



Presidential Commission  
*for the* Study of Bioethical Issues

## **TRANSCRIPT**

### Federal Oversight

Amy Patterson, M.D.  
Acting Director, Office of Science Policy; Director, Office of Biotechnology Activities; National Institutes of Health

Michael Rodemeyer, J.D.  
Lecturer, Dept. of Science, Technology & Society, School of Engineering and Applied Science, University of Virginia

Edward H. You  
Supervisory Special Agent, Federal Bureau of Investigation, Weapons of Mass Destruction Directorate, Countermeasures Unit I, Bioterrorism Prevention Program

Meeting 1, Session 7  
July 9, 2010  
Washington, D.C.

**Amy Gutmann:**

Ladies and gentlemen, if you can please take your seats, we're going to get started. Commission members, if you'd please take your seats.

We now move to our final panel of this day, which will focus on current federal oversight and regulatory activities regarding synthetic biology and potential actions the government could take in response to recent development. This is again the beginning of an overview. We will have time for deeper dives into this because we really, as a commission, are not going to be able to reach any conclusions about this part of our report until we have a chance to digest more of the science and ethics and social responsibility issues. But this will at least begin to give us a sense of where our presenters see federal oversight as it is now. And will give us a window on to the state of federal regulation and oversight and give the commission members and the public a chance to ask some initial questions.

So let us begin. In her position as acting associate director of NIH Office of Science Policy, Dr. Amy Patterson advises the NIH director and the 27 NIH institute and center directors. Her primary responsibility is to provide national leadership in the analysis and development of science policy on a wide array of issues related to the national biomedical research enterprise. Dr. Patterson is deeply involved with the work of the secretary's advisory committee on genetics, health and society, the recombinant DNA advisory committee and the national science advisory board for bio security. Welcome, Dr. Patterson.

**Amy Patterson:**

Thank you very much. Good morning, commissioners. Good morning, everyone here today. I was asked to speak to you today about the role of the federal government, especially the National Institutes of Health in the oversight of synthetic biology research.

And I'd like to start off by spending just a few moments on how science and public policy have evolved over the last four decades and have brought us to the biotechnology oversight framework that we have today. I'll spend a few minutes discussing how that framework may be relevant to synthetic biology, touch upon some of the challenges this technology presents for oversight and then conclude with some parting thoughts about the tasks that lie ahead of the commis-

sion. The caveat, though, before we turn back the hands of time, this timeline is in no way meant to be comprehensive, but it is meant to illustrate a few of the key scientific and policy highlights relevant to the oversight of synthetic biology research.

And so, with the advent of recombinant DNA and the technology in the 1970s, we move beyond simply being able to identify the structure and sequence of genetic information to being able to manipulate that structure. And the technology gave us new tools for understanding the genetic underpinnings of life and new avenues for the development of new therapeutics and other beneficial applications. This technology, however, also, prompted considerable concerns among the scientific community and general public about unintended consequences including both short-term and long-term potential adverse effects on health and the environment.

The new technology also raised profound questions, questions that will resonate today, questions about the boundaries between species, questions about the appropriateness of humankind's manipulating the genetic code. And during this time, a national dialogue grew about the appropriate role of the public, of society and the legislature, shaping the direction of scientific inquiry in a free society.

Several bills were introduced in Congress, bills that if passed would have placed statutory constraints on this technology. This proved unnecessary as the scientific community stepped up to the plate. Recognizing the uncertainties, the potential risks posed and the depth of public concern, scientists at that time called for a moratorium on future research pending the development of an appropriate oversight framework. And they assembled at the Asilomar Conference Center in California in 1975. And scientific leaders began the work of articulating some of the principles and practices that might govern the future of this research. And out of this societal debate emerged, (1) a recognition of the inherent promise of this technology, (2) the importance of an ongoing public dialogue, the development of public understanding and the importance of public input on the future use and application of this technology and, (3) the importance of careful risk assessment and oversight. And thus the foundation was laid for the oversight framework that would continue to evolve and we'll touch briefly on some of the key points over the coming decades.

A national advisory body was formed at that time, the NIH Recombinant DNA Advisory Committee, affectionately referred to as the RAC. It was established to review in public each and every recombinant DNA proposal at that time and to articulate the overarching principles and practices that should ensure the safe and ethical conduct of the research and to discuss strategies about both biologic and physical containment of recombinant agents. The NIH guidelines were published in the bicentennial year and they've been updated many, many times since. A very deliberate decision was made to publish these as guidelines rather than regulations, so that they could be more readily updated to reflect advances in the science and advances in our understanding of the risks. And despite the name "guidelines," compliance was and is a term and condition of federal funding.

The 1980s saw the advent of technologies that automated DNA synthesis and sequencing and the emerging ease with which DNA could be manipulated, coupled with the desire to apply this technology to the treatment of human disease, prompted a study by a prior president's commission. This study's "Splicing Life" concluded that the benefits of recombinant technology warranted continued scientific exploration, but it also concluded that there was an ongoing need for thoughtful forward-thinking deliberation about the potential ethical and societal implications of recombinant technology and how it might be developed in the future.

In recognition of the need to embed ethics in the day-to-day conduct of genomic research, as the human genome project got under way, a program was established to address the ethical, legal and social issues inherent in this research. And ELSI program was and is an integral part of that research program. Now, in anticipation of the first application of recombinant DNA in humans, the NIH guidelines underwent an extensive revision to address scientific safety and ethical issues and also to put in place a review process for each and every clinical protocol that proposed the use of recombinant DNA in humans.

And I also wanted to mention that in 1986, the federal government issued a document which was a statement of basic federal policy about the regulation of biotechnology products. This was referred to as the "coordinated framework." And I mention it because among

a number of things that it talks about; it articulates a principle that may be relevant for our discussion today. Namely, the notion that genetically engineered products should be regulated according to their intrinsic characteristics and features, not according to their method of production. Just a thought to keep in mind.

Now, the 1990s also saw growing concerns about the ready access to dangerous pathogens that could be used as agents of bioterrorism. And the federal government promulgated new statutes and regulations governing the transfer of specific agents and toxins, so-called select agents and toxins, and the select agent regulations cover both, naturally occurring or wild type pathogens as well as recombinant ones.

The past decade has seen several notable advances in our understanding of human genome as well as our ability as you heard yesterday, to design and synthesize ever larger fragments of nucleic acids and express them in biologic systems. And these experiments represent a continuum of genetic research and engineering and they enable important advances in vaccine and drug development, among other beneficial applications. They also raise profound questions.

These advances took place, however, in the shadow of 9/11 and the dissemination of anthrax spores through the U.S. postal system, and so concerns crescendoed at this time about the potential for deliberate misuse of biotechnology in ways that could harm human health and other aspects of national security. And these concerns prompted a national policy dialogue and the establishment of the National Science Advisory Board for Bio security or NSABB. The NSABB has issued several reports for strategies minimizing the potential for misuse of biotechnology including a code of conduct for scientists and also very specific strategies for trying to minimize the bio security risks raised by synthetic select agents.

And I wanted to also highlight that the scientific community has again stepped up to the plate on a number of occasions during the past year. There's one example shown here about synbio on this slide that they have convened in a series of ongoing meetings to discuss not only the advances in the technology, but also some of the important societal issues raised by this technology.

So from the 1970s to the present day, we've been probing and altering the structure of DNA and other biologic components using recombinant DNA techniques, and de novo synthesis techniques and other technologies and this has been a continuum of incremental steps forward in science coupled with a process of oversight evolution that encompasses synthetic biology.

