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Opportunities and Challenges in the Emerging Field of Synthetic Biology

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P R O C E E D I N G S (8:30 a.m.)

Agenda Item: Welcome – Charles M. Vest

DR. VEST: Good morning, everyone. I'm Chuck Vest, President of the National Academy of Engineering. And since we're here in Washington, how many of you know why the United States Capitol is located where it is? One person. This is good. Two, two people. Well, John F. Kennedy, when he was president of the United States, explained that the Capitol had been located here in the middle of the East Coast so that our work could combine the charm of the North with the efficiency of the South.

So in that sense of efficiency, I'm here to welcome you to this meeting when it's halfway done. But it is really a great privilege to have all of you gathered here at the National Academies to do something that I think is very important, and I'd like to explain at least a little bit while I feel that way.

Back in the sort of early to mid-90s when I was serving as president of MIT, I got a call one day from a great friend, the late Michael Dertouzos who many of you may have known who was head of the Laboratory for Computer

Science, and he said, Chuck, you know all this stuff about Al Gore and the U.S. National Super Highway, and I said, yeah, I've got a basic idea about what it's about. He said, well, let me tell you, that's not the real action is. The real action's something called the Worldwide Web. This doesn't have anything to do with the United States. What's going to happen is going to happen globally. And there's this guy called Tim Berners-Lee over at CERN in Europe, and he's conceived this idea that he calls the Worldwide Web and this is really important, and I want you to get on an airplane with me next week and we're going over to Brussels and negotiate bring Tim back to MIT in order to start a consortium to be sure that this idea can be deployed in a way that it serves all nations and is as openly and in essence freely accessible as possible.

So indeed I found myself on a plane with Michael and took a very modest part in several meetings that ultimately did result in the formation of this consortium that most of the world doesn't even know exists but is really responsible for the way that Worldwide Web was deployed.

I learned a lot from that, particularly how an engineering culture works that just wants to get something done and done right and make it as accessible as possible. But I learned another thing. I learned how to explain what it's like to serve as president of one of the National Academies or president of a great university. At least the Americans in the group, many others will have seen a movie Forrest Gump some years ago. So Forrest Gump was sort of a hapless guy that didn't add any value to anything. But somehow he always showed up at really important moments in the history of his generation. And I felt that way a little bit regarding the Worldwide Web and many other things where I was able to show up and kind be there even though I didn't bring a whole lot to the table.

And I have a bit of that sense of history in the making here today. Here, literally but also figuratively in terms of the larger dialogue that is beginning to go on and driven by some of the founding folks of what we now are calling synthetic biology. I have to be honest. I first got a sense of what was going on kind of walking up and down the hallways at MIT several years ago. You know, we read in

the newspaper all the time about the Arab street. If you want to learn about the Middle East, you just keep your eye open. Well, that's the way it is at MIT, and I heard all these kids talking about bio hacking. Well, I figured I'd better find out what this bio hacking is all about. So somehow I managed to trace down and get Drew Endy to come over to the office one day and give me a little tutorial about what was beginning to develop around a number of institutions in the U.S. and around the world and what this might actually mean.

But I have to tell you that from my own perhaps parochial perspective, I am with the National Academy of Engineering, what I really see is the emergence of a new field of engineering.

Now I know that we're going to say science, science, science, science. But this has to do with engineering in ways that I would like to explain at least from my perspective. For many years now, probably even a couple of decades, there's been a very strong feeling and indeed a number of actions taken in institutions around the world that biology was going to emerge as a new underlying

science for new ways of doing engineering in the same way that physics and chemistry and mathematics and computation to some sense had formed the infrastructure and the basis for producing goods and services through engineering in the past decades.

And what I in my sort of modest understanding of things here began to see is the emergence of that as really becoming true and that synthetic biology's a very, very major step along the way. Because after all, I would think of engineering as meaning applying design and synthesis to achieve some predetermined goal or executed desired function. And I think that's what those of you who are working professionally in this field are in fact doing. So I'm going to greet you as fellow engineers whether you like it or not.

But the really important issue here is that everyone in this room is keenly aware that we are working with the very stuff of life in a way that we have not been able to in the past. Now there's therefore enormous potential for doing good and enormous potential for doing harm. This is what Koji Omi, the founder of the Science

Technology and Society Forum in Japan likes to call the light and shadow.

So what's new? This is the case certainly for all technologies historically – good and ill, and I think what's new is the amazing speed at which things propagate today, in which ideas can emerge from fundamental concepts and laboratories out into the so-called real world. It's what's new is the enormous variety of end stakes that you could produce by your work and certainly what's new is the nature of reproduction and replication in living systems. This is in fact unlike most engineering fields of the past.

So I cannot tell you how very pleased I am to look at the diversity of institutions, professions and perspectives that are represented in this room fro academia, government and industry, from several nations and continents, people from ethics, intelligence and legal communities, from environmentalists to economists. Knowledge in technological capability should and will progress with enthusiasm, optimism and spirit of innovation, and I want to encourage that in every way I possibly can.

But it is terribly important and very rewarding that you are here today debating, considering a variety of potential consequences of synthetic biology and working together to make the dominant drive of this embryonic field positive and beneficial to humankind. To return to Koji Omi's conception of all this, to be sure that the light extinguishes the shadows.

You can't fully predict what road will lead to when you start down a path of something unusual like this. I again in the Forrest Gump spirit a little bit was very privileged to get to known Claude Shannon a little bit in his later years. And I asked Claude Shannon one time how and why he became an engineering, and here's what he told me. He said I grew up on a farm in a very isolated area up in the northern part of the lower Peninsula of Michigan. But he said my father went off one day each year to the big city, one trip to the big city each year. And every year he brought me back an erector set, whatever was the latest model of the erector set, and I sat around putting these things together and building them. And he said that's what really made me decide to become an engineer. And of course,

that launched an intellectual career that no one could have predicted that gave us a radically new field of information and communication theory that really changed the world.

So with that in mind, I've been pondering today what in the world might be accomplished by some young girl in a small town whose father goes off each year and brings her back a new bag of biobricks from Drew Endy. What an adventure.

Anyway, thank you very much for being here. I think that you're part of an enormously important dialogue, and I hope that you have a very productive day. Thank you.

[APPLAUSE]

Agenda Item: Session 4: Developing the Field: Needs of Academia and Industry

DR. SILVER: Thank you. Thank you for that really inspirational opening. As a molecular biologist, I'm honored to be welcomed as an engineer. Thank you. Something I've been striving for.

So just why it inspires me to tell a very short story about why I'm here. I did grow up scientifically as a molecular biologist, and I had the good fortune to meet

Drew Endy and I'm not going to tell the story of how and Randy and Tom Knight when they were at MIT, and they graciously brought me into their group as the token biologist. And the way we work together I really think is part of the theme of this session is that it began through education. They were involved in teaching an intercession course at MIT where students were asked to make cells that would make polka dots. And from this grew, of course, the IGEN which Randy will be telling you about more.

I also come to this session wearing a couple of other hats. I'm back in the Renaissance days of Harvard about five years ago. I was one of the founding members of the Department of Systems Biology and new graduate program that is entitled Systems Biology but we have worked hard to embrace Synthetic Biology in that.

And now I'm also one of the founders of a new – Harvard's new attempt to get into bioengineering, the Wyss Institute of Biologically Inspired Engineering, and that may in fact become the home of synthetic biology at Harvard.

Now I have a few problems as the director of a

graduate program and involved in education at all levels and also involved in the interface with industry, and so these are some of my issues of concern that I think about a lot. And I don't know if they will come out of this session, but I'd like to have other people's thoughts on this. So my first is how can we have a system at all levels in engineering and science –- I'll put them together –- that allows students to be nimble.

Now let's forget a moment the oft heard clichés about interdisciplinary science. I'm sort of tired of them. But the kinds of push back that we do get are that this is not a hypothesis driven science. Then you have to start talking about the interface with engineering. But then if you're trying to build this in a department of systems biology, you have traditionally trained faculty, traditional journals with traditional end points, funding agencies that don't understand. And so all of these things act as negative input to our students.

I think that –- and something we've tried to build as an emphasis more on collaborative projects and a reward system for collaboration, not everyone can know

everything, and I think in systems biology we've learned that lesson. We can certainly start to apply it here. Keeping with the sports theme of this meeting, I have a quote from Casey Stengel which is we couldn't do it without the players.

Now my second related question is how do we have a training environment that maintains the level of excitement that the students come to with this. I often see students coming in very excited, and then by the end of their third year, fourth year of graduate school they're beaten senseless. How do we prevent this? This shouldn't happen. If we're attracting the best and the brightest, let's keep them that way. Let's keep them engaged.

These are students that don't want to sit on the sidelines. They want to be at these meetings. They want to be everywhere, and these are the students that want to do things fast. They don't want to be waiting a year for their ligation to work. So DNA synthesis, they want – these are the students that want to be able to plug into a computer, get the experiment done as fast as possible and move on. They want cutting edge technology. And so let's figure out

how to let this be the generation of biologist engineers that make that happen.

And then the last thing that I think students are concerned about and I think this is a good thing which we haven't seen a whole lot of in the biology arena is how do we effectively drive this innovation into commercialization and students are much more interested in that. And I think they need to be allowed to play more of an active role in that much like in the development in the IT era, in the developments in computer science. Why should our students be any different? Let's engage them. Industry, take note. This is the future. So you have a gold mine here of youth. So this is very much a youth driven field, and I think that we'll be hearing more about how to maybe hopefully the answers to some of these questions. So I'll introduce all three speakers.

The first one is Francois Képès who is the research director at the French National Center for Scientific Research and the founding director of the Epigenomics Project, very interesting.

And then the second speaker is my good friend

Randy Rettberg who is officially the director of iGEM and also a bunch of other titles here.

And then Richard Johnson, Senior Counsel at Arnold & Porter and CEO of Global Helix. So take it away.

DR. KÉPÈS: Thank you, Pam. Thank you to the organizers for giving me this opportunity to attend this very interesting conference which includes lots of very, very interesting extra scientific considerations on top of scientific considerations. It is not usual, and I'm very glad to be here.

A few words of context. I'm working at Genopole. Genopole is the largest French biopark with now currently 64 biotech companies and 22 academie class along a small university. At Genopole, the Epigeonomics Project is sort of an institute of advanced studies. It became the hub of the French research network in systems biology in 2009, Synthetic Biology Institute in 2005. It is also program of foreign visitors and international scientific events.

The purpose of this talk will be to raise issues mostly –- raise issues on research infrastructure and support for further discussion with you. I'll bring some

potential answers. But you should understand them as meaning a way of raising issues and fostering discussion mostly.

As a foreword, let me simply express because I'll need to notion later on that synthetic biology encompasses applied and fundamental aspects. We heard that already yesterday. Let me simply mention that because its entailed rationalized conception is very close to applied research and to the engineering concepts. But because it allows us sometimes to distinguish between constraints and contingencies, it is also very much on the fundamental side. Let me give an example.

The genetic code is known to be quasi-universal. Does it mean that it is a byproduct of physical necessity? Or does it mean that it is a consequence of a frozen accident of evolution. The best way to answer this question is to make material with another genetic code and see if it works, right. So in this case, we are trying to answer a fundamental question.

All right, so in this spirit, given that synthetic biology is an emerging field of investigation, in

the balance between exploration and exploitation, we need to set it very much on the exploration side initially. This is why most colleagues would think that what we need are blue-sky projects which are well funded. Christina Smolke yesterday alluded to the necessity for foundational studies and this also means that initially most calls for proposals should not involve in a necessary way industrial partners in the consortium.

In the spirit of Eddington who urged us to provide enough time and intellectual space for those who want to invest themselves in explorational levels beyond the genome. But given my foreword, you understand why I'm insisting here that it is very natural in the context of synthetic biology to have a close contact between industry and academia. And this can call for having an increasing dose of calls for proposals that involve small and medium-sized companies, for instance.

We should also remember that there are diverse modalities for corporation between academia and industry. One can be the customer of the other or vice versa. There could also be true scientific cooperation. The case of big

companies seems to be different. Although we do not hear very much of what's going on in the big companies, the feelings – and perhaps we'll hear more today, the feeling is that very often they'll start from their field of expertise and strength. Let's take the example of a big chemistry company. They'll not say we are switching. We are now a synthetic biology company, no way.

What they will do instead is look into synthetic biology as an enabling set of technologies that perhaps can increase and improve their processes. From the point of view of synthetic biology, chemistry is a contributing field. So in a way perhaps these big companies are adopting proposition number four or was it five by Victor DeLorenzo on intergenerational cooperation based any advance on a contributing field such as chemistry.

Coming back to the close contact between academia and small, medium industry, if we want this close contact to last long it makes sense to have an elaborative relation. This is shown here. For this purpose, how about the following situation. My lab is purchasing some commercial pipeline because it needs it to accelerate its

discovery rate and finds out that one of the solutions within the pipeline actually has been published by my own group five years back, right. By this little story, fake story, what I'm trying to say is that it is not inadequate to think that the academia should have a capacity to retain intellectual property and capture intellectual property positions in the spirit not to do the job of industry but of retaining an included(?) relation.

Another issue on this side is also where to put tech transfer units. So I've not done a full survey, but just talking to some of my colleagues in the industry, it appeared that their wish is that that tech transfer unit should be located within the academic laboratories. So the person in charge just coming out of his office or her office can talk to the scientist and see what can be amenable to patenting, for instance, or to protection of any type of development besides other types of approaches which are very typical such as survey, outside survey and so on. This idea and, again, this is an issue for you to discuss. But my colleagues so far have been of this opinion.

Last slide on R&D, full stream transnational cooperation. Here, possibly I'm back on the European continent. As you know, we are trying to build a union. One of the ways of the scientific lab is always to foster transnational cooperation by various means and two of them which are pretty relevant to synthetic biology are shown here, course of provisions across borders of Ph.D students and post-docs with possibly one supervisor being on the biology side and another being on the mathematics or physics side for instance.

Small focused meetings of an interdisciplinary nature that could be decided bottom up to start to maintain a collaboration and prepare joint proposals. I know that these types of actions cost very little. Limited traveling funds are sufficient. They're very efficient because they're at the site where science occurs.

Two slides of technology platforms. First of all, trying to list possible service and you may want to add more. One is DNA synthesis and order not so much to compete with gene art but in case confidentiality is required by one of the customers, it makes sense to have a small DNA

synthesis unit in-house.

The second one is robotized DNA assembly. The third one is central biology resources. That's the wet part, DNA banks, cell banks and the dry counterpart is repository for biological models, knowledge bases, EBI Institute in the UK has developed such repositories. We still have to think how to adapt them to the case of synthetic biology.

Reference centers would be instrumental in elaborating good safe practice and standards, new standards and links.

Customers, this is an important point. Customers could be academia and industry. In fact, a technological platform if you think of it as a meeting platform for academia and industry. The reasons that industrialists will not go to an academy club and act as customers, they need quality insurance, quality control, traceability, reproducibility which they find in a good platform.

Financial support, we have to face the fact that an initial investment in required. You cannot have customers if you don't have the first machine or device in

your house. But the idea is that it could be come mostly self-sustaining in the long run by applying fees for services.

As for preferred location, near or within a center of excellence in synthetic biology. Why is that? Because in fact we've not talked about it, but one of the important assets in that platform is also the gray matter from the academics who bring in novel software, novel conception tools, for instance, in synthetic biology that make the platform more attractive to customers. And a totally different aspect is the networking. I mentioned that a few reference centers would be able to provide all the services and to provide a capacity to elaborate new standards and new codes or guidelines. This may certainly not be the case for small local platforms which on the other side would benefit from having access to these new guidelines.

And for this reason, we hope that – we think that it would make sense to network reference centers, a few of them, and local platforms many more at the continental level.

Okay, so my last two slides are devoted to standardization. I noted that in the program there was not a full-fledged section on standards, and of course I'll be very brief on that. But at least for further discussion I'd like to bring this up.

At the same time I'm pushing the idea that I and my colleagues are all for it when it's checked and not for in favor of it with a little circle. But again, this is for discussion. Measurements, all the omics techniques for which we have standards maintained by consortium. I mean, I suppose we have no choice if we want to publish. When it comes to DNA parts, we would actually welcome more standards and characterization and annotation. When it comes to design and assembly of DNA parts, you know there are many ways that there are already some existing standards like the iGEM standard. But it's pretty clear that other standards are possible, and it is probably too early to settle on a particular standard on that side. We can still think of improvements. Plus, as you are well aware of from yesterday's lectures, this issue is going to be less and less important as DNA synthesis capacity are

building up.

Ontologies which is in brief are a self-consistent set of hierarchical annotations. We have existing standards maintained by consortia just as gene ontology which are an infusion by informatics and systems biology.

Now here's a case where probably engineering sciences according to many of my colleagues could bring their standards in such a way that we could progressively adapt the existing standards for systems biology to become useful, more useful for synthetic biology. On the side of mathematical modeling, we have many different formalism. But it's very clear that if you want to include geometrical space in your model, you'll resort to a formalism. If you don't and if you have qualitative data and you want a qualitative output, you'll resort to another one. And there is no way that we can set a universal standard on that side at present.

Same thing for computational simulation tools. However, by definition, exchange formats should be standardized, and we have such standards such as BML. With

that I close and I thank you for your attention.

[APPLAUSE]

DR. RETTBERG: So for this group, I'm going to give a little bit of a different presentation, and I apologize for it being a bit choppy. But I wanted to go directly to point out that iGEM already has an award for best human practice events. That was won in 2008 by Heidelberg. All of this information I'm showing you is live on the iGEM Wiki which you can find yourself by remembering iGEM.org.

This is the Heidelberg Team's website made by them. You'll note that they have it actually available in many different languages which I thought was very nicely international. I think I might try to make a requirement for everybody else to make all their websites in all of these different languages so if you have a different preference your choice. They have a human practices section which talks about the kinds of thing they did. They said that only a well-informed public is able to develop a non-prejudiced and profound opinion about synthetic biology. Their words, "Science can only work successfully and

develop useful inventions if it is based on a high level of acceptance in the society." As part of their project, they went out into the public and did surveys, interacted with the public. They interacted with the press directly on the topic of how the public should think about synthetic biology.

Each team gives a presentation at the jamboree and does the sound work? Let me see if I can get sound to come out. There are too many buttons to push. There's always another way. Okay, well, this one has reached the limits of our technical abilities. But the point is that a portion of their talk they devoted to what they had done in terms of presenting to the public, to the press, what they've done in terms of surveys. And so to the extent that we start with an assumption that the students and the iGEM teams need to learn about the importance of the human side of synthetic biology, we may be incorrect.

In fact, I find that in many ways they're ahead of the rest of the world and ahead of many of the biologists I meet, and that they're very eager to do things of profound value to the world. Now we can go to my regular

presentation. I don't think it's going to be as good.

So synthetic biology from our point of view is focused on standard parts, and that comes from an engineering point of view, an engineering background. The odd situation where the early founders of synthetic biology at MIT, Tom Knight and Drew Endy and myself, had an experience which was an engineering background.

Tom and I were both actually computer architects and networking architects. I spent almost 30 years in the computer industry. I began my career at Bolt Beranek and Newman with the Arpanet Project. When I joined the network, there were only 24 computers. Along in my history, I got to write the first TCPIP for Unix, designed the computer that was used as the pack a switch in the earliest pieces of the Internet, did the link from the U.S. to the U.K., went to Apple, designed computers that were sold to many, many, many people, went to Sun Microsystems, ended my career as the chief technical officer of the storage division.

So my background as an engineer is clear. Why on earth would it make sense for me to come and become a biologist? It only makes sense because there's a gap in the

discipline which allows engineering to have real value, and in some ways it sounds like the scientists who are biologists saying we could let the engineers come in and they might offer some value, but instead the engineers are just going to bowl their way directly in and offer the value whether it's eagerly accepted or not.

So the question that I think is at the core is can simple biological systems be built from standard interchangeable parts and operated in living cells. So how many of you think that can be done? Are there any biologists who think it can be done? Yeah, okay, we have a few.

When people, when we started working on this, there was this other point of view which is biology is so complex that each case is unique. If you learn something about one organism at one temperature in one media, it's not necessarily the case if you change the temperature or if you change the media or certainly if you change the organism.

So how do you find out the answer to this question? Can you do this? You can't look it up in

Wikipedia. You can't Google it back, you know, in 2002. The only thing you could do is try. Now at MIT, we have a wonderful advantage, and that advantage is we have undergraduates and our undergraduates don't know what you can't do. Therefore, in January the four of us and then Pam joining us the year later said, well, we will run a design class in designing biological systems and we'll populate it with undergraduates and we'll tell them we're going to make blinking cells. And they believed us, and we spent the entire January doing it and trying it out and learning from the students which is the best for you to always learn.

So let me tell you a little bit about iGEM. It grew out of all of that. It grew out of this desire to test that hypothesis. So iGEM is an international design competition primarily focused at undergraduate students, although we're in fact getting some high school students and some high school teams.

The goal is to design and build a project that will impress us, and we're focused on synthetic biology not in a general way but synthetic biology specifically based on standard parts, and we have a registry of standard parts

that I will talk about in a minute.

The final part, it is absolutely critical. It's in fact one of the requirements. We don't have very many requirements. One of the requirements is to have fun and to make a positive contribution to the world. The long term goal, of course, is much more complicated than that. It would be an extreme error to think of iGEM as a teaching program where a synthetic biologist teach the students how to do synthetic biology. The iGEM program has a very large number of people, a large number of instructors, large number of schools. We're developing this field of synthetic biology at its core. The work done by the iGEM students and presented at the jamboree are some of the best work done in synthetic biology and is in fact one of the best conferences you can go to. It trains the students and instructors. We're training them in great quantities, and it's actually pretty important that we get ready for them to arrive and start to look for jobs and graduate student positions.

So above all of that, we're trying to make sure that this is all positive, that the community is focused on

that. Drew Endy will tell you about how we thought about calling this bug wars, but we decided that was maybe not the right tone for this.

The philosophy of iGEM is a philosophy and get and give. They get the parts at the beginning of the summer. They give the parts back for the iGEM teams that follow. They put their projects on that Wiki, and the teams that follow look at those projects, and that means that the teams and the students that follow start where the last year left off, and they are pushed to make it better and better and better and better.

This is also not like a normal class where at the end of the year you take the homework, you give it back to the students, you say that's great, I'm going on vacation. So we've had a great deal of growth. Right now, this year we're in the 210-212 teams. It fluctuates a little bit now because some drop out and then some have joined later. I think we may be actually right at 211. Last year, we had 84. So we've grown by about 50 percent for the past two years.

This is actually more striking than you imagine

because we did our registration in March. March was the time when the news was filled with worries of the coming Depression, global meltdown and the teams have to raise their own money. I don't send them money; they send me money. So the fact that we continued to have growth in that kind of environment has been very reassuring in terms of how strong this is.

The total number of people who participated last year was 1180 that were actually signed up and registered with teams. There were about 750 students at that point. I've projected off into the future what might happen in a year and two years because that's where I have to plan for the events that come. Two years out, we could expect that the number of teams might be on the order of 250, 270, and we might be having a jamboree with more than 2,000 to 2,500 people, maybe 4,000 people participating worldwide. You could say this is unrealistic, it has to top out at some point. I'd like to point out that the U.S. first robotics competition has 1700 teams. Their budget is around $30 million. I think we have some room for growth. The question would be which schools should not participate, which

countries do want to be left behind in synthetic biology.

So here's the list of teams, and I'll give to you. You can kind of look through and see whether in your favorite school, your favorite country is represented or in the U.S. I'll come back to that at the end.

We have teams in Asia. We also have teams in Canada, and we have five teams in Latin America. So we do have a team from Brazil. We had a team from Peru last year for a little while, and they had to drop out because of support problems. iGEM works this way: Over the November to March timeframe, teams assemble. This happens two ways. It either happens because some students have fallen in love with the idea of iGEM and they go to their professors or any adult and say can you please help us, and the professors say, well, I don't know, I'm busy right now. They go back. They get more friends. They send emails to us and say there's only two of us, can you tell us how we can help and we say go find professors.

The other way, of course, is the professors and often junior professors say this is really a wonderful thing; I'm going to assemble an iGEM team, and they worry

whether students will be interested or not. Fortunately, that worry is always resolved.

We then have teachers workshops in the spring. We have them in the U.S., the U.K. – Europe, we had them in the U.K. last time, and in Asia. We send out a kit of parts. This is more important than it appears because this is like that erector set, and it goes to all the iGEM teams and it's tangible. When the professors see this kit of parts, they realize that the students now have something they never had which is they have 1,000 parts –- or 2,000 parts last year that they can use immediately because these parts are designed to work together.

You then work at your school. All those thousands of students do not come to MIT and work in my lab. They stay at their school. They work under the instruction of their instructors, their professors. They then do come to the jamboree. The jamboree has been held at MIT up through this year. This year is going to have to be the last time it's actually held at MIT because it's outgrown our largest auditorium, and I now have signed up for all of the major auditoriums for that weekend. So we're reaching the end of

that, and it's going to have to change in some way. At the end of all that, you win your prizes and you publish your work. Many of the iGEM projects have actually been published in different journals through the years. We expect that to happen again as well.

For this audience, I'd like to point out one particular thing which is I am always asked is iGEM safe, and I say, well, we had one student pass out, you know, two years ago at the jamboree because she got too excited and forgot to eat. So there is that, and people were worried about the future of iGEM and they thought what if some student was damaged, you know, was hurt in a lab. But I'm not too worried about that. I don't find a lot of press reports which are of the forum a sophomore at Duke had their index finger eaten off by their bacteria, right. The stuff that they're doing is not fundamentally dealing with a dangerous compound.

iGEM counts on the instructors and the schools to provide the framework for safety, to provide the training for all of their students, to provide training of how to do lab procedures properly so you don't get burned by heat or

chemicals so that the projects that you're doing are appropriate.

If you look at this list which you probably have been doing while I was talking, you'll see that the issues of how the safety of your project relates to the world around you is a key topic. We will be requiring this year each team to provide a little report on this topic, and the judging committee which Drew is one of the chairs of will be evaluating that in terms of giving awards.

The impact of iGEM is number one on the students, but in a way that's simple, right. This is students being allowed to spend the summer in the school doing a project of their own design and trying to impress everyone else. The bigger impact is on the instructors who are learning about synthetic biology. It's on the schools. The simple example of that is that schools all over the world are now producing four-credit classes in synthetic biology in their spring terms. They're doing that because the other iGEM teams are doing it, too. If they don't it, they will fall behind. The competition side's working quite well, and we are even having different centers for synthetic biology

that have grown up at sites where we had iGEM.

There are a lot of iGEM projects. I'm not really going to go into them. Go to iGEM.org, look at last year. Look at 2008, and you can see all the different kinds of projects. It's an enormously broad number. The teams have been highly successful. Most of the teams have built something and had part of it work. They are also extremely ambitious. And so most of the projects didn't work completely. So there's more work to be done, but the answer to that question of can you build these simple systems from standard interchangeable parts is actually working.

The other side of this goes back to the engineering background. In the late '60s and early '70s, the integrated circuit was developed as a low-cost item and one of the primary companies was Texas Instruments. They put out the TTL data book, and the TTL data book allowed small numbers of people –- a few –- to build a computer. The entire mini-computer industry thrived on that. There were companies after companies that would make brand new computers, new instruction sets, new innovations and then go and offer them into the public. There was an enormous

explosion in the number of computer companies then.

The reason that's important now is that we now have a biology industry focused on large pharma companies. That is like when I was at MIT I wanted to design computers. I know that I would work for IBM for the bunch – Burroughs, Univac, NCR, CBC or Honeywell. There were no other choices. If I was going to design computers, I was going to work there.

That turned out to be completely false, and the bunch is gone in terms of offering computers. So I expect that it's possible that the same thing might happen with synthetic biology, that it might well be that through synthetic biology a rich and diverse industrial base is formed, and it's formed by those students who have participated in iGEM, have heard about iGEM and are desperate to do the engineering of biology.

The registry of standard biological parts –- I'm going to go through this pretty quickly. You can find that if you go to iGEM.org. It has parts in it. Right now, it has about 3,500 parts that are available at DNA. A part is a thing like the coding region for a protein. We do quality

control on this. We sequence all of the parts before we send them out. We provide all of that information on our website. We live on the Internet.

We have a standard method for assembly. All the biobrick parts that we send out –- almost all –- are compatible in the way that you can put them together. So assembling your project is something that is not a research project. You know just how to do it. People are doing it all over the world. You can get lots of help.

We have done work on robotic assembly, and that's going to be continuing. Most of the work is done in E. coli, although some work is done in plants and some work has even been done in mouse and in embryonic stem cells. The new areas are CAD, development of software. We have a software tools track. And the area which is so new it isn't even happening yet is the commercial application side. There are all of these wonderful projects done by all of these wonderful students, and what comes of them? Berkeley develops bactoblood, bacterial blood. They put the hemoglobin system in. They work on many more parts of it. This is something that perhaps should be explored by

commercial companies.

The team from Edinboro makes a arsenic detector for arsenic-contaminated wells. What's happening with that? The answer is that the students went back to their studies and the instructors realized they had fallen behind in their work. So what do we need going forward?

The first thing we need is open access. Three teams last year were not able to get their visas to attend the iGEM Jamboree. How many teams will that happen to this year? What if 20 or 30 teams are not able to get their visas and are not able to attend the Jamboree?

We had the request from Iran, from Tehran University to have a team. I had to say no. There are economic sanctions. I'm not allowed to provide you anything like that.

The next serious topic is one of patents. Is there a de facto research or education exemption? There is not an actual research exemption. The courts struck that down. There is a de facto one, and will it work for iGEM in the future? I worry that some patent troll will send a letter to MIT and I will be shut down.

We are working on making a not-for-profit. There are other questions. If this issue of patents becomes serious in the area of synthetic biology, perhaps certain core resources need to move into governmental or special situations where patent exemptions can be applied.

For this group, there's a question of I have 1700 people. What do we teach them in the topic of policy and human practices? We always need more money. We need money for the teams, and that's a worldwide problem. We need better parts and tools. Thank you.

[APPLAUSE]

DR. JOHNSON: While Steve's putting it up, I'm Rick Johnson and I am going to go in a slightly different direction here. But I think it's an important issue that a number of people have previewed and do sort of an informal synthesis and quick overview on some of the ownership and access and rights issues on synthetic biology.

But what I want to do is basically go through sort of Rick's top ten list of challenges, issues and developments but in a framework that basically has sort of four underlying themes. One is obviously many of the

aspects of synthetic biology are the dream final examination for an intellectual property law professor. But at the same time I want to suggest that really it's a lot more than patents, a lot more than just talking about open source, and it's also more than just intellectual property rights, and I want to pay particular attention to a number of sort of new tool kit issues that I think broaden the discussion and may also provide ways to deal with both openness, the incentives, the innovation that we want to achieve simultaneously and particularly around infrastructure platforms, standards, collaborative mechanisms and the one that's getting no attention in synthetic biology which is how antitrust and competition policy can be used as an antidote if intellectual property goes a little too far.

