Please stand by

Please stand by

>> John Holdren: Can I ask everybody to take their places, please. It is my great pleasure to welcome you all to the 30th official meeting of President Obama's council of advisors on science and technology, that's 30th, 3-zero. And of course a particular welcome to the members of PCAST who in many cases have traveled far to be here. Welcome as well to the staff of OSTP and the science and technology institute and work together very closely with PCAST. Welcome to the members of the wider science technology and innovation community who have joined us in the room, and of course welcome to all those who are watching us on the webcast. And let me while mentioning the webcast, take this opportunity to remind those who will be speaking to please turn on your microfonls before you start to speak. Because in this case, while the people in the room may be able to hear you without the microphone, the people on the webcast certainly will not. And I'm sure in terms of sheer numbers they represent the largest part of the audience.

Before I go any further, I want to note two particularly important personnel changes related to the work of PCAST. First of all, almost exactly two weeks ago the United States Senate confirmed Dr. Joe hendlesman as OSTP director for science and Joe is here. Congratulations, Joe. (Applause).

And on a different note, I have to record with regret that our longstanding OSTP, slash, PCAST triple AS fellow Dr. Natoki Ford is experiencing her last PCAST meeting before she moves on to new challenges. So let us thank Dr. Natoki Ford for her incredible service. (Applause).

Since this is the 30th official meeting of PCAST in the Obama administration I thought it worth reflecting at least very briefly on the extraordinary record of this group in terms of its level of activity, and in terms of the fraction of its recommendations for the President that he has embraced and that have become part of administration policy. We have done an enormous number of studies, almost as many studies at this point as we have had official meetings, over 25, and more to come.

And if one looks at those studies from the very beginning up to the most recent ones, one finds a remarkable degree of resonance with administration priorities and with executive orders, presidential memoranda and other instructions the President has given going forward to embrace and embody the recommendations of this group in his policy.

One could start with health information technology near the beginning of our record and the study of systems engineering of the health care system to get better outcomes for more Americans at lower cost in our very recently released reports, the recommendations of these reports, both the early one and the most recent one, are being embraced and embodied in the policies and actions of the Department of Health and Human Services, the CDC, the FDA, and others.

Our work on the allocation of federal spectrum continues to be acted upon by the administration, and that policy is moving forward expeditiously. Our recommendations in 2010 on accelerating energy technology innovation in that report of 2010 we recommended quadrennial technology review by the DOE which was carried out in the next year, and a new one is underway and we remd a quad renial interview, an interagency look at energy innovation and technology policy as a whole is the quadrennial interview is well under with a as an interagency led from the White House with a strong sec tear yat in the Department of Energy.

The recommendations of this group on climate change in early 2013 can be seen reflected in substantial measure in the climate action plan that the President rolled out in June of 2013, and again, that climate action plan is being implemented with really enormous focus, commitment, and coherence, led in the White House by the President's counselor John pedesta.

The report relatively recently on big data and privacy the tech no logical issues at the intersection of technology and data the interagency report to the study led by counselor pedesta is also in the process of effecting United States policy in this domain. Certainly our report on cybersecurity of more than a year ago is, implemented under the direction of the national security council in many of its recommendations.

Our report on agriculture R&D has been embraced by the USDA and with enthusiasm, and again, a large fraction of its recommendations are in the process of being acted upon.

Our report on accelerating drug development and approval, obviously a very important issue in the larger context of public health and the health care system. Again, being embraced by NIH and the FDA.

Advanced manufacturing, a major theme of an early study by PCAST has led to two rounds of advanced manufacturing partnership engaging many of the leaders of the high tech industry and our major research universities around the country, with a whole series of specific results, including initial installments in developing a national network of institutes on manufacturing innovation. Again, I think already having substantial effects on the whole process of increasing U.S. competitiveness, bringing back jobs in manufacturing, giving the United States an important economic edge in a variety of important manufacturing industries.

STEM education. This group has made so far three reports on STEM education, going on four, and the results of the reports that have been completed so far are abundantly reflected in the administration's strategic plan for STEM education which is being carried out under the oversight of one of the standing committees of the national science and technology council, which OSTP cochairs.

So I think we have a lot to be proud of in this group. It has been incredibly hard-working PCAST, with folks who of course are uncommend, except for me, I'm the one full-time government employee on PCAST. My cochair my vice chairs and all of the members otherwise serve without compensation. Quite the opposite; they get to take out of their pockets some considerable part of the expense of doing this, because the government reimbursement rules don't quite stretch to reach the full costs of doing this. And I have to say that as you know, and you'll hear it again from the President himself later today, the President is enormously appreciative of the work of this group, and the role it has played in his formulation of policies around science, technology, and innovation.

With that, I'm going to ask my cochair, Dr. Eric Lander, the head of the brode institute of genomics at Harvard if he has any opening remarks.

>> Eric Lander: No, other than to admit that I hadn't realized it was our 30th meeting. It is remarkable across 25 reports and we'll have another one that we bring to the council today for approval and another one that I think we're going to have ready to bring in September and maybe two by then, that the energy of this group has not flagged. I just think it's fantastic.

We'll dive into the meat of the reports there, but and I'm also grateful that so many people keep showing up to our meetings here in person and on the web, so both the White House the energy of the group and the energy of the broader community I think really sustains us, so thank you.

>> John Holdren: And let me just add there are two and a half years left in this administration, and we are not finished. There is a lot of work yet to do. Interesting and important challenges that remain to be addressed in the science, technology and innovation space, and we will hear about some of those in the course of this morning's meeting and we'll be again discussing them with the President later today.

Let me now again with the reminder to everybody to please use your microphone when you speak. I want to turn to the discussion of the national nanotechnology review, and there I believe that mark Gorenberg will be leading off the discussion. So Mark, the floor is yours.

>> John thank you very much, the 21st century nanotechnology research and development act of 2003 calls for a national nanotechnology advisory panel to periodically review the national nanotechnology initiative, the NNI. We've designated in 2004 that PCAST be that NAP so this is now our fifth review of the NNI and the third one under this particular PCAST.

What we're going to talk about today is actually a work in progress. To give you an idea of where we are in progression of that review. Okay.