I want to touch upon some of the principles that contribute to the oversight system. The oversight system reflects a fundamental premise, that while biotechnology offers many major benefits to society, the potential risk must be assessed and addressed. Oversight needs to be predicated on risk assessments and titrated according to risk. The framework is designed to evolve to reflect advances in science and advances in our understanding of risks, but it's also designed to reflect input from the public as it's developed.

The oversight framework is primarily aimed at addressing four categories of risk, biosafety risks result from accidental exposure to a pathogen or toxin that could adversely affect lab workers, the general public, plants, animals or the environment; and biosecurity risks results from the deliberate misuse of technology to cause harm. Risk to human subjects refer to potential adverse affects that may result from clinical administration of biotechnology products and risks to societal norms involve controversial uses or consequences of biotechnology, such as germ line gene transfer or use of genetic engineering to alter human traits rather than to treat human disease.

The next few slides outline how these major categories of risk are addressed in the framework for biotechnology research and many of these components are generally applicable to synthetic biology as a subset of biotechnology. We don't have time to review these tables item by item. I know you're relieved. But I will briefly touch upon the overall categories.

Biosafety risks are addressed by a variety of federal policies and regulations that we can discuss in detail during the discussion period. But essentially, they speak to the safe handling and transfer of infectious agents.

Biosecurity risks are addressed in several statutes and regulations that are fundamentally aimed at preventing loss, theft, and misuse of dangerous pathogens and minimizing the misuse of knowledge of biotechnologies in ways that could threaten public health or national security.

Risks to human subjects are addressed in rules aimed at insuring the safe and ethical conduct of clinical research using the products of biotechnology.

And risks to society are to some extent addressed by some of these very same policies and requirements. For example, the NIH guidelines prohibit the use of gene transfer for germ line modification and for in-utero administration, and the biological and toxin weapons convention bans the development of biologic weapons for mass destruction.

I wanted to touch upon the “culture of responsibility” because this is a very important concept. The oversight framework acknowledges that the responsible conduct of science, at the end of the day, rests upon the behavior of individuals. And federal oversight can provide carrots and sticks and it can help cultivate a culture of responsibility, but ultimately at the end of the day, that’s fostered and nurtured at the local level.

Oversight also relies on assessment of risks and threats, and that assessment is predicated on an understanding of the biologic characteristics of the agent, its host, and the environment. And one of the biggest challenges in the oversight of biotechnology, be it recombinant DNA or synthetic biology, is its capacity to create novel entities that have less and less similarity to what we know and, therefore, are more difficult to assess in terms of the risks that they may present to health or the environment or to our societal norms.

In synthetic biology in particular, the capacity to create increasingly novel organisms is, in theory at least, limitless. And so we’re faced with the prospect of increasing levels of uncertainty.

Another notable challenge for oversight of synthetic biology is the increasing ease with which one can order online sequences or parts,

customized sequences. And readily purchase online reagents and automated equipment.

Another challenge that I think you've heard about earlier in the meeting is the demographics of the practitioners of synthetic biology are changing around the world. They include not only people from multiple scientific disciplines, but nonscientists and high school students as well. So not only is synthetic biology democratized but, like most of biotechnology, it's a globalized and commercialized industry.

Now, all of these features present a real boon to scientific progress. They create a very open access environment and offer the prospect of hope for new therapeutics and other beneficial products, but they also present major challenges for oversight. And we need to expand our capacity for risk assessment and management in the context of increasing uncharacterized biological properties and in the context of a widely available technology.

Toward this end, the U.S. Government is continuing to further refine the oversight framework. We are very busily at work. We have much work to do. And I would say that all of us are still on the slippery slope of the learning curve here. For example, the NIH guidelines are currently under revision to more explicitly address the safety oversight of basic and clinical research with synthetic nucleic acids, putting in place an oversight framework at both the local and the federal level for the review of these experiments.

The U.S. Government is developing guidance for providers of synthetic double stranded DNA, for strategies on how to screen orders. The U.S. Government policy on the local and federal oversight of dual use research, so then this notion of the potential misuse of knowledge or biotechnology techniques is well under way. And it's based on the recommendations of the national science advisory board for bio security and it will be applicable to certain types of synthetic biology experiments. And the U.S. Government recently tasked the national science advisory board on bio security to advise on strategies on how to do outreach to all practitioners of synthetic biology, how to enhance the culture of responsibility and increase international engagement on these issues.

I just have three more slides.

The U.S. Government is also actively exploring ways in which the oversight system could be enhanced in the future to more reliably predict biologic function of a novel agent and identify associated risks, and in fact, we have commissioned a study from the National Academies on this very topic. Both the BMBL and the select agent rules undergo periodic revision and were just recently revised to reflect scientific advances, including those in synthetic biology.

And then as recently as last week, our President issued an executive order aimed at striking a critical balance between biosecurity and reducing burden on scientists engaged in legitimate research on select agents.

So in conclusion, the current oversight framework has evolved extensively over the past four decades. The field of synthetic biology, like much of biotechnology, continues to present major challenges to oversight. Oversight can never simply be “business as usual” and true scientific progress is predicated on public trust, a trust that is earned through a process of open transparent dialogue that encompasses frank deliberations about uncertainty, unintended consequences, and societal norms.

This commission can provide invaluable expertise and the very prominent forum for catalyzing enhanced public understanding, awareness, and dialogue about the future uses and applications of this technology and what it may mean for society. And the future evolution of the oversight framework will be, must be, informed by such a dialogue.

Thomas Jefferson once remarked that the price of freedom is eternal vigilance and this concept is certainly relevant today. And I would say the price of scientific freedom is eternal vigilance and responsibility. Thank you.

**Amy Gutmann:**

Thank you very much. Our next speaker is Michael Rodemeyer. Michael is a lawyer who has spent the last 30 years working in the fields of science, technology, and environmental policy. He teaches science and technology policy at the University of Virginia’s Depart-

ment of Science, Technology and Society. In 2009, he wrote “New Life, Old Bottles,” a study of the regulation of synthetic biology for the Woodrow Wilson International Center for Scholars. Mr. Rodemeyer has also worked in the federal government as assistant director for environment in the Office of Science and Technology Policy and is chief Democratic Council for the U.S. Congress House Committee on Science and Technology.

Welcome, Mr. Rodemeyer.

**Michael Rodemeyer:**

Thank you very much. It’s a great privilege to be with you here this morning to talk about the current biotechnology regulatory system and how it would apply to the likely first generation of synthetic biology products.

As Dr. Gutmann recognized, my comments are taken largely from the work that I did for the Woodrow Wilson Center which in turn were based on work that I did at the Pew Initiative on Food and Technology in the last decade.

In general, since it’s difficult for a lawyer to say anything in 15 minutes, let me just sort of put my concluding thoughts right up-front, which is to say that in fact the existing laws and regulations that cover biotechnology products are likely to apply to the first products of synthetic biology. Since the very first generation of synthetic biology products are expected to be relatively simple and not very different from the kind of genetically engineered counterparts with which agencies have familiarity, they are unlikely to raise in the short-term any novel risk assessment or risk management issues.

But as the technology continues to develop and as organisms become more complex, more novel, and more artificial, the challenge will be to be able to assess the risks of those organisms in advance. And that’s especially a concern for organisms that will be intended for use in the environment.

Faced with that kind of uncertainty, regulatory agencies will be in a difficult position of making decisions that balance uncertainty, benefits, and potential harms. Now, as noted in our discussion yester-

day, there is a déjà vu quality to much of the conversations we've had. Much of these same debates about bio safety took place in the 1970s and 1980s following the development of recombinant DNA technology. And while there are differences between synthetic biology tools and recombinant DNA technologies, the point I want to make is that the kinds of risks that regulators are concerned about are essentially roughly the same. I'm not talking about bio security issues but bio safety issues.