And then finally about its global. This entire group is global. We've been talking about global. But almost all of the analyses that are detailed with respect to ownership and access have really been through an American lens, and there's a growing asymmetry with a global synthetic biology community and putting it in that

broader context. So let me start. Clearly, obviously I'll come back. I'm not going to make your eyes glaze over and get into patent claims and details of patents. But I want to suggest first obviously that the complexity of the patent landscape is real. It's significant because we're dealing with a cumulative convergent set of technologies here. And so consequently, the interactions and if you look down the list of all of our many different elements and synthetic biology, almost all of these can be touched directly or indirectly by patients in way or another. The concerns that have been expressed which are real are possibilities of patent thickets of abilities that are going to retard upstream downstream the ability to do research, to commercialize, to have beneficial global impact that we want.

But patents are extremely context, and the nature of those interactions and what their implications are are not things that can easily be done. We have issues about foundational patients, how broad they are, how good they are. Artie Rye, Jamie Boyle, Andrew Torrence all have done very interesting and good work looking at some of those

potential foundational patents at the moment.

Then we have a whole range of issues around the infrastructure, the parts, the different networks, interfaces, etc. And yet, at the same time and I'm going to come back to this, frequently the reaction is, okay, let's do less patenting. And the point I just want to throw out now and I'll come back to is in some cases if your goal is openness, the best way to protect openness is through actually strong intellectual property regimes that you control as opposed to other alternatives. I'll come back to that.

Related to the patent issue, and this will be my last discussion specifically about patients is that really there are a range of unresolved patent issues that are going to have a major impact in shaping the future directions for us in synthetic biology around the scope of patentability, the range of normal questions in patents, about how prior art is applied, non-obviousness, et cetera.

There also are in the U.S. a number of pending cases and implementation of prior cases that are going to have a major impact. The U.S. Supreme Court is about to

consider the In re Bilski which goes to method patents, mental step patents which are what they say are going to be critically important.

The court has already recently talked about non-obviousness and changed that significantly, how that gets implemented. It's going to have a significant impact. And obviously some of you are familiar that the American Civil Liberties Union has recently filed a very broad complaint against Myriad that really goes to the patentability of genes as well as diagnostic methods and what happens with that case obviously could potentially have some significant impacts.

Another one is one that Mark Lemley at Stanford has been looking at over a number of years which I think is very important which is that obviously with patents and industries and applications being very context dependent, there are a range of different patent – what he calls the ten patent policy levers and how you adjust and how they mix are going to have a significant impact.

And as a number of speakers have already mentioned, we get a number of our favorite most difficult

intractable issues back on the table in synthetic biology. Randy was just talking about research exemption issue. Ken Oye has written perceptively and extensively about factors. There's a rich literature. There are no easy answers.

Material transfer agreements, obviously we haven't talked about that so far, obviously a major issue with respect to ownership access rights when we look at not only the materials side but the information side of synthetic biology. We have the broader issues about sort of university technology transfer offices, how they operate, what they're trying to do versus sort of the knowledge commons. And then we have sort of norms of openness, or whether or not, for example, around patenting that non-assertion agreements can be developed or implemented, and that could change things significantly.

But I think it goes well beyond patents. And one of the things that have not gotten much attention is in many cases the issues are really around the interaction and the bundle of rights. So when we look at synthetic biology, there potentially are some very interesting issues around design rights, very strong in Europe. There was a series of

cases in the U.K. around 10-15 years ago that when you're trying to assure interoperability among parts, and this particularly had to do, for example, with auto parts. In fact, there was a must fit, must match exemption to intellectual property rules for designs. Does that apply? It's an interesting question for synthetic biology.

Databases – obviously the EU has a database directive. The U.S. doesn't have one. There are ways in which one can get protection. And so whether it's the registry or other types of ways in which we are going to be putting this information and parts together, the concerns about how the database protections may operate are significant. The OECD has recently done some very valuable work on guidelines for access to human genetic research databases that also are important from this context.

Copyright –- Artie and Jamie and others and I don't disagree with any of their analysis, have said, ah, copyright's really not an issue. It's thin. It's not clear that it would apply. Just synthetic biology, I'm not so sure. As we look increasingly at the length of the synthesis that we'll be able to do and see whether or not

the originality and expression that copyright protects could be extended, I think a very important part and something that a couple speakers yesterday began to talk to was over time we're increasingly going to see a decoupling of design from manufacturer and process, and that I would argue is going to increase the likelihood there may be copyright issues. And clearly what about annotations and references.

There are also sui generis rights. So in the semiconductor industry, there was sort of a –- it didn't quite fit for chip designs. So eventually what came up globally was a sui generis or unique right for mass works. There's also an interesting one for plant readers rights. The interesting part of that is not only about how it operates, but it is the only one that builds in a research exemption and an experimental use exemption into the right. And then trademarks are likely to be very important. Biobrick has value. Its logo, its trademark are important quality control tools and other things. And so how that gets deployed the same way with trademark with formats as they increasingly become important.

So what are some of the things that I think are really driving and that we need to wrestle with more perhaps than we have before. Clearly one of the underlying themes here is that we have competing visions of openness, and I'll just address four.

We have open science, public domain. Outside the intellectual property system, risk is and we have free riders or by trying to keep it open we actively set up for someone else to tweak it or do something sufficiently inventive that they enclose it, and what we've tried to do doesn't work.

Open source –- Open source frequently gets misinterpreted. Open source depends on a very robust intellectual property system. Copy left and other types of licenses require a very efficient and effective intellectual property system to work. We also, however, and I'm going to talk to standards and I'm glad that Francois began to raise that issue because I think that's a particularly interesting one about open standards. And then open innovation. Obviously, one of the major changes globally in business models, value chains, university

industry interactions is around the notion of an open innovation where you don't have to do it all, you don't have to be vertically integrated. You can go and look and find the best piece of that value chain, basically, mini-synthetic biology and though that you can also increase revenues or other strategic opportunities by things that you don't need as a core part of your business by taking it outside the company.

We've until tended to talk about issues in terms of commons, anti-commons. I think from an academic and theoretical and this is a big leap from sort of real world, but I think there is some utility in beginning to talk more in synthetic biology about what some young scholars are beginning to call the semi-commons, and this is really interacting common and private uses over the same resources that are dynamic, they're scalable, they can change over time and they adjust to different mechanisms.

Alan in a seminar article in 2000 had a very – and this is grossly oversimplified by gives the point. His point was in pre-industrial England, you had communities where you had private ownership of land for farming. You

had public or common ownership for grazing, and so you had shared over the same resource you had different rules that could be reshaped and did very efficiently over time. And so the notion is are there ways in which as synthetic biology evolves where we draw lines of demarcation, et cetera can shift and also be looking very much at sort of a mixed or semi-commons approach.

Another real challenge we face is clearly we have a clash of cultures, and we have a clash of cultures around ownership and access at many different levels. We've got the multidisciplinary one. So if we look at all of the elements that are converging in synthetic biology, they come from very different backgrounds about how they view intellectual property rights, how they resolve conflicts, how licensing is done. So what Biopharma does is very different obviously from MIT. It's also very different from what a traditional chemical industry approach would be. It's very different from what systems engineers or the semiconductor industry. And so that clash of cultures obviously is a big one made more complex by the fact that we have limited alignments of interest.

We've got multiple players here in terms of companies, universities, libertarian hacker communities, et cetera. And in trying to get some alignment of interest, we have the convergence and globalization sets of issues. And I would argue we also have another emerging trend, and that's right now in this room and elsewhere we do have – there is a synthetic biology community that's built around trust because everybody knows basically who everyone else is who's any good that's doing work.

As synthetic biology evolves, it's going to get too big where you're not going to know everyone. And so I would argue we're going to have some transition from trust to contract and what role intellectual property plays as a neutral tradable bridgeable asset is an interesting question.

The next thing I want to talk about and this really comes back to something that both Randy and Francois have just been mentioning. Obviously, I think when we look, it's clearly going to be user driven innovation. What Eric Von Hippel at MIT has called democratizing innovation effort. Eric's got some interesting new data. When I was

talking to him a couple weeks ago when he first did the book about democratizing innovation was maybe 35 percent of innovations were in that thing. He's now up to sort of 75 or 80 and climbing.

And so therefore how are we going to get public policies that are really user focused on innovation rather than on the traditional producer side in terms of where we strike balances. And when we get to the infrastructure openness issues, and it's interesting because Francois and I did not coordinate presentations. But I think there is –- and I want to use one example. Obviously, characterization of the genetic parts is a critical infrastructure core function. And I think that without –- and it doesn't have to be in a government laboratory; it could be at MIT or Centers of Excellence anywhere in the country and networked around the world. We're going to need ways to leverage shared resources that have a government component.

An example, I think, that is a very interesting one as a central template and Jeff Schloss can tell us more from an NIH perspective is something like the National Cancer Institute's Nanotechnology Characterization Lab.

It's an open access shared resource, but it combines it with certain rules of the road. And by having this shared resource, it deals with some of the openness questions. And in the NIH or NCI case, it's open source. So it's any publicly funded development that's openly distributable products and data.

Open Development –- I think this is really important from a synthetic biology community. It needs to be community driven development to align its needs with priorities in the shared resources, open access and federated. And Pam said so I'm just going to skip over it quickly one of the standards.

And I think all I want to say about standards is that the intellectual property issues and the interface standards, I think, are going to be actually one of the key drivers of standards. We'll have the slides available later, I'm sure.

The second is right now the analyses have tended to focus on biotechnology and information technology. I think we need a lot more analysis of looking at semiconductors and to some extent nanotechnology because

that's where we have patent thickets that are very similar with dealing with devices. And it's interesting because we have a sharing community. In this case, it happens to be a closed sharing community that in the main works fairly well. But the key point is the reuse element and the creation of IPR blocks as a unit of reusable design. And how that gets down in the semiconductor industry, I think, has a lot to tell us in synthetic biology.

Something that the OECD has done great work on in the last few years which is looking at new collaborative mechanisms and knowledge markets. So for example, one of the areas is patent, of course. If we have blocking or other types of situations, it strikes me that synthetic biology provides exactly the type of situation where that works well particularly since it's standards driven in the future. I just want to call your attention to the international component because beyond the U.S. side, we have a range of international intellectual property both issues that are going to be out there but also some disconnects among different national regimes for the community.

And then finally I just want to close with talking a little bit about antitrust, the competition policy because what we haven't done is look at how antitrust rules, particularly in different governments can be used to deal with some of the issues in terms of intellectual property usage, strategic behavior, technology markets, the so-called essential facilities doctrine of which is to make open things that you otherwise might have closed.

So we may get back to some of these other issues. But for Pam's schedule, I will finish up here. Thanks.

[APPLAUSE]

Agenda Item: Questions and Answers

DR. SILVER: So I'd like to open it for questions now, please. Ken?

AUDIENCE: The intellectual property rights and standards and protocols issues that were raised in several of the talks are now in a funny position because as the conference has emphasized that the bundle of technologies and approaches we call synthetic biology is largely but not exclusively pre-commercial. My question to all of the

panelists from different perspectives looking ahead 10 to 15 years as the technologies and approaches prove themselves, as the parts become more valuable, the protocols and standards assume much greater value, what do you expect to be the state of the landscape, the major fights and what steps should we take now to avoid let's call it the worse visions of the future that you have.

DR. RETTBERG: So I remember when I was at Apple Computer being asked –- they were starting to do the Power PC development and I was asked to compare the patent portfolio of Apple and IBM. I thought this was a disaster. My career was over because it was going to take forever to go through the patent portfolio of IBM.

It turned out not to be quite so bad because by simply measuring the height of the stacks, it was crystal clear the problem was not of one of the details of the patents, but rather how much Apple was going to have to pay IBM in order to not continue the discussion any more since they actually wanted to proceed.

All along, I kept on running into people saying patents are very important. But I had Apple involved in

their advanced research organization, they said, oh, we get patents, we get patents, patents. But in my experience, I actually never found that individual patents were very critical.

There were always exceptions. Xerox had a patent on the copying that lasted for a very long time, and they were able to milk very successfully. But in terms of the computer industry it was like clumps of patents, and there was cross-licensing. And if you had enough patents and you wanted to do the business, then you could do some cross-licensing.

I feel that biotechnology seems to be a different thing where individual patents have extreme financial value. And that, I believe has produced a tendency in the academic community to use patents as lottery tickets to say I am doing an important piece of work. I am going to make sure that its patented. I don’t expect that I’m going to make any money on that patient. But if anybody ever makes a billion dollars, I should get my share. And therefore, a patent is put in place which acts as an intellectual block to future activity but for the most part doesn’t produce

any financial return.

So I think what might happen with synthetic biology is that it takes the path in the electronics industry of particularly as we move out of strictly the pharma industry, as we move into kind of the engineering of biology in a lot more ways, I think we'll find there's a lot of patents, more diverse.

DR. JOHNSON: I mean, as Niels Boor said, you know, prediction is very difficult, particularly about the future. And I think the issue here is that we could go in various different pathways, and I think it's too early to tell. One could be very much along the semiconductor type of line where it's a mixed system where IP is absolutely critical and yet reuse and stacks and what not work very well.

There is a risk that obviously it could go in a different direction that would either retard innovation or choke it off at an early stage. And so I think the deed is short term to preserve those options so that you're not foreclosing different pathways because I don't think we're at the point now where we know exactly what really is going

to be the most critical elements for how synthetic biology develops.

DR. IMPERIALE: Mike Imperiale from University of Michigan. I have a question for Rick. Rick, you commented a couple of times about how intellectual property would actually promote openness. And I guess to me maybe being naïve in the field, it’s a little counterintuitive, right, because we think about as soon as we put something out there, it can no longer be protected. So can you expand on that a little bit?

DR. JOHNSON: An example, Mike, would be when SARS was an issue. Most of the national health services and the NIH that were deeply involved with doing some of the cutting edge research basically made a decision, I think the correct one, by saying that we want to be the ones who can control what happens with respect to this. So if we patent it, we don’t have to go get royalties. We can make it royalty free. We get complete control over how this develops in terms of what the licensing terms are, what the patterns are. And without that protection, somebody else might be able to –- now obviously with the registry is

that, you know, the hope and the notion is that you've done enough things that there's sufficient prior art so basically patentability and enclosure become impossible or at least very difficult.

But I think there are a growing number of people who think that it is better to have either public or other types of institutions controlling their own destiny rather than taking the risk. So the notion of protecting the openness is sort of in that vise.

AUDIENCE: So in other words sort of using IKEA as a preemptive mechanism –

DR. JOHNSON: As a preemptive thing in much the same way that open source obviously relies heavily on, as I mentioned, on it needs a functioning intellectual property system to make open source work.

DR. ANTHONY: Etole Anthony, International Center for Writing. So both Pam and Randy have mentioned the issue of enthusiasm of new generation students with great ideas, and I think this is really fantastic. However, I think that having the field, I mean having just enthusiasm is like having a car having only acceleration. So I think that we

should have another break and perhaps the break is what is called peer review. And I wonder how many of these ardent critics that for the most part appear to be Internet phenomenon have really made its way into the scientific or technical peer review literature. I have been making census myself and the number of papers in connection to this contest is literature. Let’s put it like that. That’s what would be one remark.

And then the other remark is on the parts. So parts are declared to be independent, reusable and you know I think we have to distinguish between having sequences that are compatible, reusable. I know that as compared to functions and I could argue that in biology what you have to play with is with functions not so much with sequence. I mean sequences are easy to put back and forth. Functions is where we have the hot potato to handle.

DR. SILVER: Can I just say something very briefly? Personally, I hope that we don’t have to teach students to live in world that relies solely on peer review.

DR. RETTBERG: So you asked about the enthusiasm.

I have been struck with several very odd discussions. There was a person who was coming from the Education Ministry of India. He explained how they took their enthusiastic students and they drove the enthusiasm out of them. I think that's horrible.

I am struck with the enthusiasm since we're in the sports analogy. Living in Boston, the Red Sox, the Celtics, the Patriots, the Bruins, the level of excitement around sports is dramatic. There is in the dwindling Boston Globe if you notice it's gotten thinner. There's still a very healthy sports section.

There is in fact no science section. There is in fact a very detailed listing of which teams and which place has won what. There even occasionally is a multipage section about the high school teams, who they played, who scored what, who won, all the standings. There is no similar section in the Boston Globe related to education, science or engineering.

So I am very happy to have the enthusiasm because the alternative is horrible. So I don't accept the complaint about enthusiasm. I think it's fine. I hope we

keep it. I know that in the experience I had with the development of computers and I know that even now in the world of software computer people are excited. It's a good thing. You get your new iphone, right, right. You want one, right? It's great. So I'm completely happy with that. I understand completely that that does not replace doing good work and simply being excited doesn't mean your system's going to work better. But it does allow more people to participate. It gets people involved and excited at an earlier age so that they set their careers to learning the things they need in order to be successful at this.

I know that I have had several times, I have had people explain to me how their child wants to go to one of the schools that has an iGEM team in order to study biology and be on an iGEM team, and that's a great thing.

The question of the interchangeability, of course it's not perfect and of course occasionally the biological systems are in fact too complicated, and they get in the way. But very often the actual experiences that functions are able to be moved from one particular organism, one particular genome into another and they function okay. So

the actual success has been pretty good.

DR. JOHNSON: Just one short comment on the second part of the question to say that people doing genetic engineering obviously play with DNA. But I found myself recently trying to do epigenetic engineering, and in the end it boiled down to playing with DNA again.

DR. SILVER: Excuse me. Can we take a few questions, and we'll see if we can answer them together. So go ahead.

DR. TAYLOR: Terry Taylor from the International Council for Live Sciences. My question's prompted really by Richard Johnson's remark about user driven innovation and the democratization of innovation, the Von Hippel idea.

But I wonder if the panel –- I'm addressing it to all the panel really. I wonder if we're missing one very important driver that may drive the technology forward in a particular direction, and that is synthetic biology. Learning from the information technology driver which was the ordinary consumer what Freeman Dyson has called the domestication of the technology which impelled the technology forward enormously with video games, iPods and

all these other technologies that you now have in your home. I wonder if you could postulate about a future of synthetic biology with this domestication of this technology which Freeman Dyson warns us about because this is rather different, and it is affecting fundamental life processes. So it's a rather different element in relation to policy challenge for everyone. So I wonder if they could comment on the possibilities of domestication of synthetic biology.

DR. SILVER: Okay, so we have the future. Let's have another question over here.

AUDIENCE: Sure. A comment or a praise and two brief questions. As a scientist from one of the developing countries, I'm deeply impressed and so excited about the talk by Randy on iGEM. I have been in Europe and the States for so many years. I realized it before that the biggest difference or major reason for us developing country have been lagging behind is education. If what you say that impact is for today, and the research is for tomorrow and education is for the day after tomorrow.

And I would like to tell my colleague over here

also from developing countries, especially those in Asia, but really have to confess that our able researchers have not begun to do some real work on synthetic biology yet. But now you have already begun to educate the kids. That's the difference. That's what I have learned. I really would like to sing all my praises for you on your job, on your talk.

The question is very simple. First, are you going to have a team in China? I really would like to cooperate. Then I have the second question. For Rick, do you have any commons on that patent application for the minimal genome of hundreds of genes? The minimal genome is artificial, is novel. And other genes, difficult to say. Perhaps few natural. Thank you.

DR. SILVER: Okay, patenting and genome, and what was that first question?

DR. RETTBERG: We have several teams in China. Just go to iGEM.org, and you can see the list.

AUDIENCE: (Off mike)

DR. SILVER: Well, you can go to the Internet and find that out. Okay, quickly then there's one more

question, and then we'll –

DR. EPSTEIN: I'm Gerald Epstein from Your Affiliation Could Go Here. I'm struck by the difference in time scale between the legal system and science. So the Chopper Barney case, we have sort of a decade, and it seems this is ultimately going to get wrapped up in a major court case. Question one is can we bring that sooner rather than later? And two, when we have a major court case, I have images of columns collapsing and all sorts of things coming down. Is it going to be a disaster, or are we going to somehow dust off and keep going? What's going to happen when some cataclysmic court ruling says and does that mean we can do any kind of planning or policy at all, or do we just wait for the legal collusion and then pick up after?

DR. SILVER: We will lump that into the litigation question, and then the last question.

AUDIENCE: Quick one for Randy. You spoke about the expansion of iGEM numerically and geographically. I was wondering if you could comment on how the nature of the participants might be changing, in particular the age of participants, the type of backgrounds they have and perhaps

even the affiliations or lack of them.

DR. SILVER: Quickly.

DR. RETTBERG: I believe what's happening is that as we expand in size, we're getting more of the curve, the edges of the curve is expanding. So we have had a high school student participating at Penn State several years ago. We had one high school teen tightly connected with UCSF participating last year. That team has continued this year as a high school team, and we have one completely unaffiliated high school team from South Carolina participating this year.

There is another activity which is the Do It Yourself Biology Group. They would like to participate in iGEM, but they're going to have to get themselves organized a little bit more before we will be able to know that they can participate within iGEM and do it safely.

DR. SILVER: Okay, I think then we'll close. Richard, I think there's about several litigation oriented questions.

DR. JOHNSON: Let me just comment very briefly about the –

DR. SILVER: Very quickly.

DR. JOHNSON: The third point is a very important one. But it's not a new issue, and all emerging technologies and over a long period of time you've had this lag. We've had lags from telegraph, telephone. We had the issues in terms of the airplane where the airplane eventually you had to have a young Secretary of the Navy named Franklin Roosevelt step in and basically create a patent solve some of the problems. We had it in transistors where basically eventually the government had to step in and tell AT&T and Fairchild and TI to license. So basically court cases also, I think, and there's an interesting work if people want to look at it by Mark Lemley of Stanford, who I referred to earlier and some colleagues which basically is arguing which I find actually fairly persuasive historically of why you want to leave it to a sort of a messy court process and in the end maybe we can accelerate it a little bit. But it may end up with better results than with people trying to make decisions at an earlier stage that are premature and that prevent or cut off future options for the development. I think some of

Randy's things with Arpanet and the Internet also go very much to that.

DR. SILVER: Okay, so lastly there was the question of the future which seems to close every session. So would you all like to –

DR. RETTBERG: I just want to say one thing which is I'm a little bit concerned about the court case, and I hope I get to retire before that actually happens.

DR. SILVER: Okay, so that's your vision for the future. So would you like to comment on the future?

DR. KÉPÈS: Right. So what I think we are facing is really an expansion. So it is a very exciting moment actually to be involved in this new field. And from the way we will be able to deal with IP issues as well as infrastructure and financial support will come actually better field of a more difficult field.

An important issue to my eyes is how much protection do we need in order to keep the industry going without –- while minimizing the impact on basic research. This is really an important issue, and I was very glad to hear that the views of my colleague, Rick Johnson. Thank

you very much.

DR. SILVER: Anyone else want to comment?

DR. RETTBERG: I'm always surprised by people who say – have sentences that start, well, who would have imagined, right. I think of the previous President saying who would have imagined a flood in New Orleans except then you see there was a report that he sat in on before that.

People would say, well, who would have imagined computers everywhere. Who would imagine all the computers in the world connected together except I was in the early development of the Arpanet, and of course we thought about there being ten dollar computers. That's the number we thought of, by the way, and we clearly aimed too high, and we clearly thought that all the computers in the world all being connected together.

We didn't understand exactly where it would go, but Doug Inglebart had already done many things in the human augmentation project that are actually now in existence in the web and in the mice that we used. So I think that we are still in very early days of synthetic biology, and our time frame shouldn't be what's going to

happen in five years. But I think that over this next century we will find that we get to be good at matter.

In the second half of the last century, we got to be good at information, and it was fundamentally different. Biology is the core technology that manipulates matter better than anything else. And as we harness it, I believe we will get to be good at matter.

DR. SILVER: Okay. I think we'll stop there and thank everyone.

[APPLAUSE]

(Break)

Agenda Item: Session 5: Roundtable on Investment Models for Synthetic Biology

DR. LAZOWSKA: Okay, folks, let's take seats and get going, if that's okay. Well, thanks. My name is Ed Lazowska, and this is the session that's called a Roundtable on Investment Models for Synthetic Biology. I'm a computer scientist which sort of leaves me odd person out at this meeting. My really principal connection to synthetic biology is I was chair of the DARPA Information Science and Technology Advisory Committee in 2003 when Drew

Endy and a set of others led the first major sort of synthesis study of synthetic biology which in many ways I think launched the parts based community. And from a computer science point of view, there are a lot of analogies to synthetic biology.

During this session, we'll continue the discussion of open source versus open innovation, for example, which has a lot to do with investment models and investment incentives. But really from my field's point of view, we're in the business of complexity management, and complexity management is the reason that today you can design integrated circuits with billions of transistors and 25 years ago we could design integrated circuits with tens of thousands of transistors. So it's not just that they're smaller and you can fit more of them on the same die. That's, of course, the case. But the real issue is what are the design tools and what are the composable units, and how do you make them larger and larger over time and still preserve that composability that allow teams of reasonable size numbers of people and reasonable amounts of time for reasonable amounts of money to design things that are

orders and orders and orders of magnitude more powerful and more capable than they were just a few years ago. And that's the path that synthetic biology is traversing now, and that's the leverage of this parts based composable approach.

We're going to divert a bit from the pattern so far. The plan for this session is that each of the panelists is going to give you about a five minute introduction just telling you where they come from, and then we'll have a discussion with you. So we really want your active participation in this both as people asking questions and as people answering questions. So we'll say a little bit more about this, but there's plenty of expertise on the panel but there's plenty of expertise in the room, and we want to have everyone participate in this next session.

So let me tell you who we've got here, and then I'll invite them up one at a time to just give you a bit of background.

Mark Waxman on my immediate left is the Chair of the Healthcare Industry Team at Foley & Company. Greg Kisor

is Vice President for Investor Relations at Intellectual Ventures, an organization in Seattle and the world these days. Paul Olsiewski is Program Director at the Sloan Foundation, and Ioannia Economidis is the Principal Scientific Officer of the European Commission.

So we've got a lawyer, an investor, a foundation person and a European. I think that covers the bases. We've checked all the boxes, and we're ready to go. So with that, let me invite Mark to hop up here and give you a bit of introduction.

MR. WAXMAN: Thank you very much. Having virtually two lawyers in a row, you have my sympathies. I feel like kind of after hearing that last discussion, Richard, I feel like kind of a skunk at the picnic. You know, we come in with different bent in terms of what some of the issues are.

I come to the investment side, I guess. We first got involved looking at the investment side of this in the representation of FEBIT in connection with the investment of Incutel into FEBIT which was one of the investments that Cord was talking about yesterday, a particular kind of

investment model that we may have an opportunity to talk about.

What I want to do briefly is to chat a little bit about sort of a view of the investment environment taking off of the last discussion that we had. And looking at this, some of this is perceptual. But you can see this is kind of a little bit of what the public may be starting to think about synthetic biology and where we may be in a couple of years. And while this is cartoonist, of course, you can see as you look at what headlines are that are actually behind this type of cartoon, it's a little different and this is just some of the recent theme because I think this helps inform the environment.

We go from the first one that sounds good about bugs eating waste and excreting petro that sounds really great to big questions about technology to the Army Slows Bioresearch at the Maryland Laboratory. Those of you that read the newspaper articles about Ft. Dietrich and the various things that were going on there, you kind of ask the question, you know, are we one vial away from disaster here if something happens. Are we all of a sudden going to

see a different type of environment to George Church's are we creating life from scratch to something world changing. We're now interplanetary to synthesized ethics, bringing in an entirely different element and then to the ultimate pragmatism, you know, gene therapy gets under the skin, going under nails and under the skin to help cure people.

So the reason I point this out to say, look, this is as you invest into this both from the public and governmental perceptions. This is what it is that people are thinking about. The Woodrow Wilson folks who I know are here, you know, they've done a nice summary showing the news coverage going like this over the past couple of years talking about sort of the themes that people are thinking about, and I think we have to be a little bit careful as we keep talking about designer organisms, playing God, and Frankenstein like pictures coming out of this that create problems coupled with this whole notion of biosecurity. Is this really a threat that people are concerned about? Yes. But is it something that has to dominate our discussions, or do we need to again temper the vocabulary that's there.

We just heard, I think, what I would call a

fairly distressing and depression discussion about the patent thicket. The question is, you know, is this enough to just kind of kill the whole thing and we should all go home and maybe, as was suggested, await the litigation. I think a positive view of that would be no. I think the answer to that question, you know, should we get into now, I think the answer is yes. We ought to get into it now. We ought to look at what some of the patents are, and we ought to have a better understanding of where the blocks are and where they aren't.

Is it a good idea to await the litigation? You know, those of you that kind of follow the patent world, I mean the Qualcomm litigation with Broadband and Texas Instruments and Nokia's been going for years. It didn't stop innovation. It was good for our profession. It didn't stop innovation necessarily. The litigation's that gone on in the genetically engineered crop field has also been good for our profession. It didn't stop innovation. But could there be a better way? The answer to that I think has to be an obvious yes. There could be a better way, a much better way, and I think it requires some sort of affirmative look

at how this might work.

And the question is who's going to lead that affirmative look on some sort of collective collaborative basis. I think it probably has to be something in the order of trade association who says we're going to take a hard look at this or a collaborative probably on the not for profit side who says we're going to take a hard look at this potentially supposed by industry as well.

So the answer is real joint effort viable? I think my answer to that is yes. I don't think we ought to all just await the continuing expense involved in sending my kids to college.

Next piece, we touched on a little bit. You know, the lack of regulation. Yes, there's a lot of regulation out there for people who, you know, you run a lab, you have to open a lab, you have to get a license. You want to run certain kinds of facilities, you have to get licensed. You want to get patented. You want to get something through the FDA. But there isn't any real specific regulation that is focused on synthetic biology per se as a regulatory matter. So the question is, is that a good thing or is that an

inviting target.

I think it depends how you see the public perception. Sometimes when there's regulation, the public feels more protected that somebody's looking at this, they've seen what's important, they've seen what isn't, and some sort of regulatory environment may be helpful from that perspective.

Sometimes you have regulation as something else. And as I say, right now synbio may be regulated because it may be a pollutant, it may be a pesticide, it may be a contaminant. It may turn out people think it's nanotechnology. Those of you from Berkeley know, you know, the City of Berkeley wants to do something with nanotechnology. And then you end up in a regulatory problem that lots of different people may be trying to regulate the same thing, and you end up something like stem cells.

Stem cells, you could -- in California, you could have the Governor give you a lot of money to go do embryonic stem cell research. If you're in the Dakotas, you go to jail. All right, that wasn't a very good regulatory regime. So somewhere we need to step in and avoid what I

call the crazy quilt of regulation that I think we've seen with stem cells.

One of the things I think is worth a good look is why not use the proposed Amended NIH Guidelines that came out for recombinant DNA research that have now added on synthetic biology and maybe we could use those as a baseline to expand the regulatory environment and adopt it on a little broader scale.

These were published in March. The comments are in. They start talking about a taxonomy of risk as we look at, you know, synthetic biology, in that case based on certain strains and whether it's two-thirds of an existing viro genome or half or something, but it was a start. I think it was a way to look at how are we going to address the research phase, how we're going to prioritize risk and relate the risk to how we're going to do the research. I think that might be a good start. It doesn't get you to the next phase which I mentioned in my question yesterday. What about scale of distribution and sale. You know, how do we go about thinking about regulation there. Again, this is something we don't want a patchwork. We don't want to any

time you have synbio rolling through the streets of Berkeley you have to go register it as a model which obviously would pick up everything from perfumes to tennis rackets. I'm not sure what the goal there was. And we clearly need to address the need for international harmonization. I mean this stuff gets mailed through the mail all over the world. To have one set of regulatory environment here and another one there again isn't going to be very helpful.

