and, perhaps if the chairman was generous and gave more time, we can get some responses, otherwise I would like to ask you to send in a response and it goes like this.

We have been talking for a good day on this subject, maybe more, to a very sophisticated audience and presenters, on a very complex issue and my observation is, the NIH has conundrum. On the one hand, its core mission is basic research, there's passion, of

all the people working on basic research, and they have a set of expectations.

And, on the other hand, there is the American public, 50 percent of whom don't even know what the NIH is, and now what we are saying we want to explain to them how you go from basic research to translation research oh and by the way, this is only at the beginning of the pipeline. Don't have high expectations, because then you have got to depend on the pharmaceutical industry.

I believe we are giving an almost mission impossible to the NIH in this communication conundrum and within the American public there is a segmentation that goes from the highly passionate, of people who have mothers, fathers, children, sisters and brothers with terrible diseases, to the young population that doesn't even think they are ever going to get sick and die.

It is easy to sell Pepsi-Cola. You just buy three commercials in the Super Bowl

and then three more for Doritos so you eat Doritos, you get the salt, you drink the Pepsi and the thirst goes away.

But, I think, as we talk about this communication problem, it isn't simple to beat up Tony about, you know, you have got to cut budgets and explain to the public. And then, who do you explain it to? The members of Congress? There's passion across the boards.

So ,what I would -- my question is, and you probably can't answer at the minute, is it possible for people to have incredible experience in the field of communication to think through this conundrum and make some recommendations on how you approach this incredibly difficult communication problem that relates to the future of how the NIH could help the American public and people around the world deal with problems that just give you headaches? So, that is my question. Thank you.

CHAIR AUGUSTINE: Tony, well, a lot

of -- let's take three minutes and somebody can answer that question.

MS. COMSTOCK RICK: I can't answer the question, but I do want to say that in my work with the Parkinson's community, I am often in a position to -- for NIH funding, explaining CAN, funding in general and it's obviously one of the things we advocate for.

And it is not at all uncommon for someone who is new to the world of federal funding for research of any kind to say to me, what do I care about federal funding for NIH? I have -- fill in the name of the blank, whatever university -- in my community and they are doing plenty. There is no understanding out there that that is even federal funding.

And that is a key position point. I am not sure that we should require that your R01 crew spend x number of hours a year out in the community, but it is not a crazy idea. It is not a crazy idea to force them to tell you,

not in just their papers, but in their public communications, where they got their money from.

I mean there are -- it's a daunting task but you always have to start somewhere.

MEMBER FAUCI: It is true and we have actually -- again, I am not trying to counter anything you are saying, I am agreeing with you, is that we went through something and continue it up until today of making it very clear to the investigators that in their releases they should be very explicit.

It more often than not gets blunted down to the footnote by the office of communication of the university. That's -- it is what it is. That's what happens.

CHAIR AUGUSTINE: Jeremy, we will give you the last word. Greg.

MR. SIMON: So there are three guys in a truck and the high pressure hose breaks and they can't get where they are going unless

they fix it. Okay, not very interesting. But, if I told you they had to fix it with just what is on the truck, now it gets a little more interesting. Maybe you make on to Top Gear on television.

But, if I told you that they had to fix it with what is on the truck, and by the way, the truck is the Apollo 13 and they are in space on the way to the moon, all of a sudden, a simple plumbing problem becomes a dramatic story.

One option that Mary Woolley pointed out yesterday is to have more scientists die because she said 63 percent of the people can't name a living scientist. So, that is a bad option. I am not for that option.

But, the fact of the matter is the reason this country is so obsessed with movies is because stories are reality to people. Dr. Fauci, your story, you have saved lives of individuals, some of whom are in this room.

The people who developed the drug Selzentry gave a talk at the pharma meeting last year. It was unbelievable. There are stories all over NIH of individual dramas that start with something as simple as I wonder this doesn't work in children with this gene.

We have got to get this out as a story, not as a journal article, not as a New York Times article. The New York Times is in the snapshot business and anybody on any given day can look bad if all you took is a snapshot.

You are in the movie business. You are talking about movies that take 20 years to run, and we have got to approach it that way and we have got to talk about it that way.

When I tell people specific stories of how things got done in medicine, they love it. But, that is not how we talk about it, and that is what we have got to do.

CHAIR AUGUSTINE: That is a terrific point to wrap up on. And, on behalf

of the whole SMRB, let me thank each of our panelists, Tony thank you for taking the lead on this. We are now at the point we can break for lunch. There is food in the adjacent room for the panel members and for the SMRB members. Our guests, there is a cafeteria down, I think, on the first floor. We will meet back here at 12:15 promptly. We have got a big afternoon, so please, everybody, particularly the members, be sure to get back.

(Whereupon the above-entitled matter went off the record at 11:34 a.m. and went back on the record at 12:16 p.m.)

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

12:16 p.m.

CHAIR AUGUSTINE: We can begin the final session. This is an extremely important topic obviously. We have set aside about two hours for the discussion, including public comments, and Bill, as chair of the SUAA Working Group, is going to make a presentation on behalf of that group. Then we will have, I hope, ample opportunity to discuss it.

At the end of the day, we are, I think, obliged to make a formal recommendation to Francis and as you all have heard yesterday, when we do make such a recommendation, it triggers a whole bunch of actions on his part and that of the institute and so this is important. Bill, it's yours.

MEMBER ROPER: Thank you. Thank you, Norm. Before I begin, I want to thank the members of our working group and especially the staff, Amy and Lyric and others who have worked tirelessly on our collective behalf. I

think we have had a thoughtful discussion and respectful dialogue over the year and a half that we have been working on this project and I am pleased to report to you.

Our charge as a working group made a year and a half ago was to recommend whether organizational change here at the NIH could further research into substance use, abuse and addiction and to improve the public's health.

These are the members of the working group. I thank each of you for your hard work and dedication and here is what we have done. Some of this -- in fact much of this -- you have already heard so I am going to be relatively brief, though if you would wish, I can elaborate or others can as well.

Over the last 15 months, 17 months, the working group has held 12 teleconferences and three in-person meetings and they have heard from a wide array of people, some here at the NIH, NIAAA, and NIDA, but also people from across the addiction and

alcohol communities and lots of people who have given us lots to think about and discuss in our report.

First, I would like to summarize our major findings. Emerging scientific research indicates that there are similar reward pathways that underlie compulsive behavior, many substances that pose the potential for abuse may have similar effects on the brain.

There are common genetic sites associated with risks of disorders related to abuse, and addiction is a developmental disease, particularly beginning within adolescence and that causes some special issues.

Many substance abusers suffer from multiple drug dependencies or comorbidities and, in addition to these general perspectives that I share, we asked both the NIAAA and NIDA to identify some high priority areas where the current scientific work is not addressing the

things appropriately.

And this is the perspective that we got from colleagues at NIAAA. That is, that there is a need for greater understanding of the pharmacokinetic and pharmacodynamic interactions between alcohol and commonly-used therapeutics for other conditions, that there is research needed on the novel metabolites generated as a result of interactions between alcohol and illicit drugs, that we need more information on the mechanisms by which alcohol increases the risks for certain cancers, and regarding the public's health, more is needed to know how to encourage patients to seek treatment.

From NIDA, we heard that there is a lack of pharmaceutical industry interest in developing therapies to treat addiction, that there is insufficient involvement of the medical community in preventing and treating addiction and alcoholism, that there are treatments that are available that are not

being widely used and that there is, like we have demonstrated the last day and a half, challenges in translation of these research results.

The text on this slide is brief, but make no mistake, we heard from a broad range of stakeholders on the question of the optimal organizational structure for NIDA and NIAAA.

People have made compelling arguments and provided a wealth of information and evidence on these issues. We have heard from people on both sides, if I can put it that way, or maybe more properly, we have heard from people all across the spectrum.

Briefly, we have heard primarily from representatives from the drug abuse research and treatment communities' arguments in favor of a structural reorganization over there on the left of the slide.

They say that there is compelling evidence regarding synergies in the science,

that certain patient populations are under-served, particularly patients with multiple substance dependencies, and we have heard perspectives on impediments to collaboration and integration between the two largely separate and siloed scientific communities.

On the other side, we have heard primarily from representatives at the alcohol abuse research and treatment communities. These individuals have expressed a preference for a non-structural approach to reorganization here, which would maintain the current separate institutes.

This approach would involve what we have been referring to in our discussions as a functional approach to reorganization, which would involve the establishment of a blueprint of sorts across the NIH for research in this area.