Just to review those just very quickly, we are talking about bio safety concerns in the laboratory of an accidental release of pathogenic or toxic organism that might infect laboratory workers or the community. We're talking about the environmental concerns that Dr. Snow talked about yesterday, both in the event of an accidental release, but also for an intentional release for use in the environment. And we're also talking about a set of concerns about final products. For example, if we're going to be using synthetic microbes to manufacture chemicals, and drugs and foods, how do we know that those final products are going to be safe?

So in this presentation, what I'll be talking about is the existing system of biotechnology regulation that deals primarily with these bio safety risks.

As Dr. Patterson has indicated, the National Institutes of Health played a critical role in regulating bio safety conduct in research laboratories. And this, of course, is not an issue that's unique to engineered organisms. We need to deal with bio safety practices in dealing with the whole range of infectious and potentially dangerous organisms. But engineered organisms pose particular issues. One again is the issue about, how do you determine in advance the potential risk of an organism in order to know what level of bio safety you need to put into place? For recombinant DNA technology, that assessment is relatively straightforward because you can find the naturally occurring origin of the gene segment of interest and determine its function based on that natural knowledge.

Now, synthetic biology makes this assessment more complicated. A synthetic microbe can be assembled from modified genetic parts taken from several different unrelated organisms or even completely

artificially constructed in a lab. And it's conceivable that the parts could operate in the new organism in unexpected ways. In other words, that the engineered microbe could show emergent behaviors. And while it's unlikely an engineered organism could have riskier characteristics, they might be predicted on the understanding of its various engineered parts.

For the last 30 years, as Dr. Patterson has indicated, the NIH guidelines have guided researchers in making determinations about risk characterization and bio safety practices. And the NIH is I think commendably moving ahead to amend its regulations to cover synthetic biology research as well. The challenge, though, particularly as the technology develops will be to develop guidelines that are sufficiently cautionary, but without imposing unnecessarily expensive and cumbersome containment requirements that might hinder research. Ultimately, though, and this is a point Dr. Patterson also made, whether these guidelines work will really depend on the institutional bio safety committees at universities and research labs that have the responsibility for implementing.

We also need to understand whether the research not covered by NIH guidelines, for example, purely privately funded research, is a significant problem in this area or not. In the 1980s, as the first products of genetic engineering began to move out of the laboratories and into commercial production, the administration at that point was faced with the question of how do we regulate? NIH does not have the tools to do enforcement or regulation for commercial practices. So as a result, the Office of Science and Technology Policy in 1986 led an interagency process to develop the coordinated framework for the regulation of biotechnology.

Those policies are still in place today. And they've guided the development of biotechnology regulation. There were three basic findings of that group that I think are relevant to our decisions today: One is that, as Dr. Patterson said, the decision that the process of biotechnology itself was not inherently risky. It's no different in its risk characteristics than conventional breeding. And that therefore there's a second point that regulation should be based on the characteristics of the final product, not the process by which it was made. The third point was that given that, existing laws could be used by the U.S. regulatory

agencies to regulate any anticipated risks of the kinds of products that were then expected from biotechnology. The concern, the question, of course, is, how well has this regulatory system been put into place?

The way that it has evolved is there are really two points I want to make about it. One is that the United States — and this is not a model that's been followed around the world — has adopted, in effect, “technology-neutral approach” to regulation. So, for example, drugs are regulated by the Food and Drug Administration, regardless of how they are made. Pesticides are regulated by the Environmental Protection Agency, and new plant or microbial varieties intended for general use in the environment are reviewed for potential pest problems by the Department of Agriculture.

Now despite this general principle, in fact, the regulatory agencies have had to engage in a fair amount of legal sleight of hand to fit biotechnology products into existing regulatory schemes. These existing laws, of course, were written before biotechnology came along, so it's not surprising that agencies have had to adapt and in some cases are still adapting 30 years later regulations to fit new technologies. For example, E.P.A. had to figure out how to regulate a corn plant as a pesticide. The FDA had to figure out how to regulate a genetically engineered salmon as under the new animal drug approval laws. And USDA had to figure out how to create, how to regulate, an herbicide resistant variety of soybean as a plant pest.

Now, while some of these creative legal interpretations could be subject to legal challenge, the Government's authority to regulate biotechnology companies under existing laws has not been challenged to date. And I think the reason for that is largely because biotechnology companies in fact have every reason to cooperate with agencies, rather than to confront them.

It's also important to note that one other consequence of this technology-neutral approach is that biotechnology products receive widely different levels of regulatory scrutiny, depending on what the product is. Under U.S. law, some products are viewed as inherently risky and, therefore, are required to go through a mandatory pre-market approval process. Agencies must find that the products are safe to be used before they can be marketed. Examples of that include animal

and human drugs, pesticides and food additives.

On the other hand, most products that are introduced into the marketplace get little or no pre-market regulatory review, although, of course, the manufacturers have to be legally responsible for their safety. So, for example, if you want to produce a dietary supplement using synthetic biology, you will get the same regulation that other supplementary diet products have, which is to say, very little. So it's important to understand that different products will get different levels of scrutiny.

Now, it may not come as a surprise, despite 30 years of effort of regulating biotechnology, there's still a difference of opinion as the adequacy of the U.S. regulatory system for current biotechnology products. Certainly a number of groups believe that the system is not rigorous enough while others just as equally passionately believe that biotechnology products are overregulated and keep beneficial products off the market. This is not the regulatory system that you would design from scratch if you had a blank slate, but on the whole, my opinion is the system has worked reasonably well. Valuable new products in agriculture and in medicine have been successfully introduced without any evidence of public harm or environmental problems.

Now, one could argue and we've just been lucky or that we haven't looked hard enough for evidence of problems. And I think there is some force to these arguments. On the whole though, however the system and I think however imperfectly seems to be working. As a practical matter, I think the United States is unlikely to change its position, the policy position that has been in place for 30 years.

So the question is, how would this framework apply to synthetic microbes used to produce products like drugs and bio drugs? An initial question is whether the laws give agencies authority to cover these new kinds of products. As I noted previously, agencies have already had to stretch their legal authorities to reach recombinant DNA products. And I think it's likely that E.P.A. and USDA among others will need to revise their regulations in order to make sure they cover synthetic biology products.

On the whole, however, I think existing laws are likely to provide

agencies with sufficient legal authority to review new products developed through synthetic biology. Food and drug administration, for example, has broad authority to review not only the safety and efficacy of drugs, but also the process by which they're manufactured. But even if the laws are sufficient to cover synthetic biology products, I think the real issue is, and the more important question is, whether the agencies have the resources and tools they need to both assess the risks of this new technology and to manage the risks as well.

The first microbes from synthetic biology are really not likely to be appreciably different and there's no reason to think that they are inherently more risky than products we have seen all along. But as I noted before, as the technology develops, it's going to become more difficult to assess in advance the potential impacts of these organisms.

Now, risk assessment is critical for regulatory agencies because it really determines the level of containment, control, or monitoring that's going to be required in order to commercialize the product. Getting the regulation right under such conditions of uncertainty by neither over regulating nor under regulating is a major challenge. I want to mention that I think it may be particularly difficult for E.P.A. under the Toxic Substances Control Act (ToSCA). There have been a number of articles written, there are in fact some laws pending in Congress to revise ToSCA because it's essentially hybrid statute which could make it more difficult for E.P.A. to actually obtain the information it needs to make a risk assessment. I can get into more details about that in the question and answer period.