So we started earlier this year, this is cochaired by Michael McQuade, a member of PCAST, and also with great oversight and a lot of great input from Maxine Savitz and Bill Press. Tireless, tireless work by Ashley prediff who is the assistant executive director of PCAST and also oversight and great inputs and direction from Marjorie Blumenthal the executive director of PCAST. We've consulted and put together a group of 11 industry experts from academia, from industry, and also from areas like the venture capital community to look at the field not just from a nanotech expert view but also from a generalist view with the idea of nanotechnology of part of what they do. We also had two in-person meetings and we've hosted many conversations with folks around government agencies, industry, universities, et cetera, to understand their views.

Also did want to say before we move forward that we're honored to have two folks here in the room with us, one is Lloyd Whitman who is the director of the national nanotechnology coordination office, which is important in sort of the common -- the connection between the NNI and the outside world as well as work within the agencies. And also tof Kareem who is the stpbility director of OSTP responsible for nano technology and one of the cochairs of the subcommittee on neuro-scale science engineering and technology core part of this organization. Which reports under the national science and technology council.

The national nanotechnology initiative is a cross cutting national vision for development of nanotechnology within the United States, it sort of combines the federal effort in -- across different agencies in nanoscale science, engineering technology and related issues. In 2014, however, five of those agencies garnered 93 percent of the budget but the NNI is inclusive of 27 active agency units that are involved in this effort.

The definition, by the way, that the NNI put on nanotechnology was a size one, a dimension of 1 to 100 nanometers so it's actually material that -- or that is has quantum mechanical effects that could have very different properties than similar types of components at different scales. And that size threshold was used rather than sort of a particular discipline in terms of its definition.

And you can go to the site, neuro.gov to get obviously far more information on this. The FY 15 budget right now that it's proposed is $1.50 billion roughly the same as 2014. The innovation calls for healthy research effort to continue.

But international competition in this area says that, while the U.S. GAO -- 2014 property E report says while U.S. is still the lead in research, although there are some barometers like research papers being submitted now more from China and EU than from the United States, the one thing the GAO report did say that we've fallen behind some of the other countries in some of the infrastructure technology like nanotechnology manufacturing of products and that did influence some of the thinking that has already gone on in this committee.

This gives you a context of spending in nanotechnology field, overall worldwide about $18.50 billion. The U.S. government and State governments as well which have been involved, about 2.1 billion, Europe about the same, corporate spending is also up, right now it's 4.1 billion, Japan is a large player corporately. But what's really been moving forward well is the idea worldwide nanoproduct enabled proubility product revenue roughly 731 billion in 2012.

We looked at this as a transition point. So while we believe that a healthy research environment must continue, the primary conclusion of the 2014 PCAST review of the NNI will be that the United States will only be able to claim the rewards that it's made from investing in nanotechnology research by bringing together this federal initiative, federal agencies, the Office of Science and Technology policy and all these different efforts within the community to apply this research towards, having leadership for technologies into commercial products, we recall actually framing this under the concept of NNI 2.0 which is the idea of moving from neuro scale components to moving to interdisciplinary neuro systems. And we're seeing increasing distributions in nanoboiling, energy resources, food agriculture, simulation, cognitive technologies, and the number of different disciplines where this involved is actually fairly staggering to think about.

The added value of the NNI over the last 13 years has been very significant think about collaborations between the industries, there are reported only 35 collaborations between agencies in this work 205, 159 last year, that's been very prolific in their work through the agencies and great camaraderie effort.

But the international competition that we're seeing and the naturally racial of the field says that we have to do more. And the neuro ecosystem has to go beyond the government to this full ecosystem of community, industrial, government, public, philanthropic partners all working together. And we've also looked at this going beyond the current concepts. By the NNI and we believe the primary driver of what we say in our report, that the primary driver for the next wave of the NNI should be this concept of grand challenges. That it should be centered around the idea of aaddition, chiefable inspirational goals that have the cross sector involvement in the selection refinement examine pursuit of the goals. This has been a staple we're starting to see in the administration through OSTP, we're seeing grand challenge in areas like the brain initiative, the national grand challenge the grand challenge for development the administration has moved forward on grand challenges because they can ehelp in societal problems, they can serve as multi impact of collaborations, create a foundation for jobs of the future, capture the public imagination, and also inspire a next generation of scientists and engineers.

We will have some illustration of some grand challenges in the report. And actually would love to here since we're in public forum would love to hear some for the next month or two from people in the public that they think would be great grand challenges initiatives to be included in the report. But to give you some of the initiatives that we have looked at one of them is the neuro-enabled desalination of sea water to serve the emerging water crisis this is one where a nanostructure membrane can be used to control pore shapes and they can have very high selectivity separating out salt from sea water another, neuro based 18th bact yals thater at add indicate untreadable inspection in the grand cheal we're putting a year on that of 2025, using nanomaterials to disrupt the cell walls of bacteria, overcoming their ability to genetically evolve in response to drugs. Another idea reducing greenhouse emotions by nanosolid state refrigeration, the pour pruction of HVAC systems that contributes to large amounts of greenhouse casts and nanostructured thermoelectric material could enable that to be far more efficient for heating and cooling.

Those are just some examples we'll talk about things such as 3D printing, we also -- and some involved with cancers. But we also believe there could be a huge impact in neuro manufacturing and we believe one of the grand challenges should be around neuro manufacturing.

The report will talk about some of the efforts involved with commercial in nanomanufacturing today we see that a big thrust going thrurts there are such as nanomanufacturing, nanocommercial business association, has been prolific in tying together the government with the outside community setting up centers that people can use, as well.

One that we do want to highlight though that the government has put together stt national nanomanufacturing innovation that was put together 2013 are for federal investing it links institutes for inferring with common goals with you with unique concentrations.

In the budget of 2014 the President proposed creating a network of 15 regional institutes for manufacturing innovation, that has now been expanded to trying to put together 45, to solvetle aging structure of manufacturing it's a great thrust and has some great immediate success in the administration we think the NNI should be the national partner to bring forward NNI in nanomanufacturing.

One of the great areas we should commend the NFCT is its coordination of nanotechnology in R&D with environmental health and safety issues, essentially set up a subgroup called the national nanotechnology environmental and health impacts group, NEHI working group. They put out this report in 2014 that was -- talked about the collaborations amongst the agencies on the EHS and it's entitled progress review on the coordinated implementation of NNI 2011 EHS research strategy.

We've been told that about 40 percent of the effort of the NACT centers around NEH today so a small amount of dollars but important work is essentially in the government. Some of the implementation of this 2011 study included development of comprehensive measurement tools.