Insurance, you know, this is a question I've written about. Is there going to be some sort of synbio exclusion in certain kinds of insurance policies that if you're working in insurance, if you need insurance to commercialize, right, you need to protect your workers, your workers comp insurance. If you're going to make products, you've got to have products liability insurance. You know, how are you going to go about handling that.

The insurance industry, Swiss Re in particular, is looking at this. I think an intergovernmental insurance exchange as has been suggested is probably unnecessary. But it's something that we need to think about.

End of the day, you know, kind of where do you end up? Is there a possibility of public/private partnership? There's a lot of talk about this. There's a lot of talk about can you put together the screening watch list hotlines and clearinghouse altogether as an industry and say we're going to have a nonprofit center to this. I think the answer to that is yes. I think it's a good idea. I think government ought to fund it, and I think industry ought to get behind it.

You've got IASB in Europe already coming together with a code of conduct project with some technical solutions that they would like to put in place. If we could do that and adopt that internationally again I think another positive step.

Here in the U.S. we formed the Synthetic Biology Industry Association in order to start thinking about this collectively as a trade association from industry. One of the great things about this room is you have an awful lot of people from the academic side, from government, from NGOs, from the charitable side. I think we need an organized industry presence because as you heard with

respect to the patent world, industry sees these things a little different. Industry sees this can we create a market, can we do return on investment, can we get these things out. Consistent with the Bayh-Dole Act, of course, but on the other hand, they're ROI.

So there's an industry voice FEBIT, GENEART, Sutro Biopharma, IQT, Incutel, Blue Heron, Biosearch Technologies and Integrated DNA technologies have already joined this association. I'd be happy to talk to you about it if you want to do it. And the question here at the end of the day is who's going to convene the solution. We have a lot of conferences that sort of bring people together. The next step is we need to have one where people sit around the table and say, okay, if we're going to regulate, what's it going to be, who's going to do it, and how are we going to move that process through without killing it because it's an industry that everyone says has purpose and value. Let's not get caught up in the thickets. Thanks.

[APPLAUSE]

DR. KISOR: Sorry to disappoint everyone, but I didn't prepare slides. So an interesting point in my life

came on Wednesday. On Wednesday I woke up to the news that the Pope had declared patents evil, and the Swedish Pirate Party had declared Elvis evil. Now I mean I know it seems kind of strange. But in both cases, it's because they were protected by intellectual property. Elvis is protected by copyright. In fact, his current estate makes more money per year now than the collective years he was alive. It's pretty phenomenal.

The Pope made no comment about Elvis. But he did make a comment about patents, in particular those in the area of healthcare and the fact that there's just been a systemic failure to solve the developmental problems surrounding the zealousness to enforce intellectual property and keep things away from those that have real need.

So I have to tell you I was spending the day on Wednesday. I knew I was coming to do this, and I was just wondering, you know, which side of the fence should I be on and what should I do because, you know – by the way, I'm an Elvis fan. It's my chosen song choices when I do Karaoke. I was really questioning myself because even my fall back

career after patents was at risk.

But nevertheless it's true that there are definitely real issues around the use of intellectual property. And my company if those of you that don't know of us, everybody wonders whether we're evil or not because we are effectively a company that does venture investment model in intellectual property. We do do spin offs and things like that. So there possibly will be products along these lines. We really are focused on intellectual property.

Synbio is a small part of an investment in two of our funds. But really one of the things that I see is that the raging debate here, we have 95 percent of the debate taking place in something that's actually a much, much single digit percent of the developing world. But it's interesting to see this debate because we really live in an exciting time. Synbio offers promises of all kinds of things. I teasingly tell my children that I'm going to live to be 150. So they need to learn to put up with me, and I actually think there's a promise that that might be possible, although some people say I'm crazy for wanting

that.

But this is an exciting time, and we need to figure out how to encourage innovation, and this goes not just for synbio but in general. Advances in technologies and so on are just going at a rapid pace, and innovation seems to be stunted in some cases by somebody's desire to make a dollar. And I would say I actually think that those dollars are actually what's causing the desire to innovate. So before you brand me an evil raging capitalist or whatever, I'll just capitulate to it.

The debate about IPR is something that is not new at all. The earliest case of it in the United States that I could find was a debate in the 1820s over patents around heaters going into homes. They had developed a new radiating kind of heater, and it was being protected and only one producer in Pennsylvania was producing it and there was a debate that it would allow the poor to have proper heat with less material going into the heater. Therefore, it should be declared open for the public good. And it was rather interesting to see that that's a similar debate.

You go with the Wright Brothers and their aircraft. They actually before World War I the Secretary of the Navy had to basically force them to open their patents up so aircraft could be built. If you go fast forward in software, originally software, even the ability to copyright software was challenged. People said it should be free with the hardware.

And now we're of course debating patents on software and when are they valid and when are they not and so on. And I think that that's very similar to a debate that you'd have about synbio. You know, when should the patents be allowed, and when should they not and what's the scope and what should be allowed to be protected, what should be open for research and so on.

One of the things that I know because I live in this world is that regardless of how you want to do it property rights drives the ability to have wealth creation. And without wealth creation, you don't have investment in innovation. The public good alone would put us to the point where we're solely relying on philanthropy and the government basically, the governments to fund innovation.

And that even will dry up if there's no wealth creation. So property rights sort of drive the need for wealth creation. So in this we need to preserve some way that wealth creation is still possible while allowing for innovations and innovations to be built on top of innovations.

It's kind of ironic that the very property rights that most people think as a barrier to access is probably the only vehicle people have to ensure access, to ensure proper usage of the technologies because without intellectual property you have no way of saying they must open it up or they must produce for third world countries or they must allow researchers to have access to their innovations and so on.

So I welcome any questions. I welcome the debate. But I'm sort of fallen on that side of the issue, and I'm here to advocate that we need to find a space for IPR in this. We need to find a space where research can occur, and it's done such that all research is possible. It's done such that the public good is served. But it's also done that we have a growing health industry. Thanks.

[APPLAUSE]

DR. OLSIEWSKI: Good morning. First of all, as a sponsor of the meeting, I want to thank you all for coming and sitting in the audience and listening to the wonderful talks and so on. And I found this meeting to be incredibly exciting. Now I didn't have an erector set when I grew up, but –- and my parents didn't go to college. But I had a microscope and I had a Gilbert chemistry set. So maybe that's how I ended up getting a Ph.D in biochemistry at MIT. I don't know. But those early experiences make a difference.

So why do I care about synthetic biology? Well, when I took my job at the Alfred P. Sloan Foundation, I was hired to develop a new scientific program area in biotechnology, whatever that meant. I also was asked to work on our bioterrorism program, and this is pre-9/11 and was interested – the Foundation was interested particularly in issues of potentially dangerous research in the life sciences.

All right, so suddenly I'm working at the Alfred P. Sloan Foundation being paid to study, work with really smart scientists, engineers, people, ethicists, lawyers and

again both looking for important projects in basic research to fund as well as in looking at potentially dangerous research in the life science. So that sets the stage. Okay. May I have the next slide, Stephen.

I want to then mention two early important grants. We do our work by studying problems identifying smart people to work on them, coaxing them to write a proposal and then funding them. We give grants. It's a very exciting and rewarding professional opportunity. I have two grants listed here. One is a 2001 grant to the National Academies and Jo Husbands is here somewhere, the PI on that grant, and that ended up becoming the Think Committee Report which actually is called Biotechnology Research in an Age of Terrorism, and that was really a landmark report because it said there was some experiments in the life sciences where you really should think about it and then just did a series of recommendations which I'm not going to talk about but is a very important thing because should there be regulation in science? Well, there already was some. The RAC, were those –- I don't want to call them. Whatever the legal term is, was that enough oversight and

so on.

All right, so working away on that. But remember, I had the microscope. I had the chemistry set. I read Science. I read Chemistry and Engineering News, and there I see in Chemistry and Engineering News a picture of Drew Endy and some students holding up flashing bacteria, and I said, hmm, this looks good. But remember at sometime during this time we had had the anthrax attacks and so on. So the bioterrorism program got a little more exciting because people were very interested in it. But anyway, I'm not here to talk about that. I'm here to talk about synthetic biology.

So I started following synthetic biology, and I thought it was really exciting. We invited – I went to Synthetic Biology 1.0, met a number of the people who are in this room. We invited Drew to give a talk, the Sloan Foundation. The science and engineering blew us away. I said, okay, Drew, what do you think. That's how we were, got a great person in the room. And Drew said to me I think you should work on the societal issues. It takes up so much of my time, we need some good answers.

So I took the good advice, and that led to a 2005 grant which is a joint venture, the Venture Institute. They're definitely doing the science. CSIS definitely understands the security implications, and MIT, Drew's group, definitely understands the engineering. And they put together a consortium of scientists, various leaders from ethics, whatever other from soup to nuts and came up with a report called Synthetic Genomics Options for Governance, and this was our first big splash in the synthetic biology arena, and I think that's been a very important report. I think three out of the four people are in the room today. Jerry Epstein, Michele Garfinkel and Drew Endy who are authors on that, and again I think what's really important about that report is that it gives options. It leaves it to others to determine what the risks are because depending upon what you think the risks are, that will help you select your options.

So we also during that time we underwrote the societal Issue sessions at Synthetic Biology 2.0 in Berkeley, 3.0 in Zurich, 4.0 in Hong Kong. One of the things that's been really wonderful with this is I've

traveled all over the world and again meet, you know, hearing really interesting state of the art science and engineering talks in this fabulous field as well as engaging people on the various issues.

So in 2008, we decided to take another look at what we were doing in synthetic biology, and we wanted to go just beyond synthetic genomics and some of the biosecurity issues to look at some of the other issues. We see a lot of promise in this field. We hope that there will be wonderful products that will help with our environment, with our health and any other application that may come along. And so I'm going to step back so that I don't get these in the wrong order.

But we wanted, we had several goals. We wanted to improve understanding of ethical, social and policy issues by the scientists and engineers. We wanted to improve understanding of the science and engineering by the policy makers, journalists and the public. Again, we're committed to improving biosecurity and biosafety. But we also wanted to create a cadre of young scholars working on the societal issues, and I don't know if Paul's still here. But I'm

still using that term.

And so we have three projects. The current project is the one that's incubating or happening right now. Anne-Marie Mazza is the PI on that. This is this meeting. We had a planning meeting, very exciting for the Sloan Foundation to be able to participate in the brainstorming and again meeting all these international collaborators.

I'm going to mention three projects, the Hastings Center, the people from that project are here. That project is led by Tom Murray and Greg Kaebnick. They're here. I'm not going to give a lot of detail on the projects because you can meet the people. We have a project with the J. Craig Venter Institute. Michele Garfinkel is here. Laurie Knowles. Paul Thompson of Michigan State is also part of that project. And then we have the project that was alluded to in the first speaker at the Woodrow Wilson International Center for Scholars, Dave Rejeski at the back as the PI on that. Andrew Maynard is in here. And since Dave's actually giving a talk tomorrow, I'm going to say the least about that.

All right, so the Hastings Center, again, why are we working with the Hastings Center? They're a high quality ethics center. So we're interested in -- one of the reasons we funded them is to do serious scholarly research on the ethical issues in synthetic biology that will help inform policy discussions.

Roger Brent graciously agreed to be their scientific adviser with all of our projects in the societal issues in synthetic biology. It is key to have top synthetic biologists involved in the discussions, engineers, biologists, practitioners of synthetic biology working directly with the social scientists, philosophers and ethicists. And then I list the three topics that they're going to review as part of their study.

All right, then I'm going to mention the Venter Institute's project, okay, and it's called synthetic genomics. Scientists' understanding of society's concerns, society's understanding of the science and the scientists, two sides. We expect that this project will help the scientists and engineers better understand how society views their work. We also want to educate journalists so

that they can better inform the public about synthetic biology. We also want to inform policy makers to help them structure better policy.

And one side on the Wilson Center. Many of you may have already been to some of their events. Their goal is to identify and start to address the risks in synthetic biology. They've had some fabulous events. Mike Rodemeyer gave a talk. The people from the Hastings Center presented some of their work. They've had several things. If you haven't been to their website, I urge you to go there.

So anyway the Sloan Foundation has probably spent at least $2 million investing in addressing the societal issues in synthetic biology. We think it's very important. We encourage others to invest in this part because I think it's a very important area, and I'll answer questions later. Thank you.

[APPLAUSE]

DR. ECONOMIDIS: Thank you for the invitation. I'm the European. What I would like to tell you is how a European institution like the European Commission is investing in these particular parts of science, and of

course you can imagine that it's part of a whole structure of investment.

Now talking about synthetic biology, we started with a given definition back in 2003 was high level invitation of scholars where they came and they gave a definition of the field. You may agree or disagree with the definition. However, it was a working document in order to start thinking how we can proceed in this field. And the elements, of course, were to address biological systems as many times we have discussed in this meeting with the tools and the language of engineering that was the main principle.

Now coming from this document, there were two calls for proposals and they came out and yesterday there were discussions on that. Two sets of projects that came out of 18 different projects. Some of them they survived through the publications and the peer reviews and the public relations that they make some of them. Probably they went out to their final report, but some of them probably you know the acronyms like the emergence of the provocatives you have heard about it on SynBiocomm,

Synbiology, Symbiosafe, and Tessy. You have a representative here and some other projects in which we don't have really the details to go on it.

So the major elements of that were to come with some topics dealing not only with basic science but by medicine, new generation of pharmaceuticals, new chemical compounds to approach the issues of environmental energy and production of SMART materials and some issues as we just heard the last speaker of issues of security and safety. This is history.

Then we came at the era of the seventh framework program. For the non-Europeans, a little bit of background. This is the major funding system of the European system, and it has several elements. I'd like to show it to you. It's a program that has funding for seven years of the level of $53 billion Euros, and it's breaking in different dimensions. The two elements that we have to take into account is the one on the top which is called ideas, and this has the basic elements of research. You have heard apparently from the so-called European Research Council, and this open-ended type of blue-sky type of research, and

of course it has some projects of synthetic biology.

And the other ones which we care about is people because that involves fellowships. Young people, we've heard before, lectures on the importance of young people. So it's for young scholars to exchange their experiences. And the major funding comes from the program Cross Cooperation which involves different other small programs, mathematic programs.

Now you could have imagined that synthetic biology can fall between different disciplines. One can be health, the obvious one. The other is the food and environment. The other one can be nano-materials or new materials. However, it was a matter of choice. Some of these programs did not really respond to this kind of provocation of the new times, but some others they did.

I am lucky enough to belong to a program called the Knowledge-Based Bio-Economy, and I'm going to tell you a few things about that in which we responded to the issues of synthetic biology. So the Knowledge-Based Bio-Economy, it's very sketchy. It deals with three elements. One of the biological resources and one, of course, of the biological

sources can be agriculture per se. This second one is the processing. So when you have biological resources, you go to two directions. One direction is for food, and the other is for non-food.

I belong to the part which is non-food and has the most advanced biotechnological techniques. And I don't know if it's right or wrong, it may come from the discussion. Synthetic biology, we use it as one more advanced tools, one more part of the emerging technologies of biotech knowledge in order to promote bio economy because biotechnology is not science per se but is a technology. So it has to give services and economy to the society.

So we have a modest cultural proposal at the beginning, and we came out with one project. Victor De Lorenzo yesterday alluded around this kind of ideas is how to use synthetic biology for approaching, attacking environmental issues, aspects of bio mediation, and there was a modest investment of $1 million Euros and to accumulate scholars to come around and create the critical mass around this particular issue using synthetic biology

for environmental issues.

Getting more courage from this project, this project has several working elements and the one is the conceptual frame. Since this is a new discipline, the genetic tools, the design and modeling tools, the bio degradation approach going to a specific issue and as Rick said, socioeconomic environmental assessment, biosafety issues and the aspect of training and dissemination because at least with the public perception we have strong issue in Europe. And of course, training is a seminal issue of any field of science.

Now in the following proposals, we went to better investment around $3 million Euros, and we said instead of approaching the issue of environment, let’s ask what synthetic biology can do in general for biotechnology, and in this case we defined even what we want to do from the elements of synthetic biology because synthetic biology covers several issues. And this is what you see in the blue, and the most important thing to have to create maybe the tool for going through different applications biotechnology.

So it came out with this hasn't started yet. It's under discussion. The finalization is a project which has eight labs. It's to modify the chromosome of the bacillus subtilis receptors and to create the tool for having a new and more focused biotechnological applications.

Now very quickly to another program that these people are working on socioeconomic research. They have two projects, one called Synth-ethics and one called SYBHEL and they are dealing and analyzing the LC issues which can be focused new or not new because it's a matter of debate on the synthetic biology.

Now the type of investment that we do, we try to have so-called stakeholders I mean from the different affiliations and disciplines that you can see on the slide which have, of course, we need the industries as well, small, medium enterprises or bigger industries.

Now I'm finishing by saying that besides giving money and following the projects, we try to have network. And so we have three types of networking. One is the European Network of Semantic Work and one is the collaboration just mentioned. The basic research of the ERC

and the people fellowships. The second one is that we have asked every country that sits as an advisory country and we have 30 countries around the table to have a network so the KBBE, the Knowledge-Based Bio-Economy Network and to have designated specialists from their field and to come and give us more or less advice and tell us what they are doing in the member states.

And they have a working group in the initiative of Germany, the Working Group of Synthetic Biology, and that works very well. Of course, because it's a governmental, it has an irony. One of the member states has a major activity in studying biology is not represented there because they're bureaucrats or they're administrators. They haven't thought carefully about this field.

And then yesterday we discussed the European Group of Ethics where they give advice to the President of the Commission, and they come with a report now in September that will be public on the net how the European Commission and the Union are thinking about the ethical issues of that. Okay, and the second type of networks is

what we have in Europe. So we have the FP 7. We have the ESF, the European Science Foundation. We have the EMBO. They have activities. The Royal Society, that of course is the organizer of this meeting, and the Royal Academy of Engineering.

And third one and I'm finishing is that the International Network that we try to participate is the International Conferences that we just heard. The OECD Working Party on Biotechnology which would try to complement our work and their work, and finally last but not least and there are several members here, the EC-US Task Force on Biotechnology Research where funding agencies from this country, from the United States and European Commission try to discuss about the cutting-edge research and see how we can bring the two communities from both sides of the Atlantic together. Thank you.

[APPLAUSE]

Agenda Item: Questions and Answers

DR. LAZOWSKA: Okay, so this panel is about investment models and of course there are lots of possible investors. There are government funding agencies. There are

foundations. There are corporations. There are private investors.

And I'd like to begin by discussing this landscape a little bit and let me start maybe with a couple of analogies to software which I know a lot better than biology. One thing I'm interested in is understanding the balance of investment between tools and applications, all right. And my sense is that there is a large amount of funding for applications, but not a lot of funding for the tools that will allow one to build the next generation of applications. This is, well, you know I'm sorry. I was too busy solving the problem to build tools.

And if I think back to the integrated circuit revolution in the late 1970s and the early 1980s, DARPA made very, very substantial investments in tools, tools that made it possible for people who understood the architecture of systems to build integrated circuits. And that's really what created the revolution. It was the construction of those tools and the dissemination of those tools and putting those tools in the hands of people who understood system architecture rather than tapping up

integrated circuit masks.

My feeling is that one of the many things DARPA whiffed on in the past eight years was synthetic biology. We put a huge amount of effort into our ISAT study in 2003 and a lot came out of it. But it wasn't through a sort of DARPA decision to invest. It was through a set of people realizing that there was enormous promise, and they had to move this ball forward on their own. So that's sort of the first question which is what is the tools versus application investment balance, and is it appropriate. And if not, how does one change it. Maybe you folks have any opinions, and again we're happy to hear from you as well. Art, do you think about this at all or not?

PANELIST: Well, I think I disagree with you. I think there's a fairly healthy at least at the thought side perhaps the dollar side less clear as between tools and applications. I mean I see the gene synthesizers. I think those working on different types of gates. I think the people involved at sort of the biobrick effort, you know, all of those in my mind are the tools that are later on going to become the applications.

You read a lot about the applications as you look into sort of energy and things like that. But I mean I personally think it's balanced. The other question that you inferentially asked and I'll just answer it had to do with how are you going to investment, who's going to do it and how. You know, in my mind there's really four models that are out there that people do invest with.

I mean one is the standard VC model. And so you asked the question where are they investing. I think they're given the current investment cycle and others may answer this better, they're looking a little shorter term than they were in the past. And so I think that tends to focus more on tool maybe than applications.

There's the tech transfer model which was mentioned in the prior discussion. The tech transfer model looks at a little bit of each and has its own model and people can go online at Harvard or MIT and see what the tech transfer model looks like.

You know, the third is the application model. I mentioned the Incutel investment in FEBIT which actually was an investment that didn't take the form of a normal

stock purchase. It took the form of a work order that would be exchanged for warrants going in the future as a model.

And the last, I think, is kind of the Gates model or the CHAVI, CHAVI being the Center for HIV AIDS Vaccine Immunology which is sort of long term problem solving that also involves tools by a government funder with infrastructure collaboration and a centralized database. So I guess I see it as maybe a little more robust on both sides than you might.

PANELIST: So tools versus applications. I think that tools –- funding for tools does help jump start an industry, and the semiconductor integrated circuit example is a great one. But as far as the venture community, yes, they're very focused more on return and more near term return to try to bring solvency back to a lot of their current investments. But I think in that regard they're actually more focused on applications than tools. They actually want something that's going to go to market, that's going to create a return. And tools are useful only if it helps you bring applications to realization quicker.

For example, you know, the synbio area there's

people working on some what you'd call synthetic yeast to make beer and wine better, okay, and make it more consistent and make it create a more consistent product regardless of what went it, the materials that went into it initially. And that's definitely an application. It's definitely something that people are going to invest money in because there's a huge industry and so on. But the building blocks there likely have a lot of reuse for other areas because it involves a chemical transformation.

And so in that respect they look at that as sort of a tool as a basis for what other applications can be spun on top of it. But I think generally the focus is more maybe that's short sighted. But I think at least the industry and the venture community is actually saying, you know, how can I make money on this and I'll throw money into it because I want wealth creation and I want a sustainable industry. And I think that most of the investment in the building blocks, the tools and so on is coming more from either philanthropy and government or people doing core research.

DR. OLSIEWSKI: Actually, I'd like to make a

comment on this. First of all, I think there has to be data at least in terms of what the U.S., the NSF has funded in synthetic biology. I don't know what the data is. I know I saw Zoe over there. But I think that in the U.S. there should be data. Maybe it's not all collected, but it would be interesting to see specifically where the money went, okay, and how much there really is.

I also know that various companies do those reports on the venture firm. So I think it's great to sort of talk about this, that and the other thing in terms of the different opportunities. I really hope if someone has a report on the data, I would like to see that. When the Sloan Foundation was doing the assessment of what to do on the societal issues, we saw very little investment in the U.S. in the societal issues. And again, we only have a relatively small amount of money compared to the big funder in the U.S., and that is the government. So we were very careful before we entered into this area. But if somebody has those data, I'd love to see them.

DR. LAZOWSKA: Let me ask about reuse of components and sort of another software analogy which is

the sort of the open versus closed business, and we talked about this by email before the panel a bit. Rick did a great job in his presentation in the last session talking about open science, open source, open standards and open innovation, and they are different and it's easy to confuse them.

But one thing I'm interested in is whether there are adequate incentives for investment, for private investment or corporate investment in an open world in synthetic biology, all right. That is, it's possible to sort of overdraw analogies, naïve analogies between software and biology. So can you imagine investment incentives in an open world.

Another question is whether we've got a situation where the government and foundations are allowing people to corner future markets with public or foundation monies. So here to state this in the extreme and again this is referring to our email conversation, the Department of Energy has said to J. Kesling a few years ago, look, you know, here's your $100 million but you have to make these parts you develop open and publish everything you learn

through the course of this project. So I think this whole open versus closed issue is a really important one.

PANELIST: You know, it raises in my mind the question of the debate about whether the Bayh-Dole Act has been a success or not over the long haul because it raises the same issue. Fortunately, I don't know the answer to that question. But I do know that and this is why I mentioned it, you know, there are models out there which the government has looked at in other sectors which require you as a condition of getting the dollars you require to contribute to technology back into the pool in order to make it available for others. There's also the model of the stem cell patents that WARF where they have agreed in essence to license that to research uses and they'll come back and talk to you later if you start making money. But at least they want to get the technology out and principally licensed out to other non-profit entities.

I think the government, to answer your question, ought to look very hard at grants going off into the future and requiring, if there's the IP coming out of those grants, consideration of bringing them back in and making

them more generally available to help (a) fund the pool and fund the next generation of research. The theory behind that has to be that this type of research is actually going to open up an industry as opposed to close it down. You have to believe and we've seen this in software that by creating platform type technologies you're going to end up with more industry and investment in the end than you have now. There's a trade off that's very difficult to make at the beginning. But once it's gone, I mean one can compare what's gone on in between Qualcomm, Nokia and the rest to say look at that situation as opposed to other environments and say did we progress.

DR. LAZOWSKA: Let's take some questions from the audience. We've got a line at the microphone back here.

AUDIENCE: I guess I want to have some questions about how to best structure investments in tools. I would respectfully disagree that there's a significant investment in tools and very little public representation in the tool bases that are being built out. For example, construction of genetic material has largely been driven by private investments. The last public investment I'm aware of came

out of the Advanced Technology Office at DARPA in 2003.

With the sequencing projects, we saw significant public investments and thus representation in the development of tools for reading out DNA. What role should public investment have in sustained improvements to getting better at building genetic material. Second, along the same lines but as a specific example, if you look at the geometic growth of the biobrick parts collection, this is driven by a bottom up set of students all over the world. It’s a very controversial project because many people think biology’s too complicated to standardize and share in this way. Should we expect this project to succeed by itself, or do we need to see professionally staffed production facilities akin to a genome center come into existence to make higher quality parts and address some of the concerns that come from our better and more senior folks in, say, the National Academies.

As a third example of public investment, to be very specific last year 1,500 new parts showed up. If we are to assign very strong property rights to them so that we can give them away, patents would cost us about $30-40

million last year. That would be ten times the budget, if you will, of the actual event which produced all those parts. We're not going to pay the lawyers that much money if we had it. We'd probably make more parts. How do we invest in a legal framework that actually comes to life not at some imagined point in the future, but how about in the next 12 months that will solve this problem for us.

A final example. How do we make investments in community, again using biobricks. When that collection got starts, every new genetic component had a signature built into the DNA. This supports naïve colony PCR characterization presence/absence tests in the environment to figure out whether or not there's biobrick parts around. If you're interested in establishing a standard of practice as an engineer that an engineer will sign their work. If you're interested in making the future problems around biosurveillance easier, how could we pay for this. Practically, we couldn't do it with the lack of investment because the community grew geometrically and our funding sources from any source did not scale.

So it's four specific examples –- construction of

genetic material, professionalization of parts collection, a legal framework that actually works now and establishing a community. What would be the ideal balance of private/public foundational investments in getting this to happen? Thank you.

DR. LAZOWSKA: Well, great questions, Drew.

PANELIST: So taking them a little bit –- I agree that there's very little public investment, and the private investment most of us aren't going to talk about what we're investing in. So and in that respect, even if we're investing in tools, it's not necessarily going to be tools that are open based. So I tend to agree. Part of the second question, I think, was about a student-based development effort, will it succeed, does it have a chance and so on. And I would say that, yes, it has a chance to succeed in spawning people's interest and encouraging industry to take notice. There's several examples of early stages that happened. The first real sort of open source effort that I was aware of that did that was something called the Independent JPEG Group. I'm aware of it because I was working image compression at the time. But I was trying to

run a business that was about doing development on image compression, and here a bunch of college students got together and gave the code away for free and threatened my business model and I eventually capitulated and went to work for IBM.

But it succeeded, though, I think in allowing people to have a fundamental building block, a tool where they could actually try out concepts in building new products and it was quite successful as anybody who's watching television or whatever nowadays understands that digital imagery was quite successful. So I think that it's an effort that should be encouraged and has a possibility of doing a lot of great good.

A legal model that works? I think the gest of the question from Drew was about, you know, who in the heck's going to pay for the patent filings, that it's an order of magnitude, right, of the –

DR. LAZOWSKA: No, sorry. The question was is there a legal framework that preserves the accessibility of those parts while making it unnecessary to spend $30 million on patents.

PANELIST: Right, but there is a legal framework than can do it. But one of the first issues is that you don't even need a legal framework if nobody can afford to file the patents, right. So –

DR. LAZOWSKA: No, but some corporation could presumably make some of that inaccessible.

PANELIST: Right, but I think the two are inevitably tied together. There's a legal framework and a commercial framework that actually accomplishes both, and it's something that could be done now and it's one where you have an independent sort of a patent pool sort of situation. We've seen those work successfully where the patent pool in and of itself becomes sort of the independent arbiter of what should be in, what is relevant, what's valid, what's enforceable and so on. The Independent JPEG Group is one example of that. I keep going to imaging because that's part of the world I live in. But they actually also set a basis for what's reasonable royalty for commercial applications built on top of the intellectual property.

The whole Qualcomm situation that's been

referenced a couple times, one of the issues is Qualcomm requires quite a high percentage of your handset basically for the essential coverage on the radio component which nowadays is a very small part of the actual intelligent handset. And an interesting aspect would be if somebody could acquire more essential patents than Qualcomm owned in a pool and charge a much lower basis rate, that would put at risk Qualcomm's ability to say that what they were charging was fair and reasonable in an enforcement situation.

So I think there is a legal framework that allows sort of intellectual property coming to a holding environment where one of the terms is that innovation on – it's open for innovation. In other words, access for further research, access for doing early stage product development and so on is allowed for all the intellectual property within that. And I think that that or for basically public good works, supplying things to third world countries or using it for philanthropic sort of funded efforts.

But for commercial efforts, it would still

preserve the rights for people to build products and for wealth creation to occur in that area, and it would be done in a way that makes sure that the innovators get – that money flows into the system instead of buying new beach homes for attorneys which is basically what happens whenever litigation is the result.

And now that I have anything against the beach home for the attorney, I just think that we need to establish a system where it’s not by default half the money is going out of the system but it’s staying within the system and the wealth creation is allowed to spawn better and better innovation on top of it. Thanks.

DR. SILVER: I want to make a comment about the investment in the science and engineering, Drew’s point about the tools. Anybody in here who applies for grants knows it’s going to go through peer review. If it’s not hypothesis-driven research, it’s not going to get funded. I think that if –- and again, the Sloan Foundation made a decision upfront to tackle the societal issues because we felt that that was an unmet need.

But we do in other areas fund basic research, and

we always look ahead to say what is the exit strategy. And the exit strategy generally is that you make a compelling case so that somewhere in the U.S. government there is funding for this. So I think that I know the community's been working hard at this. But basically maybe that's an outcome of some meeting that, you know, there would be some analysis to make the case that in order for the synthetic biology to succeed we need the tools, we need the exploratory research and that has to be funded.

But as far as I see in the current funding mechanism, it won't be funded. Some of the things that we funded, the Sloan Foundation, in science, when I sent it out for peer review, what I have to now caution reviewers because the first they tell me is NIH would never fund this, and I say absolutely. That's why we're interested in it.