Proponents of this approach have cited the potential for loss of certain research foci as a serious risk of structural

reorganization, thinking that some things would not be paid attention to and might get lost in a new institute.

They also have said there are benefits to having multiple perspectives brought to bear on common scientific questions and having this addiction work done across a number of institutes is a good thing, not a bad thing.

We also heard examples of successful collaboration and other trans-NIH initiatives and we also heard about the relevance of the distinction between licit and illicit substances in terms of public health messages and the stigma attached to drugs versus alcohol.

In our deliberations, we were guided by the earlier work of Bill Brody and his working group, which looked at how the NIH should go about considering change, the notion of assessing the need for change, evaluating the options for change, and implementing and

managing the change.

We have been looking at this three-step process and I would like to talk about these in turn. For our purposes, at step one, assessing the need for change, we identified five criteria: is there an immediate crisis; are there unaddressed scientific opportunities; have there been changes in the scientific landscape that merit doing something different; are there evolving or emerging public health needs; is there a need to improve the quality or efficiency of research.

So, we have looked at each of those and then, in step two of the process, options for change, we have looked at a range of possibilities.

Many of you have seen this slide before, but it seeks to highlight looking at things from as they are now, the status quo at the far left, to the establishment of a blueprint across institutes, somewhere in the

middle there, beyond just NIDA and NIAAA, and then closer to the right, the merger of two institutes, or then finally at the far right, the establishment of an entirely new institute with new areas added in from the entire NIH portfolio beyond just alcohol and drugs.

So, this is how we have gone about our work, examining each of these in turn and so now I want to turn first to our conclusions and then to our recommendations.

Our first and primary conclusion, which we are unanimously of the view, is that the status quo is not ideal for fulfilling NIH's mission and optimizing research in this area. And therefore, we agree that reorganization is needed in order to optimize the science and the public's health.

Based on the criteria that I mentioned a couple of slides ago, we found evidence of a need for change in the status quo, not an immediate crisis, but there are unaddressed scientific opportunities, there

have been changes in the scientific landscape, there are emerging public health needs and there are opportunities to improve the quality and efficiency of the research that is done.

Based on this initial conclusion that the status quo is not ideal, we have identified some key features which need to define and characterize any reorganization.

First and foremost, any reorganization needs to integrate addiction research portfolios across all of NIH and I urge you to hear that point, not just NIDA and NIAAA, but addiction research across the NIH.

And this is broader than just drug and alcohol research. It includes such other substances as tobacco, but also other behaviors such as gambling addiction.

To draw a picture of what we are envisioning, we would make the point a mission statement, if you will, for a new organizational entity should include the promotion of a unified vision for addiction

research, an interdisciplinary approach to advancing that work, flexibility so that the agency could do new areas of study, and a multidisciplinary approach to the training of new investigators.

For this to be successful, we need, or the nation needs, commitment by participants at all levels, include the strong leadership of the NIH director and directors of the NIH institutes and centers, would require participation and contributions from all stakeholders including internal staff and extramural investigators, and the reorganization must be underpinned by functional integration. It can't be just a change in name only, with the identification and embracing of shared goals, enhanced communication and collaboration, engagement on the part of all the relevant parties to identify, create and sustain synergies and make the cultural shift that this is all calls for.

So, that is our conclusions, and now our recommendations.

Many of our presentations to date have included a discussion of two primary options for reorganization and, in our report, we characterize in some detail these two options.

First, a new institute focusing on addiction, or secondly, a trans-NIH initiative on addiction. We recommend again unanimously that one of these options be adopted and implemented and I want to discuss in a few minutes some of the strengths and weaknesses of each.

But, I would add that we are not recommending which of these two to do, but we will have a conversation and I think you will hear individual perspectives on one and another.

In terms of the first option, a new addiction institute. It would include addiction portfolios from across the NIH, drug

addiction research from NIDA, alcohol from NIAAA, tobacco from NCI, gambling addiction from NIDA and NIMH. This is something that we discussed at substantial length.

NIH will need to conduct an agency-wide portfolio analysis to determine which addiction-related programs should be included in the new institute, to identify then what things currently done in these two institutes would have to go somewhere else, because the non-addiction research activities would need to go somewhere else, perhaps alcohol liver disease reassigned to NIDDK, and perhaps fetal alcohol spectrum disorders research to NICHD for example.

Funding for each of these portfolios should not be diminished, but merely transferred to the new institute for addiction research or to another institute for non-addiction research.

Establishing this new institute would require the recruitment of a new

director and will need people, personnel of course, and we assume and recommend that staff would be transferred from the existing two institutes. There may be a need to hire new staff to achieve the new mission. There will need to be a new strategic plan of course.

And, given the long process for identifying and appointing a new director, there ought to be a transition committee to oversee the process, to do the NIH-wide portfolio analysis, to develop the organizational structure, to establish a time-line and so on.

The reason for laying out these points is to give readers of the report and listeners today a sense of what this would really be like, or might well be like.

So, let me turn to the second option, a new trans-NIH initiative on addiction. Our idea is to have this modeled after the two very successful NIH Blueprint for Neuroscience Research of the new OppNet

for Behavioral and Social Science Research.

This initiative, we believe, would need to be larger in scale and investment than either of those two examples. And you see what additional things would be brought into this trans-NIH initiative on addiction.

To be successful, it would have to have stable and dedicated funding. Several members of the working group put forward the notion of a majority of each institute's addiction funds would need to be devoted to this project. The Office of the Director would need to contribute as well. A larger investment than the blueprint means would be a big deal, with staff support from the two existing institutes and an evaluation plan et cetera.

The basic organization of this initiative would include a steering committee with IC directors from the relative institutes and perhaps some others, working groups tasked with carrying out the various important

activities to bring this off and then manage it over time.

Let me summarize, if I might, the arguments in favor of first one and then the other option. In regards to a new institute, proponents of this approach find the scientific evidence and the public health needs compelling, so compelling as to undertake this structural reorganization.

In their view, the scientific and public health goals can't be met by the trans-NIH initiative that I explained a moment ago.

On a related note, there is a some sense that the divergence of the two scientific communities is so severe, so siloed, that it can only be remedied by forcing them together with the establishment of a new institute.

And finally, the new institute would enable effective promotion of some high priority areas. Research on polysubstance abuse or understanding adolescent use, or

promoting the public health message that alcohol and drugs can have similar effects on the brain and body, for example.

On the side of favoring the new trans-NIH initiative, proponents have said that the evidence of the scientific opportunity and public health needs is compelling, but there is a major question as to whether a new institute is the best way to proceed.

But rather, would suggest that the trans-NIH initiative would be just as successful and, building on these two examples that I have already cited, there is evidence for such trans-NIH initiatives accomplishing what was sought.

There is also some fear that establishing a new institute would create research gaps, in particular in the alcohol portfolio. Over the course of our deliberations, we have discussed and carefully considered the cost-benefit of establishing a

new institute. Implementing that option would be a significant undertaking and would require considerable effort.

It might also cause considerable disruption in the research community, at least in the short term, and we are concerned that the benefits of a new addiction institute are outweighed by the burden of establishing it, especially given that the trans-NIH initiative would allow the agency to address science and public health needs in much the same regard.

The trans-NIH initiative would be inherently interdisciplinary, bringing unique perspectives to the table to focus in a coordinated way, we would hope, on these important issues.

So, that is what we have spent the last almost year and a half talking about and discussing and I would be happy to answer any questions if you would, or Norm, I think it is time for the full board to discuss this.

CHAIR AUGUSTINE: Okay. Bill, thank

you and thank your group. You have all had a chance to read the report, which is, as you saw, very extensive. I thought it was extremely well written. So we do have time for some questions and Steve I see your hand there.

MEMBER KATZ: Right. Thank you. I thought your report was very well written as well, without really a firm recommendation one way or the other. I have two questions. The first is was there a recommendation if there is a functional -- if that is the recommendation -- was there some time-line to assess what is happening or was that just left open? Was that discussed?

MEMBER ROPER: How long to try it, you mean?

MEMBER KATZ: How long to try it and how to evaluate what --

MEMBER ROPER: Yes. Yes. We did talk about that at some length and, I think, it's our view that it would need to be given

at least three years, or on that order, meaning it would take a while to get it geared up and then to give it a chance to prove its worth, and then to the question of what are the criteria by which it will be judged?

We talked some about that but we didn't array it in great detail.

MEMBER KATZ: And the second question Bill, is how did the group -- obviously you all dealt with this for a very long time -- how did the group come out in terms of the one or the other, or was it just split down the middle?