Collection and exposure of collection educate, enhancing modes of interaction, improved assessment of transport and transformations of E&Ms, development of principles for establishing robust risk assessment and coordination of the efforts to enhance coordination modeling simulation in order to work this work in nanoinformatics infrastructure.

A lot of this has been tied together, as Lloyd will tell you, with the NNCO.

So Lloyd will be -- is planning to go back to -- he's sort of been on loan in the interim and he's actually working with OSTP, until we find his replacement. But the NNCO director is a very important position in this and we're hopeful that the NNCO director will tie together with these new ideas around grand challenges and really be an instrumental force in helping to bring them forward.

The NNCO acts as the primary point of contact for information on the NNI as we talked about, provides technical administration support, develops the updates for the NNI website and does the public outreach for the NNI.

So with that, I guess we can open up to questions. Maybe I can conclude by just saying that again, NNI has been a truly successful venture for the last 13 years temporarily for setting up collaborations between the agencies, we think this is a great opportunity and we think actually that the international landscape requires us to take this up a notch and really bring autopsy this together, not just for research but also far more for commercialization.

And we're starting to see some great centers come together, I mean many universities had for years but particularly there's a lot of publicity recently this is a pry priority of NIT going forward, a facility of 200,000 square feet campus to bring this together we think this will be a future shining area for the next decade as we pursue NNI 2.0. Thank you. hol hold thanks very much, Mark. The floor is now open for discussion from the PCAST members. Maxine Savitz, please.

>> Mark I want to thank up and actually the whole community. Moving to the grand challenges, you know, is the right thing to do, but what about the fundamental research aspects of the government program? I mean, that's been key through the 13 years you see -- you know, what where that fits in as poornt part.

And the other one, are you starting to think more about what might -- in the other metric, how do you measure the outputs of this.

>> Mark Gorenberg: Yeah those are really good questions. We're very adamant that the research has to continue. We're not looking at commercialization at the expense of research, but we're just saying that now we're in the next phase of international development around commercialization, we're seeing far more products come to market.

So the government has to continue that research to go on, but commercialization becomes a sort of necessary component side-by-side.

The second question -- oh, about metrics. Yeah. So there's two recommendations that came forward in the 2012 report that we will certainly continue in the 2014 report and even put more emphasis on. One of them is the idea of creating an advisory committee that involves industry and academia to work in almost a continuous basis with the NNI, and NSED to bring forward these concepts. The other one that was brought forward in the 2012 report that will also be a key part of the 2014 is the idea of metrics, and measuring. And we're started to look at some more concrete concepts of that, like the star metric systems that we'll be highlighting in the report.

>> Maxine Savitz: Thank you. Have

>> John Holdren: Jim gates please.

>> S. James Gates: Thank you John and thank you Mark for the leadership of the entire group in putting together the report my question is related to that of Maxine's you responded that a continuation of research is going to be a high priority in the future and related to that of course is the ability to retain talent to actually carry that research out. Can you say something specifically about that, in the face of this fierce international competition that we keep hearing about?

>> Mark Gorenberg: Yeah we're starting -- Jim it's a really good question. We're starting to see for the first time the -- and particularly in the nanotechnology area the brain drain of some of the experts here in this country to go overseas, of being enticed. The international budgets now to rally around nanotechnology are such that they're starting to attract some of our best and brightest and some of our longstanding, you know, not just young professors but well tenured professors to go overseas to do these efforts.

So we're looking at the idea of calling for -- and we haven't formulated the exact recommendations yet -- but we are looking into the area of calling for specific grants to be granted to well-known single investigators to make sure that their research continues on here and that they're enticed to stay here in the United States to move that forward. hol hold good. Bill Press.

>> William Press: Yes, thanks, Mark, for such a clear presentation. I wonder if you could cleabt a little bit more on what makes a grand challenge a grand challenge. How is that different, say, you know, from other kinds of initiatives. And what are the differences that give your workshop this confidence that grand challenges are really the way to push this forward?

>> Mark Gorenberg: That's a great question, Bill. Most of the work that has gone on to date has been more around coordination, and in fact in the 2010 report they put together ideas that they call nanotechnology signature initiatives, which coordinated agencies together on the work that they're doing. And that has -- again, in the context of coordinating research, that has been a good thing to do. And five of them have been created.

But we see that if we brought this up a notch in terms of grand challenges what are the characteristics of grand challenges and this is something that OSTP has been talked about as well as other areas, so first of all they have a measurable end point. Second of all they require advances in fundamental scientific knowledge, tools and infrastructure to be completed. Third is they have clear milestones along the way that can be looked and can be measured. And fourth is that they're integrating. So they're interdisciplinary amongst different organizations.

And the fifth, hand in hand with that is they're too big to be undertaken by a single or even a few institutions. And even in fact just by the government. So this is one where the government becomes sort of the bully pulpit to also bring in a lot of other organizations with the agencies to work on these grand challenges.

We will in the report talk about ideas for identifying and implementing grand challenges, so those are the basic tenets but we'll have a lot more to say on that.

>> John Holdren: I see no more flags, and we are right on schedule to transition to the next topic, so let me thank Mark and all your coconspirators in this effort for the great work that you summarized here this morning.

We will turn now to a discussion of the report on antibiotic resistance, and that discussion will be led by my cochair, Dr. Eric Lander. Eric.

>> Eric Lander: Thanks very much, John, and I want to thank Chris Chyba, PCAST member and cochair with me on this study that we've been working on for awhile now.

We are are bringing today to PCAST for approval of up for your approving, that is, this report on antibiotic resistance.

We've been covering this topic now for more than six months and had the opportunity to benefit from discussions with experts in a wide range of fields, members of a working group that we put together covering topics from public health to the development of drugs to basic research to agriculture, and many, many other fields, as well. As well as having heard, I must say, and very helpfully so from many different members of the public and from organizations.

I don't remember a topic on which we've gotten quite as many different inputs, people sent in, read this scientific paper, read that scientific paper. Wait a second, I don't believe this scientific paper. It was a really rich engagement and there may be people here on the web or here in the room who helped out in that discussion. And we're really, really grateful for that.

We also had the opportunity to talk extensively across the federal government with the many different agencies that have expertise in this area. The USDA and the international institutes of health and the CDC and the FDA, -- National Institutes of Health CDC, FDA, CDS, OMB, almost every three letter acronym you can think of was involved in this discussion.