So I think here is a case where, you know, the Sloan Foundation that doesn't have that much money and we don't spend it all on science and societal issues and science. But I think the community, we as a community have to sort to make the case and sort of get this rolling, and

I think it's essential to the development.

DR. LAZOWSKA: Okay, Mark had a comment.

MR. WAXMAN: It sounds like a request for a grant application we'll be sending you shortly.

DR. OLSIEWSKI: I invite you both to –

MR. WAXMAN: It's coming. You know, short comments to Drew's comments. First, I mean there, as Greg said, I mean there are systems that allow for intellectual property exchange. What seems to be required and I don't think these are secrets is an analysis of what are the key patents. There's not tons of them out there.

Second, whether those who are holding the key patents are in fact prepared to license them and, if so, on what terms they're prepared to license them, it may well be that the terms that are being offered are very beneficial to the continuing development at least on the research side of the technology. I don't know that those people have said no, or that they've been asked appropriately whether the answer's yes or no or on what basis they would contribute.

So I think that also has to be tested. And just in the interest of time, I'll answer your other question.

Could all this be done in 12 months? I doubt it.

DR. LAZOWSKA: Okay, over here.

AUDIENCE: Yes, as far as tools and applications, just to define for the European Commission grants, those are consortia. And as I said, it comes from the different affiliations, academia, research or industry. In this case, the industry has to apply with the public rules. They cannot hold the data. They have to publish, and they cannot create patents immediately but after the finalization of the projects. The projects are usually from three minimum to five or six years. So in this case, as far as the tools versus the applications, for emerging technologies you start with the idea that, well, if I have to arrive to an application, I need some tools. So you have the excuse or the roadmap or whatever, the roadmap of five, six years to develop the tools in order to apply to even the beginning of some kind of applications. And of course, those are recommended applications, are not applications for ready for the market.

DR. LAZOWSKA: So I want to come back to the roadmap question in a couple of minutes because I think an

important question is, is there one. All right, in semiconductors, the roadmap has played a very important role. And I don't know if a funding agency or a government has a roadmap in synthetic biology. It's arguably, you know, I think we have to talk about outcomes here. And the question is what are some possible outcomes of this meeting, things that we could undertake that would actually make things better for both innovation and investment in synthetic biology. A roadmap is one possible outcome.

I think it is the case in this country that most research is very heavily application driven, you know. I spent Tuesday with a bunch of folks, Wednesday a bunch of folks from NIH, and I confess sort of astonished to learn that NIH doesn't do healthcare, right. You've got a disease, you've got an ear at NIH, right. You're a basic biologist or you got a healthcare problem, forget it, right. So and you know if you look at big investments in synthetic biology, it's, hey, we want to tackle malaria. And as Drew pointed out yesterday, that doesn't necessarily translate into generating the next malaria vaccine when a resistant strain shows up after 18 months, all right.

So I think the money even in the research domain is in the applications. Let's go over here. Sorry.

DR. TAYLOR: Terry Taylor from the International Council for Life Sciences. I have two short questions on risk and really related to investment risk in this area. And I was wondering whether –- this is addressed to all panel members, whether they could say something of how in a methodological way that is it possible to bring in the public policy risk that is being driven by public perception and how that is handled and what a deterrent that is through private investment particularly.

My second question is perhaps addressed to Dr. Economidis about the European Union's sort of background, if you like, policy element on the precautionary principle and how that is interacting or the implications of that for investment in the European Union and perhaps possible division between European Union and other parts of the world, particularly across the Atlantic on that aspect. Thank you.

DR. LAZOWSKA: Great. So those are great questions, and let's try and have short answers so we can

get to more questions. But I think the important issues here are that there is uncertainty related to public policy and uncertainty related to public perception and both of those potentially affect the investment environment. Comments?

DR. ECONOMIDIS: Well, our program, I'm not so worried about the investment environment. People in investments will make their decisions. We're just worried about just the field in general, and that's why to sort of air these issues, shine bright lights and come up with some innovative ways of dealing with some of the issues that get identified.

No one in this room – I was trained in biochemistry. There's not a biochemist who would say, oh, we've already discovered all the interesting biochemistry. So in terms of dealing with some of the societal issues and managing risk, I don't think we've come up with every idea. So I'm quite optimistic.

DR. LAZOWSKA: Greg, comment?

MR. KISOR: Yes, I think there's a very good question about how does the investment community, how do

they perceive the public perception and how does that create risk. And I think that at least as far as our investment decisions go, it seems that we definitely shy away from the areas of highest debate, the areas where it tends to be controversial and instead we invest in things like, you know, food or making better wine or things of those nature that aren't necessarily going to have a lot of public –- I mean, it's already, you know, the public debate on that, people will want better wine. So the public perception risk.

Whereas other things where you talk about, you know, especially in areas where security is worried about and opening up the wrong vial and so on, those are areas where people are waiting to see and let the debate rage for a little bit longer before they put a ton into it. But I think part of it is because it's not clear, I mean, a government can legislate overnight something that destroys an investment, and they'll do that because of public perception, in reaction to public perception.

So, therefore, it's marked as high risk and it becomes an even smaller part of any investment portfolio

because it's high risk.

DR. LAZOWSKA: Okay, let's get a few more comments on the table from the audience.

AUDIENCE: I have a comment that segues into a couple of questions. This is Sheila Johnson. I'm from Harvard. Yesterday, we began with Dr. Bement talking about the need to get society out in front of the science or the public out in front of the science.

But by this roundtable, we're down to a lawyer, an investor, a foundation person and a European. Now with all due respect to Europe, even that does not constitute a highly representative imaging of the public. And yet, everybody seems to be aware it's the last set of questions suggested that something about who the public is or who publics are and where they're situated and what they think is not irrelevant to investment decisions about synthetic biology or indeed anything else.

So there's this famous perhaps hypocrofal quote about George Bernard Shaw meeting a famed beauty and the beauty saying to her, effusing to him, oh, Mr. Shaw, just think if we were married, we could have children who would

have my beauty and your brains, and Shaw quipped, but Madam, supposing they were born with your brains and my beauty. So in talking about synthetic biology as a sort of semi-outside of it because I've done a lot of work on biotech but not that much on symbio, I get the impression that there are two large analogies in the background for people who are thinking about investment and one is information technologies and the other is biotechnologies, and that's not surprising because synbio is seen as a combination of streams coming from both of these areas.

Now with regard to the risks and benefits or the challenges and opportunities, it also strikes me as a somewhat informed observer of these kinds of debates that as long as people are talking about opportunities, they're analogizing more to the info side. And as long as they're analogizing to the risks, they're analogizing more to the bio side.

Now the bio side has been characterized by a mixture of complacency in high places and rejection in low places. So the complacency in high places says there's nothing much new here and so we don't need to worry. The

ethical issues are the same, and the regulatory issues are the same and so on and we've heard a lot of that.

Now who would there who could –- well, so the question there might be what does the panel think of this. But the further add on question if I'm right about the possible genetic reversal where you end up with Shaw's beauty and the famous beauty's brains, how would you know, what would you need to do in a meeting like this but also out there when you get out into society to get a sense of the pitfalls that might be lurking. So, for instance, one could ask, well, what's missing at a discussion like this. And one would immediately notice that several Americans and a few Europeans and one or two people from China do not represent a sort of good mapping of the globe when one is talking about globalization as a major theme here, right. I mean, you know, we're talking about investments where things that get invented in America will have value if they have markets worldwide. So what are those markets about. So that's one question.

Another question is what about representatives of the public? I mean, why isn't the Union of Concerned

Scientists sitting there talking about investment decisions or Greenpeace sitting there talking about investment decisions. So I'll stop there.

DR. LAZOWSKA: Okay. Comments from the panel? Let's again, Mark, please.

MR. WAXMAN: I guess I take your question a little bit to be who regulates the world. In terms of, you know, is there some regulator that's going to convene all the relevant resources and come up with a balanced decision that takes the risks and rewards of development and concludes what development will go forward and what development will not.

And we don't have that model right now. It might be a good model, but I don't think we have it. What I've seen which is somewhat a response to your question and brings it down to a totally different level which some levels works and some levels doesn't is rulemaking types of things that we have here which goes back to the question about regulation. At least in a rulemaking type of process, anybody that's interested has an opportunity to comment and at least have their views heard with the goal at the end of

the day of getting a decision.

One of the challenges we've been talking about is whether we want to have that decision now or whether it's really premature to have that decision. And as we listened over the last two days, there's a lot of comments. Some would say it's very premature. We don't know enough to start making the decisions. Others would say, gee, we're a long ways down the road and it's kind of too late. It's somewhere in the middle, I think, and I'm not representing anyone other than our side, the legal side and the trade association that I happen to work with. I think there's a view that we ought to go about creating some type of rulemaking process so there is some sort of format and forum that is going to result in a decision on some specific types of issues.

DR. LAZOWSKA: Okay, let's hear from a couple of other audience members.

DR. OLSIEWSKI: Can I just because I think –

DR. LAZOWSKA: No, we're running out of time, Paula.

AUDIENCE: I just want to interject the question

about entrepreneurship here in terms of investment models. And obviously there's a wealth of evidence from the OECD, from the Kaplan Foundation, from Commission and many other sources about how critical entrepreneurial ecosystems, entrepreneurship variations on the theme or to realizing the promise of emerging technologies particularly when built around some broad and generally applicable sets of technologies.

So I just wanted to ask the panel how they see the role of the entrepreneurial ecosystem in realizing the promise of synthetic biology. And second, is there anything that you see as where we are today or down the road in a short time is likely to be different about how entrepreneurial ecosystems work. And here, I don't mean just for profit. I'm also talking about the major trends with social entrepreneurs, et cetera, but how entrepreneurship links to the investment models and the future direction of synthetic biology.

PANELIST: I actually think that my company, well, part of the reason why I joined the company that I'm working at now is because of our belief in entrepreneurship

and our belief that entrepreneurship actually can thrive if it can be kept away from the boundaries that are put on it, say, for example, most by traditional roadmapping or company strategy or things of that nature.

What I find very fascinating is most of what you would call inflection point technologies or something that was truly disruptive to the industry that caused people to throw out all their old products and make new ones, of course, that wasn't on the roadmap of those companies, okay. And in fact in many cases you see even today like the music industry fighting against digital music distribution and things of that nature.

So one of the things I think is key is that entrepreneurship in all areas, if it could be –- there's people that are really, really good at being entrepreneurs. They're really good at being innovators and inventing new concepts and doing that, and then there's people that are good at building major product lines and businesses and so on out of it. And if you had some way to continue to encourage people to create new concepts, new models, new products, new ideas and that's what they were allowed to

focus on, meanwhile there is a vehicle that takes it once it becomes jelled enough that it can be involved in wealth creation and continue to feed them and allow them to continue to innovate.

That's part of why we advocate intellectual property not necessarily being used as a barrier to keeping people from building products but actually being used as a tool of aggregating and allowing people to build. And so I think that something that encourages that community and I think synbio's a perfect play for that and there's people that are going to be great at innovating that will probably be pretty bad at building businesses around it and that we need to find a way to make sure that they can continue to invent, they can continue to innovate and that the community as a whole can innovate on top of those innovations, but also that there's a path that they're rewarded when somebody else takes it and has wealth creation.

DR. LAZOWSKA: Paul, you've been in line for a terribly long time.

AUDIENCE: Just a small comment. Professor

Jasanoff has pioneered the concept and the research on the co-production of science and society for a very long time now, and there is a strange sense of an absence of a vast amount of work in literature in SDS. And I'm not an SDS person. I'm an anthropology science person and a philosopher which is strange. Just on the one hand, you're looking for people doing new things when an awful lot has been done already. And yet, somehow it's different.

And as to Pam Silver's point about peer review with two minutes to go, this is not the time to get into that. But I mean you funded somebody who wrote an article about technology saying there were no new questions already and please fund us, and you did. Nothing against that –- and I'm also clear I never asked you for money. I'm fine, so he's been terrific. But when we responded –

DR. LAZOWSKA: Now you'll never get any, but go ahead.

AUDIENCE: I know. I got a famous comment I got turned down for the Elsie Project when I suggested that PCR about which I wrote a book might have some social implications. I still talked about those in those days, and

the panel led by Charles Canner wrote back and said that's absurd like the transistor technologies have no social implications. So this was – I'm not sure the Elsie model is really the way to go.

All I'm suggesting here is I think as other people have and Drew in a different domain has been suggesting, in an emergent dynamic complicated field, bringing in the past and, again, what you're doing is great. But there's plenty of room for people who are not yet experts in a field which essentially has no experts, okay.

DR. LAZOWSKA: So as we close, let me go down the row and I want to ask Drew Endy to chime in on this as well and ask each of you if there were one or two things that we could do or change that would improve the innovation and investment environment, all right, improve that ecosystem, what would they be? If someone were to come out of this meeting and say, okay, I'm going to tackle something that's going to make the environment better for innovation and investment, what would you have them tackle?

AUDIENCE: Well, I guess the first part of it

would be a second stimulus package. Beyond that, I think what we need is for a government investment on a strategic basis in the industry to try to create a better knowledge base about what is possible and what is not in the not too distant future.

DR. LAZOWSKA: Sorry, government investment in the industry?

AUDIENCE: That’s right, government investment in the symbio creation that says we’re going to fund a certain amount of dollars into innovation through a collaborative of the leading primarily not-for-profit universities and other research houses to assess where are we, what does the patent thicket look like, what’s a reasonable place to be in in a couple years, and how should we best try to promote the technology.

DR. LAZOWSKA: So you’re looking for an investment in assessing the policy environment? Is that my understanding or not?

AUDIENCE: No, assessing the scientific environment.

DR. LAZOWSKA: Okay.

AUDIENCE: And making an investment in those areas where there appears to be the most promise for the broadest platform for future development.

DR. LAZOWSKA: Okay. Greg?

MR. KISOR: I'm just going to harken back to a closing that I made in my opening remarks which was we need to create an environment where new innovations can be created in synbio that they can be accessed by all researchers, and that innovation can be built on top of innovation and make sure that that's the case but done in such a way that we ensure that public good is served in those cases where it's applicable and done in a way where it also allows for a growing healthy industry to be built because without wealth creation there won't be money coming in. Even governments rely on wealth creation to fund their grants.

DR. LAZOWSKA: Great. So that's putting to place a regime in which you can innovate on top of innovation and at the same time create wealth.

AUDIENCE: Correct.

DR. LAZOWSKA: Great. Paula?

DR. OLSIEWSKI: Well, I think that in order to get there, we really need to deal with some of the issues. And again, maybe that's by having a roadmap for synthetic biology that the U.S. puts together and again gets all those things on the table. How did we fund iGEM? That again is the future workers. How do we make sure that the synthetic biology community has sort of the tools and the resources that are currently not available with the current funding system. I think that's a big gap, and if we address that I think a lot of things would happen faster and there would be more to invest in.

DR. LAZOWSKA: Ioannis?

DR. ECONOMIDIS: Right, well, when the European Commission evaluation system is a rather complex peer review system in which you have a panel of the evaluators of different disciplines. So in this case, several of the topics that again I don't have time to elaborate like risk of the public concern, the precautionary principle and stimulating the industries and for us industries are other small, medium enterprise or bigger industries involving the research and then having that as a jumping board going

further.

With this kind of complex review system, we try to compensate all this sometimes contradictory elements. I mean contradictory in the sense of if you want to have risk, you are not sure really about the outcome. So the investment is a risk investment. This is one hand.

Now if you want safety or security, those are you take a more conservative approach to a more, let's say, aggressive approach. So there are –- we try with this kind of elaborate system to compensate. I cannot say that always the outcome's right. However, I mean we try our best.

DR. LAZOWSKA: Okay. Drew, do you have a comment? What would you have us all do?

DR. DREW: If individual countries could by themselves and collectively develop a strategy by which it becomes possible to make sustained investments and improving the process of engineering biology, developing biology as a technology, realizing the promise which we hear about this being the century of biology as a science and engineering as a discipline coming together and actually doing that, having that be an integrated strategy

that makes it okay for people to explore improvements, say, in DNA synthesis without being derailed by political concerns around biosecurity.

All right, so not only do we have to have sustained investments in tools that support the process of engineering biology, but these need to be coupled to political and social considerations relating to equity, ownership, safety, security, anything else you want to talk about, humanity. So let’s get that going, and give everybody an umbrella in which we can continue to pull this together responsibly.

DR. LAZOWSKA: Great. Thanks. Thank you very much. Before we thank the panel and you get lunch, I’ve been asked to request that all of the session chairs remain here for just five minutes to set up a panel that will take place at the end of the day today. Thank you, panelists, very much.

[LUNCH RECESS.]

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

Agenda Item: Session 6: Governance Issues Related to Synthetic Biologic Health/Safety/Environment

DR. TORGERSEN: Ladies and gentlemen, let’s start the next session, biosafety. First of all, let me thank the organizers for giving me the opportunity to be here today and to be part of this very interesting and high level conference. I’m enjoying myself very much, and I was asked to give some introductory remarks on the issue of biosafety coming from a country that is renown mostly for classical music and skiing resorts rather than for a track record in synthetic biology, namely Austria.

Nevertheless, we have a second track record and that is hostility towards biotechnology. So it is perhaps not so my fortune that someone from Austria is introducing biosafety because that was used as an excuse for not permitting biotechnology especially in the area of genome food and crops.

But looking at biosafety, I think we ought to take a fresh look. Biosafety was invented or brought on

track by the Asilomar Conference and the subsequent NIH guidelines. And obviously, these NIH guidelines have functioned quite well because we have no accident so far which could also be due to by technology being inherently safe rather than the successes of risk assessment.

Nevertheless, if we consider synthetic biology as an extension of biotechnology, then we have to acknowledge that most of it is quite fully regulated. Researchers assert that it is inherently safe and we have no reason not to believe them. So new regulation is not steeped necessarily for the moment as new regulation could also stifle progress in the field.

Some adaptation nevertheless seems to be necessary, and there is one big issue that lurks behind and that is biosecurity. But this is the subject of another part of this conference. But let me make a plea for not separating them too much. You need a framework that determines what you can do and what you should not do, and both are dependent on risk assessment or something like that. So you end up with the same problem, namely how to assess the potential risk.

Now there are some problems with risk assessment these days, especially also coming from some approaches from synthetic biology. For example, the identification of the agent classically the system by taxonomy, but for synthetic biology this is sort of inappropriate. Also sequence seems to be a bit problematic especially when it comes to tracing back sequence and properties or relating sequence and properties, properties such as pathogenicity or the capacity to spread a bit different or difficult to videos from the sequence.

Even more problematic does it get if we have completely novel organisms that synthetic biology presents us because we have no clue, no experience what we could draw some comparisons to. I get the feeling that conventional tools may no longer fit not today perhaps but in the not too distant future. So how can we arrive at tools that get not stretched to the limit?

A second problem I would like to address is that the world has changed since the days of Asilomar, especially science has changed, not only politics. One issue here is proliferation. We have experienced a vast

increase in knowledge and an increase in the sharing of this knowledge worldwide and across communities. This makes oversight a bit difficult or increasingly difficult.

This might be considered the problem for regulators only because they lose track of what is going on. But I think, as I stated before, it is necessary to know what you can do and what you should not do. And this has to be based on sound science.

Another problem might evolve from different disciplines being involved in synthetic biology, and many or some of the researchers that enter the field might not be very experienced in handling organisms. So this basic lack of lab skills might become a problem in the future and might be addressed by professional bodies as well.

The third thing is that the societal context of biosafety may have changed, especially the definition of harm. What is it exactly that we want to prevent, and how do we do that? For example, talking about the environment, over the last 20 years or so we have had fierce discussions over what a natural environment is that might be in danger or may be jeopardized by technological interventions.

Another thing is the rationale for regulation as such especially in Europe. There were at least allegations that the strict regulation was more a result of reacting to public anxieties than real scientific established need. So I think we have to rethink the meaning of biosafety and the chances and opportunities of risk assessment a bit deeper, and we could perhaps take synthetic biology as an incident or a chance to rehearse these concepts and perhaps synthetic biology can also provide us with some clues on how to better relate sequence and properties.

We have two speakers today, one covering the scientific side, the other one covering the regulatory side. Takuji Wakita is a medical doctor and has considerable experience in handling hepatitis virus which is quite unpleasant stuff. He is currently director of the Department of Virology at the National Institute of Infectious Diseases in Tokyo, and I would like to ask for your presentation.

DR. WAKITA: Thank you, Dr. Torgersen for my introduction. And today, I’m going to talk about the synthetic biology. I’m not directly working in the

synthetic biology field, but maybe I hope our experience is useful for that field.

And the disease here, very old relic, maybe probably this is oldest record over the occasion, and this is one of the most recent patient, polio virus, itself is going to eradicate. And virus is classified into very many kinds of virus, and may be divided into its genome is by RNA and also DNA. And one of the DNA virus, the variola virus has been already eradicated. And another one, polio virus, is going to be eradicated.

An RNA virus which has different kinds of genome, for example, single-strand positive-strand RNA or negative strand RNA. Even other virus, double-strand RNA genome. And there are several RNA viruses, namely, Norovirus, JEV, Polio, Coxsackie, Influenza, Mumps, Measles, many and different viruses and different life cycles.

And for the analysis of RNA virus, it is important to think about central dogma because DNA information, genetic information is this is the central dogma is proposed more than 50 years ago by Dr. Click and stable DNA can solve the genetic information and DNA

replicated by DNA polymerase and DNA information is transcribed into RNA. But this RNA is unstable and translated into protein.

And RNA virus has RNA genome. But from the research of RNA virus, there is not always a case because RNA is replicated in RNA virus by RNA-dependent RNA polymerase. And also from the retro virus research there is a reverse transcription by reverse transcriptase. So this is very important for the RNA virus research because the unstable RNA information can be stored by DNA form by reverse transcription.

So now the unable RNA genome or RNA virus can be stored in its stable DNA form. So this is the life cycle of RNA virus. The virus can attach to the surface of target cells and get into the cells and the viral RNA is invaded into the cell and RNA genome replicated and viral parts are assembled and entered again. And we know from the research of the purified viral RNA can transmit into the cells and produce the virus particles. So in the 1980s the first infectious cDNA clone of RNA virus. Scientists reported the transcriptase. So that complementary DNA or RNA genome of

poliovirus was constructed into the plasmid, and this plasmid is transcripted into the cultured cells and produced into such virus.

So this is a simple system to produce infectious poliovirus. Because of the genome of poliovirus is single stranded positive-strand RNA, so the genomic viral RNA can be the messenger RNA. So only single RNA can be constructed to produce infectious virus. Take for example this system. We have established the infectious system of hepatitis C virus. hepatitis C virus DNA was isolated from non-A non-B hepatitis from chimpanzee, and this is a structure of HCV RNA genome. It is similar to the poliovirus which has about 9.6 kilobase positive strand RNA and which has a long operating trail in the center genome flanked by short five frame, three frame region. And this operating frame translated into the three stem by proteins for formation and replication. And once hepatitis C virus infected to the patient, most of the patients cause a persistent infection which was the chronic hepatitis, liver cirrhosis and hepatocellular carcinoma more than ten years, of course.

And the literature reported more than 170 million

HCV carriers reproduced in the world. Now we constructed from the one specific patient who had HCV DNA like this and in vitro synthesized RNA was transmitted into naïve HuH7 cells and produced the virus particles was visualized by an immune microscope which has a double strand double membrane structure following inside structure is nucleod capsules. And infectivity was confounded to infect the naïve cultured cells.

So now we can have the HCV infection system using this system, and this is very useful to analyze the virus entry and virus replication and other things. And research for the hepatitis C virus is going forward very much. And most importantly, we can now do the antiviral drug screening and also vaccine development is ongoing.

And this system is also applicable for other viruses. This is the measles virus. Measles virus is malatable strong single stranded RNA for its genome. So the stories do become difficult compared to single-strand positive-strand RNA. So this is a scheme of the genetic construct of Measles virus and several proteins necessary for the viral particle formation.

So to construct of the measles virus reverse genetic system, we need at least four plasmids to produce infectious virus particles because we need to messenger RNA plasmid to produce the virus protein necessary for the virus particle formation. And also we need another virus genome construct to produce the negative-strand RNA for its genome. So these four constructs is together transcriptive into the cells, and we can produce an infectious measles virus.

And also the system for the influenza virus is much more complicated because influenza virus has negative-strand RNA and also the virus RNA is separated into eight segments. So we need at least eight plasmid or expressed in the viral RNA. So eight plasmid for the viral RNA and also virus protein expressed in plasmid we need four plasmid. So a total of 12 plasmid is transmitted together into the cells, and we can find infectious virus production.

But this system is quite efficient to produce the artificial reassortent which has a different character over the viral type influenza. So it is very useful for producing the vaccine strength, for example, Avian flu is

highly pathogenic to the A. We need to produce a vaccine using A. But the virol type Avian flu is very toxic. So we can change the parts of the virus genome.

So there are many benefits and risks for the reverse genetics system of RNA viruses such as it is useful to produce recombinant viruses. We can put any reporter genes or other genes into the virus genome and, for example, geno express and analysis of viral life cycles and pathogenesis is very useful and antiviral vaccine development. But there are some risks spread of artificial virus through the nature and production of artificial virulent virus with or without intention. And there is a concern for the bioterrorism.

And smallpox is declared for eradication in 1980s, and vaccine was terminated in 1976, and they are only stored in the United States and Russia. And there are increases in population in the younger generation without vaccination. So increased risk for bioterrorism.

However, it is very difficult to synthesize this giant DNA genome of smallpox virus. However, for the polio cases, they’re still endemic in four countries and maybe a

vaccine will terminate it after education. But however, some scientists insist to continue the vaccination.

And in 2002, Dr. Edward Wimmer who has proposed t continue the vaccination has synthesized the polio virus DNA only from the sequence information. So he synthesized the cDNA from oligionucleotide synthesis and construct it from poliovirus cDNA and produced very similar character of the virus compared to wild type produced. So there is a risk. Only chemical synthesis can be used to produce the virus. It is very cheap. We can synthesize the poliovirus DNA only for about $7,500, and with basic molecular biology technique and cell culture facility very easily found in most laboratory and the university or institute. So there are risks of reintroducing viruses because smallpox is once leaked from the laboratory and also there are laboratory infection of SARS virus and also the laboratory strain of poliovirus is leaked from the laboratory. So these kinds of viruses should be contained very securely.

And there are only four countries in the poliovirus endemic in Nigeria, Afghanistan, Pakistan, India and many other countries with green color has already

contained the storage of the polio virus in their laboratory, and Japan and China also finished this report in the last year.

So in conclusion of my talk, reverse genetics system has been developed for RNA virus analysis and is obviously important for the progress of medicine. On the other hand, these kinds of experiments should be regulated by any guidelines or the law and monitored by the authority. And wild type polio eradication program progress and only four endemic countries of poliovirus. Appropriate containment should be necessary for highly virulent virus or highly spreadable virus. Thank you.

[APPLAUSE]

DR. TORGERSEN: Thank you, Dr. Wakita. Our next speaker is Jacqueline Corrigan-Curay. She holds a degree both in law and in medicine and is acting director of the Office of Biotechnology Activities at the NIH. And as such, is executive secretary for the NIH Recombinant DNA Advisory Committee and responsible for the recent modifications and view of policy and NIH guidelines that have been put on the web in May for comment.

DR. CORRIGAN-CURAY: Right, so these are still proposed changes and thank you for having me here today to talk about our proposal to bring synthetic nucleic acids, synthetic biology under the framework of the NIH guideline, and everyone has referenced the Asilomar Conference. And, of course, the importance of that it was premised on scientists taking responsibility for the risk of their own research. But also out of that came a guideline framework and the establishment of a new federal oversight committee which you're probably familiar with, the NIH Recombinant DNA Advisory Committee fondly known as the RAC. That launched the process of guideline development, the first guidelines published in July of 1976 and made recommendations about local oversight. So though these are federal guidelines, they're implemented at each institution that receives NIH funding for recombinant DNA research.

And the RAC continues to advise the NIH Director on recombinant DNA research as well as human gene transfer. They meet quarterly.

So we're going to fast forward a little bit 30 years, and we have a report by the National Science

Advisory Board for Biosecurity on assessing the biosecurity concerns related to synthesis select agents. For those of you who are not familiar with NSABB –- we always use acronyms, it is chartered by the government and advisory to the HHS Secretary and NIH Director and the heads of all federal entities that conduct and support life sciences research and it’s staffed and administered out of our office.

Now the focus of this report was as it said, the biosecurity for synthesis of select agents. However, they noted that some practitioners of synthetic genomics are educated in disciplines that do not routinely entail formal training in biosafety -– chemists and engineers and therefore are uncertain about when and if to even consult a IBC, the Institutional Biosafety Committees, and they thought it was important to ensure that biosafety principles and practices are applicable to synthetic genomics and easily understood.

Well, by the time the report was published, we had the NIH guidelines which is, as I said, applies to institutions that receive funding from NIH for recombinant

DNA. If you receive one single grant, all your research for recombinant DNA is covered by these guidelines at the institution, and it's a term and condition of the grant which makes it mandatory.

Other government agencies also adhere to these. For example, the Department of Defense, and then we have the CDC, NIH, BMBL which is agent specific and not technology driven and references the NIH guidelines. Well, the recommendations by the NSABB Report were considered through a trans-federal policy coordination process, all of the recommendations. And with respect to the need for biosafety guidance, U.S. government accepted that recommendation with the understanding that implementation would be through modification of the NIH guidelines and then referenced by the BMBL.

So just to let you know where the NIH guidelines were, this is the definition and defines the scope. Obviously, you probably are familiar. Its molecules are constructed outside living cells by joining natural or synthetic DNA segments, DNA molecules that can replicate or molecules derived thereof.

So as written, it did not cover synthetic DNA that is synthesized de novo only that that is done by recombinant means and does not cover synthesized RNA viruses unless there was recombinant DNA involved. And the scope just to also –- the report by NSABB was focused on synthetic genomics. But really the NIH guidelines only cover research with nucleic acids. So once you place them in a cell virus organism, if you just synthesize them in a test tube, it’s not under the NIH guidelines yet, although we did propose as part of our amendments that if you manipulate them, for example, put them in a liposome so they’re more easily able to enter a cell that we will capture them under the NIH guidelines.

And then, of course, it also captures all human gene transfer experiments, and those are defined as the transfer recombinant DNA or DNA or RNA derived from recombinant DNA to one or more human subjects. So we turn to the NIH Recombinant DNA Advisory Committee, and we said consider the application of the guideline system to synthetic biology to what degree is the technology covered and does the scope need to be modified. And if it does need

to be modified, think of – develop draft recommendations regarding principles and procedures for risk assessment and management of research involving synthetic biology.

And the review process to date, we started in October 2007 with actually a joint meeting between the RAC and the NSABB on a state of the science of synthetic biology. And then we formed a biosafety working group which is a subgroup of the RAC. It included former and present RAC members, many of them virologists expertise in infectious disease, and we asked one of our bioethicists to join the group as well.

And then we consulted experts in synthetic biology, and Dr. Endy was kind enough to join us as well as Dr. Weiss who is at MIT. And the proposed revisions were developed and then reviewed at a full public RAC meeting and approved by the RAC. And after extensive internal review, they were published in the Federal Register for comment. And about two weeks ago, we held a full day meeting in Arlington, Virginia for the public to talk about some of the outstanding issues.