Now, since risk assessment is itself likely to become more difficult, it's all the more important to have effective controls for preventing the spread, the unintended spread of synthetic microbes, particularly in the environment. And in fact, such controls will probably be necessary in order to do any kind of field testing for us to be able to understand the actual function of these microbes in the environment.

Now our experience to date has not been encouraging, as I mentioned yesterday in biotechnology, we know that it's very difficult to keep biologically active materials segregated in the environment. We've had a number of instances where unapproved genetic technologies have been found in the seed supply and there's been widespread

gene flow from G.M. crops. So we clearly need a better set of tools for doing this than we've done before. But it's critical that such tools be developed publicly and tested publicly and shared widely in order to avoid some of the controversies that have attended terminator-like technologies in the context of genetically modified crops.

Now, I also want to mention that everything I've talked about so far, of course, is irrelevant to the garage biology phenomena because regulations that I'm talking about presume an industry that understands what its obligations are and has the capacity to comply. It's clearly not the case that people doing work in their backyards or in their garages are going to be likely to know they've got to file a ToSCA permit in order to do their research. And I think we don't have a satisfactory model at this point for doing this.

So in conclusion, I'd really like to make the following recommendations to the commission:

One is that the federal government really needs to conduct a full and transparent review of the current regulatory system to ensure that the agencies have sufficient authority, tools and resources to assess and manage the risks of likely future products of synthetic biology. The recent DOE grant to the Venter Institute, which I'll be working with them on, hopefully can provide a process for beginning that assessment.

Second, federal research funding agencies such as the National Science Foundation and NIH should fund robust programs of risk assessment methodology and risk research on synthetic micro organisms so that regulatory agencies can have an independent basis for making risk assessment and regulatory decisions.

Funding is also needed to develop tests and assess biological controls that can allow for the conditional releases of synthetic organisms, even where the risk assessments may have uncertainties. And unless the risk research keeps pace with the development of the technology itself, agencies are likely to respond to uncertainty by overregulation, potentially keeping beneficial products off the market. Such research needs to be done in an open and transparent way in order to provide credibility and public engagement.

Finally, I would recommend that the federal government needs to meet with stakeholders, particularly including state and local governments as well as the do it together community to begin to discuss rules and regulations that might apply to all research on synthetic biology.

Synthetic biology and synthetic genomics offer promise for harnessing biology to address some of our most pressing environmental and public health needs. Having a credible effective regulatory regime in place, when the commercial products begin to move through the pipeline is a key part of ensuring that society receives the maximum benefit of the technology while minimizing any risk. Thank you.

**Amy Gutmann:**

Thank you. That conclusion is something we will definitely take to heart.

Our last speaker of the day is Edward You, Supervisory Special Agent in the FBI's Weapons of Mass Destruction Directorate, Bioterrorism Prevention Plan. Mr. You is responsible for creating programs and activities to coordinate and improve FBI and interagency efforts to identify, assess and respond to potential biological threats or incidences. He also serves on the working group of the National Security Council Interagency Policy Committee on countering biological threats. Before joining the FBI, Mr. You was a human gene therapy and cancer therapeutics researcher. Your background couldn't be more relevant to us. Welcome, Special Agent You.

**Edward You:**

Thank you very much. And I want to thank the commission for inviting the FBI to present today and being last, I actually have the advantage of building upon the previous presenters.

So let me go ahead and start on building on Dr. Patterson's talk on the NSABB recommendations, many of which are very relevant to the discussions that we've had. They've come up with reports on addressing bio security concerns related to synthetic biology, on dual use issues and most importantly, I think, is the outreach and education component of it all. And I would also like to bring to the com-

mission's attention that the White House actually released in this past November a national strategy for countering bioethical threats and I have included some of the highlights which include reinforcing norms of safe and responsible conduct, addressing emerging risks which synthetic biology could be included, and taking reasonable steps to reduce the potential for exploitation and also international engagement.

Just to provide you a little bit of background, the Weapons of Mass Destruction Directorate was founded in 2006, so we are just celebrating our fourth year. I do want to caveat right now that the FBI is not a regulatory body, but a law enforcement agency. But, however, in light of 9/11 and especially the anthrax mailings, we have taken a proactive stance now. And through the consolidation of the different WMD units, we now have the three items I listed there, and counter measures of preparedness, investigative and operations and intelligence analysis for chemical, biological radiological and nuclear WMD threats.

So from the bioterrorism prevention program, I've listed some of our goals here. Most of them operational in regards to addressing bioterrorism. But I want to highlight the third bullet is that enhancing bioterrorism, scientific, industry and academic outreach.

Why is that the case? Well, the challenge is, when it comes to particularly synthetic biology is how to engage the different communities about bio security? Now, the commissions have already seen the past day that synthetic biology is already difficult to define. Well, within that, we're dealing with different communities ranging from industry to academia to your amateur biologist. They're very different cultures. We're dealing with advances in technologies on different levels. And it requires educational awareness, not only for the communities themselves, but for the agencies that interact with them and gain a better understanding of who they are and what they are doing.

Now, while the FBI's responsibility is maintaining Homeland Security, we also understand that any type of bio security program has to ensure that there's not a negative impact that impedes research in all these different fronts because that in itself would represent a national security risk because there's a chance that you're now impeding valu-

able research and counter measures development or in bio defense as well as some of the more important entrepreneurial efforts that are going on as well.

So striking that balance. This was brought up already yesterday. And also, in 2006 the NSABB came up with a report on addressing the risk of the acquisition of DNA sequences coding for dangerous pathogens or toxins. Well, in the U.S., the synthetic DNA companies took that to heart and actually instituted best practices in looking at how do you screen your customers and incoming sequences to insure that that risk is addressed?

Well, the FBI took the NSABB recommendations and ran with them and conducted outreach to these companies. The challenges the companies found was that although they do their due diligence, they ran into the question if they had come up with a red flag, a suspicious hit, what do they do?

Well, by conducting our outreach, the FBI engaged our WMD coordinators, these are special agents that are dedicated to WMD related matters and there's one in each of our 56 field offices across the U.S. The companies now know that if they do come across that quote-unquote hit, they can contact their local coordinator who then can reach back to headquarters where we have our own subject matter experts and then we can also then reach back to other federal partners like the C.D.C., NIH, Department of Health and Human Services so we can do a proper assessment of the issue. And so as I highlight there, the industry is, as a result, very happy of that question of who to call.

And then that falls into what Dr. Patterson just mentioned that just recently a draft of the screening framework guidance for synthetic DNA providers was released in November. This came out of HHS's Office of Assistant Secretary for Preparedness and Response. And it highlights customer screening recommendations, sequence screening recommendations, and government notification recommendations. So this actually gives the DNA provider some recourse as to not only what to look out for but then who they can contact, such as FBI or if there are export considerations the Department of Commerce. So these are all listed in the guidance. And this is all voluntary as well, too.

Now, the FBI also hosted in August of 2009 its first synthetic biology conference in San Francisco. We did this in partnership with the Department of Health and Human Services, the State Department, and the American Association for the Advancement of Science. And at this event, we brought together representatives from the communities from academia, industry and DIY bio, to come together and not only talk about the state-of-the-art, but by having a law enforcement presence there, can we come to a meeting of the minds in identifying what are some of the risks and can we come up with strategies to help manage and mitigate those risks without, again, negatively impacting their efforts on all fronts. And it was overwhelming well received. And as I said before, the FBI gained a better understanding of what the different communities represented and what they had at stake as well, too.