And we learned a lot. It's a big and complicated problem.

All that said, it's sort of simple at some level. There are really three things that have to be done. Well, we know that there is no permanent vick tree against microbes. Mike robes continue to evolve in response to selective pressure. If you use antibiotics, whether in human health care or or in agriculture you will overtime see resistance.

This was pointed out by Alexander Fleming in his no bell address, it's not a surprise that there are lots of mutations that occur in bacteria and lots of exchangeable pieces of DNA that transfer between bacteria that create ways to spread and create new resistance.

It is a cat and mouse game played at this microscopic level between our agents, our therapeutics, and these microbes. There is no permanent victory in that sense.

Nonetheless, we can stay ahead of it. And the simple triad of strategy is surveillance, stewardship, and continued development of antibiotics or other treatments.

It's a rate question. If we can survey and see that's going on and we can slow town the rate at which we lose antibiotics through stewardship and speed up the rate at which we create new antibiotics or equivalent therapies through science and other such measures, science both in academia and industrial scientific development, we stay ahead, we win. We have a pharmaocopia of agents and collection of treatments that make us large yeah stay ahead.

If we fail, if we fall behind in our stewardship in our creation or if we fail to surveil to understand what's going on, it's a very real risk to see a resurgence of what life looked like a century ago when we had bugs we could not treat. It is a terrifying prospect. Now, I don't -- it doesn't help to do scare tactics around these things, but it's just plain scary. Members of PCAST has commented to me I now worry when I go into a hospital whether I might get an antibiotic resistant infection and that is not a crazy prospect anymore.

We're doing okay I think two decades ago, but it was really becoming clear we were in trouble on the point. A decade ago it was clear to wise observers and many folks, the infectious disease society of America and others were raising alarms that we were going to be in trouble. Today we see something like 17 really serious threats that emerged. And give rise to something like 23,000 deaths, much, much larger numbers of people who are sick, and a total economic cost, including the health care costs, and the associated loss of productivity costs, that are somewhere between $50 billion and $70 billion a year.

It costs this much in lives and money. If we could reduce it it's certainly worth putting money behind that problem if we could reduce that $70 billion by 10 percent that's a savings of 5 to $7 billion, in the crassest economic terms but it's more than that because this is a curve that's getsing away from us so one should shouldn't be doing arithmetic based on today's numbers one should be arithmetic on what it looks like five years from now and 10 years if now which is a much more serious thing.

It's something that has been of interest to all of PCAST. Now, we have a report, and I'm going to say in advance our usual practice at PCAST is, because when we're done and we vote on a report, it still has to get cleaned up and edited, various people have editorial comments, and so my expectation is that we certainly will not be able to publicly release the report today, my expectation is, as we always do with PCAST reports, within the next several weeks as soon as the editorial work is done and it gets properly set by White House graphics we'll be able to release this report in the next several weeks, but I'd like to sort of sketch today for people who are listening roughly where we're going with this. And I'm hoping with the actual report is publicly released there will be an opportunity for much deeper discussion of all of these points.

So the first thing to say is -- it's going to take federal coordination and leadership. And so PCAST has looked at the coordination that's been in place for the last 15 years or so, there has been an interagency task force working with this, and it was probably the appropriate thing for the time. But I think it's clear to us right now that given the new focus and new investment that we're going to call for, it's very important that that investment be coordinated and managed in the most serious and I think strengthened way. With an appropriate interagency task force at high enough level involving voffleg the leadership of the secretary of those agencies, and also with White House coordination, with appropriate office in the White House being tasked with -- that is with an existing office in the White House, being tasked with responsibility for ensuring that the interagency coordination goes on.

And we also suggest that there be a standing advisory council. So this is a pretty serious suggestion of coordination, interagency coordination, making sure that the White House itself stays on top of a national plan here, and is accountable annually for how we are doing against that plan. Someone tasked within one of the existing offices needs to be accountable for the progress annually on such a plan, and as I say, an existing group -- a new federal advisory group, that will be able to involve the external community.

This we hope will keep the spotlight on progress. And this is a measurable goal. We can ask what is the incidence of each of these antibiotic resistance organisms, what are the new ones that are popping up, is it going down, there are many things it's hard to know if you're making progress. We can tell if we're making progress. Do we have more antibiotics in the pipeline, are more getting approved. We should have in the next several years a scorecard. And we ought to know each year how we're doing against our scorecard. I wish many things could be as crunchy as this, but this one is crunchy and we ought to make sure we stay on top of it.

So we're going to make -- we have some recommendations about concrete actions like that.

Now, the second area that the report will touch on is surveillance. Being able to systematically surveil the problem and respond to the problem is very important, and there are two directions in which we make recommendations. One has to do with strengthening state and local public health infrastructure for surveillance and response. The CDC does provide some funding for states and localities to do this kind of surveillance. It's a small amount of funding, and it is a crucial life blood toes those agencies that do -- that are on the ground in states and municipalities, and do the actual traditional surveillance using existing microbiological methods in connection with the clinic the don't have funding in many of the states the CDC fund something essential, and this is a case where additional federal funding would make a huge difference. And we call for that.

But there's something more that's needed. We need to have new high-end technological surveillance of a sort we could never have before. When you see that somebody has a particular antibiotic resistant infection, carbopenum resistant bacteria it's hard to know whether three patients in the same facility got it from each other, each brought it from the same location, or whether they arose independently. Because when you play it out on a petri plate you can't see the difference.

But the DNA contains a record. If these things came from the same recent source, like spread from one patient to another within a facility, the DNA sequence will be almost identical. If they had totally different origins, there are tail tail genetic differences spread all over the genome. And you know what, one is also going to be able to tell whether this came from another country or whether this came from agriculture. There remain great debates over how much can be exchanged between humans and animals.

Well, with DNA sequence, deep DNA sequence, you can establish the provenance, you can reconstruct the evolutionary tree and the exchange tree of genetic material.

We could not have made a recommendation like this five years ago because the technology wasn't up to it. It would be a ludicrously expensive thing to do. But technology is advancing dramatically here. By next year we expect sequencing an entire human genome will cause a,000 and a microbe is typically about a thousand times smaller than a human genome. Now don't get me wrong we're not going to get the one dollar microbe, because sample costs things like that, but in a world where that's the direction we're moving, we ought to be getting as much information out of this because with awareness, awareness of what's the rate what are the numbers of different types of mutations where they coming from, we can take informed action.