In general, I would say there is support for the

incorporation of synthetic nucleic acids within the guidelines, although there are still some outstanding issues we're working on. So the overarching themes of the way we work was to capture the same products made by synthetic techniques that are currently covered under the NIH guidelines. And the level of review should be based on risk, not on technique and then to develop a risk management framework that is based on the current science and what we can see in the foreseeable future. We really can't anticipate where this technology is going, and you can't develop a framework on that and just recognize that the NIH guidelines would need to be updated periodically.

So our new definition, we tried very hard to combine it into one simple definition. But after going back and forth, decided that the definition recombinant DNA and now recombinant nucleic acids just to make it clear, it's RNA and DNA had served the scientific community and was so well known there was really no reason to change that, and instead we added a new definition of synthetic nucleic acids, those that are chemically or any other wise synthesized, amplified and that may partially contain

functional equivalent nucleotides recognizing there may be chemical modifications.

We then spent a lot of time talking about replication because it's a unique risk characteristic of recombinant DNA, and it's actually part of the definition. The potential ability to propagate in the lab and the exposed lab work and the environment is one of the things that creates the risk. And the questions are whether the non-replicating synthetic molecules when used in cells or organisms really is a risk comparable. And we looked at it both for basic research and for clinical research.

And after much debate, we decided to propose an exemption from the NIH guidelines for synthetic nucleic acids that cannot replicate provided they're not used in human gene transfer. And the rationale was that that's consistent with what we do with recombinant DNA laboratory research. It's usually limited to molecules that can replicate or are derived from them whereas in human gene transfer we often use replication and incompetent vectors. And so we think the difference is based in part on the increased risk of the delivered human gene transfer

compared to an inadvertent lab exposure. So just going through this, our assumption was exposure in a lab to a low dose non-replicating synthetic nucleic acid sequence is considered low risk because it really cannot replicate spread. It cannot get into the environment, and it's somewhat similar to a chemical exposure of nucleic acid are much less toxic.

In contrast, human gene transfer for those of you who are familiar, we're talking about administering 10 to the 11, 10 to the 12 viral genome copies. Many human gene transfer trials already use replication incompetent vectors. And yet, the toxicities are safety concerns we've seen come about from transgene effects, insertional mutagenesis and other immunologic effects.

And there is still a concern that human gene transfer raises unique scientific, medical and ethical issues that warrant the transparent oversight of RAC. Now as I said, this was not a decision that we came to lightly. And so we went out to the scientific community in the Federal Register asking them do you think this distinction holds up, is this the right thing to do. And we had a

number of questions including what about non-replicating synthetic nucleic acids that may not replicate but produce toxins or oncogenes.

And for human gene transfer, are there classes of experiments that use non-replicating nucleic acids such as antisense RNA or RNAi that deserve to be exempt as well. And these were two of the areas we spent probably half the day on about two weeks ago in Virginia debating. And I think there was a general consensus that there is some classes of nucleic acids that don’t replicate when used in basic research, do not need to come under the framework of the NIH guidelines. But we need to really think through the language and the scope of that exemption.

And for human gene transfer, again there were arguments made that some of these classes of nucleic acids are much more analogous to small molecule drugs. However, we had some debate about recent literature of unpredictable toxicities or functions, and perhaps we don’t understand these as well. So again this is an area that we’re still working on.

I mentioned that we asked the RAC to also look at

the risk assessment framework and say does it apply to synthetic biology or is it so fundamentally different we have to think about this in a different way. For those of you, many of you are familiar with the risk assessment on the NIH guidelines. You start with the risk group of the agent that you're going to manipulate starting in agents are either risk group one through risk group four, depending upon their ability to cause disease in healthy individuals and the availability of preventive and therapeutic measures moving up to risk group three, agents such as rickettsia, yellow fever, hunta virus and risk group four, things like Marburg and ebola virus.

Now the containment level is not always equal to the risk group of the parent organism. It can be raised or lowered depending upon a risk assessment. And the NIH guidelines has a number of factors to consider within this, and this is actually not the complete list but it is what the IBCs start with and work.

So we looked at this risk assessment, and we asked our consultants in synthetic biology to give us some examples of what kind of experiments an IBC might see today

or in the foreseeable future. And the members of the Subcommittee tried to apply this risk assessment to that. And in general, their conclusion was the risk assessment is really not fundamentally different at this point. What we recognize as the technology moves forward, we may be able to develop very complex chimeras for which apparent organism is not obvious and how should that be dealt with.

Of course, a risk assessment should consider the organisms from which the sequence is derived, and it may be prudent initially to consider the highest risk group classification of any agent sequence in the chimera even if it’s not the majority sequence. And all things being then equal, you would also look at the percent contributed by multiple parents and the predicted function or intended purpose.

And we thought to take the conservative stance again to assume that it’s going to function as it does in the original host until proven otherwise. And finally, something that may be unique is there may be synergisms that we haven’t seen or haven’t anticipated when we start combining sequences that have not been –- are not easily

combined in nature by recombinant means.

Now again this is all general and it has to be implemented by the local IBCs, and we realize that we cannot anticipate where this science is going, and I think the NIH guidelines has a clause that really sums it up and it's what we refer to as the spirit clause because it really says, look, we cannot anticipate every experiment that's going to come up with and the responsibility for safety and biosafety lies ultimately on the person conducting the experiment. And this is guidance that is for the ICB, the biosafety officer, and the principal investigator.

And to this we've added or propose to add a couple of other caveats that we do recognize that the utilization of new genetic manipulation techniques may enable work previously done by recombinant needs to be done faster, more efficiently or at a larger scale.

But to date, the assessment was the techniques have not yet yielded organisms that present safety concerns that fall outside the current risk assessment framework used for recombinant. And as the field develops, we will

need to look at this again.

So in conclusion, I would say that research for synthetic nucleic acids in most cases appears to present biosafety risks. They're comparable to rDNA research, and the current risk assessment framework can be used for the attention to the unique aspects of this technology. There is probably certain work with non-replicating synthetic nucleic acids that may not even need to be within this framework. But this is –- it's not that no biosafety standards or other standards will apply and defining those exemptions is something that we will be working on before we publish our final recommendations. So thank you.

[APPLAUSE]

Agenda Item: Questions and Answers

DR. TORGERSEN: Thank you very much, and may I ask for questions and contributions.

AUDIENCE: I'm Mark Siegel from the Environmental Protection Agency, and a disclaimer. I'm not a lawyer. So for those of the rest of you who are lawyers here, some of the statements, you may want to quibble with. But throughout this conference we've heard several people make

statements that synthetic biology is not regulated. In the U.S., that's not true. We heard it yesterday from Amyris and I want to repeat it that in fact there exists and have existed for a dozen years at least regulations into which synthetic biology would fit when it's used for commercial purposes.

However, synthetic biology, as was stated before, per se is not regulated because it's synthetic biology. It's regulated generally by how the device is used. So there are regulations for industrial, commercial, consumer use. There are regulations for agriculture or for pharma. Different parts of the U.S. government deal with different things, and that was established 30 years ago or 25 years ago by the coordinated framework which sort of parceled out who does what. So it's been around for a while. You shouldn't assume that there are no regulations. But it doesn't mean there are no rules. But it doesn't mean that the rules force an agency in the U.S. government to regulate every case of the use of synthetic biology. There are exemptions. There are exclusions, and it's often done on a case-by-case basis.

You should become familiar with the law and understand that there are those rules that are in place. I don't know if you want to comment on it from the NIH perspective. But a lot of the rules do refer back to your guidelines.

DR. CORRIGAN-CURAY: Yes, they do. And so that's one of the issues in the ARC guidelines. And so any change in our guidelines may affect that to the extent that the language remains like that. And certainly what we're looking at is research. So we don't look under the NIH guidelines. It's contained in the lab. Anything that's released out of the lab is under the purview of the EPA or USDA or other agencies. So we're just looking under our guidelines certain aspects of synthetic biology were not covered because we were a technique or we are still until this has to be finalized a technique-specific guideline.

AUDIENCE: I'm Mike Rodemeyer with the University of Virginia, and I have two quite, well, they may not be quick questions. But the question is the Institutional Biosafe Committees have an increasing level of responsibility to handle biosecurity, other issues.

Clearly, synthetic biology may require additional disciplines, for example, to be included on the biosafety committees.

So one question is what is the NIH doing to help institutions develop the capabilities of biosafety committees to keep up with the science so that they can properly apply the guidelines and assess the risk.

And my other question is what are the equivalent to the NIH guidelines in other parts of the world? Do we have similar kinds of restrictions or guidelines that would also deal with biosafety concerns that would cover synthetic biology or not? I think NIH should really be commended for their foresight in anticipating this, and I'd like to hear that that's happening around the world as well.

DR. CORRIGAN-CURAY: I appreciate what you're saying about the IBCs. At this point, we in our office have an outreach to the IBCs. We go out a lot to teach and educate them on the guidelines inasmuch as we can. Is there any direct funding to them on how to increase? Not that I know of at this time.

I realize, yes, this is an expanding area. Now there are some –- we don't know, though, what is, you know, the technology has to develop, how it's going to develop, how rapidly it's going to become more complex and what they've dealt with, we don't know. It will depend upon what we decide to exempt and not exempt in terms of what they have to review.

There are some IBCs that are already reviewing some of this work. At our conference, it was one of our participants from MIT thought that her work was already under the NIH guidelines and was taking it to her IBC.

But you raise a good point. In terms of –- I'm sorry, but I can't comment on the European, and maybe since we have a number of colleagues from Europe who might want to comment on the comparable frameworks that are set up in Europe, it may be country specific. I don't know.

DR. WAKITA: In Japan, we have followed very similar guidelines for NIH. But a few years ago, we have th law to regulate DNA combination experiment, and we have to report every application for the DNA experiment to the Ministry of Education.

DR. TORGERSEN: Yes, similar situation in Europe. There's a EU regulation that is essentially shaped after the pattern of the NIH guidelines. So there is pretty much the same ruling and is complementary anyway.

AUDIENCE: I'm Jermaine at the Woodrow Wilson Center. Jacqueline, I'm interested in the public meeting that you held in June which I think you variously described as an opportunity for the public input, for the stakeholder input and for expert input. I'm interested to know whether you felt that you had the right people there and whether the dialogue, the discussion, the input there was finely, bold and important to what finally came out.

DR. CORRIGAN-CURAY: I would say that we advertised it widely but was somewhat disappointed with the amount of public who showed up. But we had, I think, very good panels. And all of this actually I sort of went through my slides. I thought I had a 15-minute talk, but I think I was ten minutes. So I went very rapidly, and my slides are available.

But all of this is available on our website. So the agenda and the participant list. And I think we really

did have quite good discussions, and it really focused on this issue of what should be exempted for basic research, and then what about human gene transfer. And we had representation from the two main companies that are working in this area with RNAi messenger RNA and their perspective as well as basic researchers, representatives from the IBCs on each of the panels.

And so I think it was a very good discussion. We'll have transcripts from that, and we'll distill that and continue our work on it. But you're welcome to go to the website, and you'll be able to see the agenda and the participants.

DR. TORGERSEN: Okay, please and could you please pose a short question.

AUDIENCE: Yes, very short. My name's Allen Pearson. I'm from Biotechnology Regulatory Services at APHS, part of the U.S. Department of Agriculture, another one of the regulatory agencies involved here.

The question is where the RAC looked at the question of whether synthetic biology posed any fundamentally new challenges to risk assessment and decided

that right now it didn't, did it have any sense of if and when it might? At what point might fundamental challenge be posed, or was there a sense that we might be able to incrementally get there so that we'll never maybe have a fundamental challenge because we'll evolve as the field evolves.

DR. CORRIGAN-CURAY: I think it was more the latter. You know, one of the things, synthetic biology has a lot of great promise, and then there's also this thought that we may come up with organisms that we never saw and therefore that's where the risk assessment will be challenged. How do we evaluate something that we have no framework for.

But that seemed to be off in the distance, and we thought that the field, we don't know. Maybe it will develop like this, maybe it will develop like this. And if it develops like this, then yes, an incremental knowledge will develop and risk assessment.

And as I said, we haven't really changed the scope of the guidelines, the definition in 30 years. Synthetic biology may make that time frame shorter.

DR. TORGERSEN: Could we please collect the rest of the questions and then answer it together, please.

AUDIENCE: Mike Payne from the U.K. Health and Safety Executive. I just wanted to give a European perspective and add another element to it. As has already been said, the European legislation is based on two directives which then implement it into the law within the member states and the union. And that brings with it a legal requirement to comply, and there's a Regulate III involvement of inspection and checking compliance.

I was just curious whether the NIH guidelines are in fact guidelines and aren't actually legislation, and how you check compliance with the guidelines.

DR. TORGERSEN: Okay, yes, please. Oh, okay.

DR. CORRIGAN-CURAY: The NIH guidelines are indeed guidelines, but they are also a term and condition of the grant money that you receive from NIH. So any repercussions would come through the funding mechanism or the cessation of the funding mechanism.

Now as guidelines because they're implemented at the local level, is the Institutional Biosafety Committee

that has the responsibility for making sure that the PIs comply with the guidelines. There are reporting requirements to NIH for any incidents that happen in the lab. But we are not a regulatory agency. So we rely in large part on going out and educating IBCs. We do do site visits to IBCs. We have an active site visit program.

We have a lot of information on our website to educate IBCs. In fact, they've just developed sort of the pre-checklist for IBCs which really also lay out the requirements under the guidelines and gives IBCs a framework to evaluate how they are doing. But you know, unlike a regulatory system where perhaps there's financial penalties, we do potentially have financial penalties. But we really work on trying to work with the communities, the investigators, the IBC and getting the message out, and most people want to do the right thing and they want to comply with the NIH guidelines.

DR. TORGERSEN: Okay. Then I thank you for your contributions and for the contributions from the panel and from the audience, and I close this session. Thank you.

[APPLAUSE]

Agenda Item: Security

DR. GILLESPIE: Okay, folks, biosecurity. Here we go. Let me introduce myself first because I've been quiet so far, and that's going to change for the rest of the afternoon, I'm sorry to say.

I want to conquer the world. Here's the world that I want to conquer. I come from a place called the OECD, the Organisation for Economic Cooperation and Developments. And the first thing I have to say is organization doesn't have a Z is in it. It's got an S. And I'm just saying this so we all remember.

[LAUGHTER]

DR. GILLESPIE: And this is an OECD meeting. So it's British English, and I speak British English.

AUDIENCE: Oh, you lost the war. Get over it.

DR. GILLESPIE: Bench war.

[LAUGHTER]

DR. GILLESPIE: You see it works already, ah? Put a Scotsman up and that's what happens. Okay, so what I want to do for a minute or two before we get into serious stuff is tell you why we're here, and it's not just to take back

the good old colonies. It's to talk about some serious things.

The serious thing is basically one thing and one thing only. We're the organization for economic cooperation and development, and what you want is economic development. God, we need it now more than we've needed it for such a long time. What a crisis. What a set of stimulus packages. Aren't you guys lucky with the amount of money that's being spent. So let's spend it on things that are going to matter.

And the key issue for us is how much does synthetic biology matter. So the first question for the OECD and our reason for being involved in these discussions is we now start to talk about biosciences and biotechnology being what many of us have always thought it probably would be –- a really transformative generic general purpose technology. If we can do what people like Drew Endy tell us we can do which is take these building blocks of biology and engineer them and synthesize them and assimilate them in a way that we've done with engineering and with ICTs. Then to use a sporting metaphor, with a proper game with

bats and balls, cricket, we can knock the ball for six.

AUDIENCE: What is that?

DR. GILLESPIE: Well, you know, I don't know the equivalent in rounders. But, but in order to do that to knock the ball for six or knock it out of the park or whatever it is you call it, we need to make sure that we create a really effective, really efficient supportive ecosystem environment for innovation. And that's what the OECD is trying to do through our various working parties.

And you have heard already in coffee and over cocktails and the like that we've got representatives from two of our intergovernmental working parties here From the biotechnology guys and from the nanotechnology guys, and it ain't any accident when it comes to this set of discussions.

But up to five things that I worry about in synthetic biology, and I worry about them across the range of science and technology issues we deal with. First of all, how do we enable, how do we create the systems for the networking, the collaborative work, the convergence of technologies and the real movement, the capturing of the

benefits of globalization.

And that's what these guys have all been talking about telling us about these great advances and getting young kids involved in synthetic biology. What as governments can we do to enable them.

Secondly, we believe in open innovation. We believe in open innovation because that's the way people innovate in the life sciences. Let's get real. Nobody does all their own thing any longer. We have to go for open innovation. So how do you get open innovation and maintain a return on investment? It's the open/close debate. It worries us a lot.

Thirdly, and here is where synthetic biology starts to get really interesting. We're interested in bringing supply and demand side together in participative innovation, in user-driven innovation. Sure we see a lot of this in the software industry. But are we going to start to see this in the biosciences as well. There's a real set of governance issues in there, and that's going to play into what some of the comments these guys will make.

Fourthly, are –- I don't know if he's still in

the room, but are we going to innovate in a way that will meet societal expectations, whatever they will be? And again, societal expectations are probably higher now with all these billions of dollars with all our government's spent on Stimulus packages. So we'd better damned well make sure that the innovations that are coming out of these Stimulus packages actually meet societal expectations. Will synthetic biology?

And fifthly, and the purpose of this session, governance. Can we create sustainable forward looking, dynamic governance systems that allow the innovation to come through, that allow the inventions, that allow all these great things we've been talking about but also protect societal interests.

And that – and you've taken my slide down, Steve. Can I have it back again? I'm still conquering the world. He's having problems with Windows. It doesn't matter. Forget it.

The OECD is 30 member countries plus 10's knocking at the door. And between them, they make up about 80 percent of the GDP of the planet. It's the rich man's

club, but it's also the real big growing nations. So the Chinese, the Indians, the Brazilians, the Russians, all of them are now getting more and more engaged in our work. They're not members, but they're engaged.

Now we really want to see some global networking of the research and also we want to see common international governance systems. On security, we've done some modest work in the OECD. We have a site called biosecuritycodes.org which I encourage you to look up. One of the tests on this will be to see what the write up of this meeting is on that site.

But it tries to act as kind of an oasis in the desert in information and a plethora of activities we see in biosecurity. And the second thing is last year our council of member countries adopted guidelines for biosecurity particularly focused on large culture corporations, and these are guidelines which are now being put in place not just in the member countries but also in key accession candidate countries, key countries joining the OECD like, for example, Russia.

So we've done a fair amount of work in this. But

we have really only scratched the surface. And the question for us today in our session of biosecurity is what challenge and opportunities, what challenges particularly here do synthetic biology bring in biosecurity governments. And we have two speakers today because I'm going to shut up in a second, I promise.

We have two speakers here today to give us slightly different but complementary perspectives, and the innovation is we're going to change the order and the agenda. So we're going to start with Michael Imperiale who's as well as being a professor of biology and immunology at the University of Michigan, you all here will know him well, he serves on the NACBB. He also serves on the National Academies Committee for New Government University Partnership in Science and Security.

And after Michael, we'll turn to Nicolas Bécard who is from the Office of Francois Fillon, the Prime Minister of France and he is in the Secretariat Generale de la de Défense Nationale where he's responsible for the bio issues related to non-proliferation and security. So, ladies and gentlemen, I hope that you with me will first of

all welcome Michael to the podium. Michael.

DR. IMPERIALE: Okay, thank you, Iain. So I'd really like to commend the organizers for holding this meeting. It's been really fascinating and to get this group of people together in the same room, I think, that in and of itself really says a lot about this field which I'm very, very excited about even though I am not a practitioner of synthetic biology. I'm a virologist.

But my interest comes from my service on these committees that Iain just told you about. But what I'm going to talk about today really is my own opinion and is not anything having to do necessarily with the opinions of the National Science Advisory Board for Biosecurity. So I'm speaking as a private citizen today.

So I'd like to tell you about how I view the issue here, and let's just start with some premises. So first of all synthetic biology present risks, but so does all biology and in fact so does everything we do on a day to day basis. We're going to walk out the door and cross the street, and that's going to present the risk.

So I think we have to acknowledge that there are

risks there. Now the thing with biology is that the consequences of something happening are potentially devastating, right. However, we don't know how to quantify the risks that are associated with synthetic biology, or I would argue, with much of biology at all with maybe a small subset dealing with the types of very dangerous agents that we've heard about already.

And so given this, how do we approach the issue of biosecurity as it relates to synthetic biology? And so the way that I've been thinking about it is that there are four factors that come into play here. First are the technologies themselves. The second are the practitioners of that technology, and then the biology. And by biology, I mean I should have put a capital B on biology, and I'll come back to what I mean by that in a minute. And then the public because the public factors into this discussion because in effect the public are those that are being put at risk if there are any risks that we need to worry about.

So how do we look at these things? So let's think about the technologies. I'm going to arbitrarily divide synthetic biology into two classes for the purposes of my

talk –- genome synthesis and engineering which is pretty much everything else. Okay, so with genome synthesis as we just heard, it's very easy these days to synthesize the genome of pretty much any virus, and a little bit harder but one can then derive a virus from these genomes. The technology for synthesizing bacteria is with us. It's not as easy to do right now, but I'm assuming that that's going to move along quite quickly.

And then of course there's the issue of new organisms, however we want to define those, whether that be mixing and matching parts of existing organisms or maybe trying to develop something completely de novo and the kinds of things that we just heard about a little bit earlier.

And then with respect to engineering, there are design circuits or the kinds of things we've heard about during this talk. Molecular shuffling that we haven't heard about too much during this conference but I think is an important part, and also self-replicating systems which have been mentioned. But again, we haven't gone into a lot of detail. There are probably other things that fall under

this category. But from my simple way of thinking about things, these are the –- I think at least present examples of what the risks might be.

Now with respect to the practitioners, I have four categories here. The first are traditional scientists, and I mean these are the scientists who work in university labs, government labs, that sort of thing who are sort of what we would consider the scientists.

Then there are other organized groups like iGEM. Maybe laboratory courses in colleges or in high schools even, and then the DIY community. I'm not sure what this is really to be honest with you. But to paraphrase Stephen Colbert, it's real because they have a website. And then finally terrorists, but I'm not going to talk about terrorists today because I think what we really are worried about are the risks that are posed by the scientific enterprise itself. And obviously if there's someone who's really intent on doing harm, that sort of risk is there, and I think we have to just live with that.

And then the biology, and the point I want to make about the biology is that to some degree it's

predictable. But to a large degree, it's unpredictable. And in fact, what excites most of us scientists about biology is the fact that it is unpredictable. And so as we are undertaking our experiments, there are results we're going to get that we did not expect, that don't fit a hypothesis, and they're just as exciting and sometimes even more exciting as the predicted results of our experiments and there's no way to anticipate those, right.

So what are some of the things that are more or less predictable or unpredictable? Well, the design principles for some of the circuits that we're thinking about here. Selection, right. So we're dealing with biological systems here, and there's always going to be the potential for selection that we did not anticipate as we design these things.

Virulence is a very fuzzy term, and we don't understand enough about virulence to be able to point to something without any prior knowledge and say this is virulent or this is not. And then there are probably other intangibles that I'm not even thinking about right now, but I'm sure that they exist because, again, we're dealing with

a biological system.

So the question is what do we do? How do we integrate all of these things and come up with something that's going to allow us to advance economic considerations, the science itself and all the things that we would really love to do while making sure that we're not putting people at unnecessary risk.

And so I want to talk about some things, some ideas I have. Some are ongoing efforts, and some are just some ideas that I'm going to throw out there for discussion.

So first of all, let me just push aside right away equipment and supplies. I think that at this point in time we can't even consider trying to regulate the equipment and supplies that are needed to do this type of research because it's most low tech, it's inexpensive, and most of it is widely available. So as far as I'm concerned, I think this is really off the table. And unless there are new technologies that come about where we can start from day one and think about should we be regulating those technologies, right now I think we have to live with the

situation in which we already exist.

Okay, so what about synthetic genomics? So, you know, one thing that people talk about a lot is screening orders, and in fact ENSEB has made as part of its recommendations in the same report that you just heard about orders should be screened for the potential match to something that's dangerous. And so what this requires is buying from providers and for the most part the synthesis community has agreed to do some sort of screening. But I think what we need are better and more uniform screening tools so everybody's working on the same page in order to be able to determine if something is dangerous or not. But I'm going to talk a little bit more about this in a minute and come back to it.

And then I think we also need rational list of agents. What's really the most dangerous thing, and what should we really be screening for? And again, that's going to be a little bit difficult to derive again because of our understanding of these agents which is not where we would like it to be in order to really be able to manage risks on a more definite basis the way that one might manage

traditional recombinant DNA research.

And engineered systems, I think that in terms of circuits as the predictability improves, the risks will presumably go down. And what I would like to recommend is that we start building a database of what sorts of combinations of things are okay and what sorts perhaps are not okay. And then that will allow us to try to start stratifying things. And so I think at this conference we've been referring to as Asilomar as some sort of God of biological research. But again after Asilomar, what was done was to start keeping track of, okay, well this type of experiment really isn't that risky, and so we can put it into a lower category.

And I think we can start to try to do the same thing with synthetic biology. Molecular shuffling, to me presents the highest risk. And the main reason for that is that the potential outcomes are unknown because pretty much you can get almost anything that you might want to try to select for. Now I realize there are a lot of technical issues dealing with that. But again the whole issue of shuffling is to try to make a large pool of sequences and

then try to pick out the one that one wants.

And so similar to the situation that's post from a biosafety standpoint, I would say here one wants to be conservative regarding containment and be very prepared for unintended outcomes. So if something bad does come about, you're prepared to contain it and to do the appropriate thing.

And then finally self-replicating systems. I think at the present time the technology's not far enough advanced that we need to worry about these things. But as the technology does begin to advance, it's something that we need to continue to discuss.

Okay, people. So this is now going to be the last part of what I want to talk about. So first of all, there's the traditional scientific community, and everyone especially recently here in the U.S., we're concerned about the so-called insider threat. The threat is certainly real, but it's probably very, very low. But it's something that we need to think about. And so I think what that means is that we just have to have awareness. Again, we need to be aware if results of the experiment points towards a higher

risk of what's being done, and we also just have to be aware of others. So you know, although we don't want to be sort of spying on each other, we do want to keep an eye out if someone's behavior seems inappropriate. You know, if someone's sticking a vial in their pocket or something like that, you know, those are the kinds of things we normally don't do in the laboratory. And I think we just have to be more responsible as a scientific community so that if something bad were to happen, at least we can say, hey, we have done our part to minimize the risk.

With respect to the other synbio communities and again here I mean maybe the kids who are working on iGEM, those sorts of things that are not in your traditional laboratories. First of all, I think we need to try to identify who's out there, especially in this DIY community and engage them in a dialogue. We need to make them aware that there are potential risks so that they know about it.

Now my fear is that if we are dealing with some high school students, I think we all know when we were teenagers even though we were told not to engage in certain behaviors, you know, we did it anyway. And so even though I

think the intention of these kids who are working on these projects is all very, very good, I think there is a little bit higher risk in terms of that particular community.

And then finally I want to talk about the public, right. So the question is why do we engage in biological research at all, and to me there are three reasons. Number one is it's an intellectual pursuit. We like discovery. We like learning about things. The second is that it's fun. And to me, synthetic biology sounds like a lot of fun, and I actually wish I were doing it.

But most important probably is that we engage in this because we want to benefit mankind on many levels from public health, agriculture up to increasing our knowledge. So on many different levels, we're really here for the public. And so we work for the public. They pay taxes. They make donations to the private foundations that fund the research, and they're the beneficiaries of the work that we do. And so I think we do have to be engaged in a dialogue with the public about the risk. And so I would say we have to listen to the public and listen to their concerns. We have to educate them. We've talked about some of these

issues already in this conference.

I think we have to be humble. Someone raised this point yesterday, I think, in one of the question and answer sessions. And I think that we can't say that we're the scientific community. We know what's best for you. You know, I think we have to be willing to accept that the public, if they're educated, may not be willing to accept certain risks. And so I think we have to be willing to accept that.

We have to maintain openness. Openness builds trust, and people have talked about this already. I don't need to go into it. And again, we need to be honest about the possible risk. So I think we'd be doing ourselves a disservice if we went out there and say, you know, synthetic biology doesn't really present any risks. Don't worry. We're going to be fine. We're going to take care of everything. I think we have to be honest that there might be some risks. However, there are these other risks that you have to put this in the bigger context of when one is thinking about that.

And so let me just end on a more positive point.

These are the things I think are the good news. First of all, is that I've been impressed that the synthetic biology community is already engaging in discussions. This is one example of that, but there are many other things with respect to meetings, websites.

So one example that we haven't heard about today is the Steve Moira at Berkeley has initiated a portal where if one has questions about whether an experiment might pose a risk, one can submit that question to this portal and then a group of experts will anonymously discuss it and provide some advice. So these kinds of things are going on already.

The science and security communities are talking to each other which is good because we really do need to educate each other as was mentioned either earlier today or yesterday. It's great that there's an ongoing international dialogue because obviously it doesn't make sense to have regulations or rules in one country and not in another country because we really must think of ourselves as a global community. I'm preaching to the choir here obviously.

And then finally, the government actions that have been taken, at least the ones that I'm aware of and I'm mostly aware of those in the U.S. have been measured which is good because I think that it shows that the governments realize the importance of not impeding the research as it moves forward. And so I will end there. Thank you.

[APPLAUSE]

DR. GILLESPIE: Thank you very much, Michael, and I'm glad to hear that you sound like you've given up bad behavior. You talked about being badly behaved when you were a teenager. You must tell me the secret on that.

And you've given us a perfect segue from government action into what's happening in France. So without further adieu, Nicolas, the floor is yours.

DR. BÉCARD: So thank you very much to give me the opportunity to be here today with you. So I work for Secretariat de la Defense Nationale. It's run from the Prime Minister office, and we are in charge to coordinate all issues in relation with security and defense. So we're looking for and matching demands and we have initiated a

great deal of cooperation about synthetic biology and biosecurity.

So I would like to presently choose the first analysis of this research and approach for synthetic biology and biosecurity. So my talk will focus only on biosecurity. So I would like just to remind quickly the definition from the OECD who is an organizer of this meeting. Biosecurity is intended to deter or detect the loss or theft of dangerous biological materials for illicit or malicious purposes. So who can use this for malicious purposes is going to be from a range scale from individuals, crime organization, terrorists and we could then exclude country with biological program.

So the generic tools to improve biosecurity are regulation, recommendation and a sensitization. So to talk about biosecurity, we need to identify the potential risks. So currently the potential risks are on the biological demands with biological synthesis de novo, biological agents and with de novo synthesis of new biological agents. So the major concern is about de novo synthesis of non-biological agents because we have a lot of regulation

control listed, biological threat agents and synthetic biology can offer a new opportunity, a new way of synthesis to create these agents to escape control.

And there's a concern about de novo synthesis of new biological threat agents and more exactly about modification of threat agents to improve the biological property about, for example, pathogenicity about resistance in environments.

So we can imagine other appreciation with other potential risk of funds. So we're just giving two examples. We can identify disease of known and chemical precursors when you have a lot of regulation to control the precursor of chemical or biowarfare agents. And if we can not pursue with imagination, we can imagine also some potential risks with nanotechnology. But it's difficult to –- to identify all the potential risks open with synthetic biology.