MEMBER ROPER: There are eight of us and, I think on a good day, we split pretty well down the middle. I'd be happy for people to speak on each of their own perspectives, but we polled the group, I polled the group many times, and there were times when it was six to two, or four to four, or two to six, or whatever, but we were pretty split on this.

I think, if I can be more

forthcoming to you and especially to Francis, the best way I can formulate the question is what I touched on in one of the slides towards the end, and that is, is this the issue that rises to the level of the director and your time and attention and involvement? Is this what you want to make one of your three or four things to get done in the next year or so here at the NIH?

Some of us, and I am just going to be candid and speak just for myself, believe that the answer to that is no, that given the projects on your desk -- let me be clear, I am speaking for myself, not for the working group -- the things on your desk, I would not encourage you to take on a structural reorganization of merging these two institutes.

But, there is compelling information that says if it could be done, good would result. It is just a question of is the -- to use an overly trite expression, is

the juice worth the squeeze right now?

CHAIR AUGUSTINE: Let's see, I saw Harold and then myself.

MEMBER VARMUS: Well, having sat where Francis is now sitting, I don't understand why you think this would take so much time. There's obviously some problems to work out, but from everything I have heard, it sounds like the new institute is the way to go and I just don't -- Francis is already doing a lot of things, as are we all, and most of those things that we are doing clearly are much more time consuming than this ought to be.

You have outlined a pretty good plan for how to do it. We know, in general, what programs are being moved around. Yes, it would take a few meetings and the good will of people who are involved, but it doesn't seem to me that Francis' attempt to do translational research and build a global health agenda are going to be undermined by

taking on what, I think, would be an important, but only moderately exertional task.

MEMBER ROPER: Well, Harold, I just would ask others from the group if they want to comment. I would say that you have done a very good job of describing what led many of our group to say let's get on with it. It's a pretty close call. I wouldn't say it is overwhelming. I am going to sit down if I could and then I will just join in the conversation from there.

CHAIR AUGUSTINE: Okay. Bill?

MEMBER BRODY: So, Harold, I approach this as a slam dunk. I mean this was obvious that you would merge the two institutions, without any data. And then we gather the -- and I was not on the subcommittee -- gathered data, but as this whole thing unfolded, I think yesterday somebody made the comment you can -- it's hard to herd cats but you can move the food.

But, the difficulty is --

MEMBER KATZ: That was Francis.

(Laughter.)

MEMBER ROPER: But, in this case, you know a lot of the angst and vehemence and perceptions came from the external community, where you really can't move the food bowl. I think, within the NIH, yes I would agree there would be disruptions and dislocations, but in the end, everybody will follow because the budgets are there.

But, I was struck by the deep-felt, deeply-held feelings of the alcohol community that this would be a horrific mistake and so where I would come down on this is to give this a chance to do the functional integration, you know, perfect is the enemy of the good, but that might be a better way to approach.

Meanwhile, also to give the external community some reassurance that life will go on in this transition and then if it

works great, if it doesn't then you can take the nuclear option.

MEMBER ROPER: Can I make one other point that I should have made earlier to Harold's good point? Again, speaking just for myself, if this were to be taken on, and there is an argument and you have done a good job of making it, I think that argument is much more far-reaching than just merging these two institutes. I believe you earlier made this point.

But, I would go from 30 to 10 institutes and, you know, really have at it and make some significant change.

CHAIR AUGUSTINE: Go ahead.

MEMBER VARMUS: Ten years ago, I did make an argument for six institutes and I would be happy to make that argument again, but that is not on the table today. I think, what was the result of the furor that I caused by making this drastic, but I think actually quite reasonable suggestion, was to try some

things that looked like low-hanging fruit, things that really made sense, could be rationalized scientifically, and would really improve things.

There will be resistance to that, because what is at stake in the minds of some is whether I am still going to get my grants, whether the money will still be there for my programs and this is a place where a group like this needs to exercise leadership and judgment and obviously there is going to be anxiety about making any change that might affect whether individuals have the programs and access to funds that they want to have.

And, I think, the group has done a good job of identifying the sources of those anxieties, saying these programs to have the support that they need -- institutes, including mine, would probably see some cost-shifting if we created a new institution. Frankly, we are prepared to do that. I think it sounds like the right thing and I think

just to say, you know, I understand what Bill is feeling, because when I offered my proposals 10 years ago there were a lot of people shooting at me, and you know, nobody likes to be shot at.

But, I can just tell you from my experience as director in trying to establish collaborative inter-institute programs that depended upon good will and these things have a limited lifetime that there is no assurance -- they may have vulnerabilities of their own. I am not sure the functional test that we are talking about, having a trans-NIH addiction initiative, would actually tell you whether it would be better to go ahead and make a new institute.

I am not sure it's the right test and that could fail for reasons that I don't know what the metric is for judging whether this is satisfactory. It might fail. Is that a reason to have the new institute? Possibly not. I don't know how you would evaluate what

these functional Band-Aids would do. I think they are very much less than half-way measures to doing what ought to be done.

CHAIR AUGUSTINE: Tom and then me.

MEMBER KELLY: You know, I thought the report was really extraordinarily well done and made a very compelling case on the basis of the science, at least that the creation of a new institute would probably be the best route.

And I guess it is not completely clear to me that there is a huge delta in terms of effort of going down one route versus the other.

I mean, if we are truly going to have a -- fix this, some kind of a trans-NIH initiative that is going to be truly effective and actually get the scientific synergies we want, that is going to take an enormous effort as well, especially given the resistance that is apparent here.

I think it is probably unlikely

that going the second route will really achieve the results that the committee wants to achieve, which is to really change how addiction research is organized and functions in NIH and so, I view it as really sort of postponing the decision for a merger, which is probably the best outcome, then perhaps we should not do that.

CHAIR AUGUSTINE: Thank you Tom. I had two questions Bill for you. The first one is that all of the members of your group, you indicated, felt the status quo was not the appropriate circumstance, but there was a split between option one and option two.

Were there those who believed that the option that they didn't prefer just wasn't workable, or was it strictly a matter of believing that they had one option they thought would be better than the other?

That's my first question and well why don't you take that and I have got one other to follow on.

MEMBER ROPER: Since most of them are here, I would prefer them speak for themselves and I meant and should have asked them to do that in general about whether I fairly summarized the group, so maybe I would just invite them to answer your question.

CHAIR AUGUSTINE: Fine.

MEMBER ZOGHBI: I will be happy to start. I think, I just want to reiterate that the reasons to merge the two institutes are scientifically driven, public health driven, objectively driven. Most of the arguments we felt against -- we heard against, really rest on two issues: one issue that alcohol is not a drug. We don't want the stigma.

And the truth is, in teenagers and adolescents, alcohol is illegal and it is a drug and this is the double message we send to the youth, so at least for someone really thinking about it from public health, if you are really going to educate youth that alcohol is bad, you have to put it in the same

category.

For its age group, it is just as bad for the brain. And then, there are all the scientific reasons. They are well delineated in the report.

The second big reason was a fear that alcohol has so many other effects on health and other organs, that those would be lost by a merged institute and the truth of the matter, the science will be better on a brain or fetal alcohol syndrome or a developmental disorder section of child health or in liver disease or whatever disease, the effect of cancer, all these will be much more really dealt with deeply, in a more integrated way, if they belong in another institute where that institute has rigorous science going on.

So, to me, the two major sort of arguments for the non-merger, I think, the reasons are not there. And last, but not least, to do a real successful trans-NIH initiative, that means the majority of the

addiction money in any one institute, which means a large sum of the alcohol institute money, over 50 percent or more of their budget, if you look how much of their budget is addiction, has to go to that trans-NIH initiatives.

And that is really structurally quite a challenge to now start moving them from their very institute, so it is much cleaner and simpler, as Harold just stated, to merge the two institutes. So. this was my rationale, why I preferred the merged institute option.

CHAIR AUGUSTINE: Richard.

MEMBER HODES: As I recall, the evolution, we went from six to two, to five to three, to four to four, probably, not to give the impression that we were vacillating a lot --

MEMBER VARMUS: Six-two for the merger?

MEMBER HODES: No. It started as

only two for the merger and six were functional, so I guess self confessional is permitted. I was one of the six who thought that frankly, if this was being -- that simply the merger of these two institutes was in the context of addiction a half measure. If it was a convenient way to start down the line, but look -- pardon the rephrasing here -- but the low-hanging fruit, you know, I was not impressed that that was high motive.

So actually, a couple of us raised the question about taking this more broadly. If this was seriously being science-based, and we look at addiction across all of NIH, didn't we agree that this was really the goal? Once we got there, to me it was no longer a half measure and I also became concerned about how the functional measure would work now across so many institutes.