And then this also then on the international level, Dr. Schmidt mentioned the International Association for Synthetic Biology, they too, instituted best practices. They held a workshop in November of 2009 to look at customer and sequence screening matters as well, too, and to also look at a code of conduct to codify these best practices. Well, the FBI, the U.N. Biological Weapons Convention, and the U.S. State Department were also in attendance and looking at what was instituted here in the U.S., how we might assist and maybe potentially translating this notification process that the FBI had to an international level.

And then we've talked, of course, about iGEM. It's an undergraduate competition hosted by MIT. This past year in 2009, there were 1,200 attendees, 26 countries, 100 universities. It's an undergraduate competition and Dr. Randy Rettberg, the director of this competition, he states it, and I can't underscore it even more, that it is fun. And it is all about synthetic biology and it's amazing what these teenagers can do in a three-month time period. And they come to MIT at the end of the summer and show case their summer projects. Well in this past iGEM, the FBI actually was there because of the international component.

**Amy Gutmann:**

Do the students all know you were there?

**Edward You:**

The first question was, why is the FBI here?

[AUDIENCE LAUGHTER]

But because again the international representation, we invited the U.S. State Department and the U.N. Biological Weapons Convention to bring representatives there.

And we hosted a workshop and actually manned an outreach booth to really promote responsible research. So in this instance, it was outreach, not oversight. And it was blue jeans and not men in black. [laughter]

And then DIY bio, the community held its first formal conference at UCLA and they talked about their state-of-the-art, where they stood, looking at citizen science and the expansion potentially of the community. And they got the measures. And to their credit, they actually invited the FBI to come in and give a presentation on promoting responsible research, and also to promote some career opportunities as well.

And then just recently, the U.N. Interregional Crime and Justice Research Institute (UNICRI) had a synthetic biology, nano-biotechnology risk and response assessment. It's basically an exercise to parallel what the commission is doing here. They brought together experts from across Europe from academia, industry, policy makers, and the FBI as well as the U.N. BWC to look at what is the state of the art, looking at future bio security implications of synthetic biology and then hopefully come to some possible response measures or policy recommendations. The timeline is that the report is due out, hopefully, by this coming September. So that might be something that the commission might want to take into consideration.

And then also just recently, the FBI co hosted with the Massachusetts Society for Medical Research its first bio security conference. The significance of this is that this was a conference that had attendees from academia. And as I listed there, they're representatives from institutional bio safety committees, institutional review boards and institu-

tional animal care and use committees. As Dr. Patterson mentioned, these are the gatekeepers. They are the ones that ensure that the NIH guidelines are followed and instituted. They look at ethical issues on research and grant proposals. And at this conference, and with all of the federal partners that I have listed there, we were able to bring down to the academic levels what do we mean by bio security from a federal perspective, from a law enforcement, from a security perspective.

And by working together with the research community, can we come up with ways forward in addressing bio safety and bio security. And again in a way such that is not negatively impacting research and in a way that is commiserate with the risks that are identified. Well this again was overwhelming well received, so much so that the majority of the attendees stated that any future bio safety, bio security meetings or trainings should absolutely have FBI or federal participation. So it was really great. And as we talked about over the course of the day and a half, there are these terminologies, dual use, concerns of properly handling materials, physical security and exploitation. And again, as Dr. Patterson mentioned, all the FBI activities are looking at fostering a culture of responsibility. It's empowering the community members themselves as to what we mean by bio security. Help them to be able to self-identify what some of the risks and harms can potentially be. And then working together in trying to manage those risks.

If the commission will indulge me, I want to share an anecdote that it is not so difficult to engage these different communities. I'd like to highlight one professor Jean Peccoud from Virginia Tech. He's a professor in their Bioinformatics Institute. He received an invitation to the FBI Synthetic Biology Conference and his first initial reaction was like "I don't work in a laboratory, why should I bother?" But then on second thought he said, "Well if the FBI is inviting me, it must be something important so I guess I should go."

And he went and listened to the message. And he actually took it to heart. And on his own, at Virginia Tech, invited the FBI to come down and give a bio security workshop, but not just for bioinformatics students alone, but he extended the invitation to entire campus and to four other universities in the area and brought together undergraduates, all the way on up to faculty members and administrators,

including the vice president of research and vice president of compliance. And it was a great success. He himself has a great success story.

But at the end of the day, and I'll never forget this, but there was a student who was going to be a sophomore, and at the end of the message, she basically raised her hand and stood up. She was like "I understand, what can I do?"

So through iGEM, through the outreach that we have not only for the faculty members, we're equipping them to become the next generation of synthetic biology practitioners, researchers, entrepreneurs, to understand that there are these issues that should be addressed. And so we're effecting that change, we're fostering this development of this culture and from the faculty side helping them to become the mentors and advisers to address the concerns that have been brought up in the commission's deliberations.

So what's the role of the FBI in all of this? Well, as we talked, there are certain identified and as yet to be identified threats and how that relates to the scientific community. Well, the FBI addressing the threat, that's our job. And engaging the scientific community, our job also, our responsibility is to engage them and provide them the education to have a situational awareness that I had mentioned, to empower them from industry academia all the way down to the DIY bio to be able to address and understand that there are these threats out there and within the community potentially. But it doesn't stop right there. That there is, it's a two-way street. That there is communication back to the FBI, not just as far as like, a notification, like a 911 call, but basically to help us--and as we mentioned, the synthetic biology is screaming forward into the future. And from not only the FBI side, but from a policy making side, it is going to be very difficult to keep up with the state of the art.

So that's why we absolutely relied upon the scientific community to help us, to guide us, to ensure that we are addressing the risk and threats appropriately. That we are aligning our resources in a matter that is commiserate with the risk that make sense to not only to actually addressing national security but to make sense to the constituents who make up the scientific community. So, in sum, mitigating the risks. [beep noise]--Good timing-- It's conducting outreach well then

develop partnerships, not oversight. And the end result will be effective policy making, meaning that the FBI and our federal partners are engaged in all of this can advise bodies like yourselves to make the policy recommendations.

But I think even more importantly, too, is that to get engagement from the scientific community, from the stakeholders themselves, the practitioners themselves to advice bodies such as yourselves, to ensure that the policies that come out are commiserate and make sense to the stakeholders that this will be applied to. With that, I thank you, commission, for your time.

**Amy Gutmann:**

Thank you for a very engaging presentation, which brings up this vivid image in my mind of agents in jeans educating teens, right?

[AUDIENCE LAUGHTER]

It's really quite something. I'm going to ask Jim Wagner, our vice chair, to ask the first question.

## Q & A

**Jim Wagner:**

Thanks very much. And wonderful presentations, all of you. Thank you very much.

I do have a quick question. Dr. Patterson, I understand and it was reiterated by Mr. Rodemeyer, that this notion of facing regulatory focus and activity on product, in fact, product performance. And I'm comforted to know, Mr. Rodemeyer, that you feel that in the near-term with a little bit of extension of what our current regulatory regime, I believe you called it, we're in pretty good shape.

But I found it striking that it was Agent You's presentation that focused on something we heard yesterday. And that is that part of the distinguishing element apparently, synthetic biology, is that so much of it is in information. It is in coded sequences. It's not in product. Do we imagine that another dimension that needs ultimately to be added to the regulatory regime, again using your language, is some-

thing that will address not just product and performance, but will address also the early stage information and its exchange?