There's a need to create a national capability for this kind of surveillance, and we think there are probably two directions that you ought to proceed. Regional laboratories that can do this for many facilities, and then also for some major hospitals, being able to do this on-site in the hospital makes sense. It certainly isn't going to be possible I think for every single doctor's office to do this themselves, in many small hospitals, but some large facilities ought to be doing this, and we ought to have regional capabilities for this kind of surveillance across -- serving the rest of the national health care system.

And many things go along with this. You're going to need to have reference databases of sequences of all these bugs. And the CDC has huge collections, and the USDA has huge collections, we ought to get them sequenced and the database freely available. And we ought to have the software easy to analyze this in different places so we're really saying let's apply the genomic revolution to the surveillance here.

But also let's not forget that the basic state and local public health infrastructure is critical. Those are not in competition with each other; we need both.

Now, the next area to speak of is fundamental is the creation of new antibiotics. There are multiple components to that. Why is it hard to create new antibiotics? One gap. Scientific knowledge. Bugs are smart, they're really smart, and they've got a lot of tricks. Take gram negative bacteria they have this funky cell wall and it's really hard to get molecules into a gram negative bacteria and if you get them in they have a lot of ways to pump them out they have a lot of different pump mechanisms to pump these things out.

It's important to take on the range of scientific problems related to beating back the tricks of bacteria.

In the report we'll lay out I think we've picked out 8 or 9 examples of many are bubbling up in the ferment of scientific community of things that we could learn that could accelerate this. Like how you get things into gram negatives. How you can take a bacteria that's nonsensitive and resensitize it by hitting the mechanism and leading it back to the initial antibiotic.

By understanding how it is that a tiny percentage of bacteria can hunker down in kind of a persistent state and be tolerant to not genetically resistant but tolerant to because of their physiologic state the antibiotic. There are important scientific questions that simply won't yield to brute force they will take the cleverest investigators of this generation to work on those problems and provide a scientific foungss.

And we call for increased funding, there. That's clearly the NIH but I think other agencies as well have roles, the FDA has roles here, DARPA, DITRA I think have contributions to make here. That's with regard to human health. There's also a basic research question with regard to agriculture.

Ideally we would like to have ways to be able to provide the benefits to agriculture that are currently associated with antibiotic use through other means. So finding alternative approaches to either do growth promotion, disease prevention for agriculture and decrease the need for any antibiotics there or human relevant antibiotics.

I don't just mean medically useful I mean relevant, the ones if you got resistance to, the animal, that resistance would cross-transfer to resistance in human even if it's not the same antibiotic it's in the same class or could be transferred.

So I think there's a lot of work in agriculture that says let's find scientific ways, maybe probiotic combinations you can feed animals that will be effective at driving out a particular bacteria. So tremendous creativity is needed there.

All that said, there are other things that are needed to create new antibiotics, so in addition to calling for more research in those areas, and serious funding in those areas, we've got to think about the clinical development path for new therapeutics. One place where you run into trouble is clinical trials. It's not so easy to do a clinical trial. If I have a cancer patient and I try to run a clinical trial, I discover the cancer patient and I could enroll them in the clinical trial for that patient, might start three weeks later or a month later or whatever.

If I have a patient with a serious antibiotic resistant infection I've got to enroll them instantly. I don't know when I'm going to see that patient, I've got to enroll them instantly, I'm not going to have that many patients in any one facility. So we need to have the most streamlined, efficient clinical trials sfrawrs to decrease the cost to the developer of a new antibiotic, of testing that antibiotic, as safely and effectively as possible.

So we call for the federal government to help stand up a national infrastructure for clinical trials of new antibiotics. I think there are pieces already in place that will provide some of that infrastructure, but it needs to be knitted together. And obviously the sponsor of any particular drug should pay for the cost of that clinical trial. This is not to substitute for the fact that developers should pay for the cost, but it's to put in place the ongoing, continuous, as they sometimes say, warm infrastructure, that somebody can drop into, rather than having the huge cost of assembling a clinical trials network for this one antibiotic you want to test.

In addition, there are things that the FDA can do with regard to the regulatory pathway for new antibiotics. If you have an antibiotic that treats individuals with a serious life-threatening antibiotic-resistant infection, you could test it in such patients and show that it was efficacious and had acceptable risk profile. That's not that hard to do.

If in addition you have to test that agent in many patients with other kinds of conditions, where the risk-benefit profile would be very different, that's a much larger and more complicated study.

So if there was a way to approve an antibiotic for a limited special use, and with a screamingly clear label that said this is only intended to be used in the cases of, the FDA could proceed with an approval in that case based on a focused clinical trial. But then we have to make sure in protecting patients that the system is there, that everyone understands that. And I think the FDA is, and has been for awhile, this came up in an earlier PCAST report -- thinking hard about does it have the authority, is it clear that it has the authority, would it be be a good idea for Congress to give it the authority. Think there are many who believe that it has the authority but it's a close call and it might be better for the Congress to signal that. But we think the FDA should be doing this and that should be resolved. Because we think it is in the benefit of patients that a clear system be set up for people who desperately need these drugs can get it and we do do everything possible it's just those patients that get that.

Subject that physician in this country have a right to prescribe as they see fit so we have to strike those balances. It's worthwhile putting in that space.

>> Now with basic research it is a economic proposition to develop an antibiotic.

We attend to the question of commercial development. We tried to analyze what is the economics of antibiotic development look like. And it's not pretty. It's not an accident that there's hundreds and hundreds, perhaps a thousand agents for cancer in development take it in pipelines. Cancer, while it's there has been a lot of progress it's a chronic condition, and it's a condition where for a variety of reasons the reimbursements have gotten to levels of sometimes $100,000 for a course of treatment.

And effective antibiotic should clear an infection in two weeks.

It's really not intended to be a chronic treatment. And the idea of paying $100,000 for that is just -- but when you think about an investor either at a large investor at a pharmaceutical company scratching their head saying which which one should I invest in, and they say there are a lot of risks around developing this antibiotic, if I succeed it's not such an attractive proposition economically maybe I should allocate my capital elsewhere. We do rely on a market and in order to rely on a market things have to be attractive economic propositions.