So, I am a big fan and participant in the neuroscience blueprint. Nonetheless, there is a big difference between seeing two

institutes putting a substantial part of their money into a functional rearrangement and now seeing three, four, five.

So, it was a combination of seeing this as a more rigorously science-based, trans-NIH, rearrangement, weighed against what it appeared to me would be a more challenging functional solution involving components from so many institutes, and that was the evolution of my own thinking.

CHAIR AUGUSTINE: Thank you.

MEMBER ROPER: Can I just add a point? She should be here to represent herself, but Josie Briggs is a member of our group and I think what Richard said was pretty much Josie's views as well.

CHAIR AUGUSTINE: Gene?

MEMBER WASHINGTON: Yes. I don't know where I was in the beginning, but at the end I was still in the trans-NIH group and principally for the reasons that Bill just articulated. First Bill, you did represent, at

least to my view, sort of the balance in terms of the discussion.

But, at the end for me -- and Harold you are right, there is no way to do a randomized clinical trial here and I felt that the functional solution would work. I felt like we had no evidence that the structure one would work any more effectively, given what was perceived as being some of the resistance that it would cause, not just internally but externally, and some of the disruption that it might cause, and that one approach would be to in fact see if this works, thinking of it in an evolutionary way. And if it worked, meaning that we saw that there was an improvement in the science in particular, then there would be no reason to take on the additional burden of overcoming resistance and the disruption that it might cause.

So, at the end I came down on the side of the functional.

CHAIR AUGUSTINE: Steve.

MEMBER KATZ: So I am still coming down, but my question to me Gene is really similar to what I asked Bill and that is how is that assessment going to be done? In other words, if it's two years or three years, when you say "improved science," how -- what is the metric?

MEMBER TABAK: Do I have permission from my boss to revert to my old role for about two minutes?

DIRECTOR COLLINS: Permission granted.

MEMBER TABAK: So I was --

MEMBER ROPER: And Larry, let me just do my part to day Griff and Debbie need to talk after you do. Go ahead.

MEMBER KATZ: Are you going to address that, the metric?

MEMBER TABAK: Well, indeed. So whilst director of NIDCR I as a member of this subgroup and no longer am a member of the subgroup I guess.

The problem, Steve, is -- Huda made some comments about the quality of the science and I respect her as a scientist enormously. But frankly, I am not prepared to say that the science being conducted at AAA is any better or worse than any other institute at NIH.

And I would love to see the data that proves it one way or the other. Beauty is in the eye of the beholder. The angst and capital that will have to be expended is not really internal. You are right, Harold. You do it. People squawk and whatnot, but internally that is not the issue.

The issue is externally, and those of us on the subcommittee who listened to many, many, many, many, many individuals describe their angst. And what was the angst all about? The angst is about how many loci of decision-making do you have? It is going to be a person making the decision, or is it going to be two people? And if it's one person

making the decision, the possibility exists that what they hold dear and think is very, very important scientifically, will go away.

It doesn't mean it will, but that is what the angst is all about. Now, I think there is a lot less angst about a functional merger, because you still have the failsafe of having two different people making decisions, okay?

You may disagree with that view, but that is the reality. There are still two people making the decision. I think the angst is less because people have observed the value added by the neuroscience blueprint. No doubt this would be more challenging because of the magnitude, but if you are really serious about merging all addictive research, then if you are going to do that, then you have to put NIMH on the table right now. Let's be honest. Harold already indicated there's a section of the NCI that would have to be put on the table.

So if that is what you really want to do, okay, then do that. But, let's not just pick out these two things because they are "low-hanging fruit."

Okay, last point. If we are going to go back to the original three institutes, I think that is a great idea.

MEMBER HODES: Just to clarify. The two recommendations, I think, actually both involved the trans-NIH all institutes involved, that was not a distinction any longer between the two.

MEMBER ROPER: Richard is right.

CHAIR AUGUSTINE: Let's see. I saw Gene and then Griff.

MEMBER WASHINGTON: My thinking was that whether we went with structural of functional you had to come up with some metric of success and my thought was that that in fact would be a task, one of the first tasks of whichever approach was taken. So, I don't see where one is different form the other, in

the case of the structural, likewise there would be some metrics and if it wasn't that, there would be have to be some remedial action taken.

And so, I don't see the difference.

CHAIR AUGUSTINE: Griff.

MEMBER RODGERS: Can I just make a point? The -- this has truly been sort of an evolutionary effort, and certainly initially with the idea of just really merging these two institutes just because of its convenience and the situation as existed, really -- the scientific argument notwithstanding it would appear more reasonable, that if you are going to have a single institute for addiction research, that all addiction research should be on the table.

And I think that is how we evolved and that is reflected in both of these options.

Bill was very good -- ecumenical -

- during these discussions with these various groups that we met with, to understand from their perspective, if a merger were to occur, what is your greatest angst? What would be lost?

And correspondingly, it was to ask the groups, if we don't merge, what is it you feel that we would absolutely need to be done in order to achieve the overall goal?

And I think that is the starting point for what the metrics would be in terms of understanding what would be needed to be accomplished in two or three years, whether the experiment is a success or not.

I think we have a lot of paper, several dozen trees were killed during this experiment, and I think you summarized it in about 15 slides. But, we actually have a number of action points that we could actually start with, in terms of what are the deliverables that one would likely see that would be a mark of success or failure over a

course of time, if this was done in a staged fashion.

CHAIR AUGUSTINE: Griff, you led into the second half of the question I wanted to ask actually, which I was going to ask you Bill, in the report you did lay out a set of conditions with regard to option two, that if not met would met would trigger going to the director and presumably then going to option one.

In other words, I kind of viewed as option two as being a conditional move where you could end up at option one. Option one was just let's go with it.

MEMBER ROPER: Yes. I think it could be undertaken in that fashion. You are right. Under either of these, and I have tried to say this, but I will just stress it, is from Francis and the folks in OD and across the institutes and centers and whatever, there would really have to be a serious effort to try to make this work and under either option,

to be sure.

I think Dr. Powell wanted to talk, Norman, if I could ask her?

MEMBER POWELL: Well, I think that the discussion from the members of the committee shows, I think the amount of work and energy and really considerable thought that went into this report, which I thought was a wonderful report and Bill really did a good job steering the committee.

And, I think, we all respected very much each other's opinions about this. We also, and I think maybe this point wasn't emphasized enough, in addition to the testimony that we heard over and over again, we read all of the reports that have been done about this question, over decades.

So, that this is not a new question. This is a question that has been before various groups and bodies for many, many, many years. And, I think, we came to the conclusion that the science has evolved

considerably over those years, so what might have been a very much simpler question several decades ago, was a very complex question now, which really brought us to the conclusion that addiction research with the real importance that it has for society, is a very important thing, and that the science of addiction research has really progressed and that we really felt something needed to be done about the spectrum of addiction research, which was much broader than merging two institutes, so it was not a simple question anymore.

And we thoughtfully considered it, and I think the pragmatic arguments that were made were very valid and very important ones. But, for myself, I think first of all, it is the time to make a decision, not a staged decision, but a decision, because this has been going on for a long time.

And I don't think a functional solution will work. I think small, functional initiatives like the neuroscience blueprint

have done good things. This is a major, major initiative, if it is to cross institutes without a structural reorganization.

So, I guess, my pragmatism is that it's -- for me if was time to do something definitive and it was really time to do something that I really thought scientifically would be to the benefit of the public, rather than simply tweaking around the edges.

CHAIR AUGUSTINE: Thank you. My understanding is that Dr. Shurin is on the line here. Is that correct? Not yet. She is dialing. Okay.

All right. Let's see. Gene and then Harold.

MEMBER WASHINGTON: No, I am done.

CHAIR AUGUSTINE: You are done.

MEMBER VARMUS: I am going to just speak briefly to a really critical point that Larry raised about this perception that it is one person versus two people making decisions.

It is more than just people, it is

also a budgetary number signed by Congress, and that is reflective of there being one versus two. And the argument that the decision is based on this idea that more might be better -- I am not saying you were making that argument but that is an argument that is being made -- could be applied and it has been applied over the years to proliferate the institutes.

Your institute of course is very easily divided into four, maybe even more, that we could have not one cancer institute. We have got institutes for various types of cancer. We could have an institute for mouse models of cancer. That would make me very happy.

In the appropriation process, in general, despite what everybody says, things more or less happen in lockstep. That means you end up with institutes locked into their budget priorities. I know there is occasional deviations, but not too often.