A lot of recommendations have been published for governments and authorities to improve biosecurity. So we can original recommendation academies of science. So the French Academy of Science has not published a specific report about synthetic biology. But a report on biological

constraints, biological security and scientific responsibility.

We can also name national authority and some specifics to these like students from 6th FP as it was presented previously in the NSF Program more exactly. So we are here with some recommendations that we have analyzed in the French –- so we can just mention the federal regulation to permit monitor of application, control of DNA synthesis, guidelines, harmonization and controls, sensitization, education and training and the last one on thelist is the committee to check and control synthetic biological research.

So the first recommendation was about adaptation to limit malicious application. So we are looking for and we have an existing framework for analyzing the risk of biosecurity. So we have international regulation with United Nation resolutions. The Chemical Weapons Convention and the Biological Weapons Convention which normally limits the risk for development of new agents.

We have also European regulation for export control. So this regulation assumes national and

automatically placing all European countries. The control regulation, the name exactly in Europe is Regulation No. 1334/2000 which requires you to use items including software and technology to be subject to effective control when they are exported from the community.

So the list of biological and chemical items is determined by the Austrian Rule. European regulation for biological risk and warfare is more for biosafety but is involved as well in biosecurity which can be complemented with national regulation. And we have in France but we are not alone. You can find in a lot of countries some specific regulation for biosecurity to control order of parts and by parts it’s included in the DNA synthesis, DNA sequences, micro-organisms and toxins.

For all this we cannot assume that all this regulation can cover all the biosecurity for the potential risk of synthetic biology. So these works are still in progress, and we continue to pursue the analyses. But to be sure that it will be completely covered we need to look for and identify all the potential risks to check if it’s not controlled with the correct limitation.

So the second recommendation was about control of DNA synthesis. So we have two approaches. The first is about control of DNA synthesis. So we are looking for initiation for some work by EISB about the control of the DNA synthesis, but it is looking very difficult to control all the DNA synthesis in order of biosecurity. Moreover, we have an uncommon use of such control. So it could be very difficult to place them.

Moreover, we need appropriate database. So I know that a lot of people work in this way. But currently the database is not enough for us, and to be very, very effective we need an international control. It’s not the case because for the companies on the streets it shows that you have international consortium, but it is not with all of them.

So the second approach is an approach in territorialized in France. It’s about sensitization of gene synthesis industries. So it’s reserved from a group, analysis group from Australia, Australian group with communication to industries of a demonstrated list of industries to identify suspicious orders of gene synthesis

sequences and to remark with some national point of contact in case of suspicious order.

So I know that here in U.S. there is the same kind of approach has been in place. So just to remind because it’s very important we are not against control of DNA synthesis. It could be a good approach, but currently it is not appropriate. We do not have all the appropriate tools, and it is very important that for the control of sensitive synthesis must be international to be effective. It’s very, very important for us.

So another recommendation is about sensitization of scientific community. So for France this is very important. It may be the best way like it was reported by the French Science Academy with things like biosecurity can be improved by sensitization of program in scientific community. So it’s while you have a sensitization program, biosecurity in each research institution.

We have in place as well conference by good monitoring agency from -– we are seminar from the international information charter direction. We try to expand the risk and to give some example which is a relief

for scientific people and we explain the risks. We have also program of education with some specific university degrees in biosecurity. In fact, it's not exactly biosecurity but in biosafety and biosecurity. So we have a university, one university degree in place in France. And we have probably the national forum to sensitize the scientific community. So sensitization of scientific community is considered a very, very important approach to improve biosecurity concern of scientists.

So the last recommendation was about monitoring and control commitment for sensitization by the researcher. So we are naturally willing to analyze this proposition. But we are sure of one point that such committee should be ready international and has been the framework of unity if we want to be sincere, and maybe you could be taking charge by the biological and toxic weapons convention. So it is what we have and we are naturally learning this way. Some nationals of the scientific community and emergent scientific fields. So it was led by the French Academy of Sciences. It is not in place currently, but it is in progress and is not restricted to synthesis biology but for

all emergent scientific skills.

So in summary, I would just like to remind that sensitivity by Europe provides further application including biodefense. So it is very important to be interested by these new fields, and we are aware as well that regulation without discrimination could handicap research. So we are conscious that we need maybe to control and regulate these new fields but with regulation if we need it and to take care about developing research.

So biosecurity can be improved by sensitization of scientific community as you can understand in a very important way that we have identified. So tools for education and training will come. You have control of synthetic order for industries is supported. So it is in progress in France. It’s more and first step is probably the best approach for the control of DNA sequences currently at the moment. And analyses of biorisk and synthetic biology is still ongoing. So we continue this work with a little step and guidelines of good practices for biosecurity of synthetic biology also will come. So thank you very much for your attention.

[APPLAUSE]

Agenda Item: Questions and Answers

DR. GILLESPIE: Well, thank you very much indeed, Nicolas. And I think you nicely summarized some of the key issues that we might follow with some discussion on. And before I turn the floor open to the questioners, let me just pose three things that I've heard.

The first one is ask simply a question. What's different about synthetic biology? And the thing that strikes me from the conversations we've had is the individuals, the types of people, the communities that are involved here because quintessentially we're talking about trying to involve the bright young future generations. We're involving engineers as well as scientists who have very different perspectives on some of these risks. And we have the speed and the ability of bio hacker to work here is something which is certainly from my experience the bioscience is rather different.

And the second question I want to throw out on the table is one about infrastructures. And I think both of you mentioned that you wanted to see some better guidance,

some better tools available for issues such as looking at synthesized sequences. I'm a mushroom. I'm kept in the dark, and they feed me bullshit.

And then the third thing is who needs to be doing what. So I want to just put these on the table, leave you to ponder them and in the meantime throw the floor open to questioners. And I know that one of the targets for your comments, Nicolas, as the biological toxic weapons convention, chap. So I think we'll start with Pierce.

AUDIENCE: I was going to thank both speakers for a fantastic set of presentations and point out that it looks like I might come and hang around with you guys at future meetings if some of those recommendations came true.

I'd like to start off by picking up on the point about the DIY bio community to point out that they do have a safety and security working group, that myself and other people in the room are on that group, and that those channels of communications are beginning to be open. That is something that some of the leading figures in that community are particularly concerned about resolving. So that there is some good news there.

But if you'll indulge me, I had some thoughts, feedback and questions on what we've just heard. I think first of all I would start off by saying I absolutely believe the first message out of our mouths when we talk about security is to say how good this community is on that issue. You know, it really is the case study of engagement and community-led engagement on security issues. If we could only do this with other biological science disciplines, my job would be much easier.

Secondly, I've listened very carefully to the words that are used in association with security frameworks. Now I think that we're still missing a trick here, and I think these frameworks should allow beneficial applications. I think they should enable beneficial applications. I want to see what is eventually put in place as the door that you go through to get to Randy's fund from yesterday. I think that's what it is. This is part of a much better process.

And I think the relationship between security community and synthetic biology community is more than just a relationship. It's more than just communicating. I think

that both fields will dramatically alter each other, that synthetic biology will drastically impact the security field because it's going to, if the potential comes true in a couple of decades time as we've heard, the really big stuff, it's going to blow traditional approaches to arms control out of the water. And equally, if you flip it around and do it the other way around, I think we've heard exactly the right thing that security is a part of doing biology in the 21st century. Good biology is safe, secure and beneficial biology, and that requires quite a big shift in thinking amongst how you pursue biology.

And that leads me to a recommendation that both security and the synthetic biology communities are going to have to go through a fairly big shift, and that's going to require new tools and approaches. And finally, I think we need to start looking at reframing this issue from a negative to a positive. The question we're now asking synthetic biologists shouldn't be are you part of the problem, are you doing something that's wrong. It's a question of are you part of the solution, how are you helping us prevent others –- not you, others from doing

something wrong.

So my five things are acknowledge the work, ensure security frameworks, enable, not restrict, recognize it's a two-way relationship that will have a big impact in both directions, actively pursue new tools and approaches and reframe the issue.

DR. GILLESPIE: I love these points, Pierce. I love them particularly that point about enabling. I'm going to take a few points, and I encourage people to not just ask questions, but as Pierce has done, voice opinions. We want a discussion. So off you go.

AUDIENCE: I actually want to come back to the biohacking issue. And I'm still trying to get a sense of whether this is really a myth or a speculation or whether it's a very real concern. When I look at this and there are a couple of things which I think are very clear. One is we know the people that are either young in years or young at heart like to do disruptive things.

You look at the chemistry community. I was dying to ask how many people here who started off as chemists experimenting with explosives as kids. I'm not going to ask

that. But certainly most people will know of people that have messed around with high energetic systems as kids.

We also know obviously about the computer virus community where people will write things just because they can, not because they have bad intentions, just because they're flexing their muscles. The question is, is that tendency to try and flex muscles like that actually going to become a reality within the fringes of the biohacker community, and I'm not talking about the organized biohacker community that are going to be responsible, they're going to hit some sort of code. But the people at the fringes of that community that decide they can do something and they want to see how far they can push it. Is this something that can really happen, or are we just making myths for ourselves.

DR. GILLESPIE: Another great question.

AUDIENCE: Well, continuing from the two previous questions, I would like to draw some comparison between the information communication technology and the synbio technology, nanotechnology, et cetera. We have the information technology transform our productivity of our

system and completely made us dependent, our economic benefit on the information technology and therefore the information hackers created economic horror in doing some hacking.

Now I'm not worried whether it is a myth or a reality. This technology, unlike nuclear technology, is not dependent on the equipment. It's purely knowledge dependent. And science being democratic and open and transparent, the knowledge is freely available. If it goes into the misusing hands, how are we going to prevent it. All that I heard today is sensitizing the scientific community and self-regulating. I don't think that is a huge issue here.

Coming from a health department, I'm worried about health security. If this is misused in some way or the other, where is the firewall that will be used in information technology? Where is the biological firewall? Is someone looking at it? Is it possible to build that firewall simultaneously as we build a whole new system of new synthesis, new synthetic biology. I think it's time to start thinking along those lines as well because health

security is where this will start, where this will be affected leading to economic insecurity. That's my comment.

DR. GILLESPIE: Thank you. We'll take one more before I invite answers.

AUDIENCE: Thank you. I'd like to argue that the security connected issues to synthetic biology for the next ten years is going to be zero or close to zero because of the following. Virulence factors as we know now from the result of research for 20 years are the result of an intimate evolutionary intimacy between the host and the agent that expresses the virulence. So the one, the virulence factors that are the worse probably happened already developed by nature. They are out there, and nature has produced all possible combinations of them and evolution. So I have serious doubts that even the smartest engineer, the smartest biologist can come up with something that is more pathogenic than the agents that we have out there.

So basically I think that the security issue is connected through the direction of more virulent bacteria, more virulent agents. At this point, I want it to be very,

very limited.

DR. GILLESPIE: Okay. So let's just pause on I think there's four key points come out there from these questions. One, we need to reshape the debate and to security enabling innovation and recognize the interdependence between the innovators and the security community in looking at these issues.

Secondly, while there is a fair degree of responsibility in the DIY hackers, but will that responsibility be held at the margins. Thirdly, do we have to and can we build a firewall, for example, for health security. And fourthly, while maybe we don't have to do it right now, we've got some time. Michael, do you want to start?

MR. IMPERIALE: So first I completely agree with Pierce. And as I said, I think that that discussion at least here in the U.S. is occurring on many different levels. And so my sense is that it's also occurring outside the U.S. So I think you're absolutely right.

With respect to the biohacker situation, you know, I guess my feeling is that if someone is really

intent on doing harm, you know, they're going to find a way to do it. You can put up an impediment here. You can put up an impediment here. And you know, depending on how large of a firewall one can build, you might be able to more or less stop more people. But I'm not sure you can ever really control every one. That's just not going to happen.

And so then the question becomes what's the bigger risk, someone doing biohacking or someone driving a car bomb up to a building or things like that. And again, since it's very hard to quantify these risks, I don't know how to wrap my arms around that question. But I guess my bottom line is we're never going to be able to stop everyone from doing something bad. And then I actually would dispute the last comment that nature has already sort of sampled the entire set of possible combinations that can lead to virulence. I don't think that's the case. I think if that were the case, most viruses would infect any species that they want because they'd have more places to replicate. That's just one very simplistic view of it. So I think there are a lot of things out there that we don't know. We don't understand virulence. There are many, many

ways to accomplish virulence. It is dependent upon a clear sort of choreographed interaction between the pathogen and the host. But I disagree that there are not more virulent things that are potentially out there that nature has not yet found.

MR.GILLESPIE: Thanks, Michael. Nicolas.

DR. BÉCARD: Just some comment about biosecurity. We have not in France currently, but it’s why we recommend control of suspicious orders from DNA synthesis industries and normally to check that no individual can order some DNA sequence to try to make biohacking. And I think that the concern about biohacking is more about biosafety. That’s my mind.

About to come back about United Nation. So I just give an example, maybe I’d use not appropriate terms, so I just give an example like existing chemical which we would create an organism which Internatonale Authority to control. So if you need to control it for sure, by means you should be by United Nation and these organizations. I mention this way. So and to finish with infrastructure because that was something very interesting. And we are

looking forward to maybe discuss this in this place.

DR. GILLESPIE: Thank you, and I'm going to take five minutes off your coffee break. I'm sorry, but it's because I want one more round. Paul.

AUDIENCE: I am here, and I'm not going to talk about society although I'm very happy to notice that several people are at least a little nervous about it which they never were before. Okay, a few points.

There's a distinction between risk and danger which I think is worth drawing. Most of what you said are about dangers. Risks are something that are quantified in a series. So we don't know as you've said what the risks actually are because we haven't encountered any. So it's tricky to look at the currently existing risk assessment and risk analysis technologies because we're in probably a different situation. So we have a topology of danger. We know very little about risk. So that's point one.

Point two, something that I've encountered with many biologists is a simple distinction but one that seems to be missed between terror and warfare. The response that it's very hard to do anything with anthrax or the virulence

thing and I agree with you about virulence is of course important. But all you need to have had is that H1N1 which could have killed nobody came out of some lab and you would have dramatic consequences even if no one was actually harmed. So it's not really going to cause a loss of life is one thing. But anything synthetic that starts something else or a set of ramifications is going to have a lot of effect.

And then finally I think the third point is preparedness. That is to say, I think we would all agree whether it's rambunctious, overly testosterone youth, unknown genders or not, once something happens, then what? And in my experience, not enough attention has been paid to that because I fully agree with Michael that you can't control everything and we don't want to live in a society where you can control everything. Do you hear, society?

So the question is once something happens, then what? And that's what I think we need to pay more attention to in addition to everything else that you've been saying.

DR. GILLESPIE: I knew we could bring you back to society. Next question.

AUDIENCE: Okay. This session actually has something in common with many of the previous sessions. We're talking about a technology and a set of methods that have not had immediate effect, but the effects are coming. So as was true in our discussion of intellectual property issues, as was true in our discussion of environmental effects, so too with reference to security. We're not talking about immediate two, three, four, five term effects. It's longer term.

That said, if we look to the effects of synthetic biology as distinct from ordinary good old fashioned recombinant DNA work and look to the effects on both offense and defense over the longer term, I think that we have to actually take this quite seriously. We've had an emphasis on diffusion which has been entirely appropriate because deskilling and access of a larger group of people to the methods is part of what's intrinsic to synthetic biology.

But at the same time, there are other potential effects of synthetic biology that we may want to be looking at in terms of offense and defense, specifically if

thinking back to Drew's presentation at the very outset, you have a set of methods that allow more reliable, more rapid, lower cost –- again, more rapid and more precise methods for redesign that may have both offensive and defensive implications. On the defensive side, good news. There's the possibility of developing countermeasures not just to artificial but to natural problems more quickly. The revolution in medicine that we were discussing earlier should be part of a discussion of defense and security. On offense, the potential for designing more discriminating. You know, we talk about ebola or smallpox. But there's also the potential that more discriminating biological weapons may be developed, and that may be actually the greater threat because they may be more usable by states.

You put that on top of the hackers longer term, and we need to be more careful in our characterization of offense and defense and then take advantage of the time that we have now to do appropriate actions to emphasize the defense and perhaps weaken the offensive implications.

DR. GILLESPIE: Okay, one more.

AUDIENCE: I think the first speaker rightly

mentioned that all these equipment are easily available, cheap and widely available, and these are the right combination for people with wrong intentions. As many sites of al-Qaeda and Los Quativa I know Torra Borra has laboratories, and they actually constantly look for those types of people. So as a scientific community, we have to be right all the time and these people don't have to be right one single time. So I think my recommendation to this community would be not only to find ways to look for these types of synthetic biology narratives but also countermeasures such as the firewall which was mentioned by the previous person who posed the question from Canada. So I think we need to look at the measures and countermeasures which is already pointed out.

DR. GILLESPIE: Okay, and the last question.

AUDIENCE: This is really just a comment and it relates a point that Michael made. I just wanted to correct unless I have potential misconception in relation to iGEM. With iGEM, we don't have 1100 students kind of running around and doing these projects. It's really important to understand that the iGEM teams work with faculty is well

regulated laboratories within well known universities.

And three weeks ago, at Imperial College, we ran the European Teach the Teachers Meeting with Randy and his colleagues, and all the people that attended that meeting, about 60 of them, are all very well known or well known research scientists who are regulated by the regulations of their various countries, et cetera.

So are these really important that, you know, that make the point that as far as iGEM projects are concerned, these are all done within highly regulated laboratories and under the supervision of research faculty that really understand what they're doing.

DR. GILLESPIE: Thank you for that. And so I think the key points there are and it's a very difficult ones in the last kind of minute or two of the session. How do we deal with that which is unpredictable, not just unpredicted. How do we deal with different tolerances of risk depending on the origin of an event.

How do we create preparedness and then a response for an unusual but potentially very harmful event. And can we spend some time thinking a little bit about the pros and

cons of different characteristics of synthetic biology in a more sophisticated way than it's black or white. So Michael, would you want to start.

DR. IMPERIALE: First, let me apologize if I came across as thinking that iGEm was this unregulated group of kids just running around willy knilly because I realize that's not the case. With respect to the response, I think that's a very, very important issue and I would argue that the public health response can be thought of as another one of these dual use issues that we talk about all the time in that the same system that allows us to respond to naturally occurring events would also allow us to hopefully respond to any kind of event that may come out of a laboratory or be manmade. So I think it's very important that we invest in the public health response for two reasons. Even if nothing were ever to happen out of a laboratory, we have to have public health response in place. I'm going to come back to this issue of thinking long term versus short term. You know, I'm not sure that all of the issues are really long term because right now if someone, I think, with a little bit of money and wherewithal could buy all of the

oliogos that they need to construct a select agent, the synthesis of oliogos is not being screened at all. And they could try to do that, and that could be done today. You know, it took Eckard Vimmer I don't know how long, but the technology is a lot more robust right now.

And so I think we do have to be thinking short term as well as long term.

PANELIST: So the difficulty for us is that the long term risk potential is not clear. So it's how we can try to regulate something that we cannot fully define now. So it's very difficult.

DR. GILLESPIE: Well, thank you very much. To have the last word in this session. The four messages I take away are think about synthetic biology and security as being things where security a positive or can be a positive framework by condition for innovation make sure it is.

Secondly, acknowledge that we have a very responsible, very engaged community here on this set of issues, and we should congratulate ourselves for that. Third, there's certainly some short term imperatives, and I think the biggest short imperative that I've heard is the

availability of skilling tools and skilling tools which can be used and exchanged internationally. So there's a common playing field for that. But nevertheless, fourthly, there are some longer term issues that we do have some time to think about, although complacency would not be rewarded.

Ladies and gentlemen, I think you've earned your coffee. Please join me in thanking the speakers.

[APPLAUSE]

Agenda Item: Session 7: Public Engagement and Participation

MR. RODEMEYER: Good afternoon and thanks for staying with us through a really interesting day. There's a lot of good discussion and information. I'd like to think that we're now at the very top of the roller coaster and ready to go down that last ride. So hold on the next hour or so.

My name is Rodemeyer. I'm with the University of Virginia, and it's my privilege to moderate this panel on public participation and engagement. This seems to be the elephant that has been lurking behind many of the prior

panels. So I'm glad we'll finally get a chance to tackle this head one.

What I'd like to do is actually address just at the beginning a view questions if I can get the PowerPoint up. First of all, it's interesting that we've got a panel on public participation and public engagement. So why are we doing this in the first place? I mean, geologists don't engage with the public before they go out and do their research. And most people, most technologies get introduced without the benefit of public engagement. Nobody asks the public about introduction for the internal combustion engine or MS DOS. So one question is what really makes this different? Why are we doing this?

So one question and maybe this is provocative is what is the assumption that we're making about what we need to have happen here. I think there may be an assumption that the public needs to be informed so that they will not be scared and shut down this technology. It's the ghost of the GMO debate in Europe.

Now I think we need to be somewhat explicit when we talk about these issues because the question is what is

it that we really expect to get from public engagement and public participation. This assumes, for example, a deficit model of understanding that the problem is simply that the public is ignorant and therefore fearful and that therefore the remedy is simply to educate the public, so that if they know what we know they will accept this technology and allow science to move forward. A lot of debatable assumptions there. So that's a question about whether or not we're asking that.

What I think we're beginning to see is an effort at this very early stage to begin to frame this technology. We've seen it throughout a number of the panels already today and yesterday which is, is this in fact some new and dramatically different technology that therefore has novel and perhaps unquantifiable risks, or is this, as Jim Greenwood said yesterday, basically like making beer.

So the question and that's really where the divide has come on the GMO debate between Europe and the United States. The question of really whether this is something that is a continuation, a natural extension of existing technologies or something that's radically new.

That framing process is taking place now, and the question is what's the relationship between that process and our desire to engage with the public.

The second question really is and I think it's the time that we actually have to ask Paul's question seriously in this panel, which is what do we really mean by public. Are we really talking about every man, child, woman on the planet understanding synthetic biology and approving it or accepting it? Probably not.

Then what are we talking about? Are we talking about potential social actors who may have the power to block the technology by their opposition through either political means or through appeals to consumers, for example, to be concerned about the product.

So I think we need to discuss specifically what we mean by the public in terms of this issue and in terms of how do we discuss this in a global environment. What does the public mean when we're talking about a globalized economy.

For the third question, it's how do we do this? Assuming we want to do this, how do you engage the public?

There's been more efforts in Europe than in the United States to look at these kinds of issues. We need to understand what has worked and what has not. We don't really have successful models for this as far as I'm aware. Most people are too busy, too tired with their own lives, too broke, too distracted to kind of deal with these issues. So how do you actually engage them particularly before in fact there are actually any products to talk about.

Another question that we have to ask is of course the role of the media. The media has, particularly European media, has been blamed for much of the European reaction to GMOs. But that again was 20 years ago, 25 years ago. What happens today when the mainstream media no longer have science reporters, for example. What happens in an environment where we have completely fractured media system where people are simply looking at the media outlets that support their own preconceptions of the universe.

And then finally a question about do applications matter? Does it even make sense to talk about public acceptance or public understanding of synthetic biology? Do

people really care about technological processes, or do they care about products? And in fact, do products make a difference? Do they matter what the applications are?

I think the answer to that is obviously yes. Even Europeans wear blue jeans from genetically modified cotton. So applications matter, and in this area that may also be equally true. So we need to be careful about painting with a very broad brush notions about public attitudes.

So these are just a couple of things that kind of have occurred to me, and I hope our panel will take on today. We're very fortunate to have three panelists who are very well qualified to address many of these issues. Many have been experienced through the genome wars and through the nanotech battles and genetic technology issues. Dave Rejeski from the Woodrow Wilson Center, Robert Cook-Deegan, the Director for the Duke University Center for Genome Ethics Law and Policy, and Adam Bly who is the CEO and Editor in Chief of the Seed Media Group and Seed Magazine which I'm hoping that Adam in particular will be able to address some of the media questions.

And in the spirit of public participation I'm

hoping we'll be able to get through this with plenty of time for this particular public to ask some questions and interact. So with that, David.

DR. REJESKI: Okay, well, thank you. It's great being here and thanks for hanging around for this discussion, end of two days again. From the Woodrow Wilson Center, as you probably know, this work is funded by the Sloan Foundation.

And so I'm going to spend a little bit of time talking about what we've found out recently and also in the past about public perceptions. So what I'm going to try to do is I'll reveal a little bit of the research that we've been doing on synthetic biology. I'm going to try to compare it with some of the new work from the Royal Academy of Engineering and also backward to what we did on nanotechnology because we have about four or five years of work on nano right now.

I'll share some observations about the larger social context in which synbio's evolving. And I'll end with some near term needs which I would preface by saying these are sort of my own perceptions and ideas.

So we've done two studies. The first one was a phone survey that we did last August of over 1,000 adults in the U.S. And we did two focus groups up in Baltimore last August, and we'll be repeating both of those both the national survey and the focus groups this August. So we'll have another set of data points.

Okay, what did we find out from both of these? Well, not surprisingly not many people have heard about synthetic biology. Now about 2 percent have heard a lot, 7 percent have heard something but probably close to 90 percent heard little or nothing. Not surprising.

If we compare this with nanotech, we also looked at that last year. A little bit higher saturation of nano. This by the way hasn't changed in three years, okay, in terms of public perception and awareness of nanotech. And I think it was Dan Seroes yesterday that asked this question which I think is an interesting one is do we reach a kind of systemic saturation point in society about how much people really know about stuff like this, whether it's nanotech, nanobio, synbios. So it will be interesting to see what happens to this in August when we look at it again

and see whether the nano awareness meter has moved a nanometer in the past three or four years. I doubt it, but it will be interesting to find out. Now even though they don't know anything about it, people venture a guess when we ask them about risk and benefits. A lot of them say nothing, 34 percent. But 21 percent said, ah, sounds interesting, sounds like the benefits will outweigh the risk, 16 percent say risks will outweigh the benefits. We give them some basic definitions. That shifts around a little bit and a lot of them shift to risks are going to outweigh the benefits and benefits outweigh the risks, this middle piece. Benefits and risks being equal, it stays about the same.

This is out of the focus groups. This gets back to this issue of apps. There's one particular apps people really focus on, and that was biofuels. They liked this. We ran a bunch of things sort of treating diseases, cancer, environmental contamination, sensing. There was a lot of interest. This is a very small sample, okay. But there was a lot of interest and excitement around biofuels.

This when we looked at the U.K. Eleanor Pols –

where's Eleanor right here -– did kind of a quick side by side. There was a lot of interest in biofuels in the Royal Academy of Engineering study. So that there seemed to be some kind of convergence around, and this is an interesting app. When we do the work in August in the focus group, we'll focus specifically on biofues. We want to get a sense of Americans are feeling about biofuels and whether if we sort of insert this piece on synthetic biology. We also asked him who should manage or regulate the risk. Their own government comes up high. And this one group of the females actually they want the scientific community in there. The male group wants to ban all this work altogether. There's a lot of – I'll explain this as we go on. There was a lot of sort of fundamental Christians in that group.

Nobody really wants to trust the company. But this is kind of interesting. We always ask this question, now how do we do this. Well, again going back to the U.K., no real support for a band but they like checks and balances. They like independent scientific involvement in the regulatory process. It's not really that surprising.

They think scientists should be part of the team.

They want to ban it. They don't want to shut it down. I think most people see the promise here. Again, some of the recommendations. They like the idea of openness and transparency. That's going to increase public trust. Again, I don't think there's a lot of things you wouldn't expect to see here. Open dialogue, listening and understanding. A lot of this, of course, is easier said than done as most of us know.

Now when we did about 30 hours of focus groups for nanotech, and we were always testing these propositions, do you want to shut down the technology, or do you trust people to self-regulate. In the U.S., we did them all over the U.S. in Seattle and Dallas and Philadelphia. There was never any support for shutting down the science. There was no support for self-regulation. So the idea that people are just going to self-regulate, nobody supported. Those are the book ends.

Now if we asked people this question, okay, how do you increase public confidence in nanotech, when you sort through all of the answers, there's absolute convergence on three things. The first one is more

transparency and disclosure, free market testing. We don't want you to test the stuff on us. And the third thing is they like the idea of independent testing. So they like the idea of kind of a consumer's reports, underwriter lab, companies working the NGO, some balancing of power. They don't trust industry doing all the testing.

Again, whether this translates to synthetic bio, I don't know. But these are not unreasonable kinds of demands, I think, if you're dealing with emerging technologies.

I think some challenges right now, it was astounding to watch these people react to this term, synthetic biology, absolutely stunning. It just pushed buttons that nanotech never pushed for them. Nano was that small technology. As soon as they heard synthetic biology, artificial light cloning, I mean you could see the neurons firing in their heads.

So it goes back to one of my favorite books by Reese & Trouss(?), when a name is bad, things tend to get worse. When the name is good, things tend to get better. These are the marketing folks. They know that. So I'm not

sure you can change the name. But I think you're dealing with that as a liability. I mean it's just amazing. That was one of the most stunning thing sitting behind the one-way glass is the impact of this term on people. And it was almost impossible to pull them back after their initial reaction no matter what we told them about synthetic biology.

Other problems obviously a lot of definitions floating out there. I think what happened with nanotech is the NFS came in, produced a very precise definition, three-part definition early on, and enforced it aggressively. Whether that's possible with synthetic bio, I don't know, because a lot of issues, definitions. The playing God issue won't go away, and there's no communication strategy. I can't find one. I can't find one in this industry. I can't find one in any government, and I don't think the scientific community has one.

I think there's a huge potential for a risk amplification. We're in the middle of a global pandemic. I mean I think that heightens people's anxieties around biological threats and issues. Good science journalists are

gone. They're dying out. So your ability to get anything covered well and in a balanced way is disappearing. This is an incredible difficult area.

We work with journalists sometimes for six or seven months so they can write one halfway decent story on nanotech. Nobody's going to put in that kind of time if they're blogging, right. So your ability to get anybody to cover really deep and well, anything about synbio is disappearing very quickly.

U.S. NGOs learn something from nanotech, they're fairly engaged right now. They've already had a teach-in in San Francisco. They will do more than that. There will be other actors entering this space obliquely. Lloyds of London just put you guys on the emerging risk list. The report on synthetic biology, Lloyds of London doesn't write insurance, they essentially shape the insurance market. Of course, the insurance folks were all over nanotech. The reinsurance folks, the insurance folks. So all over.

What's going to happen now is the space is going to open up, and there will be all kinds of actors coming in here from the financial sector, from the insurance sector,

from the press, from the NGO sector that's going to change the dynamics of operating. American public has experienced lots of failures of regulations. We can't deal with E.coli, Salmonella or Rickettsia. Those are pretty simple. So you've got this huge trust gap.

So we've tracked trust in government agencies for five years now. Every single year, it's gone down by four or five points. Underneath the government agencies are the businesses. Below the businesses are actually the White House and the Congress. Now that might change. We're going to do this again this year to see whether the Obama Administration is changing the trust curve. But you've got to live with this fact because that trust plays a huge role in your ability to attract investments, to get insurance, to get into the marketplace.

This was something that came out of some work at the cultural cognition project that Yale did. This was a web-based survey that was done of about 1500 people on synbio. Tony Lazare which is up at Yale. He basically does a lot of work on perceptions of environmental risks. And what he's found out is there's certain people in the U.S.

that basically are environmental risk naysayers. So as soon as you try to sort of tell them there's a risk involved with something, ah, nah. Those people tend to white male, political conservative, highly religious. This is what they found.