So we spend a bunch of time trying to think about what are the ways around there. Well you've either got to decrease the cost tore increase the incent people in this market you can decrease the cost in a number of ways you can do it in push mechanisms or pull mechanisms. Push mechanisms provide good cofunding for projects.

BARTA the agency BARTA have done this for example with agents to -- bio trrt effects it would be worthwhile to take on projects for serious by oyct conditions, and this will cost money of course.

It could dangle market commitments saying if you develop this we'll guarantee that there will be a market for it, so you don't have to worry about that, that's another approach.

There are still other approaches you could take. CMS could, in theory, although it would probably rir legislation, say we're going to pay a lot more for antibiotics that do X and Y. Is another way.

There are linkage mechanisms involving lump sum payments, and if you want a totally market based solution you could simply have tradable vow chers. Anybody who produces an antibiotic that meets this critical public need defined in some way, gets a voucher that they could trade to some other thean that they could trade to some other company to extend the patent life on some other drug

We're mindful that somebody is going to pay for that. Whether it's gooding to come through the federal budget whether it's going to come indirectly through tradable vouchers whether it's going to come through insurers. I think it's a fund amount theorem that one is not going to be able to incent new commercial development without putting some money on the table.

I think that's a basic law of economics, here. This is a partially public good we're talking about, and as a public, we must partially pay for it. Now, there will be economic benefits to themakers of these drugs, and they should be coinvesting with it, and we've got to strike that balance. We've laid out a number of options we've suggested what these things might cost. And I think PCAST has not said that we have done a deep enough analysis to say what's the right choice economically, what's the right choice commercially, what's the right choice politically. Because what would be politically feasible is an important part of this equation, too.

We tried to scope out the problem here, and there's just no doubt without attention to the economic incentives we're not going to see major investments in new antibiotics, enough to produce the numbers that we want to replace the loss.

Finally, stewardship. And I realize -- tell me when we're going here -- we're doing okay. Doing fine.

Stewardship. Two areas of stewardship, health care. Well, there are best practices for stewardship of antibiotics, making sure that they're used in the right cases, that they just don't get prescribed willy-nilly, somebody comes in, and they might have a bacterial infection, they might not, and why don't we give them antibiotics because they're cheap is not a good solution anymore. We really need to know who should be getting these antibiotics, and when they get them, they should be used for the right amount of time so as not to produce antibiotic resistance. There's a whole set to have guidelines that are implemented in a number of institutions are for high quality antibiotic stewardship.

It is time to use the levers that the federal government has to promote complete adoption of those stewardship principles. Some of the best levers we have are at CMS, the centers for Medicare and Medicaid. They have an ability to set requirements for reimbursements or for more or less reimbursement, and that's used in certain cases, and we believe that having an antibiotic stewardship program is a reasonable expectation. Having certain reporting, the physicians quality report system, is a reasonable expectation. And we lay out a set of expectations that can be, yeah, I'm going to say imposed. But the truth is everybody knows this is the right thing to do, and they're not that hard to do. This isn't that hard. This is a question of rationing is all up to what are the best practices for antibiotic stewardship. And we know this works, and we know this promotes the health of the individual patient.

This isn't just, quote, just for the benefit of the population, although that's a pretty big benefit, it is shown through many studies that these antibiotics stewardship measures on the whole benefit the individual patient. So there are tradeoffs here. There's just no reason not to be doing good antibiotic stewardship.

The federal government itself should practice what it preaches and lead by example, by applying this in its own health care facilities. And also, where the federal government gives grants, the federal government should be attaching conditions around this for grants related to health care, for example, in various communities settings there should be an expectation. It ought to be universal expectations we are practicing. High quality stewardship.

All this stewardship will be aided by better and better diagnostics. flt doc in her office is able to know rapidly whether this is a bacterial infection and whether it's resistant infection she's going to be able to prescribe correctly.

But that means we need a really rapid, really cheap diagnostic speed being available. That's great progress, in hospitals now there are pretty impressive technologies that can turn around answers in a couple of hours for a number of things and we're ven curjd by that.

We think this is a great place where the federal government including the hich nism ought to be hanging prizes out there prizes for companies and innovators to be able to develop rapid diagnostic technologies that will actually shift clinical behavior, shift clinical treatment.

Totally by accident, we found after we wrote this in this report, and socialized this to find that the United Kingdom has reached the same conclusion and decided for its famous longitude prize it has just announced they're picking the same topic. I think it's not an accident that the US and KC that the diagnostics would have a bigger impact.

Finally there's animal agriculture. I admit up front this is a very controversial subject and we've heard a lot about it. I'm going to make some statements about it and there will probably be people who disagree with me about these statements, but I'm going to tell you what we've done is tried to read the literature closely and understand the literature as best we can. We -- you know, we don't always sit down and read primary papers, but we did sit down and read primary paims.

So -- on objectionable things, you can use antibiotics 80 where in health care culture you develop a antibiotic resistant bacteria. If you use it in human culture you develop antibiotic in animals I don't think that's an objectionable statement at all can that antibiotic resistance transfer to humans? Yes ne can, they do sometimes transfer, there's clear documentation that there is such exchange.

Where we are truly unclear is how much of the problem can be attributed to agriculture. I think there's very serious concerns, we share very serious concerns, that it can be a very important reservoir. But if you ask can we pin down all of that transfer, most of the scientific literature until recently has been indirect and correlational.

In the last several years with the able to sequence genomes you can actually see because of all the little genetic bread crumbs scattered up and down the genomes that things are going back and forth but it's still a limited number of such papers. So I think it's fair to say that over the next several years we're expecting to see an awful lot more data like that. But it's clear it does happen in agriculture, it can transfer, and I don't think we're in a position ourselves to take a position on how much of the total problem it accounts for, even how to think about that question.

It still means we have to act. The things I've stated alone are enough of a reason to be acting. And I think everybody -- and I'm impressed with the people we've talked to in agriculture feel strongly that they have to be highly responsible. That judicious use in agriculture right now is absolutely essential. There may come a point where one will say it's justified to say no use. But a very important stem the FDA has taken is a set of guidances it has issued where the FDA has done something very interesting.

There's a voluntary part and a mandatory part. The voluntary part is companies that make antibiotics for agriculture are asked voly, would they please withdraw from the label the claim that those antibiotics can be used for growth promotion in animals.