If you want to generate flexibility in responding to scientific opportunities and give institute directors more authority to do things that Congress is unlikely to do, I think there is an argument to be made when the scientific basis for making those decisions is appropriate, to do some lumping.

And, I think, this is a situation where there is a pretty broad agreement, even by those who would like to temporize with a functional solution, to the notion that this is an amalgamation that would work. And my view is that -- I agree entirely with what Deborah said, that this is a -- we have been talking about this for a dozen years and it is time to do the right thing.

CHAIR AUGUSTINE: Dan.

MEMBER GOLDIN: I deeply believe that it is time to do the right thing. I think a creeping solution of testing and with a functional and then waiting another five years

and having another team come in and review it again, would be a big mistake.

The science clearly is driving it and in science, things change. Going back always feels good. It feels comfortable. No one likes change. My biggest concern about a functional organization, I don't know how many billion it is -- 2, 3, 4 billion dollars, that is a very big organization to oversee with good will.

We talked this morning about the complexities of getting across the NIH mission to the public. And, in fact, I thought I had the right number. I quoted a number that 50 percent of the Americans don't know what the NIH is or does. I was corrected at lunch and told it is 85 percent.

Now, if we add a complexity to how the NIH is going to manage itself, and it is going to manage itself on good will, and it is addiction that needs to be addressed, you cannot address a complex issue of addiction

with three or four billion dollars a year through good will.

It is a no-brainer and, from my perspective, I also think of the constituencies. I could be wrong but what I hear is the constituency of concern are the people doing the research and if that is the case, I subscribe to our director's metaphor about move the food. And that everyone is not going to be happy, change is never comfortable.

But, unless this organization has a little backbone, and shows leadership, no change is ever going to occur.

CHAIR AUGUSTINE: Tony.

MEMBER FAUCI: Norm, I just have a question just to clarify the -- since I wasn't involved obviously in the subgroup discussion, but when we were talking about if you are going to merge, that you should, apropos of Larry's question, all of addiction research, not just two institutes. In the institutes

like Mental Health I can see that they are almost unable to separate addiction issues from mental health issues.

But, in the cancer institute, Harold, in the work that you are doing with tobacco, is it the physiological effects of tobacco and its relationship to cancer, or are you actually doing addiction research?

MEMBER VARMUS: It is behavioral as well.

MEMBER FAUCI: There is. Okay. So there would be some impact on --

MEMBER VARMUS: We would look at the portfolio carefully --

MEMBER ROPER: You would know the numbers but I think the amount of addiction research that you do is about the same size as what the NIDA, NIAAA do.

MEMBER VARMUS: I should have looked for numbers last night, didn't, I am sorry, but it is probably a significant number. Sorry.

CHAIR AUGUSTINE: Has everyone had a chance to weigh in that would like to? I would like to give Francis an opportunity, or Susan, are you on the line? Hello? All right. Francis, would you like to make any comments?

DIRECTOR COLLINS: Well, I think this discussion has been reflective of the challenge of what initially appeared to many of us as maybe one of the simplest examples of the organization that you could contemplate when you looked across NIH and yet, as you started looking a little harder, it wasn't as simple as it might have first appeared, certainly reflected by the fact that the advisory council of one of the institutes involved, NIDA, voted unanimously in favor of the structural option, whereas the advisory council of the other major institute, NIAAA, voted unanimously against it, which is a reflection of how strong the feelings are in the scientific community.

And again, I think there are

certainly elements there of anxiety about what happens to research funding for particular grantees and that is not what we are about here. We are about trying to support the best science.

I do think in some of the other meetings that were held and going along this long pathway, and Bill you did a fabulous job of leading this complicated story, and in a very thoughtful way.

There certainly were consumers also who had strong opinions about this and we shouldn't lose sight of that, and particularly groups like Mothers Against Drunk Driving who --

They were certainly strongly in the camp of wanting to have special attention to alcohol. But again, I am glad to see that during the course of the deliberations, the structural model expanded in the way that it has, because clearly if we are going to do something of that sort, and claim that it is

being driven by science, then it has to be driven by science, and that means addiction, which clearly touches other areas than these two institutes, has to be on the table. And I appreciate very much that evolutionary process in your discussion, which I think makes a lot more sense scientifically.

In terms of this sort of question of cost to the Director and others around him, making one choice or the other, well that really shouldn't be the defining issue here. I do think that a structural merger probably creates more of an eruption in the shorter term than what seems to be more of a temporizing measure and that is a reality that will need to be thought about.

I think this discussion around the table of the broader group has been very helpful, because I think to have a fresh look at this from those who have not been so completely embroiled in it over more than a year is exactly what needed to happen.

I think the opinions put on the table have been strong and well-defended. I am not prepared to say what the decision from my perspective ought to be, but I think you have given me all that I need to reach that conclusion and would intend to do so in the fairly near future.

CHAIR AUGUSTINE: Susan, are you on the line?

MEMBER SHURIN: Yes, I am.

CHAIR AUGUSTINE: Would you like to make a comment? We have been going around the table sort of giving everybody a chance to share their views.

MEMBER SHURIN: Well, I think a closer relationship on the science would be incredibly helpful and, I think, that it is really difficult to mandate any structural change. It ought to be driven by the scientific issues. Clearly, there is huge overlap of -- so I think these are institutions that have been in place for a

significant period of time and the evolutionary approach makes a lot of sense.

MEMBER ROPER: I was going to ask, Norm, if you want to turn to -- I think there's some folks in the audience who want to comment.

CHAIR AUGUSTINE: Yes, that is what I intended to do after all the members had had this opportunity. Let's do that at this point then.

MEMBER VARMUS: Could I ask a procedural question. Wherever we are headed with this discussion, are we going to approve the report as a well-written report, or are we going to take a position?

CHAIR AUGUSTINE: I think that is up to the group. Someone needs to make a motion Harold and we look forward to that.

MEMBER ROPER: If I may, and this is going to sound like I am making light of something and please don't anyone take offense, but there is an old joke that says

that somebody got up at the end of a public forum and said everything that needs to be said on this subject has been said, but not by me. And those of you in the public who do want to talk, I would just ask, if you don't think I fairly reflected your point of view, please tell us how we did not, but I would urge you not to remake all the points that we tried to make.

CHAIR AUGUSTINE: So we have six members of the public who have signed up. I am going to kind of enforce the five-minute rule here, so if you will forgive me, but it is appropriate the public get the last word in this discussion, just as you got one of the early words.

So, the first person is Mark Goldman, the Research Society on Alcoholism. There is a microphone right here.

DR. GOLDMAN: Okay, thank you all for allowing this comment. I am President-elect of the Research Society on Alcoholism.

You should also know as well that I served for three years on assignment as associate director of NIAAA from 2003 to 2006. I also was head before that time of the national task force on college student drinking and then was very involved in setting up the underage drinking initiative at NIAAA.

All of the points that I could make have been said around the table and as suggested, I won't repeat them. I think it should be obvious to you that RSA probably still does not feel that a structural merger is the right way to go.

But, let me address something that I think maybe goes a bit beyond what you have all talked about here. The report begins, very early, and I actually wrote it down I think, line 192, with discussion of addiction.

And the public health problem and I can speak to this because I worked on underage drinking, I worked on a lot of domains in which addiction is not the issue

despite the huge cost to the public domain.

And, in fact, not only is addiction not the issue, but addiction is not the endpoint of the issue. There are many people who will have problems in relation to the kinds of substance use and other kinds of things we talked about here who will never get to addiction. It's just not going to happen. The numbers are way higher than the number of people that are ever going to be called addicts.

So, in light of the issues that have to get addressed, I think I would like to broaden your scope in thinking a little bit when you are talking about putting pieces together for multiple institutes, that it is even perhaps larger than you are talking about, because it is not just addiction.

We are talking about developmental processes that don't have anything to do with addiction, but do lead to use of substances and behaviors that perhaps are not because of

substance challenges but rather because of behaviors intrinsic to people, to humans.

They have to do with epigenetic factors that are not because of the substance. You touched on gambling, but there are many, many others. And in fact the number seems to be ever-growing.

What we are really talking about here at the end of the day, is something that falls in the domain and I realize when I use this word, it is one certainly when I was in NIH was a bit touchy.

It's behavioral dysregulation. It's overdriven behavior that pops up in all kinds of places. So you mentioned OppNet, one player in this mix that has not been mentioned is OBSSR, where we are all talking about behavior, but we don't really have one of the major players in the room.