So going back over a bunch of different studies, basically this effect held for nuclear power, global warning, Mad Cow. They really –- these people weren't concerned. This is what happened with synthetic biology, okay. So there's something going on here that deserves a little bit more research, right.

What's going on with these folks who really didn't care about any of this stuff. They didn't believe there were any risks here. Why are they up there, right? Also, what happens with polarization. There's this idea that we're just going to dump lots of good scientific information on folks. We've had this discussion upstairs and with other people about who is the public.

Let me tell what happens when you dump more information onto African Americans or Hispanics. Their trust goes down because they don't particularly trust

industry. They don't trust the scientific community. So this is what's going on here with more information. When we gave them lots more information on nanotech, they started compared to the white folks up at the top with a huge gap. And the more information we gave them, it went like this. Same thing where there's a gender gap, all right. The people who love this are white males. Females, very little. I mean they basically start with the gap, the trust goes down. Political party not a big factor between the Democrats and the Republicans. Ideologically, you know, these are your liberals, and then there's conservatism progresses.

But the huge one, we start breaking this public down into pieces, you realize that you're going to have to have an incredibly differentiated strategy for dealing with folks. This is no one message, okay.

Okay, let's do the experts. Who would you believe? This is Bernie. Bernie worked for an NGA, teaches environmental science in Middlebury College, all right. And Stewart up at the top works for the Cato Institute. Now whatever the equivalent is.

What happens if I now give these people messages about nanotechnology, and how does that track into you folks. Now what happens is most of us make an association with these people within 150 milliseconds, and it's not surprising what we learn from this research was they decided to basically trust the people that kind of look like them and think like them. So who's giving the messages about synthetic biology or nanotech or any new technology becomes pretty critical.

And what we found was if I expect Bernie to say nano's going to kill the world and he comes out and says, you know, there's actually some pretty interesting stuff going on here and it's not that risky and I happen to relate to Bernie, I'm much more likely to believe him than Stewart up at the top. Not surprising again, but you have to think about what the messenger is.

So who are you going to listen to on synbio? You've got some incredibly articulate scientists here, right? Some of them are even in the room. But what happens if it's the new science adviser, Malcolm Gladwell. He's got to write a book on this right? What if you turned Oprah

loose? Someone talked about Rolling Stone. Well, it could get into Rolling Stone, but you may not have any control over what they write.

Zerhouni, NIH, the new head of the Food & Drug Administration, M.D., a woman, that's a fairly U.S. centric group. But one can imagine the group for the U.K. or Germany or EU or who would the dream team look like or who would be in there for the globe? This matters, and I think the one thing we found out, okay, is that basically the worse thing that could happen is if there's one or two people that become associated because the ability to create polarization is very high.

So what you have to do is create a very, very balanced, diffused and dispersed and very, very sort of wide open deliberative climate that kind of neutralizes all this potential biases, and you have to think about how you're going to do that.

So some near term needs, and I'll finish up. We definitely need more research. I mean that's always the standard answer, right. We need more research, and we need it soon because of the fact that this area is moving very

quickly.

I think based on the research, then we need a lot more public communication data strategy. Run the scales. We have an awful lot. We ran millions of dollars of experiments in public engagement with nanotech. We scaled up none of them. So all we've been doing is reaching about 20-30 people at a shot, and nobody's really figured out, you know, what really works and how would you scale that up to have an impact.

Risk research, I mean, the one thing that's going to calm the insurance folks down, there's only two things they care about. They want regulation, and they want risk research and basically we don't have it. And we're just beginning – I might get one study for us on regulatory adequacy, but there's hardly any of that. So Paula asked for these numbers. It's taken us five months to figure out what the federal government spent. We don't have all the 2009 numbers. But it's $130 million in synthetic biology. It's about $30 million a year. When you peel the veil back, it looks almost exactly like nanotech. That means 98 or 99 percent of the money is being spent on applications, and 1

percent on implications.

There's no money in there for public engagement. There's a little bit of money for LC studies. There's nothing we can find on risk assessment. I'll be more than glad to take anything from anybody in the government that changes that. But that's all we've been able to find. Those numbers should be on the web now transparent to every single person out in the U.S. or any other country.

It shouldn't take us five months to figure out what the government's doing about this. Lastly, obviously people have talked a lot about this more international cooperation. I think that's going to be key. I'll end with this little quote from John Didion. We tell ourselves stories to live. The one thing that's exciting about this area, there will be hundreds of stories told about synthetic biology. There's going to be stories about collaboration and cooperation and discovery. There'll be stories about caution. But the thing that I would say is that the words we pick to tell those stories and I don't care whether it's Swedish or German or Swahili or Chinese are critical. The narrative structures are critical, and

the people we pick or use to choose those stories are critical. So we have to start thinking about that. And if we just kind of leave it to chance, then I think the whole system can become fairly chaotic fairly quickly.

And those are some references that I tagged on there that if you need them you can get them from the web. Thank you.

[APPLAUSE]

DR. COOK-DEEGAN: So I don't have any slides, and I'm going to save a little bit of time by just staying here because I'd like it to be a dialogue. But if I could just quickly summarize, it's a very nice segue.

If I got the message, basically you've got a really scary name, no communication strategy, an unidentified leadership and no journalist channel through which to channel the message. But other than that, things are just hunky dory. And we're talking about public engagement. And I've been to several conferences probably in just the last two months where a similar set of questions is raised but about very different fields of enterprise.

I was just two weeks ago at a gene and environmental interaction conference. We could have a conference like this about neuroscience, about stem cells, about green biotech, about ag biotech. I go to a lot of meetings about genomics where the same kinds of generic issues are posed of very rapidly moving technologies that are in the life sciences and look like they're going to ripen into things that matter in real people's lives in the foreseeable future, and people are a little bit uncomfortable with what's going to happen, and they're wondering what are we going to do about that and how do we engage the public.

And we've just seen some public information slides that suggest that people don't know very much about it and haven't thought about it. This is again what you would expect. This is not a surprise. This is in fact what you always fine. Moreover, if you got opinions, you would know that they're not very reliable. It was like asking the folks in the Huntington's families are you going to get tested before the technology was there, and then suddenly when the technology is there you get a very different set

of behavioral choices that are different from what people thought they would think when they hadn't really thought about it very much. So I think actually the question about public engagement is not how do you engage the public because it's a hopeless task of educating the whole public up to the level of sophistication that you would need to make sane policy decisions which is actually very important to think about in advance. What's the framework into which these technologies are going to fit.

Rather, it's about what stakeholders, what people are going to be affected and what would they think about it if they were fully educated and trying to bring a broader set of stakeholders into the dialogue especially if they're going to be affected by the outcome. And it strikes me that there are – that's a whole set of procedures and we do have some examples of that. And in fact, I think that there are three basic stories that have come out.

I've heard resonating histories to at least three historical episodes that we've had in my lifetime that are connected that we all think, oh, this is like that in the past. One of them is recombinant DNA. That's a 40-year-old

story. And the story there is scientists realized risk of biohazard imposed self-restraint successfully, changed rules, put in place a review procedure, and moved forward with the important science that transformed into biotechnology and now pharmaceuticals.

We have a story about genetically modified crops that's different across both sides of the Atlantic. And the lesson there is about public perceptions of risk and having one dominant corporate partner driving the agenda and what do we get from that.

And a third is, although I've only heard it mentioned once so far, I'm going to actually spend some time on it and that is the field of gene therapy. I'm going to use that as an example because if there's ever been a technology that had lots of writing and thinking by people outside the sciences about a technology before it actually existed, then that's the technology that you would look to. And yet we have this catastrophic real world event of a death that was associated with that technology that deeply affected the field and still affects the field. And you can't talk to anybody who's in that field without them

knowing what happened in 1999. So that's a one decade old catastrophic result that actually literature that goes back 40 years. It goes right back to the recombinant DNA story.

So what can we say about that? Well, one thing to observe about synthetic bio as the field is first it's a little bit hard to know what we're talking about because we've ranged, if you talk about what the biobricks foundation and that kind of engineering approach to molecular entities, that's very different from the kind of synthetic biology that we're talking about with a card dimmer or creating a whole new organism or Jay Keysling trying to use an engineering system to produce a drug. The things that people are doing in the lab is very different, and yet they're in the same category.

But even with that caveat, what can we say about the ways to approach that. One thing that I think we can say that is truly distinctive about synthetic bio is that it does feel sociologically different. It feels like the industrial ecosystem really is different. And what do I mean by that.

If you think of the personal computer business

where it quite literally was drop outs from Reed and Harvard who starts absolutely crucial companies, Microsoft and Apple, and they did it quite literally in garages or warehouses and they could do it basically at a high school level. And you think at the other end of the spectrum about developing pharmaceuticals and big pharma with a vertically integrated billion dollar a molecule model of innovation. You would think that –- it feels like synthetic bio was actually way further towards the personal computer end of that spectrum where the ecosystem is likely to be lower tech approaches to new ideas and lots and lots and lots of ideas coming out of places that you would never predict as opposed to really, really, really systematic R&D that costs lots and lots of money.

And if that’s true, that actually has some social consequences about who you engage in the policy process. It means it’s going to be much harder, and you’re going to need to hit a broader network of people.

Let me go back to why do we care about doing public engagement? Well, it strikes me that we do have some templates and you saw them in the slides that you just

showed. We have stories of how do we introduce a new technology responsibly. One model that we have is the Food & Drug Administration which is before you get to sell something, you prove that it's safe and effective. Now that's really costly, and that's part of the reason that it costs so much money to bring one of these drugs to market. So that pushes you in the direction of it's really going t cost a lot of money, and that's actually against the personal computer kind of a framework.

We have the Recombinant DNA Advisory Committee which was talked about here. That grew out of first thinking about biohazard. But please notice that same structure is precisely the structure that already existed from the late 1970s to deal with the problem of biohazard. But when the President's Commission for Bio Ethics in 1992 came out with splicing life, they said, oh, you know, these people are already looking at recombinant DNA and we are now facing the prospect of putting recombinant DNA into human beings. Why don't you ask those same people who have that expertise to think about the clinical risks and benefits of introducing DNA into people.

So they put a structure that was in place to regulate biohazard and inadvertent environmental release of nasty bugs, and they used it to become essentially a super IRV for testing safety and efficacy protocols for clinical trials of gene transfer. That is the very same structure that the Fink Committee turned to to now deal with yet a third social problem which is dual use. That's what the Fink Committee said that still exists. The IBCs have the requisite expertise. Let's use them to think about this new problem of dual use.

So what do we know about the system? Well, we can notice that it's highly adaptive and the common thread there is it has something to do with DNA. So we do have that, and my guess is whatever's going to evolve in the way of dual use is going to have something at the institutional level that will do ad hoc review of the science that's coming out of the structures that already exist.

But let me just end with a couple of kind of random observations about how that interacts with the observations I already made about the ecology, and that is we are one of the places that has started to do some dual

use review. We've looked at protocols, and it's because we're part of one of the consortia that supports bio defense and emerging infection research. One of the things that we observed is as we looked at protocols, we were really, really, really poor at thinking about what we should really be worried about when we first looked at those protocols. There are actually people who thought about what are the risks associated with doing research on nasty bugs which is mainly what we're talking about when we're doing this dual use review.

I have to say most of the attention has gone to the biology, how do you make the bug nastier. But in fact, the protocols that have really raised our – that kept us up at night if I could put it that way were not things that would require a new bug. You could take an existing bug, but they are about delivery and weaponization and dissemination, and you don't need the new bug to wreak havoc. All you need is a way to get into lots of people's bodies secretly before they know it and get into the system to cause incredible amounts of chaos.

Two things fall out of that. One is most of the

expertise we have is actually about the engineering of the bugs and the biology part. That may not be the most important thing to be worried about if we're talking about firewalls and all the analogies that were used. It could be that we actually need to be thinking about that part is really about the other parts that need to be dealt with as risks in thinking about real live how nasty people are going to think about using biology if they want to hurt people.

The other was that –- and here we're going back to the iGEM framework, one of my episodes with dual use review was actually one of the students, the head of the first Duke team on iGEM had taken my course, responsible genomics, and we had a module on dual use review and bioterrorism. So this is a kid who was well attuned to it, and he actually voluntarily –- they were working in their group. He waves me in with Artie Rye who had just given a talk on patenting and said, hey, come look at what we're doing. And Artie said, well, they had three incredibly good projects, and they were really, really interesting. Two points. One is I'm supposed to be responsible in part –-

responsible for thinking about this stuff for my institution. I didn't have a clue what was going on. It was the student voluntarily pulling me in and saying, hey, look at what we're doing that made me aware of what was going on which signals to me that actually there's probably lots of stuff going on and will continue to be going on that if we think that we're going to capture it through the structures that we exist for funding and for publication, we're probably going to be missing some stuff at the margin that may be just as important as the stuff that's going on through the main funding channels and things like that.

The other thing is when I asked him questions about dual use, even though he had taken my course just six months before, he hadn't asked himself or the team had not asked itself the questions that we would hope they would have. That's not his fault because we're all like that, right? But it suggests that we actually need to be thinking about a culture that's constantly raising these questions on itself and it just gets built into the sociology of the field.

So those are some –- it strikes me that we're

actually faced with something that's at once much more serious than it might be in other domains precisely because it's so decentralized. And on the other hand, there are rays of hope that in fact maybe the risks are not so catastrophically large as we might at first think if in fact we have students like the one who actually thinks to drag somebody into a discussion on their own volition. It seems to me that's a social system that if we can inculcate that in the field as a whole, it strikes me that that's really important.

I just want to end with one thing which is one of Drew's questions was can you in the next 12 months come up with a legal regime that will help us deal with the issues. One observation after about five years of thinking about genomics and intellectual property, and this is probably the thing we do more research on than anything else that we do. I've been studying a lot of history of technologies, and I have to say I don't know of a single friction-free technology field. I don't think I've ever seen a tech –- now of course if there were such a thing, probably I wouldn't know about it because there wouldn't have been

conflict and there wouldn't have been court cases.

But as I'm looking at the history of sewing machines and computers and radio broadcasts and all these technologies, bad things happen out there no matter how much people think about them. And it strikes me, Drew, that the solution to that that has been used in biotechnology and seems to be being used in your own field is actually just kind of conscious attention to that cluster of issues and having the leaders of the field try to think through it a little bit in advance of the bad things that might happen.

And it strikes me that the combination of public domain strategy and patenting strategy that seems to be evolving in synthetic biology may be about as good as you're going to do. And it's probably an unsatisfying answer because it's not a legal framework that is designed for your purposes. But it does strike me that the problem may be possible to work through. But the main message there is don't expect it to be pain free because I can't think of very many fields where it is.

[APPLAUSE]

MR. BLY: We're going to pick up on those rays of hope because I think that I'm going to paint a largely optimistic point of view from the public engagement's perspective.

Despite the points that were raised earlier in the introduction about the infrastructure of science media that you're dealing with today which is extraordinarily poor and frankly bankrupt and the fact that nobody knows what you do, I think these are both actually reasons for great optimism.

First, it's extraordinary that so few people know what you do and what the synthetic biology community does and is now entering a moment where understanding and engagement with it will increase under a culture, under an environment in this country that is now pro-science and now recognizes scientific integrity and ultimately trust in the scientific community as essential to the vitality of the nation.

And so I think that this is a very, very, very interesting moment and rather opportunistic that that's what the figures look like. Had it been any other way and

had the rise of engagement or literacy surrounding synthetic biology have risen over the last eight years, I think this would be a much more dire situation. So I think timing is exceptional. That's first and foremost. So I think to the extent that this alliance with the broader theme is being voiced by President Obama and by his advisers is a very fortuitous moment.

The second point I might make in terms of scientific literacy so this is sort of the area that we think about quite a bit and look at scientific literacy from the standpoint of the public, from the standpoint of the media, from the standpoint of all stakeholders and across the sciences, here's a case where I don't feel a kind of lowest common denominator strategy is necessary. I don't think that Oprah is essential. I think sort of that's actually the wrong framing through which to look at public engagement frankly because the community of synthetic biologists is much more attuned, I think, to the ways of communicating their science to the public through new approaches to communication than many other scientific communities.

I think that might be a function of just the sort of self-selecting nature of scientific fields. The scientists who are drawn to synthetic biology are perhaps different than the scientists who are drawn to geology and -- not attacking the geologists, but I think the very fact that the synthetic biology community is quite self-selected, this presents a really interesting challenge and opportunity.

I think that the confrontation that scientists often feel with the general media, mainstream media actually is not quite relevant to the communication of synthetic biology. I think that science has in this case as it so often does outpaced society, and we now are at a point trying to catch up in a regulatory, legal and other frameworks. At the same time, the opportunity is that technology and in particular digital media has in fact kept up. And I actually think that there is a rather extraordinary opportunity for this community to bypass to frankly by all accounts bypass the mainstream media in its concerted efforts to raise public literacy, raise engagement.

So to the point about blogging and that, you know, a blogger won't take the time to sort of really properly think through and articulate a point of view on synthetic biology, that's actually not the case, and I'll give you an example. I'll give you an example from our own work.

One of the ventures we launched, one of the experiments we launched a few years ago is called science blogs where today we now have 500,000 scientists communicating to two million non-scientists using social media, publishing 150 different blogs around the world in different languages, and the scientific community that's involved in this new digital media environment has recognized that the best channel of communication is direct. This is an area where the media will fail you, and speaking as an organization that employs many freelance and many full-time science journalists, by and large this is a community that will be failed by mainstream science media because it lacks the requisite scientific literacy to deal with something this complex, this challenging, this risky but also at this pace.

And so I wouldn't even contemplate the need for mainstream media and really bypass it and focus on new tools for scientific communication. I think this can be done at scale. This is not kind of fringe any more. This is not just about reaching another 5,000. Our quest in our organization is universal scientific literacy. We don't think about scientific literacy as the pursuit of 10,000 more. We think about of it as 300 million, as 700 billion, and I think that this is actually one of the unique fields that has the potential to employ digital media tools to its advantage in public engagement.

Because I feel quite optimistic about generally where this community is at in terms of its public engagement efforts and strategies, I'd even venture this. This may in fact be the community that can reform scientific literacy itself. And at this great moment where we're thinking as a society, as a country, as a world about how to revamp scientific literacy so that it doesn't mean that we are competitive with the Soviet Union and we're going to produce more scientists because they have more scientists and we'll have a Sputnik because they have a

Sputnik, but that we start thinking about scientific literacy as something more intangible and something more indigenous to a culture, I think the scientific biology community has a few things going for it that should figure into a new framework for scientific literacy.

The first among them is this sense of social responsibility that is in fact rather pervasive in this community. There is an understanding among this scientists who practice synthetic biology that there is a risk. We hear it today, and it's noteworthy that the public engagement session follows the securities session. You understand and you recognize and you speak publicly about the risks associated with it. And I hear a real sense of self-awareness about the potential dangers alongside the potential opportunities.

And so I think that presenting this new sense that scientists in fact care, scientist are in fact people, too. They're fathers and mothers and daughters and teachers and will be affected by the same consequences as the non-scientific population by the risks presented by their science, I think this dimension of social responsibility is

rather prevalent and will be a part of the way we think about science going forward.

And other is that it has the potential to be and is a participatory science. It has the citizen science qualities and the DIY qualities that are often so much a barrier to public engagement in science. We can't all go make large hydrogen colliders. But we can participate in DIY biology. We can participate in the life sciences increasingly.

And I think that that too, this participatory citizen nature that is indigenous in synthetic biology will become very important to new scientific literacy as well. The way synthetic biology operates, actual infrastructure of the community I think is something to be proud of. I think to the extent that openness and transparency in its approaches to sharing information, sharing tools and to many extent its own publication and approach to publishing resonates with where the tendencies are in the broader scientific infrastructure and towards openness, towards open access, toward transparency, and it presents a hope for a new model for open science.

And so I think in that respect as well, it can have positive benefits to scientific literacy. And then finally and perhaps the biggest challenge and most interestingly is this very point of unpredictability. This is a field riddled with unpredictability. But that is what scientific literacy should be all about. It should be about preparing the population for rampant unpredictability, for change.

Scientific literacy should be more about a methodology and philosophy rooted in the scientific method where science itself provides the boundaries within which to work and within which to think, and it’s the very weakness, it’s the very sort of unstable nature of science. It’s this very unpredictability that is in fact science’s greatest source of strength and sustainability.

And to the extent that we can communicate to the public that despite this unpredictability we move forward because we have this methodology, we have this philosophy, we have this empirical foundation that guides us and bounds us, I think that actually may be one of the most significant contributions that the community makes to

broader scientific literacy.

So I in summary would look to new media because you can and because I think it's my sense that this is a community of scientists that enjoys it and recognizes it and can frankly advance it and be bold about the extent to which the advances and culture of this new community can actually impact broader scientific culture and scientific literacy.

[APPLAUSE]

Agenda Item: Questions and Answers

MR. RODEMEYER: I have some public participation of our own here in about 15 minutes. Go ahead.

DR. OTT: Thanks. I'm Jermaine Ott. A quick comment and then a quick question. The comment is I always get really worried about talking about science literacy because it seems like we begin to talk about a process of proselytization where we're trying to convert society into a certain way of thinking and doing things. And I think there are more sophisticated ways of looking at that.

But I want to present one side and once comes the question, and the question is and I would like the

panelists to try and answer this as honestly as possible. If we didn't pursue a program of public engagement with synthetic biology, would it really make any difference.

MR. RODEMEYER: They're pondering the question. I don't mind thinking that in some ways I think that's in a sense what you were saying. You were already doing what needs to be done.

MR. BLY: I would say precisely that. I'm not sure you need to over think this in my opinion.

MR. RODEMEYER: Veterans from the genome wars or nanotech wars?

PANELIST: It wouldn't change NSF's budget.

MR. RODEMEYER: That's a cop out.

DR. REJESKI: I mean I think some of it is this kind of reactive. I mean I think it is going back to some of the analogies, and I think one of the things that was quite stunning with the GMO wars is that we had the ability to actually monetize the losses. You probably know this as well as I do. But I mean the estimates of lost market were $300 or $400 million a year for U.S. markets. That was a significant amount. That's just kind of raw inputs into the

EU market.

So I think that's something that went beyond just kind of -– so I think that's always in the background, and I don't know because you obviously lived through a lot of that. I think that's something that comes up continually when you talk to people in the synthetic bio world is whether there's going to be some sort of economic impact down the road. Or obviously if the insurance companies get involved, whether it's going to raise insurance and things that kind of scare away investors.

I think we're also in the middle of a massive economic collapse globally. So I think there's also a significant kind of overlay of less capital going around for innovation.

MR. RODEMEYER: Anything to add on that?

MR. COOK-DEEGAN: This may be an unsatisfying answer because it is for me. I'm not sure what your question means. Does it matter in the real world? Because let me use the example that I used in my remarks. That is human gene therapy.

What was the history there? Well, it was the

three denominations pointing to the President of the United States saying we're worried about this. That goes to a President's bio ethos commission that says they're worried about it and they should be worried about the following very specific things and they provided a map to FDA and NIH and said, okay, so here are some very specific steps that you need to do if this is actually going to happen in the real world.

Now would NIH and FDA have figured that out if the technology is what drove that decision rather than some foresight and some previous worry by religious denominations. I'm not sure. I do think that there is serious value in having people think about what policy should be before they're actually confronted with the choices of actually having to do something about it. And I think you can count on the fact that at least some of these technologies will come to fruition. And when they do, you're going to have to make real decisions. So I think it's an argument that in fact it does help to think at least a little bit in advance. That said, I do think I take it with a grain of salt because, look, gene therapy, there

was a lot of spilled ink. But in the end, what really mattered in the Gelsinger case was not any of the not having a good framework. It was the very specific implementation and the five or six stakeholders any one of whom could have made a different decision to change the outcome and the catastrophic outcome is avoided. So that is not – no amount of bio ethics is going to solve that problem. And yet, I do think that bio ethics had some value in setting up the framework that got them to that point. So I don't know what to say.

MR. RODEMEYER: Question over here.

AUDIENCE: Hello. This is probably more of a comment than a question. I'm Suzanne King from People Science and Policy. We were commissioned by the Royal Academy of Engineering to do the reports that the project that they referred to. So I was the person who actually sat in facilitating the group discussions and designing the questions for the survey on it.

And I thought it was just worth pointing out I think actually the people in our -– we had a group of 16 people and it was one big group rather than two focus

groups. I think the reaction was more positive. I mean it was a small group in London, but I think they seemed to be more positive about synthetic biology, and their initial reactions were a bit more I'll wait and hear a bit more about what you're going to tell me it is before I jump to conclusions, and they seemed to be more enthusiastic than talking today about the people on this side of the Atlantic, although the survey findings and some of the other discussions as you saw are remarkably similar. Awareness is absolutely the same -- 60-70 percent were unaware of it.

But I also wanted to make a couple of other more general points. I think once somebody said –- one of the speakers said something about educating the public to some sophisticated level. In Britain, one of the things that people like me go on about is the public don't actually need a PhD in any of these subjects to be able to engage intelligently if you can work out the right pieces of information to tell them about the science, and we found that time and time again.

I mean I've been involved in running these sorts

of things for 15 years now. And really people don't need to know a lot of information. They just need to know the right pieces of information to be able to engage in a fairly sophisticated debate. And I think the other thing that somebody's just alluded to as well is it's not a marketing campaign. We talk about having a dialogue with the public and scientists and policy makers. Increasingly, we're talking about the three parties, people, the public, policy makers and scientists and it's about mutual understanding and changing scientists' feedback on these events so that they actually impact some of the way they think about their science and some of the research they're doing. So it's not just about convincing the public or educating the public. It's about changing the nature of what you're doing which I think might have been something Adam was slightly alluding to as well, taking on board people's concerns and being seen to address them, and that's really the basis of confidence. I'll think I'll stop there.

MR. RODEMEYER: Thank you. Yes, lets' take the next two, so go ahead.

DR. TOLLSBY: Susan Tollsby from one of the seven

research councils in the U.K. What I was going to say really kind of builds on what Suzanne was just saying. A lot of the research that we're supporting at the moment, the different schemes a huge part or certainly a quite significant part of that we've been encouraging the scientists to take in social, ethical considerations in their work, and that's been very positive so far. And they're actually getting a lot out of that is all the positive and happy messages we're hearing.

And I had another very important point, for sure. And it's like in the centers and in the networks. They're all really driving to engage the public and whether it be on a small scale or a big project, it's an engagement in dialogue. It's all very important. And the Council's are also going to undertake another public dialogue activity over the next year. So please keep an eye open for that.

MR. RODEMEYER: Thank you. Yes sir?

DR. TAYLOR: Terry Taylor from the International Council for Life Sciences. Just two points. One is perhaps I'm wrong but I sense, one, that there is a certain amount of under estimation of the dissemination of the technology

that stands at the moment and the speed at which it will disseminate in the future. In the case of our work around the world, we hear some elements of this debate whether we're in Karachi or whether you're in Amman, in Jordan or in Singapore or Dubai. The debate, it's already a global debate and it's not something that within the hands of a relatively small number of large countries and the experts in those countries. And for probably the reasons that Adam Bly has outlined, there is an active and interactive debate and absorption of the technology, and it is, I think, certainly true that breakthroughs will come in the most surprising places around the world. So I'm a little bit worried about being too complacent on that particular point.

But overall, I'm viewing this as a positive statement. I think it's a great thing that it's disseminating rapidly in the same way that information technology in the 19th century disseminated rapidly. I think the outcome will be positive because most people want to do the right thing. It's not to say there aren't risks to be thought about. So I fully endorse David Rejeski's point

about the need for methodologies or new methodologies for some form of overall risk assessment but not with synthetic biology on its own, and this is where I'd be interested in the panel's view. But it needs to be wider than that because if you don't put synthetic biology into a full context of biological risks, you're not going to get the right answers.

And this risk assessment is urgently needed not only for communicators but also for policy makers and for public understanding. And just as a little bit of a commercial at the end, with my organization, ICLS, the raw society there's a report being published this month on this idea of net overall risk assessment and perhaps making some suggestions the way forward. Thank you.

MR. RODEMEYER: Thank you. Any comments on that? You know, one of the speakers earlier did refer to this notion of maybe it's sort of new emerging technology fatigue. We've talked certainly about genomic technologies, nanotechnologies. Every time something new comes along, we try to look at this, the risks without the context of others. Is it possible to kind of cut across that in terms

of how we deal with some of these issues.

MR. COOK-DEEGAN: Sure. Going back to the policy story, one of the things that I think is the case in synthetic biology is that you do have some structures in place that are right next door, and they've been alluded here today. That's very different from stem cells because they can't turn to and the National Academy has basically said, hey, you need a new apparatus for looking at cell biology that's different because you don't really have the structures in place that you do have in place through the institutional review process.

I'm thinking at the very policy level. So that synthetic biology in that respect actually has a smoother pathway than some other technologies that are going to have to jump start that.

MR. RODEMEYER: Questions? Let's get two other speakers.

AUDIENCE: David offered a very, very concrete suggestion from the survey. The survey said the public demands or requests testing in advance of introduction by credible third parties preferably with an evaluation.

A couple questions. First, with reference to nano, did that happen and, if so, by whom and how and by what third parties? And if not, were there any consequences?

Question two: How should we apply that principle to synthetic biology? And then of course the nasty question is question three. There aren't many examples of preventive measures being taken, the sort of systematic pretesting without disasters taking place first. From Upton Sinclair and the slaughter houses through car crashes with Nader publicizing the consequences, teaching therapy in a dead patient and there are lots of other examples. The exception would actually probably be GMC. And do you think that there's any prospect of the survey says recommendation for serious efforts to be made on pretesting. Is there any realistic prospect of that taking place without a disaster first?

MR. COOK-DEEGAN: Well, actually if I could just correct on the gene therapy, actually that would be a counter example to that because the structures were in place well in advance of the first protocols. And I would

actually say that was a failure of implementation rather than a failure to have in place the policies.

So the Gelsinger case was catastrophic, but the procedures that could have avoided it, I just don't think it fits in your framework. It's different from the FDA crises and thalidimides.

AUDIENCE: But the point being that the characteristics of the tests, how they're done and by whom bears very essentially on issues of credibility.

MR. RODEMEYER: Paul, let's get to your question or comment.

AUDIENCE: Two points, one quick. The two percent who know a lot about synthetic biology, I wonder what they know because as an anthropologist, the figures are probably higher if anyone's wasted their time and money doing a survey on that. But I can tell you from airplanes and the rest that Indiana Jones is the equivalent of anthropology and nomus, et cetera. So a little caution on that. I don't even bother any more. So that's point one.

But the more interesting question to me is where Adam was going because I saw Chris Anderson on the BBC the

other day basically saying newspapers are going out of business, who cares. We're going to have new media. We have new venues. We have thousands of bloggers. And I think at some simple level something like that is obviously true.

And so this question of the public which is large literature demonstrates arose first with literacy and the rest and then in the enlightenment with cafes where people could come together and read newspapers and the rest is endless literature and that which is there. So we have new media, new venues, and new forms not so much of literacy but of some kind of communicative exchange going on which is definitely new, and we need to know a lot more about.