**Michael Rodemeyer:**

I think that that's, in terms of where the regulatory agencies come into play, again it's a reactive system--essentially the agencies wait for industry to develop particular products, that then they need to move forward with to get the appropriate regulatory approval in the case of particular products. So agencies are not generally in the position of going out and trying to get — even though there's an effort to try to keep track of what's going on so that they can anticipate what's about to happen, unless there is some legal requirement to come to that agency for some sort of regulatory review, the fact that there may be previous work being done is not something that's likely to engage the regulatory agencies. So I think that would fall, if anywhere, more in the realm of the NIH responsibility. And certainly, that's been an issue with the security side as well.

**Jim Wagner:**

Dr. Patterson.

**Amy Patterson:**

If I could, I'd like to add a couple of comments.

First of all, genetic sequences are overseen. Let me give you a few examples. On the bio safety side, genetic sequences are looked at for their capacity to replicate or encode. But the sequences themselves, the constructs themselves, there is an oversight framework for how they are used, how they are handled, how they are distributed.

On the bio security side, the select agent rules have a genetic element section to them. So there is regulatory oversight of genetic sequences. But the threshold for oversight is, what can that genetic sequence encode? Can it encode an infectious form of one of the pathogens that we're concerned about? Can it encode one of the highly lethal toxins that we're concerned about? So it's not all genetic sequences. It's that subset which could potentially encode a pathogen. Yeah.

**Amy Gutmann:**

Let me just ask a follow-up to that. You were very, I thought, clear

and open in your presentation that we have a set of regulations in place and practices. But to quote the American philosopher Will Rogers, “Even if you’re standing on the right track, even if you are on the right track, if you’re just standing there, you’ll get run over.”

We need to think about where we have to move. Where are the gaps? Can you just say a little bit about where — I know we can’t be comprehensive—but say a little bit about where the gaps are now as you look at synthetic biology and where it might be moving.

**Amy Patterson:**

Well, I think many of the speakers yesterday and today have touched on really the major issue. And that is this notion of uncertainty. And as the constructs become more and more novel, we are less able to extrapolate from what we know from similarities to known sequence, to known agents. And I think the question becomes, is the construct or the new entity guilty of being pathogenic or innocent until we have data? And how do you treat it in that interim period when you don’t have the data? Do you treat it with maximum controls and maximum containment and assume the worse? So I think this is one of the biggest challenges. It’s almost a conceptual framework for how we think about these things and move forward in a responsible way.

**Amy Gutmann:**

Raj.

**Raju Kutcherlapati:**

I want to follow up on the question. Both Amy Patterson and Michael Rodemeyer made the case, I think, that synthetic biology is a part of the continuum of what has been happening with the recombinant DNA and genetic engineering the last 35 years and also talked about how the NIH promulgated guidelines for using recombinant DNA and how other agencies that came in and began to implement a strategy for even those institutions that are not funded by the NIH. So one of the questions that I have for you is: Do you feel that based upon all of the things that we are hearing, that we have an adequate infrastructure to examine the issues raised by synthetic biology and be able to promulgate the right types of guidelines or use regulations? Or do you need new infrastructure that needed to be built to deal with any special issues relating to synthetic biology? Both of you.

**Amy Gutmann:**

Michael, why don't you start?

**Michael Rodemeyer:**

First of all, I don't think it's politically realistic to talk about a new system of regulation for synthetic biology. I think this is the system we have. And I think the question is, how do we improve this system to make sure that the particular challenges that may be faced by synthetic biology, which I agree are really around this issue of risk assessment and knowledge — how do we build in better capacity for the system to be able to deal with that?

I think there are any number of relatively small things that could be done, both in terms of agencies writing regulations to make sure that that information is obtained, and that there are incentives for industry to develop that kind of information as these products are being developed as well so that that information is made available.

I'm hesitant to say that the system is adequate in the sense that I think there are — I have real concerns about both resources and tools that agencies have. It's difficult for them enough to deal with the fires that they have to put out today, thinking about what may or may not be a problem 5 to 10 years from now is really difficult.

But I think the system is flexible enough and adaptable enough to be able to learn and change as knowledge grows. And I think that's the lesson that we have learned really over the last 30 years as well. So I wouldn't throw out the baby in the bathwater. But I think there are definitely some things that need to be done to improve the capacity of the system.

**Amy Gutmann:**

Amy.

**Amy Patterson:**

I would agree with what Michael has said.

I would also remark that if one were to take a blank slate and design an oversight system, in my view, again the three attributes would be

the ability to foster beneficent, beneficial applications of technology while minimizing any risks and managing those risks. That there would be a role of society for input into that infrastructure and to cultivate public awareness and understanding. And thirdly, that the system could evolve.

While I think the government isn't necessarily very good at cultivating public understanding and awareness, we try very hard and we're not always the best at that. I think by and large, those three components, those attributes are present in the current system. But it needs to evolve.

I think the most important thing it needs is the tools for appropriate risk assessment here. I think another question to ask is the applicability across all sectors. We see this technology is widely available. It's practiced not simply in academia dependent on the dreams of federal funding but it's privatized. I think another consideration when one thinks about scientific progress and our relationship to other countries, as a citizen and in the world, is the question of what position the U.S. takes with regard to oversight comparative to other countries and the degree of our international engagement on these issues.

**Amy Gutmann:**

Thank you very much. Nelson.

**Nelson Michael:**

Yes. My question to the three of you is really a follow-on to the question that Raju asked, which is, it seems to me based on all three of your presentations that you describe a very similar context that we have been dealing with that's been evolving over, you know, nearly 40 years. You described in your presentation that you thought there was adequacy, even though that you wouldn't — and wouldn't necessarily have built the framework, the regulatory framework and legal framework but it stood up to the challenges to date. And the FBI, which seems to me to be the answer to a question raised yesterday about who is the person you dial 911 for when there are issues, it's not only passively engaged, but actively engaged in making sure that that 911 entity can stay up with the state of the science and is definitely improving its ability to surveil and become part of the field.

So, in that sense, what I'm wondering is if the existing regulatory or federal oversight bodies that exist simply need to add this as a mission, rather than creating a new framework? And perhaps not even creating a new office, but simply adding this mission to the existing federal system, so that there can be obviously a very quick learning period and the ability to make the quickest impact in a field that's evolving quickly. So that really is the specific question: Adding a mission or creating a new framework?

**Amy Gutmann:**

Mr. You, would you like to begin?

**Edward You:**

I think it's evidenced by the fact that the FBI, as I have mentioned, we are foremost a law enforcement agency. And in criminal investigations, that is inherently reactive. And if anything is better testimony of the fact of adding a mission is the fact that we have now become proactive in WMD matters in general so, as evidenced from the agency, it is possible. And again, I cannot comment from a regulatory standpoint. But at least from the FBI's standpoint, the mission has changed and it has adapted.

**Amy Gutmann:**

Amy.

**Amy Patterson:**

Two comments:

First of all, I think we have underscored a theme of continuum here. But I would also add the caveat, that that should not make us complacent. And I think I can speak on behalf of my colleagues at other federal agencies, we think a lot about these issues. And we're very much trying to grapple with them and look forward to the input from the commission. But I think complacency or turning a blind eye to what may potentially be novel would be a mistake.

All that said, I do think that synthetic biology is within the mission of biomedical research and much of the oversight framework that we have today, we've tried today bring together, for example, the National Science Advisory Board and the Recombinant DNA Advisory

Committee for a joint meeting that examines the state of the science both from the top down and bottom-up approaches and examined what were the current issues and what was on the horizon and what might be beyond what we can't see in terms of the bio security risks and the bio safety risks. We're also very actively trying to engage an international dialogue. We've been sponsoring a series of international webinars; the first one was in the Americas. We did that with PAHO. We are just about ...