And I think that what I would encourage you to do and the reason I would still support, despite everything that has

been said, this more temporized approach if you will, is because I think the size of the scientific endeavor has not yet been fully handled.

In other words, it is a larger problem than addiction and its full scope has yet to be defined. All the institutes that might be players in this have yet to be named because of the nature of the problem that is being addressed and if you want to talk about science driving something, I think it is time for NIH to take head-on the notion that an awful lot of the cost that is still going on, the burden of disease in the United States and other places, has to do with behavioral choices that are not yet fully understood.

And, I think, the science could go on for some time expanding itself into what that domain actually is before, perhaps, a consolidation into a single entity that would handle that kind of problem. Having said that, thank you all.

CHAIR AUGUSTINE: Thank you very much. Tom Donaldson from the National Organization on Fetal Alcohol Syndrome.

MR. DONALDSON: Good afternoon Chairman Augustine and board members. Thank you very much for the opportunity to be with you. I was here in April of 2009 and expressed my angst as the director of the National Organization on FAS and on behalf of our constituents, and concern for a potential structural merger.

Fetal Alcohol Spectrum Disorders has had sort of an intuitive home at NIAAA for about 30, 35 years, and it has functioned very well, at least in my field. So naturally, consideration of disbanding NIAAA causes a great deal of concern and worry within our field.

It also seems to me that during the deliberations, that I heard often that drug and alcohol use was very common, that the prevalence of individuals who used both, if

you use one, you use the other. The research that we have looked after from NIAAA and operated on, doesn't show that at all, so I am concerned that that is still an open question that I hope we all consider.

We see that most people who use alcohol do not use drugs. Certainly women of child-bearing age that we work most closely with. I was struck in looking, in recalling the last meeting, a number of people seemed to say, in thinking of the process over the last 18 months, that they were surprised that the overlap wasn't as broad in the science.

And I haven't heard that here today, but that is something of course that we have always seen and we have always believed and I think sort of fits with the data from NIAAA that people use alcohol, that most of them don't use drugs.

In the report, I think that -- I am pleased that Fetal Alcohol Spectrum Disorders is mentioned. Right now, some of the

research is in the neuroscience and in the addiction area on FASD and some of it is not.

So, if there is an addiction entity, whether it is the structural change or it is the new initiative, in my field at least, there is then going to be a division. So, that comfort of being able to be informed, have our work informed by what NIAAA has found, will certainly be affected.

Perhaps a small consideration, but obviously in my area, of great concern. And the other thing that I was struck with is from the very beginning, the resistance from, yes, alcohol folks in the field, the researchers, patient groups, groups like mine, even internally.

That certainly seems to still exist. Hopefully, there would be good will if a decision was made one way or the other, but it would be a concern. So lastly, it was mentioned that -- by a board member that we have all have the courage to make the decision

today, also I hope the wisdom. Include that in your deliberations. I know you will.

And, for what it is worth, from my perspective, we are pleased and I think a great credit to the board, Chairman Roper, and the work group to come up with the option for the trans-NIH functional change. I think that could be a great credit and could be made to work. Thank you very much.

CHAIR AUGUSTINE: Thank you very much. And the next speaker is James Jorkasky from the National Alliance for Eye and Vision Research.

MR. JORKASKY: Thank you Chairman Augustine. Late yesterday afternoon I was up here. I guess I was the only public commenter. But, I talked a little bit about the vision research arena, the National Eye Institute work -- by the way I am with the National Alliance for Eye and Vision Research, which serves as the Friends of the National Eye Institute. We don't speak for the NEI. We

speak about its accomplishments.

And yesterday, I spoke about its accomplishments in the translational research arena, as Dr. Varmus would say, the rich repertoire of patient solutions that it has shown in both front of the eye or corneal research, and back of the eye or retinal research.

Well, why am I back up here again talking about alcohol and drug? Simply, because NAEVR maintains that the breadth of what I spoke about yesterday in terms of NEI's deliverables over the last 40 years, as a freestanding institute, pulled out of the old national institute for neurological disease and blindness, would likely not have happened, particularly in the non-brain arena, that is related to front of the eye, eye disease and vision impairment.

As I commented to you in May earlier this year, NAEVR opposes the concept of the mergers, and again, I have spoken to my

colleagues in the alcohol research arena, and I am concerned, they are expressing similar to what we have expressed in the past, that a portion of the research could go away based upon a merger. Thank you.

CHAIR AUGUSTINE: Thank you for those thoughts. The next speaker is Stephanie O'Malley with the Research Society on Alcoholism.

DR. O'MALLEY: Good afternoon. Thank you for this opportunity to speak with you briefly today on behalf of the Research Society on Alcoholism, and I think many of the comments have been made already and they are included in the report, which is clearly a large undertaking by this committee.

The Research Society on Alcoholism is certainly in favor of the functional reorganization, and it is for scientific reasons as well as reasons of meeting the needs of the constituents.

I think that it is critical to

know that alcohol is more than addiction. But, I think the part that I would want to emphasize is that there is some real value to having an institute that encompasses different aspects of alcohol use and addiction as well.

And my analogy would be, as a participant in the trans-disciplinary tobacco use research centers, which was a collaborative venture between NCI, NIDA and NIAAA, that the emphasis was on the idea that you had to have depth within your own discipline or your own area to be able to collaborate across disciplines.

And if I were to think about investigators at NIDDK who are working on the problems of obesity or behavioral dyscontrol of eating, their work would not be as good if they were disconnected from the work that is going on in metabolism and other areas of food intake that they get through that participation in that institute.

So with this, I really believe

that the functional approach can address research on addiction while preserving the expertise and dialogue on the effects of alcohol on multiple organ systems within the alcohol research community and the dysfunctional approach will provide greater flexibility, ultimately, to approach problems that come up and new opportunities.

So with this I would like to stop and thank you very much for your attention.

CHAIR AUGUSTINE: And we thank you. The next speaker is Lyle Dennis with the AASLD.

MR. DENNIS: Thank you, Mr. Chairman. I think I am the last speaker. Oh one more, okay, so I don't get all 15 minutes. It was just a thought. All right, so I will take seven and a half. Mr. Chairman, my name is Lyle Dennis. I am a partner at Cavarocchi Ruscio and Dennis Associates and I have been privileged to represent the American Association for the Study of Liver Diseases

for the past 14 years.

As you know, because I have testified before this group before, the AASLD is the leading organization of researchers and clinicians in liver disease and liver wellness in the world and the members are deeply involved in alcohol-related liver research.

The association's position essentially has not changed since I first spoke to you in April of 2009. We are opposed to merging NIAAA and NIDA or any other action that would undermine the unique portfolio of life-saving liver disease research, which currently is supported solely by NIAAA.

Members of the AASLD believe that any action that is taken by the SMRB and ultimately by Dr. Collins must clearly benefit patients. They don't conduct research for research's sake. They do it to keep healthy people well and make sick people better. And if merging these two institutes does not specifically -- as well as the other steps

that may be taken -- does not specifically enhance that mission, or it may even impair it, then it ought not to be done.

There are 18 institutes, centers and offices at NIH that are currently involved in liver disease research. We consider that to be a strength of the system, not a weakness. I will make just a couple of quick points and then I want to address one point that was raised earlier.

About two million Americans suffer from alcohol-related liver disease. More than 30,000 die from it every year. About 100 people a day. About the number of people in this room will die today from alcohol-related liver disease.

It is heavily -- it heavily interacts with hepatitis C and hepatitis B and you are going to be seeing some reports in the very near future on those two subjects following up on the IOM report about the effects of alcohol with regard to people with

hepatitis B and C and in fact it is believed to be a co-factor driving disease progression and the risk of liver cancer even when consumed in very modest amounts.

NIAAA is the sole source of extramural NIH funding on alcohol liver research, although NIDDK is -- I am going to get presumptuous now and talk about NIDDK, as if the director were not six feet away from me -- although NIDDK's research portfolio is six times larger than NIAAA's, alcohol related research is only done by NIAAA. And the result of that focus has led to some significant scientific milestones over the years.

The report acknowledges these points, which we have made both at the SUAA and before this board, but in one section suggests that the research could simply be moved to NIDDK and this is where I am going to get presumptuous now.

AASLD has some problems with that notion. First, in an era in which the Office

of Management and Budget is asking the NIH to present an FY'12 budget with a five percent reduction, actual dollar reduction in spending, that creates a very easy place to remove some money, essentially moving the portfolio but not moving the money.

Secondly, scientists recognize that a systems biology approach is essential to study alcohol's interconnected effects on the brain and other organs, an addiction institute would certainly not be involved in that type of research that involves the liver but also the heart, the pancreas, the immune system and others.