You could worry that because that was just voluntary it wouldn't happen. But as of today 26 out of 27 companies said they would withdraw those claims. Once those claims are withdrawn it is no longer voluntary. It is then illegal to use those antibiotics for growth promotion.

We ought to see a decrease as a consequence of tha it must come under the care of a veterinarian and be used for either disease prevention or disease treatment. Now, we are very aware of there are people who are concerned that disease prevention could be a big loophole. You might say we're going to suddenly want to use the same antibiotics and just say we're using them for disease prevention. I don't want to cast aspersions because I think veterinarians will be responsible -- are responsible people here, and I don't think they will do that. But that's something we're going to have to monitor. If we don't see a decrease in use of antibiotics when one of these major uses, growth promotion, has been now -- will be withdrawn, then that's a pretty serious signal.

And we support the FDA's path, and we support monitoring of this, careful monitoring of this. And if in fact, you know, one does not see a response one will need to take further actions on it. But I'm being straightforward and I'm expecting that what we'll say -- you know, there are folks who probably will be unhappy because they would like to go further and folks unhappy because they'd like to go less far, and I'm telling you this is at least -- I'm trying to read carefully -- I've got to thank all the people who wrote to us this is where we're coming out it's important to move down the path here.

I think the details are in the report.

Finally, international cooperation we run toward the end of our time, I'm going to say simply this is a topic of eenormous interest across the world, and we can't do this alone. And we call for international cooperation on these topics. We can't do this without the World Health Organization and the U.S. has been playing a leadership role here in the World Health Organization has recently announced an international agenda and we should coordinating wi. I've gone on long because it's an important topic I realize I haven't gone into enough details to say specific things, I'll ask people to await the report's release because I didn't have time to go into more details but I'm going to stop, and my partner Chris chib a if he would like to add anything then I'll ask if there are questions.

>> Christopher Chyba: I think there's very little I want to add to Eric's remarks, as he said this is an issue that has been brewing for a very long time and yet there's a feeling I think in the infectious disease community that it's approaching a crisis.

And that means that -- that in part, our report has to focus on immediate steps, that in the short term can help mitigate the challenge that we face. But as josh yeah letterberg pointed out 15 years ago, and Eric has done a very nice job reiterating, this isn't some kind of conflict that can be won rftion our relationship with microbes is a relationship that has to be managed forever. And therefore -- and this is I think the strength of the report -- we also need to be thinking about steps we take in the medium and long-term, that will manage that relationship in a more effective way than we have done to present.

And I believe you will find, I believe you have found, that in many of the sections of the report you'll see immediate steps that need to be taken, and then you'll see ground work being laid, whether it's in fundamental research, whether it's in calls for certain type of development, that for managing that relationship in the long term. And in particular, I think in terms of the managing the relationship situational awareness is especially important, and that has to do with surveillance, traditional public health surveillance, and also the opportunity that we have now to establish DNA -- rigorous DNA based surveillance on a national scale.

And also, data collection. So we can understand better than we do currently, the effect of steps we are taking and steps that we will take in the future.

And finally, I'll reiterate Eric's comments about how this is an a fundamentally international problem, this entire problem exists in an international context. Diseases cross borders with ease. The good news there is that the World Health Organization has recently -- is recently putting in place a global action plan. And the United States has a global health security agenda which would help fund the financial resources to make international steps possible.

It is very much to our advantage, and this is true not only for fundamental moral reasons but also for national self-interest reasons, to address as much of this problem overseas as we can, in addition to addressing it within our own country.

That's all I have to say.

>> John Holdren:

>>
>> ERIC: Let's throw it open to questions from PCAST. Susan.

>> I want to check my understanding of some of the things you just said. When you wrou a new antibiotic, the role of surveillance is to detect the resistance, and presumeably, as those techniques improve, we're scofrg resistance -- or more broadly, knowing that there's residence, faster than we did in the past.

>> Eric Lander: We're knowing about its spread particularly I think that's often -- some resistance problem has been browing and exploding on us and we could know that a lot faster but we could also know where it's coming from.

Hospitals want to do the right thing they could know it's spread within their own institution for example. That's very powerful knowledge.

>> Susan Graham: So country terg that is stewardship which extends the --

>> Eric Lander: Life.

>> Susan Graham: Lifetime of an antibiotic.

>> Useful Life tism exactly.

>> Susan Graham: What I'm trying to understand is the balance there and if we were to attempt to project into the future, which side is going to dominate.

>> Eric Lander: Look, stewardship is critical because once you put all this work into getting an antibiotic if you could get four decades out of it rather than two decades out of it that would be great. Sometimes we're seeing antibiotic resistance skyrocket much earlier. So the stewardship is critical. But how would you know it's working well, how do you know what to be prepared for in the future without surveillance. So they're both components.

Surveillance will help your practice in many ways so I think they're two parts of the same equation there, of good management of the antibiotics we have, while on the other hand we make sure we develop new ones. Chris castle.

>> Christine Cassel: Thanks ERBG my congratulations to Eric, my congratulations to both you and Chris on masterful and really thorough look at the literature about this.

I just want to -- this is not really I think in the report yet, but to add to the definition of stewardship in two ways. One is we think of stewardship as not prescribing antibiotics unnecessarily. But there's another kind of stewardship, which is reducing the risk of infection so the person doesn't need the antibiotic.

And there's a kind of a math effect that can occur if we think about American hospitals I'm putting in -- with systems engineering.

>> Yes.

>> Medicare and Medicaid particularly the innovation center programs have incentives in place now under the partnership for patients and other kinds of things, to reduce hospital acquired infections, which is where some of the more dangerous ones are.

And we learned that just in the last year that's down 10 percent. You may say 10 percent isn't a lot, 10 percent is half a million adverse events, and 15,000 lives. Not to mention lots of dollars, but also lots of avoided need for antibiotics in the first place. And for exposing those bacteria to more antibiotics.

So I think there's a way in which looking at the prevention of infection is an important thing. And then the other thing I wanted to say, which particularly on behalf of my physician colleagues, is that particularly in the ambulatory setting if there is a -- there has to be a partnership with the consumer and the patient.

>> Eric Lander: Yeah.

>> Christine Cassel: Because patients sometimes instantly and mistakenly think I'm not getting good care if I don't get an antibiotic when I go to the doctor. So there needs to be a whole community effort about educating people about actually that's not the case, and sometimes your doctor is exactly right when they're telling you that you don't really need an antibiotic, and call me you know in three days if this doesn't get better kind of thing.