**Amy Gutmann:**  
Web MRs?

**Amy Patterson:**  
Webinars.

**Amy Gutmann:**  
Is this in Webster's now, online dictionary?

**Amy Patterson:**  
Online interactive sessions where the notions of dual use and synthetic biology are discussed and people can log on and call in. And we have one coming up. It's going to be based in Europe in the fall. But it features synthetic biology. And then we have one later on in the year in China. So I just say that to try to underscore that we are trying to address the issues. And I think they are very much within the current mission of many of the offices and agencies, either implicitly or explicitly and increasingly explicitly.

**Amy Gutmann:**  
I will go to Anita next, then Christine, then Barbara.

**Anita Allen:**  
Thank you. Assuming that proactive government and law enforcement oversight is appropriate, I want to ask a friendly version of a question, which you might get sometimes as an unfriendly question. But my intention is friendly. And that is: what concerns or push-back or resistance might you expect or have you gotten from the idea of government oversight in this area from researchers? And I mean concerns about academic freedom, intellectual property or industrial business secrets or concerns about civil liberties of freedom from gov-

ernment surveillance.

And I had in mind a particular push-back that was received from researchers in the academic setting when the government began to regulate encryption controls and export controls. So my question is, what sort of push-back have you gotten or do you anticipate from the innovators and researchers around issues of academic freedom and intellectual property and so forth?

**Edward You:**

I guess that's my question. Our outreach activities have been relatively new. There has been some initial pushback but I think when we come in with-- and I address this in one of my very first slides is that, how do you engage the different communities?

So how we approach an industry representative, for instance, would not be the way we would approach somebody from the DIY bio community. It's very different. But the message is still the same. Is that there are some inherent risks and potential threats. But by working together, can we manage and mitigate those risks because, you know, what's the flip side? If there is an accidental or intentional release or event, from the law enforcement side, that's already kind of a given what's going to happen.

But for engagement in academia, they now understand that — and maybe yet another act would be appropriate here. One of our engagements we provide a tabletop exercise where you give hypothetical scenarios where it could be accidental or intentional release. And we pair it up with a representative from law enforcement and a representative from academia. The information exchange is phenomenal because the representative from academia now understands what the role of law enforcement is. What our responsibilities are. And when they come that understanding, it makes the message that much more understandable.

But then it doesn't stop there. For instance, say it's an accidental release. From a law enforcement side, we now understand that if we're, you know, from a criminal standpoint, we're done. We're finished, if it's an accident. But we gain the appreciation that if you are a university, that's just the beginning. That now your funding might be at

risk. All the liability issues that come into play, that's just the very first step. So there's an appreciation and understanding from both communities--both from the intentional aspect of it and from an accidental aspect. So the different scenarios, by gaining and understanding of the different communities I think is extremely vital. So the initial--and I think once that understanding is there, the pushback decreases.

**Amy Gutmann:**

So I'm hearing proactive education.

**Edward You:**

Yes.

**Amy Gutmann:**

Proactive risk assessment. And question as to whether we can do that, whether you all can do that without a crisis, you know, before a crisis happens. It's very good.

Christine.

**Christine Grady:**

Thank you. Thank you for your comments. I wanted to ask a question in light of the questions before, about whether we need to change the regulations. One of the things, I think Amy said, was the ideal situation would be a system that is easily evolvable. And being a federal employee, I know that we work hard to make things respond. But the federal government is not known for speed in changing or reacting or responding to new fields. This synthetic biology, depending on how you think about it, is moving pretty fast. And maybe not as fast as some people like to think it is. But certainly moving fast. And Dr. Wolpe said this morning, speed is an important thing we ought to think about.

So I guess my question to you is: Is there anything we can think of in terms of how the federal government might address this issue of having to evolve faster than it normally does given the current structures? And slightly different than that, but I think related is this issue of coverage. You know, who do we reach out to? I'm happy to hear about the outreach efforts. But what else can be done from the government level to reach constituent use that it doesn't normally reach.

**Amy Gutmann:**

Amy, you want to take that?

**Amy Patterson:**

Sure. For your first question, Christine, I think the strategy of embedding in law and regulation, the overarching principle, so for example, that the products of biotechnology or pathogens should not be misused to threaten public health or regulations that ensure the safe conduct of research. And then setting forth the specific procedures and practices in guidance so that you have the standard, but the way that it is achieved can be more rapidly evolved and tweaked as new data comes in. Our understanding is enriched. How we might go about ensuring that goal embodied in the statute or regulation is achieved will change. And I think we need the flexibility to have tools, oversight tools that change in that fashion. But yet uphold the principle. And we see that, for example, in the select agent rules that speak to

knowing what you possess, knowing what you transfer and registering it and coming under that oversight framework. But the voluntary guidance to synthetic double stranded DNA providers of how they go about screening — how do they go about knowing what they have made? And that's, that's embedded in guidance rather than embedding in a regulation. So that would be my thoughts on that balance.

**Amy Gutmann:**

Thank you. Barbara.

**Barbara Atkinson:**

We heard yesterday about licensing at various steps along the process as one of the ways to monitor who is doing what. And I am particularly concerned not about the NIH people who sound like they have a fair number of areas of scrutiny, but by industrial uses and then the amateur uses. And if you had it, do you think it would be valuable or not valuable to have some kind of licensing of either the products or steps along the way, particularly to get at the bioterrorism issues and the people who aren't licensed then, therefore, being subject to some other regulation?

**Edward You:**

Well, I can say that through our engagement with the DIY bio com-

munity, they are taking that into serious consideration. Some of the things that they've considered as model rocketry, for instance, there's products where it's just over-the-counter and you could just take it and launch it. And then there's all the way to the more — the example they show is that last year, an amateur rocketry enthusiasts built a 1/5 scale of the Saturn Five Rocket and launched it and had to get FAA clearance. They had to get all the permits and licenses that are required. And they are likening a potential possible safety security framework along those lines.

I know Dr. Endy mentioned amateur radio. That licensing structure. So they understand what the impact potentially could be if something should go wrong, how that could really affect not just the community, but the perception of their community. So they are taking that into serious consideration. How it will flesh out, again I think that's where it's extremely important that we engage the different communities because it's not going to be a one size fits all. It may work for industry. It may not work for the amateur community. But unless we engage, we won't know what will actually work.

**Amy Gutmann:**

I'm going to — it's a testament to everything that you've told us and we're going to engage you more. But I'm going to go to members of the public for questions, so we can address some questions to our presenters. And go ahead. Yes. Why don't you go? And we'll take a few. Yeah, I think we should take a few because this is our last session. It's not — it's our last session for this meeting. It's not our last session. So please, introduce yourself and ask the question. And I will keep track, as will our presenters so they can answer them.

**Eric Hoffman:**

Great, thank you. My name is Eric Hoffman, I'm with Friends of the Earth. I want to go into more what Dr. Patterson was saying and also Dr. Rodemeyer. Moving forward with these new synthetic organisms, where does the burden of proof lie when we're trying to analyze risk and we're putting the brakes on research or letting it go forward? Is the burden of proof on those that are doing the research to prove that it's safe? Or do we let them go forward and then react if something bad happens?

**Amy Gutmann:**

Thank you. Yes.

**Rob Carlson:**

Rob Carlson. I am concerned — two comments.