Just to summarize, AASLD would urge the adoption of a functional approach to addressing concerns about addiction research while leaving the remaining end-organ damage research in its current successful mode. If you go forward with a structural merger, it would be impractical then to go back to the current system.

But, if you merge certain functions, you can reassess the quality of that research you have discussed and for a reasonable period of time, and reconsider a structural merger at that time if it is necessary.

I would just say one other very quick point, because I am still under my five minutes, which is on the issue of the burden on the director of NIH -- I am getting presumptuous again, talking about people as if they are not here -- on the issue of the burden, one of the differences between this and some of the other burdens is that under the statute, there is a 180 day congressional review period, and if elements of the community turn this into an issue, I am afraid that we may have the director of NIH up on Capitol Hill testifying before 14 additional committees beyond the ones that he normally has to testify before.

So, on that basis, I will stop and

thank you for all the kindnesses that the board and the SUAA have extended to AASLD over the last six 16 months. Thank you.

CHAIR AUGUSTINE: Thank you for sharing those views. And our last speaker is Mack Mitchell form Johns Hopkins. Dr. Mitchell?

DR. MITCHELL: Good afternoon. I want to start by thanking the committee for some very thoughtful deliberations that I know have taken place over the last year.

I want to just say in introduction that I have a background in alcohol research having started my career in that field more than 25 years ago, but my primary role today is really taking care of patients.

I spend the vast majority of my time today taking care of patients with liver diseases as well as other gastrointestinal diseases. And so, in that context, I do often see patients who have both alcohol and substance abuse issues. But, I also, as an

internist, see a lot of patients who come to me with concerns about their alcohol consumption that have nothing to do with concerns about addiction, or even how it might have caused liver damage.

They really come to me seeking advice about what they should do with their behavior of drinking alcohol and how that might really impact their risk of other diseases, particularly coronary heart disease, and diabetes, which are still two of the primary conditions that affect the majority of people here in the United States.

When I talk with those people and I try to explain to them what the risks are of their consumption or what benefits there might be associated with that, I rely very heavily on research that has been sponsored by the NIAAA. The NIAAA over the years has taken a real lead role, not only in looking at alcohol and its properties of addiction, but also looking at the entire spectrum of alcohol use

and trying to assess how that impacts on health and behavior.

And I think that is a very important aspect of what the research portfolio of NIAAA has offered us.

I also know that when I talk to these people, they are really not concerned entirely you know with the issue of addiction although that is a very important public health problem and I do think that a functional reorganization that stresses addiction would be a way to enhance what the public knows and understands about addiction.

But, at the same time, I think that if we were to say to the American public that the NIH no longer has an institute that is devoted to the study of alcohol, that would be disappointing news that I would have to take to my patients and also to many other people in the public.

So, I really hope that the committee will, as someone said earlier, do

the right thing and vote in favor of a functional merger where we can have both our cake and eat it too, in other words we can have more of an emphasis on addiction, so that the public really sees that as an important issue.

But, at the same time, we do not lose the benefits of what we have learned about all of the other aspects of alcohol consumption on health and behavior. Thank you.

CHAIR AUGUSTINE: Thank you very much and I thank all the members of the public again for sharing your views.

MEMBER ROPER: I just want to say that on behalf of the working group, I think what you have just seen the last, whatever time this is, 45 minutes or an hour, is a fair reflection of what our year and a half has been like and I appreciate everybody's respectful hearing and conversation so I turn it over to you.

CHAIR AUGUSTINE: And I will be

back to you, Bill, but I had a --

MEMBER BRODY: Just a question. Procedurally, what are we going -- are we going to vote on the two options to get a straw poll or a real vote or --

CHAIR AUGUSTINE: You are about one second ahead of me here. I want to ask two questions of our general counsel that advises us here. The first question is Dr. Shurin is on the telephone and I assume that she can vote. Is that correct? She left. She sent me an email with her vote. Can we count that?

MS. MCGAREY: Oh okay, I didn't realize, yes.

CHAIR AUGUSTINE: Can we count her vote?

MS. MCGAREY: I believe so, yes, but we have to look and see if proxies are allowed. No, I agree, I think this is probably advice in advance of any motion. Right.

CHAIR AUGUSTINE: I am just trying to get the ground rules here.

MS. MCGAREY: Okay, I will get back to you. Quickly.

CHAIR AUGUSTINE: Okay, we will find out. The second question I had for the counsel is there are two ways we can handle this. One, we can get somebody to make a motion and vote it up or down and then let the other one go.

The second thing we can do is just vote option 1 or option 2 without getting a formal motion. The latter would be easier but is that okay?

MS. MCGAREY: I didn't bring my rules with me. In other words, you are saying can you vote without a motion to consider the two options?

CHAIR AUGUSTINE: That is what I am saying.

MS. MCGAREY: Yes. I think you have discretion to -- you are the chair.

MEMBER KATZ: It's voting on two recommendations. Either it is going to be one

recommendation or the other one.

MS. MCGAREY: The working group --

MEMBER WASHINGTON: Just for the record, there is a third option.

CHAIR AUGUSTINE: Don't vote.

MEMBER WASHINGTON: No. No, which is where I thought, actually I thought where we were, and maybe I am just -- I was not clued into the discussion but I thought we were saying to the board that we recommend these two options for Francis to, in fact, do his due diligence and further analysis and make a decision.

CHAIR AUGUSTINE: Okay.

MEMBER ROPER: Gene, if I could answer that, at least from my perspective, we did have that conversation. You didn't dream that up. But, I am inferring from body language as much as anything else, that the NIH leadership would like us to go ahead and declare more plainly what we are in favor of. So --

CHAIR AUGUSTINE: I think we better do it by the book even though it is more complicated, so the Chair would welcome a motion, first of all with regard to the group's sentiments on whether the current process needs changed. Would anyone want to make that motion?

MEMBER ROPER: So moved.

CHAIR AUGUSTINE: Is there a second?

MEMBER GOLDIN: Second.

CHAIR AUGUSTINE: Okay. All those in favor of the motion -- is there discussion, further discussion? All those in favor of the motion please raise your right hand where we can see it clearly.

(A show of hands.)

CHAIR AUGUSTINE: That looks like it -- could you --

MEMBER TABAK: I can't vote because I no longer have that role, so I can -- one way or the other.

CHAIR AUGUSTINE: Will you count the votes? Will counsel or somebody count them? It is unanimous I think. Is anybody voting against? All those opposed? That is unanimous. Okay, would anyone want to make another motion? Harold.

MEMBER VARMUS: I would like to move that we create a new institute of addiction.

CHAIR AUGUSTINE: Okay. A motion has been made. Is there a second?

MEMBER GOLDIN: Second.

CHAIR AUGUSTINE: All right. Is there further discussion?

COURT REPORTER: Who seconded?

CHAIR AUGUSTINE: Goldin.

MS. MCGAREY: Can I make a suggestion? Do you want to amend your motion that you recommend to the director? I think you said that we create --

CHAIR AUGUSTINE: Yes that is --

MS. MCGAREY: I thought I heard --

CHAIR AUGUSTINE: Okay, it's recommend is I'm sure what you --

MEMBER VARMUS: It's recommend.

CHAIR AUGUSTINE: We are not going to usurp his position here today. All right.

MEMBER FAUCI: It was just -- it has been discussed but the recommendation of an institute, a merged institute, all the discussion about what goes into it is a different story. It is just a straightforward recommendation, is that correct?

CHAIR AUGUSTINE: No, my assumption is you are talking about option 1, basically.

MEMBER FAUCI: Right. Right. Create a merged institute.

CHAIR AUGUSTINE: As described in the report as option 1.

MEMBER KATZ: With all the accoutrements. With all the accoutrements.

MEMBER ROPER: Which would include other institutes on addiction.

MEMBER GOLDIN: If he words it as

option 1, we are in business.

CHAIR AUGUSTINE: Right. Harold, do you want to move option 1?

MEMBER VARMUS: Yes.

CHAIR AUGUSTINE: And Dan, do you accept that change, or that interpretation?

MEMBER GOLDIN: I accept the change.

CHAIR AUGUSTINE: Is there further discussion?

MEMBER BERG: One thing to consider, I mean, the motion that Harold made on addiction I think one should leave open the possibility of other descriptions such as addiction -- substance use, abuse and addiction.

MEMBER VARMUS: Yes. I didn't mean to give it a title.

MEMBER BERG: Right. But, addiction but also my suggestion that we should consider also including, in light of the discussion, substance use and abuse.