>> Eric Lander: Yeah.

>> We just need more understanding of that.

>> Eric Lander: We do. There are risks in prescribing antibiotics, and your point about infection control inspired us. There is a condition of participation in CMS for infection control. You have to have an infection control program. So we're think antibiotic stewardship should follow behind it.

I've got Bill, Joe, and Jim, and we'll come to the end of our time, I think.

>> William Press: Thanks, Eric. I think this is a terrific report, and I particularly liked the rational and dispassionate way that it looked at the agriculture question, because that's a question that attracts a lot of heat.

I think sometimes the heat is just from communities that aren't really talking to each other, or aren't communicating well enough. I wonder if you could just say a little bit procedurally about how you made contact with those communities, were you able to bring them together around the same table, how did you reach the conclusions that you reached?

>> Eric Lander: Well I must say within the working group we assembled, we had people from agriculture, people who work for big agriculture companies, and people who are are passion sdealt from the public health community, and there is quite a diversity of use.

This is a PCAST report but it's informed by the whole working group. So as we sought people's views, as we asked people to point us to literature we then asked everyone to critique the literature that was being cited in all directions.

And then as it became known through the mechanism of our having PCAST meetings and reporting on it, we received a very large number of emails from people. And the scientific public at large wrote with many, many different suggestions and studies, and we put those in front of the working group we had and said what do you make of these.

And then after we collected all of that input that had been received, we sat down ourselves and read all the papers. And so I fully understand the passions on all sides of the question. And I think we feel passionate about it, we'd like more data on some things, but we also recognize that there are actions that have to be taken, given the data we have.

So it was a really great learning experience for us. And at least in that conversation, it was very respectful conversation because it was about the science. I think there are many people within agriculture who want to use antibiotics jurksly who would be thrilled if they didn't have to use antibiotics I thrink there are people who feel there is too much use of it not to justify the risks, and I think we're on a path right now but I hope it's a path that gets us to the right place.

And I think this is a good place where having the discussion focused on the science was the right thing to do.

>> John Holdren: Joe.

>> I have a question

>> John Holdren: The honorable Dr. Johann sen.

>> I have a question, the last thing Dan said as we were coming into the room, more economics work, if people eat or broccoli there will more broccoli produced. It seems like that that failed with antibiotics, why didn't the price go up because people are dying?

It's very immediate it's like cancer except quicker, they need drugs, their families want them to have drugs, yp haven't the prices gone up and just made it more of an incentive? And sit different from broccoli, Dan?

>> Well we take refuge in the report hat president's advisers Fon technology, and theue should be answered by the if financial advisers when you think about unsirnt plays a very big role here knowing you're going to have a market, you need a very risk premium. Not having very many precedented cases. You can say I'm going to try to get $100,000 for antibiotic but there's period when nobody was sure they would see those reimbursements in cancer.

When you saw precedent in cancer -- not saying that's a good or bad thing, treatments are so expensive but I know it have produced a tremendous amount of interest in producing treatments. There's not a precedented path right now that says that's going to solve that. Moreover there's a bit of ca catch 22 here. If you've got a lot of money for it, you probably want to promote the broad use of those antibiotics so you'd get more money.

We actually don't want those antibiotics to be used broadly. In a certain sense the optimal world is to have those antibiotics and have them be used jurksly. That's a very perverse incentive for the manufacturer. So for a lot of reasons I don't think we have a perfectly functioning market, because here we have an Exeter nalty your use of an antibiotic screws up Mario's use later because you're contributing to -- through your use you're creating an expernlty of resistance.

So situations like that markets can fail.

>> I beg to differ with that -- honorable --
>> Sorry not Jo's use of the antibiotic but someone's judicious and less honorable. It's a complicated thing, it might be the economics of why people would do, and we talked to people at length in the industry as well, about this we voffled some of them in the working group.

And they walked us thu and we compared to other people's analysis of the economics. You know, there's just a big premium to pay to come into it. And some of what government cosponsorship can do is erase that premium and set it back to the right level.

Finally, Jim gates I see the last flag up.

>> S. James Gates: Thank you, first of all congratulations to Chris and all of you in the group this is a fabulous report and I'm confident that it's going to meet with the full approval of this group.

As I was reading the report, and practices I missed this, I want the answer to a question,

In an article I guess let's see in March one of our colleagues said that physics isn't sexy but everybody looks up.

Meaning that one of the reason that astronomy gets so well supported is because everybody can relate to it.

So when we sort of bring this issue over to AMR, is there some -- and in particular, the philanthropic community has in recent times become a remarkable source of funding for science. So the thing that I didn't see in the report was our kind of reaching out in that direction, saying there are other resources that could perhaps be brought to this problem. And as I said if it's there I missed it and I apologize.

But my question is can we make AMR sexy in the way that some of these other diseases are and generate community interest

>> Eric Lander: Things like the gates foundation take these things very seriously and puts significant funding behind it and there are other organizations as well that take the antibiotic question pretty seriously. But is it sexy.

I think it isn't yet, because the way it arises, is a patient comes into the hospital, gets something, it's not a sexy thing, and I think -- I don't know which presidential council has expertise on sexiness, it's probably not us. But -- in any case. (Laughter)

It is a worthy question to ask about how to get more public attention on this question.

So I realize we're at the end of our time. And I want to first thank the people who are involved in the report, and then I'm going to turn to John, who I think will ask for a vote on this. The members of PCAST who were involved in this, men's of the working group but I also want to thank the two people played a erole in this, Ashley, and Stanley who is down from Boston here for the public session to thank them for putting us through inum rabble have drafts of this thing I'm turning it over to John.

>> John Holdren: Thank you and Chris chib a for cochairing this session, let me now ask for a show of hands from PCAST members all of those in favor of approving this report contingent on the usual final edits please raise your hand. All those opposed? Abstentions? Seeing none, the report is approved with the usual condition of further edits.

>> Eric Lander: Great and I am sure there are people in the press who will say, can I get a copy in advance of the edits. And I'm going to apologize in advance we have to get it properly edited but the public release we'll have availability by phone to talk to people by phone about details.

>> Thank you.

>> John Holdren: Good w that we are going to take a 10 minute coffee break, or maybe 12, be back here five minutes later than scheduled, 10 minutes to 11:00 promptly, please, and in the meantime happy coffee.

(Break.)