So I have three websites. So I'm not opposed to what you're saying at all. I just think that's something that's worth a lot more discussion particularly among younger people who are growing up after all as cyborgs with iphones and everything else, and it's not a moralistic good, bad or anything. It's what's happening and then what in that –- just automatically saying it's good that newspapers are disappearing is a little scary. But maybe it is, but the question is what's coming next and how can we

be active participants in forming that so we're forming better publics in some sense of what I call flourishing. So I think that's an open question. But I really appreciate where you were going.

MR. RODEMEYER: So Dave, perhaps you could take the nano question first about what happened in terms of the recommendations and if there were any consequences. And then we can try to tackle the –- maybe combine the questions to sort of ask are we in a new paradigm where we may not need to have the big crisis to happen in order to either galvanize the public or engage the public in a way that requires policy response. But –

DR. REJESKI: The question is whether we can think through some of the potential, right.

MR. RODEMEYER: Where there's a third party testing to that end up happening.

DR. REJESKI: Yeah, it did happen. We did get Consumer's Reports to do some independent testing of nano-based sunscripts, not a lot. And whether it made a huge difference, I don't know. The other thing I would say is they were already on the market. And so we talked a little

bit about the FDA, and the FDA obviously does protest in the case of biomedical devices and drugs. But there's question if you put novelty into that system even though it's a fairly long system that requires interaction with industry, whether if there's a lot of novelty whether the existing in vitro, in vivo, biolacity methods are going to work with the new stuff. But that's something they have to think about. And there's an awful lot of stuff that they don't test.

I think one of the biggest surprises when we did the focus groups, we did a whole bunch of focus groups with women and cosmetics was how shocked they were when they found that the cosmetics were not really prescreened.

So there's this kind of sieve. There's all this stuff going on in the market such as dietary supplements and cosmetics. The Consumer Products Safety Commission has 390 people now. They're looking at a I think it was a baby pacifier that was coded nano engineered silver, and I asked them have you tested this, and we looked at the test protocol and all the test protocol is could they swallow the pacifier. And so actually testing for that is non-

trivial. So I think there's a whole bunch of need to sort of before you even get to sort of looking at the possible 1 in 20,000 or 1 in 100,000 potential failure of just the stuff that's out there, and you know can we test it, can we look at it, and a need to at least go partially upstream in a lot of these cases so you can see kind of what's coming down because I think the scientists and the regulatory agencies actually benefit from that conversation, and there could be tremendous benefits in synthetic biology. The same way we did one exercise in nanotech that looked at food packaging where we went upstream with industry and with regulators and looked at things that hadn't actually been commercialized.

AUDIENCE: [Off mike]

DR. REJESKI: Right. I mean the insurers get involved. The other group that's already looking at synthetic biology is a socially conscious investment group. So you're talking about people that move a lot of money or have impacts on the economics of business. I think the other thing that's behind this and I agree with Adam. I'm optimistic about the shift in the Administration is behind

all of this is this issue of trust. This is kind of dark horse, and I think that it's eroded considerably over the past few years and an awful lot of that. A lot of the sort of the public's intensity or interest in technology, a lot of them have got – I've got plenty of stuff in my life to do without worrying about nano. But if I feel that there's nobody covering my back and I can't trust the government an I feel that there's basically there's holes in the system and there's nobody else out there, and I think that heightens kind of people's awareness of what's going on. So I think actual trust in government matters – I mean if you go back, it's something that's knolling at industry right now if you go back and look at Harvard Business Review, McKinsey, you'll find issue after issue about the trust gap. And I think if we don't do something about that, it really has a long term kind of pervasive impact on our ability to innovate and commercialize these technologies.

MR. RODEMEYER: We need to wrap up. But Adam, did you want to have a –

MR. BLY: I thought briefly I'd just tackle that point. You know, so I don't think that it's as simple as

proclaiming the end of newspapers to be a good thing, and it's important as characterized I would strongly disagree with that sort of sentiment.

What this means here is that there's sort of the economic dimension of that story of media, and there's the sort of fourth estate dimension of the importance of media and trust and authority and all of that. The economic is irrelevant to this audience. The latter is more important.

One of the things that we need to do so the media community, the media industry needs to take on, the publishing industry needs to take on its own share of responsibility here is to ensure that as we're blowing up this structure and building a new architecture for new media that we ensure that we think about some of these first principles of authority, of trust of openness, of preservation when it comes to a scholarly record so that as blogs and social media are used, we tackle these problems.

We are working with the Public Library of Science. We're working with Cross Draft and with Pub Med and all sorts of organizations to ensure that the kinds of disruptions effectively that we're advocating and trying to

introduce into the media landscape ultimately do serve to both advance science and service of society by holding true to some of those first principles of the fourth estate of media.

So it's not just about blowing it up and allowing the chaos to just run rampant. It's about blowing it up and very quickly establishing what the first principles are that we need to uphold as we rebuild the media architecture for science.

MR. RODEMEYER: Thank you. Please join with me in thanking the panel for their presentations.

[APPLAUSE]

Agenda Item: Session 8: The Path Forward

DR. GILLESPIE: I'm tempted to do a cultural joke. How many Brits are in the room? It's Friday, it's five to five and it's cracker jack. I'm sorry. But you know, I've sat through two days of U.S. jokes and U.S. anecdotes. I can't resist it. Cracker Jack was a great program when I was a kid, and it was on Friday at five to five. It's a child's program, and they always pulled something magic out of a hat.

Well, I don't think we have to pull anything more magic out of the hat than synthetic biology. I mean it is the magic thing that's being pulled out of the hat. And certainly I'm convinced of that.

What we want to do in this last session, though, is just bring the moderators and as you'll see in a couple of places the moderators have immoderately got on airplanes and headed off back home. So there are a couple of august replacements in here. What I want to do is simply turn to the panel one by one in an undisclosed order so I can keep that free sort of unexpectedness amongst them to hear from them what they think are some of the key messages they've heard and one recommendation.

The reason I want one recommendation is I'm going to reverse order a little bit, and I'm going to say first of all what happens next and then I'm going to turn to them. I'm going to start with Drew, but after that it's a surprise.

First of all, in two weeks' time or so there abouts, you get the transcripts of all of these discussions. You'll see how embarrassing your questions

have been and how very embarrassed some of the answers have been. You'll also get the PowerPoints up on the web and our very good friends, our hosts in the National Academies will send you a note and let you know when that happens. So that will be kind of the immediate next step of the report.

But there are two other things as well at least that are going to come out of this meeting. One, as I think we mentioned yesterday, there will be a kind of shorter possibly slightly more targeted report which in the first instance will be prepared by ourselves and the OECD together with the Royal Society and of course in collaboration with our hosts in the National Academies.

That will take a little bit longer to do not least because the big bureaucracy in the room or at least the difficult bureaucracy in the room is the OECD and we have certain procedures to go through. But in that we want to try and come out with some recommendations. And really now we want to try and get a sense of what some of these might be. Now in my own organization –- I can't speak for the others, we will take that report and the outcome from these discussions into our internal intergovernmental

discussions which are certainly not transparent and I'm sure are completely untrustworthy and don't involve the public at all and definitely not society or even Paul's notion of society, and the OECD countries, we hope, will think about trying to identify where some of the areas for public policy which might be developed should be prioritized and I hope are taken forward.

So I've given you that introduction now because I really do want to stimulate all these august people here on the panel to come out with their reflections and their one or if they've got two, two quick recommendations. And then once I've done that, we'll quickly see if there's any comments or additional points in the audience and then, well, by then it will be five to five and it will be cracker jack.

So Drew, I'm going to start with you.

DR. ENDY: I'm a poor surrogate for Ed Rejeski who gave me this piece of paper to read to you which I'm now not allowed to do, and I'll thus paraphrase it by starting with two quotes and make one thing and be done.

We reject kings, presidents and voting. We

believe in rough consensus and running code, so says Dave Clark and the Internet Engineering Task Force. Let's get it done. And then a quote about Ed from his webpage if you've not seen it. If you're not part of the steam roller, you're part of the road.

[LAUGHTER]

DR. ENDY: So to paraphrase Ed, the last positive integer number of years have demonstrated the promise of synthetic biology, and it is now our challenge to achieve this promise. And this requires getting stuff done. Focused investments in technologies, science and policy and pulling it off. I return the remainder of my time to the chair for use by the honorable gentleman from Cambridge, Massachusetts.

DR. GILLESPIE: Anyway, so Drew, I'm going to move on next to Sheila.

DR. JASANOFF: Thank you. I guess what I'm struck by is that we've been debating two utterly different things. One is an emerging technology and how we get it out of the heads of people like Drew and get it into making money for us which we desperately need as societies.

And the other is how to construct the public's fear in the 21st century in which science and technology play incredibly important roles and in which we do a lot of the work of governance through science and technology and not only through things like law which we're kind of used to doing.

So my recommendations under each heading would therefore be rather different. So with regard to the point about emerging technologies, I think there's a lot of lack of clarity about how the experience and knowledge from other emerging technologies is being drawn upon and used. And so I would suggest that in thinking about all these quite technical issues that have come up about regulation, about the nature of intellectual property law, about the relationship with insurers and so on and so forth, that a lot more thoughtful and clear drawing of the analogies to other emerging technologies around which we have had more discussion would be appropriate. And I thought that Bob Cook-Deegan's attempt to relate gene therapy to the discussion of synthetic biology was an example of the kind of scholarly and research-based and historically grounded

analogizing that we should see more of.

But when we talk about the other point, the construction of the public's fear, I think the discussion has been not particularly illuminating to somebody like me. So I would get more excited about Adam's use of the term science literacy if I didn't know that Seed Magazine actually did science literacy in much more like what I consider to be the right way to go about constructing the public's fear in that it's not only sort of educating larger than two percent of the public about the nitty gritty of particular scientific and technological developments. But if we want to think about making a public sphere, then the points on which I think we've walked in a gingerly fashion up to even framing them and not really gone there include globalization, how do we really get a global discourse given such things as language barriers that came up on day one but people seemed to have forgotten them.

People seem to think that the only language barrier is between scientists and non-scientists. This is not the case. There are language barriers of all kinds. You

do not according to political theory get a good public sphere unless people are capable of speaking the same language. So that's something to be taken very, very seriously, especially in a globalizing world.

Scientists are not aware of the fact that what they do is not mere play and fun and sports, but also governance. I mean this is the point that really needs to be got across. The fact is that you can by technological means control people in much the same way that you do through law. And yet, the system of governance we have in place for technology is not the system of governance we have in place for constitutional law. So I think once one recognizes that technological innovation is a very deep going way of changing the very circumstances in which people live, then it becomes a challenging multilateral and ongoing progressive discussion how we're going to channel that innovative capacity in a progressive direction. I think many people have commented on the fact that this does need to be a progressive thing and not a punctual one-short decisionistic solution oriented thing. How we engage in those ongoing conversations is again something to think

about, and I think the OECD countries have the resources, but they don't put them to good use in thinking about them.

DR. GILLESPIE: Thanks, Sheila. And certainly for me one of the things that struck me over the last two days was the one of inclusiveness and trust and bringing in a broader body of opinion, a broader body of awareness and I don't use the word understanding here necessarily because I'm not quite sure what understanding means into governance, decision making and shaping the way that we harness and use these technologies. And I was struck this afternoon by the way this part I think Bob Cook-Deegan made about high tech fatigue, and this is certainly one of the challenges that we have. We have I think now three different sorts of working party in biotechnology, two different sorts of working paper in nanotechnology, and that's just in one organization. I really hope we don't end up with a working party in synthetic biology unless, of course, it's the start to think about some of these framework conditions. And one of the other things that struck me, Caroline, and I'm going to turn to you momentarily, was the demand for investment in tools and

techniques. So I really appreciate your thoughts.

DR. AJO-FRANKLIN: So just a first comment, one of the things that I've really been struck by over the last couple of days is this dynamic tension between the complexity of driving investment and global regulation of these technologies in contrast to the fact that this is being driven by large groups of excited young people who don't have the foggiest idea generally of such issues. So there's a real issue here of how do we keep them interested and engaged and yet still educate them about the real impact that they will have as they continue their career as synthetic biologists.

And I think the first stabs that iGEM is making are part of the solution in terms of scientific literacy. That's one thing. As your question about tools and techniques, so one of the very clear things I think you'll see throughout the community again as Christina said so eloquently, is this gap between what people want in terms of applications and the real need for basic investments in both tools and techniques. The fact of the matter is that most of the scientists doing this work spend 80 percent of

their time piping liquids from test tube A to test tube B. So we really need to go ahead and make investments in being able to not only synthesize DNA cheaply but also to be able to combine it in many different – in a combinantorial way so that we can actually go on and do the business of synthetic biology more quickly.

Accompanying that is, of course, investment in standards and basic tools. And we need to put in both the resources not only in terms of money but also in terms rewards in publishing and advancement to really propagate these technical innovations.

DR. GILLESPIE: Thank you, Caroline, and I was also struck by a lovely paper that Drew and Ed just passed to me this afternoon, and there's a title in it which gets the metaphor prize from OECD for this year, tools of mask construction. It's just absolutely beautiful. But I think that's kind of the message, isn't it. It really captures it.

Now let's turn to some of the applications rather than the tools. Unfortunately, Jim Greenwood's not around. But Dick Kitney is, and I'm going to turn to you, Dick,

just to give a sense of not just the health and medicine angles but your perception more generally on applications and indeed your key messages from this meeting.

MR. KITNEY: Well, thank you, Iain. So in terms of application areas, we look to this probably in terms of their role, the Academy of Engineering Report. It is of course quite difficult to predict what's going to happen over the next 25 years. But some of the developments which may occur are certainly new types of bio materials that we think are going to come about from synthetic biology leading to the ability to create, for example, new types of tissue. Other examples are advanced biosensors where you can think of biosensors, for example, in the bloodstream that can attack arterial plaque and potentially have the ability to release drugs, et cetera.

Then I think another very important area which we haven't really touched on in this meeting is the developments in a number of laboratories on both sides of the Atlantic of the biologically equivalent to computer gates. I mean somebody, actually it was Christina in her presentation talked about some end gates, et cetera and

that's certainly something that we're very interested in because we can see the whole developments of the equivalence to digital devices but biologically based. And when you think about putting those inside cells, for example, that becomes extremely exciting by way of biosensors.

In more general terms, I think it was Bob Winston yesterday who quoted Lord Calvin who in 1895 predicted that heavy in-air flight would not be possible and eight years later the Wright Brothers achieved it. And I think for me the message there is slightly different which is the problem with the Wright Brothers is nobody told them that you can't fly. And I think that's the issue here in terms of, for example, I chairman the whole field of synthetic biology. I believe that nobody has told us you can't do a lot of this stuff, and we're actually going out there and doing it collectively. So I think that's very important.

Next, a lot of comments have been made about why engineering, why are we taking this engineering approach. Well, of course, as many of you in the room, I'm an engineer and I would argue that the reason we're doing this

is because this is the way forward through into hopefully this really exciting future of industrialization using synthetic biology methods. And one thing also I think people haven't touched on here are the close parallels I would argue between synthetic chemistry in the middle of the 19th century and synthetic biology today. And if you look at the developments of synthetic chemistry in the 19th century through the 20th century, you can see quite clearly that it was the basis of many of the major industries in the 20th century including the micro electronics industry of today. So that's why I think that they're pretty close parallels. And that's why it may not work, but the reason why people are focusing on Drew, et cetera and ourselves on the engineering approach is because this is the way through to industrialization.

In terms of recommendations, I feel quite passionately actually that the way forward here, this is probably a no brainer, but the way forward here is that we need around the world to create a number of sort of really key centers in universities which combine not only research in synthetic biology but also teaching in order words

programs that are based on masters leading through to Ph.Ds where the researchers and the students interact within a single center. And I think that's extremely important. I would say that's what we're really doing at Imperial College. So I probably would say that. But I nevertheless think it is very important developments.

And finally, I think it's very exciting that we've had this meeting actually because, you know, without my knowing a lot of people on the United States side of synthetic biology and obviously the community within Europe, for the first thing I think we've actually through the OECD, Royal Society, et cetera managed to bring all these people together into what is a common meeting and hopefully in the future a common community. Thank you.

DR. GILLESPIE: Thanks, Dick, and I must say just to comment on what you said there. One of the things that struck me looking at the various emerging technologies is I've been impressed by how I think probably realistic people have been about expectations and time frames both in the Royal Academy of Engineering Report but in the discussions here. I mean sometimes we tend to throw

ourselves into the hype and say what we can and what we will do and then the delivery doesn't match the promise. But it seems to me to be a more measured and thoughtful debate that we've had in the past few days.

Except, of course, in iGEM which is going to change the world, Randy, isn't it?

DR. RETTBERG: It already has. So iGEM is certainly changing the world, and it's also –- iGEM is changing the field because what we have is kids who have a different point of view, different approaches. I was thinking about the speakers in the last session that were talking about the change in the press, in the media. And then I was realizing that, of course, in iGEM I have about a thousand students. Those students are very young. They are completely fluent in the Internet and I make them go and make web pages about their projects so they can tell everybody about them, and they tell everybody they put blogs, they put pictures of themselves, they put pictures of the parties that they have during iGEM. They put videos of the activities they do. So they are in fact creating their own news reports about the development of synthetic

biology.

And one of my tasks is to make sure that 40-50 years from now you can still get access to those websites. I feel a little bit of an obligation to capture that history and not simply power it down or install a new version of the operating system and destroy it all.

For me, this meeting has grown on me. It started off with some very pleasant discussions. And then I felt that there was a bit of a gloom that descended as we all had to worry. We didn't know how much we had to worry. Maybe we had to worry a lot, but we should start worrying soon and in many languages. And so that was very discouraging.

And fortunately, we've gotten past that a bit, and I have some to realize that quite a few of the people who were involved in the policy work here I think perhaps because the policy actions that they take actually have effect, they take those actions seriously, and so I'm optimistic about that. There is a piece that I think I see that maybe many other people don't see, and that is their presumptions about how technology develops and the

presumptions in the purest form and most incorrect form is that scientists test hypotheses in the lab. When they have that all worked out, then some engineer comes up and measures the market opportunity of that scientific discovery and then forms a company to take advantage of that. In my experience as being an entrepreneur and being in industrial environments, what I find is that the entrepreneurs are crazy and that they fall in love with the ideas and they just to make it happen. And everything else about how much money you're going to make, what the market is and all of that is all added on later, and I think that's a wonderful way to do it.

And so the discussion in the last session about explaining to everybody how science really has vast amounts of uncertainty in it. It takes a path that appears to be somewhat of a directed random walk is all just great. So in terms of the things that I've learned in this and things that have been different, it's been that the regulatory part I think has been focused on how the scientists will pay more attention to the public, how the scientists will pay more attention to the risks and the ethical issues and

the humanity. But I'd like to suggest that the people in the regulatory side need to again understand that we have a brand new field that's starting up and the excitement and the opportunity of that field is overwhelming. And the time frame is really not five years. The Internet has been around with us for 40 years. We didn't have the Worldwide Web until about 25 years into the Internet. It came in around 1995, and the Internet started around 1970. So if you had looked at the Internet, say, 10 years in, you would have said let's file transfer an email, that's it. And email hadn't penetrated very well.

So I think the right time frame is to think of this in kind of a 40 year time frame and say that's enough time to have learned many things. We have to get there safely. We have to get there with some bumps. But that's our goal.

In terms of the recommendations, I think that the biggest recommendation I would make is that we're carrying quite a few presumptions, and we're hoping that we don't have to change them as this world of synthetic biology changes. We're holding a presumption about stated clearly

and again I think incorrectly, innovation doesn't happen unless you own patents, and I think that's clearly cleanly wrong. Innovation happens when you share. When you have the patents, then you don't have to innovate so much. So the entire issue of the patent and legal framework, I think, needs to be a bit reconsidered. I like the discussion about comparing synthetic biology to the semiconductor industry where new things had to be worked out. I believe that is almost certainly the case with synthetic biology. I can't imagine that the current model will be –- that synthetic technology can in fact be successful in the current model of strict patents and high charges. So I think that has to happen. Then the next thing I think that has to happen is that the field is still extremely young. I think the practitioners in the field will have a very difficult time getting money from the funding agencies because they run into things like peer review where nine out of ten of the people doing the reviews will have a completely different point of view. And I think that the sooner the different areas in the world come to understand that this is in fact an important and serious thing and that it has to be dealt

with in that light in terms of funding, I think the better off we'll be.

DR. GILLESPIE: Thanks, Randy, and for me the IP question and the innovation exploitation model here is particularly exciting but also challenging as a synthetic bio author. One of the first of the truly convergent technologies bringing together the different disciplines of engineering and different applications of science and what that model actually looks like is something which certainly I will take a powerful message back to our constituents saying it's something that should be explored more. The role of patents, the role of IPs and that, I think that's one that we need to debate.

I think the other point here that really struck me was the non-linearity of some of the innovation practice here, and that's something which in my day job one of the things that I run is called OECD's Working Party in Technology Innovation Policy, the TIP which has pioneered much of the shift away from linear to innovation system thinking over the last 20 years. But when you look at policies, although we talk about innovation system

thinking, we still see a linear policy response and synthetic bio issue is really one that challenges that.

Which is a very clumsy segue into beginning to think about policy and the safety and security issues. So Helge, would you like to comment.

DR. TORGERSEN: One thing that struck me while listening to the presentations over two days is how strong a certain fear seems to be that the public could turn hostile either on the ground of risks emerging or other reasons that have to do with possibly wrong way of interfering or doing probably breach activities. Coming from a country where we have a fierce biotechnology debate, we've had that for 20 years now, I've been into many debates and many events that dealt with seemingly hostile public. And listening to what has been said about synthetic biology here and now, I think that synthetic biology may be different.

And taking up what Sheila said, yes, of course you can and you should learn from past experiences. Please do not take it for granted that there will be a public controversy or something like that over synthetic biology.

It can't be taken for granted. There's no reason to believe that.

Controversies are very much dependent on contingent factors on a particular point in time, a situation, a particular country. They mostly have to do with things entirely different and remote from the technology at stake.

Concerning the recommendation, yes, I think you should and you ought to go out and talk to the public to make it clear what the challenges are, what the opportunities are, who is involved, try to build trust, but please don't do that in order to prevent the public becoming hostile. Because if you do that, I can bet it will. Thank you.

DR. GILLESPIE: Clear words of warning there. I think that's a good segue, Mike, to you and then we'll come to Matthew last.

MR. RODEMEYER: I wanted to first of all, I think what we heard was that this is an extraordinarily broad technology, and we really don't know what will end up surfacing first in a public way, and that that may have a

large impact on the way that the public perceives this technology. Again, the framing issue about whether it's seen as new or whether it's seen as simply an extension of technologies that we've been comfortable with for a long time. Given that breadth, I think the notion that several people have raised including Sheila that we need to be cautious about applying what we think are the lessons from the past that this may be different. We need to both have a more nuanced understanding of how past episodes with public perceptions have actually created problems and how this will actually apply to the specific technology. It sort of reminds me of the old Woody Allen joke about talking about the lessons of Vietnam, and Woody Allen says, yes, the lessons of Vietnam is never get involved in a land war in Southeast Asia. So the issue is we don't do biology any more, that's probably the wrong lesson.

I think the second point is that a communications strategy is not the same thing as dialogue and engagement, and that there has to be more than a simple one-way communication effort that goes on here and that frankly I think the United States has much to learn from some of the

European efforts as we think about our own engagement here.

The third point is that trust is socially constructed. It can be created. It has to be earned. But the point is that it's all so easily lost. And once lost, it's very difficult to get back. And I think that leads to a fourth point is that what happens anywhere happens everywhere today. So that if there's an accident in Europe, that will affect the United States. If there's an accident in the Philippines, that will affect Europe. If there's opposition in one part of the world, it will happen everywhere. So there needs to be at the same time that we are thinking about how we globally connect research, we also need to be thinking about how we globally connect engagement with the public for which there may be some new models and new opportunities.

So again I think the issue of public participation captures very much the theme of the conference of both opportunities and challenges.

DR. GILLESPIE: And from the table here, Mathew. You get the last words.

MATTHEW(?): Yes, I'm not the more glamorous

colleague, James Wilson who's off to sigh for Google. So you get me instead. But I'm sure that he would concur with what I'm about to say. I want to thank you for inviting me and for organizing this particular symposium to help crystallize our thoughts around synthetic biology, and we're like kings moving questions to start working on and helping others, I'm sure.

I've worked towards answers to some of those. I mean, the questions will never end cropping up. But we won't hesitate to start working on some answers and I'm sure there's many in this room who would like to do the same.

But as we think through which particular answers we might be able to provide, I need to think about which particular questions are amenable to policy interventions, some questions are not. And as a secondary supplement to that, which of those questions might the Royal Society actually be able to help with and which ones might be able to intervene with.

Now I'm going to stick my neck out and pick two things which have been propping up during this symposium

that I don't think we can intervene on. But I'm happy to be told otherwise. One which hasn't come up too often but is the question of standards. I see that as an incredibly technical and important issue. But I'm not quite sure it's one which is amenable to policy intervention. Happy, again, to be corrected there. That's certainly a tentacle which I watch with much interest. But if someone knows a policy intervention which might help, I'm happy to hear it. But that's probably not something that we'll focus on.

I was extremely grateful to Rick who I'm not sure he's in the room, but yesterday for finally bringing the elephant and sticking it on a slide for me, the elephant in the room being intellectual property. It's a topography which I kind of knew was complicated, but I had no idea it was that staggeringly complicated. I'm not quite sure on that particular case the Royal Society has the expertise to resolve that one.

But I think I will move on to some things which I think we could assist on. My first thought and this is kind of my recommendation is to immediately investigate international and indeed national, actually, but

international collaboration and cooperation around the oversight of governments in the regulatory environment for synthetic biology. I think the Royal Society is well placed. We have along with other partners we have a couple of functions which we could play up. The Royal Society and similar entities work as useful honest brokers on an international stage. But we can be more than that. We can actually be powerful policy analysts and indeed to make policy recommendations. And so that's certainly an action which I'll take with me and we are indeed already in conversations with international partners, potential partners, collaborators and so on and so forth and taking forward that agenda.

Possibly falling under that very, very broad heading are a couple of other things like Terry Taylor in terms of life sciences has already mentioned some of our work on the security aspects. But perhaps slightly different to many of the other synthetic biology discussions around the security aspects, and that's Helge you mentioned this yesterday, the attempts to not only biosecurity for the full spectrum of risk and biosafety

including biosecurity and having synthetic biology as a component of a much broad spectrum of analysis of risk, something that we will be taking forward, and I think that falls under the oversight regulation and governance theme.

The other one for which we have gained some reputation in the U.K., the public engagement agenda which has been possibly the most recurrent theme over the past two days and we had some fun yesterday when we found out how many people don't know what a fossil fuel is.

I think we all need to remind ourselves that you only have expertise to a particular domain of knowledge or skill, and it's quite easy to make someone look like an idiot by asking them a question about which they don't have any expertise.

I'd rather return to Sheila's perfectly pitched challenge yesterday that really we need to actually ask who gets to imagine the future of science, and that doesn't necessarily need a detailed understanding and the expertise of a synthetic biologist to help us understand who gets to think through and imagine the future of science.

So I'd probably go to challenge to drop the word

public, but I'd replace it with the less passive and much more active word citizen. People are active participants in the political and social culture. And so we need to find mechanisms by which we can invite citizens to engage with the innovation agenda of synthetic biology, not just as litmus tests.

So I don't know an iGEM team yet which has decided to bring non-scientists onto their iGEM team to imagine what innovations in a collaboratively imagined innovations which might possibly use synthetic biology. That's the kind of imagination which I'm talking about involving citizens. I wasn't making that as a recommendation that we're going to try. But I don't know. We could explore that agenda. It's an important one.

DR. GILLESPIE: Okay. So it sounds to me like the Royal Society's going to enter an iGEM team, and Mathew's going to be on it which I think you're a bit old, mate, but hey why not.

Ladies and gentlemen, this is your last change to make an intervention before I close out. I'm not encouraging you to, but I don't want to stop you. Sally?

AUDIENCE: [Off mike]

DR. GILLESPIE: Like Sally. Pierce, Ioannis, Paul, if you go to the microphone because otherwise you won't get on the transcript.

AUDIENCE: I think that was the most incredible sort of overview of all of the broad discussions that fall sort of under the chapeau of synthetic biology that I've ever come across in half an hour. But there was one thing that struck me as not being on that list, and I want to get it in there is the question of professional societies.

You know, you have very nascent industry and already two industry associations. I know there have been discussions over an institute of synthetic biology or society professionals, and I think that as a governance option worth having on the table even if it's a bad one.

DR. GILLESPIE: Thank you. Ioannis.

DR. ECONOMIDIS: Just one addition to comment on Mathew's comments on standards to tell you just an activity that's undercoming now. On my talk, I alluded to the ECUS Task Force on Biotechnology Research, and there is without having a formal working group on that, another working

group on OECD. But we have a working relationship with the colleagues of the NSF and we're trying to bring scholars from both sides of the Atlantic together to think how we can establish in a meaningful scientific way standards and which can help this community to go forward with their work. But still this is, let's say, a very early advertisement. But since the word standards were mentioned and really we have that in our mind and we're trying to work and soon you're going to get some news from us.

DR. GILLESPIE: And I agree with you, Ioannis. I think there's a lot the international community can do to move standards forward. Paul?

AUDIENCE: I would just like to follow up on James' comment which I really appreciated and we've been talking about what is enlightenment with a small essay by Canter on that theme. He also wrote an essay on item for universal history with cosmopolitan intent. And so we citizens is much better than public since society. But it's cosmopolitan citizens in a global world and not nationalist citizens fighting each other.

So I thank you for that.

DR. GILLESPIE: And the final comment from the audience.

AUDIENCE: As Sally's employee who's confident that the regulators will be brought into the discussion, my recommendation to the synthetic biology community would be to actually remember something that one of our colleagues from Health Canada said yesterday about the difficulties of defining the boundaries in this area because having gone through this process of trying to define boundaries in the context of our regulations myself, it's very challenging.

And what strikes me is that it's really too simple to say, you know, as some might say, well, the issues are now or in the next few years, and it's too simple to say it's decades off. The field is broad. It encompasses a lot of different kinds of activities. It's my perception that there are debates within the field about what's counted as synthetic biology, what's not. So if the synthetic biology community can help the regulators define what some of those boundaries are, where we are now and where we are heading over what kind of time frame and do this repeatedly as the field evolves over the years, I

think that's going to make a very big contribution in that aspect. I suspect it will also make a contribution to public or citizen engagement as well.

DR. GILLESPIE: I do hope so. Any burning final comments from the panel? Well, ladies and gentlemen, I want to give the last words to Ed Lazowska who left me some notes here. And I'm not going to read out all of it, although I'd like to. But I'm going to read two paragraphs of it, and it's this: "During this decade, we demonstrated the promise that we will someday be able to engineer biologic skill to develop and deploy biology as a technology to address societal challenges such as energy, disease and nourishment. The challenge for us now is to achieve that promise. This will require a concerted and coordinated effort on both technology and policy fronts. And I think that you will want to join with me in thanking the moderators, the speakers, and perhaps most of all, the unsung hero of this, Anne-Marie Mazza and her team, the organizers here and National Academies for this really excellent meeting. Please me in congratulating them."

[APPLAUSE]

DR. GILLESPIE: Safe journeys home.

[Whereupon, the meeting adjourned.)