MEMBER VARMUS: I agree entirely with that.

CHAIR AUGUSTINE: Is there further discussion. Amy, my interpretation is that Susan votes no. Am I right?

EXECUTIVE SECRETARY PATTERSON: Yes.

CHAIR AUGUSTINE: Okay. Would all those in favor of the motion please raise your right hand so we can count it.

(A show of hands.)

Twelve. All those opposed.

(A show of hands.)

The motion carries 12-3 and let me just thank everybody for your reasonableness in dealing with this and the constructive approach people have taken. This is obviously not an easy one and it is not -- in my mind, it's a close decision.

And Bill, I thank you again for your leadership. I thank your committee for its work.

(Applause.)

MEMBER ROPER: I assure you, it's the pay that we got that made it worthwhile.

(Laughter.)

But, on a serious note I would say, again, the conversation today has fairly reflected what we have heard and lived with for the last year and a half and I think this has been a very carefully done process. I thank the whole board for that.

CHAIR AUGUSTINE: And I think at this point, it is a question of everybody getting behind and helping Francis deal with this in whatever fashion you deem appropriate.

And I am unaware of any other business to come before the group but let me just go around the table quickly, if anybody wants to add anything. Jeremy you want to say anything? Steve?

MEMBER KATZ: I would just like to ask, what actually happens now? Barbara said something about a 180-day period, what are the

rules for Francis here?

EXECUTIVE SECRETARY PATTERSON: Well, actually, I will call on Ben and Barbara to respond to this, but I would also just like to note for the record that this is advice to the NIH director. It is not a decision. So, there is a whole deliberative process.

CHAIR AUGUSTINE: Did that answer your question Steve?

MEMBER KATZ: No, I think --

MR. BUTLER: Sure. Under the statute there are various reporting triggers, I think it is fair to say that they are somewhat convoluted in how they are drafted and this will be our first time down this road, so we will sit down with the report. There will be a report from the board, I assume, and sit down with the director in the director's office and work through what steps are required and what steps are permissive.

But, it shouldn't -- certainly from our perspective, we wouldn't want the

procedural issues to impact the board's decision-making.

MEMBER FAUCI: Amy? Just can I ask a question related to that?

CHAIR AUGUSTINE: Sure.

EXECUTIVE SECRETARY PATTERSON: I just want to add that we will also prepare -- take the work group report, reflect the meeting today and the discussion so that it becomes a report of the full board so that it reflects the whole process.

So, that is one immediate next step. I'm sorry, Tony?

MEMBER FAUCI: I think I know the answer to this, but I want to make sure it's clear to me and to others. If Francis decides to take the recommendation of the board, would the creation of a single merged institute require congressional authorization?

MS. MCGAREY: No, the director and the Secretary of HHS have organizational authorities and that includes establishing or

abolishing institutes, so it is at the secretarial level. Congressional notification, yes.

CHAIR AUGUSTINE: Of course it might not allocate any funds, but --

MEMBER RODGERS: But, just to follow up on that question, wouldn't it be a requirement for the creation of a separate board, wouldn't that require a congressional action? A separate --

MS. MCGAREY: Advisory council?

MEMBER RODGERS: Advisory council.

MS. MCGAREY: We would have to look at that.

EXECUTIVE SECRETARY PATTERSON: And Barbara, can you just clarify, as part of the Department's notification of Congress, Congress has a specified time frame to come back to the agency or ask questions, or when is the -- when is this process stuff done?

MR. BUTLER: I think, Amy, that what you are referring to is, if at the

secretarial level, there is a consolidation or establishment or combining of institutes, there is generally a 180-day period where the report would go to Congress and Congress could decide to take further action or not, before it becomes effective.

MEMBER FAUCI: Because I think it's important for us to understand what might happen -- so let's say Francis agrees with the recommendation. The Secretary does the thing the Secretary is supposed to do. Can it -- other than what Norman alluded to, that the Congress decides not to fund it, which would be unusual, does this require an official congressional approval or not?

MEMBER ROPER: Tony, if I could answer you. We explored that at some length in the process and it does not. The appropriations subcommittees and in the appropriations committees are the two bodies in Congress, who will have to take note of this and alter their funding in the future.

But it doesn't have to be approved.

DIRECTOR COLLINS: But nothing prevents them from rejecting if they feel they want to object, of course.

CHAIR AUGUSTINE: Steve, did that take care of your question?

MEMBER KATZ: It did, yes.

CHAIR AUGUSTINE: Bill, do you want to add anything at all? No comments?

Come back -- Gene? Harold?

MEMBER VARMUS: I would like to add a point having to do with our discussion yesterday. Glad to see the floor today take a motion and make a decision. Yesterday, there was, I think, unanimity of opinion about an issue which we deferred to the next meeting for reasons, probably reasonable reasons, that Francis voiced.

I am concerned that the translational research initiative that we are discussing is a large, difficult murky one on which we may not have a report for longer than

we would like.

And I am concerned about seeing repeated deferral of a decision about the funding of the Clinical Center and attendant issues, because we don't have that other report on translational science.

I would like to think that we have some clear guidelines about -- funding the clinical centers is a very important issue and I would hate to see it deferred and deferred while we are waiting for a translational science report.

CHAIR AUGUSTINE: I have talked to Arthur about that issue and I will do so again. And if, in December, we discover it has slipped, which I hope it won't, we can address what we want to do.

MEMBER VARMUS: Okay, I just wanted to make sure we had that on the record.

CHAIR AUGUSTINE: It's a good point. Gail, do you have anything you want to add?

MEMBER CASSELL: No, in fact, all the impressions I have as a member of that group is we have a very specific charge. We have no alternative, but to be through with our report by December, right, Amy? Right, Francis?

MEMBER VARMUS: That part of it seemed clear. The questions we were trying to answer seemed less clear.

MEMBER CASSELL: Well, yes.

CHAIR AUGUSTINE: Griff? You have anything else you want to add? Anything? Do you want to add anything, Bill?

MEMBER ROPER: No, sir. We thank you for bringing this to a conclusion.

CHAIR AUGUSTINE: Dan?

MEMBER GOLDIN: I was very appreciative of what the committee did and the fact that they had the courage to bring us two options, I thought, was outstanding and I just wanted to thank them for that.

CHAIR AUGUSTINE: Tony?

MEMBER FAUCI: Nothing to add.

CHAIR AUGUSTINE: Okay, the last word Francis is all yours.

DIRECTOR COLLINS: Well Norm, you quoted Shakespeare yesterday and I don't have a quote but it does seem to me we have been living through a bit of a Shakespearean play here, which had a lot of early acts in terms of deliberations and uncertainties about where it was going to go.

And today, with the addiction and substance use issue, I think we got to the climax of this particular bit of theater. But, that is Act 4 and now it seems Act 5 falls back on the shoulders of the director to figure out exactly how do you take that climax and bring it to a conclusion that leaves everybody walking out of the theater going, well, that was worthwhile spending our time there.

We shall see whether Act 5 lives up to that expectation. And meanwhile, we have

TMAT barely into Act 1 with a very short rehearsal period, so it will be interesting to see what happens in the next couple of months.

In that regard, I just want to say thank you to everybody who has put their time into getting us this far and whose time will now be called upon in a very intense way to try to get us to this decision by December, a recommendation about where to go with translational research.

Because I agree completely with Harold, this can't slip and, if there is an issue here about whether the charge is precise enough, then we need to deal with that as well and maybe try to be realistic about the level of specificity that can be achieved in that timetable and not get so far down into the details that we drown in them.

And I hear the concerns about that from yesterday and I know Arthur did as well.

And I am pretty optimistic that based on the track record of this group and

their willingness to be both wise and hardworking, that we will have something pretty interesting by December.

So and Norm, thank you again for being the one who makes all of these things happen by your remarkable leadership.

CHAIR AUGUSTINE: This is the one here. Francis, thank you very much and a special thanks to those who are here form the public. I realize that some of these results are perhaps disappointing to you. I hope you realize they were reached in good faith and we appreciate your interest in being here today.

If there is no further business to come before the group, Gene.

MEMBER WASHINGTON: I want to publicly acknowledge Amy and her colleagues.

(Applause.)

CHAIR AUGUSTINE: Everyone have a safe trip. Oh, excuse me.

MEMBER GOLDIN: One more piece of business. I would like to know what the third

assignment for Arthur is going to be.

CHAIR AUGUSTINE: Right, okay the meeting is adjourned, safe trip home.

(Whereupon the above-entitled matter adjourned for the day at 1:53 p.m.)