First, I'm concerned that the words regulation and licensing have been used very casually the last two days. And would observe also that the press coverage so far is leaning very heavily on regulation and not with bioethical issues or anything else that was said. The reason I'm concerned is that no one has really talked about the costs of regulation. It is assumed that regulation and licensing equal safety. And it is demonstrably the case with many historical examples that safety and security are reduced by regulatory enforcement actions. And I just urge you to keep in mind this issue has two sides and we don't want to make things worse.

The final comment I would have is that the strategy, national strategy for countering bioterrorism or biological threats that Agent You put up, the first sentence of the second paragraph of that document said garage biology is good.

**Amy Gutmann:**

So noted.

**Victoria Sutton:**

Dr. Victoria Sutton, I'm director of the Center for Biodefense Law and Public Policy at Texas Tech University. I'm a lawyer and scientist. I would like to address a question that was raised about gaps. Madam Chair and Raju Kucherlapati asked about gaps. One that comes to mind, one of the big gaps is, a lot of the things we've talked about are about oversight mechanisms, but apply only to people who have government contracts and who are actually spending the money as part of the oversight. And if we're thinking about the broader picture here, the broader public, that scenario that probably should be addressed in one way or the other. If we can learn lessons from legal history, the states, local governments, may fill in regulating at that level, but it might be a point that would be good to address.

Another point Dr. Grady raised was the speed and that is certainly a

relevant question when you have a technology emerging as quickly as this one. And I would suggest if I had the opportunity to ask the agencies and departments to look at this. I would ask them, first of all, to inventory what existing regulations they had that apply and secondly, issue guidance on how synthetic biology applies. Guidance doesn't require noticing comment. It's simply a guidance, nonbinding guidance for the regulated community. Yes?

So I would suggest those would be two things I might say would be a really good step forward, assess what regulations exist and then issue a letter of guidance as to how that applies. The big picture, I think, also we learn from lessons — and we had a great walk through the legal and scientific history of biotech, the tension we have explored here is really the tension between the need for regulatory oversight against the need to optimize research and development without unnecessary impediments, but also those factors include the ethical and values constraints. So I think that this is not a luxury, it's a necessity and a role for the federal government and certainly it's doing exactly what it should be doing here today.

**Amy Gutmann:**

Thank you very much.

**Rich Boston:**

Yes, thanks very much. My name is Rich Bostin and I'm an environmental journalist who has written on genetic resource access. I have a question for Mr. Rodemeyer.

All the presentations were very enlightening and I have a question about his suggestion for federal review and how this might encompass the international connects or disconnects. He mentioned, for example, widespread gene flow from G.M. crops in the United States. That's an important management serious issue. But internationally becomes very ethical and politicized. And within this question is implicit international agreements, United States is not a party to, also. Thank you.

**Amy Gutmann:**

Good, thank you very much. Where does the burden of proof lie? I'm going to ask Michael to answer that. What are the — do we take the

costs of regulation into account? Amy, would you answer that? And international — how do we factor in the international community? I'll leave that to any taker. Michael, why don't you begin?

**Michael Rodemeyer:**

Well, the burden of proof is really set out by the various laws that apply to specific products. So, for example, if you are a drug manufacturer, the burden of proof to prove safety is on you. And the agency will deny the product until you can prove to their satisfaction that it's safe. But for other products, again depending on the law you are dealing, the burden is really on the government to prove risk in order to justify regulation or some kind of enforcement action, the answer is it depends on the law.

**Amy Gutmann:**

But it is an open question ...

**Michael Rodemeyer:**

Yes.

**Amy Gutmann:**

... as to where in the various risks involved with synthetic biology, what would apply.

**Michael Rodemeyer:**

Exactly.

**Amy Gutmann:**

Good, good. Amy.

**Amy Patterson:**

When it comes to the oversight of research, assuming that there's a standard, a regulatory standard or policy in place, then the burden of proof is on the researcher to demonstrate that they have adequate evidence, proof of concept that support moving forward. I just wanted to underscore that.

**Amy Gutmann:**

Very important point. Thank you.

**Amy Patterson:**

You asked me to speak to the cost of regulation.

When regulations are promulgated, there is an economic analysis that is done for them, with them. The burden of regulation is assessed and is usually published along with the regulation or just made available to the public. Now, one can always quibble about are those assessments accurate? Do they adequately capture all the costs? Or do they overlook costs? So the costs of regulation are important. I agree with the gentleman who offered that comment. But I would also offer that there's a cost of not regulating. And so both need to be considered.

**Amy Gutmann:**

I think from the commission's perspective, I might say just to clarify, we will not assume that regulation is justified or not justified regardless of the cost. So that, to us, is an open question. Rob has been reading the news articles more than we have probably, since we haven't had a moment in the last two days. But whatever they say, I just want to put us on record that this is something that we would definitely consider. The cost factor as something we would consider.

Who would like to take — these are really important questions and we're not going to do the deep dive today. But the question about the international community and how does that get coordinated. Michael.'

**Michael Rodemeyer:**

Well, there are two aspects. Obviously, the biosecurity issues are critical. And I'll ask my colleagues perhaps to respond to that part.

But on the regulatory side, this has been a real challenge because we've had, of course, a global controversy about genetically modified crops and food. So other regulatory systems around the world are in fact process-based regulatory systems. And we have this problem of asynchronous regulatory approvals where products may be legal here but not legal in other parts of the world, which is very difficult when you're dealing with a commodity like corn. It becomes very difficult to manage. These issues obviously are engaged at international levels in a variety of areas. There have been obviously a number of efforts to try to harmonize both U.S. and European approaches, the technolo-

gy, the world trade agreement organization, and free-trade agreements all have some—it's a complicated answer and I think that there's no clear response or no clear one place where you can kind of to bring all of those issues together.

**Amy Gutmann:**

Thank you. Mr. You.

**Edward You:**

I will comment that the FBI does have international engagement, such as through Interpol. I had mentioned earlier the U.N. I would also like to bring to the commission's attention that the U.S. State Department has an overall international bio engagement strategy so that might be another avenue that such a question could be addressed, so it deserves follow-up.

**Amy Gutmann:**

We have reached the end of our time for this first inaugural session. I first just want to say a simple observation: The number and diversity of members of the public who have turned out is truly heartening for anyone, like myself, who believes that education first and foremost is at the heart of a lot of the issues that we face in our democracy.

And secondly, it's a testament to how many members of the public stayed till we are adjourned.

Let me just say a few words and then ask Jim if he wants to say a few words. First, I want to remind everyone that we have issued a call for commentary on the topic of synthetic biology. And any group or individual who wants to offer public comments on the topic is encouraged to do so. I assure you, we will read them. Please check our website for details. Our website is [www.bioethics.gov](http://www.bioethics.gov). The email address I can give you is [info@bioethics.gov](mailto:info@bioethics.gov).

So on behalf of the commission, I just want to thank you all for coming. Our next meeting will be held September 13th and 14th at the University of Pennsylvania in Philadelphia. And as the case with all our meetings, it is open to the public and free. Our meeting after that is in Atlanta at Emory. And with that, I will turn it over to Jim.

**Jim Wagner:**

You have covered everything. Just allow me to add again my thanks to everyone. Special thanks to the commissioners and our experts throughout the session. It's just been fabulous. Learned a great deal. Thanks to the public for their contributions as well. Please continue contributing through the mechanisms that Amy outlined. And, Amy, I guess there's no convenient way for you to thank yourself. So allow me to thank you for your wonderful leadership.

**Amy Gutmann:**

I want you all to thank yourselves for really two days of excellent discussion and deliberation. It will serve us very well. Thank you. And one more time: Thank our three presenters who did a marvelous, marvelous job.

[AUDIENCE APPLAUSE]