

**TEXT OF SPEECH OF**

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I want to say we're very excited about not only your being here and participating with us, but learning from you about this senior leadership program that you're having because we're looking into some of the whole issues about leadership training ourselves as well. And, one thing I want to say before I go in to my official presentation is I think there are going to be real opportunities for us to enhance the collaboration between our organizations. Certainly for those of us who are co-located down here. There's, you know, a lake with a nice trail around it, and there are certainly opportunities as we offer leadership and management training opportunities to our staff that they can be jointly sponsored and jointly participated in by some of our people. I think it's a real opportunity that we have only begun to take advantage of.

So what I want to do today is just briefly talk about how we can, who we are, and then some opportunities for us to work together, more closely in the future.

So, you all know something about us. You know

that we're here, and for one thing that makes us very unique compared to all the other NIH Institutes, which are all located in Bethesda or the greater Washington D.C. area. There are 27 institutes and centers.

Another of the things that makes us unique is that, unlike the rest of HHS that essentially gets all of their funding from the Health and Labor committees, we get some of our funding from the Superfund, from the Environment and Energy committee. Which makes it a little different and, very honestly, sometimes when NIH goes up to the hill to talk about appropriations, they forget about us, or they forget about that part of our program, which actually funds Superfund.

We also have, are the home for the national toxicology program which I'll talk about in more detail later, which is a cross agency program, and involves FDA and CDC. And EPA serves as a critical member or members of our executive board, which provides overall leadership and guidance to the NTP as well.

Our mission, as distinct from the mission, for example of EPA, is basic research not regulation. So, much of the work that we do may be useful for decision making when it comes to regulatory decision making, but that is not the goal of the work that we do. Our goal, again, is largely basic research directed. And I'll talk

more about the Superfund program where we do both the fund research and the worker training, which is actually funded through the Energy Appropriation, and I'll talk some more about the different kinds of programs we have.

And one thing that I want to make is that, our commitment is translating Ben's science in to environmental public health. So while for much of NIH, when you talk about translation, you're talking about bench to bedside. That's part of what we do, and you had the opportunity to tour our new clinical research unit today, for which Darryl Zeldin is the acting director.

But, environmental health is really an issue with public health. So, in many ways, our mission is public health. So when we talk about translation, we're talking about translating bench to public health. Now, sometimes the bench to public health also involves going through policy. So it's often bench to policy to public health or an interactive function. Again, something that makes us rather unique compared to many of the components of NIH.

So I wanted to talk about our different divisions of our institute. Our intramural research is the one that I think many of the people in EPA think about and know the most about because that's what's located here across the lake from EPA's research facilities. And here

we are looking both at basic applied and epidemiological research to understand the biological consequences of environmental exposures. We have a highly interactive and interdisciplinary group here. And the mission of NIH's intramural programs, in some ways in contrast to their extramural programs, is to do high risk, long term research. Things that would be very difficult to get funded in a grant proposal, or things that take too long, that they're not -- they can't be accomplished in a two or a three or a four year grant approach. So, again the focus of intramural research is supposed to be high risk, and then, potentially high payoff research.

We have, at the moment, twelve laboratories and branches and we're working in a number of different areas. So I wanted to just give you an example of a study that's going on right now in the clinical research unit, which is the environmental polymorphism registry. In this we're going to be recruiting about 15,000 subjects, maybe as many as 20,000 of people living in central North Carolina. And we're trying to GIS code where they all come from so we can have opportunities for some environmental information. We are having a very diverse population here. I mean we live in an area with a lot of racial and ethnic diversity and so we are actually actively recruiting to make sure that we have extensive minority

involvement, and we're getting both DNA and personal information.

Now, at the same point we're screening the DNA here, for genotypes of interest. So that we're hopeful that we're going to be able to also recruit subjects who have certain kinds of health characteristics, certain kinds of phenotypic studies and relate that to their genotype and this will enable us to look at gene environmental actions, between -- with the phenotypes of interest. And in some ways, this study has some potentials to be kind of an adult counterpart in some way to the National Children's Studies, which is a partnership that we are involved in with EPA, as well as National Institute of Child Health and Development in CDC.

So far, we've got at least 25 investigators who are involved in this effort. We are focusing so far in at least 110 different environmental response genes. We're genotyping some of the functional snips here, and we're beginning the phenotype in studies this year. This study has the potential to provide a great deal of information. We consented all of the subjects so that -- when you do human studies you have to get informed consent and you have to make sure that you do this properly with attention to protection of human research subjects, but all these subjects were consented with the ability for us to go back

and ask them more questions, go back and take more samples from them if they are willing to participate again. We made sure that that was in the original contact with them.

So, I want to switch a little bit and talk about our extramural program here. Now like in any NIH institute, the extramural program is the majority of the budget. So, our extramural program, our grants program, what Gwen Collman, Interim Director, is in charge of, is close to a 400 million dollar a year program. And this is largely involved, again, with investigator initiator research grants and a small number of contracts and cooperative agreements, but it's largely grants.

And some of the areas in which we focus, are for example, the Children's Environmental Health Centers which are co-done with EPA. And this over all has been a great success story. We've just gone out and the funding is in progress, I believe, for the second round of these studies with EPA. Some of these have taken a little bit longer than we would have all hoped to have. There are a couple of centers that may be funded just by EPA or just by NIEHS, but in general, I think it is an example of cooperation that we would like to build upon. And I know Gwen has been talking to Bill Sanders and people in his group to try to lead to additional opportunities there.

We've also been involved, for example in the

Centers for Oceans and Human Health. And these are centers that this year we were able to keep them going because of the stimulus package, but we're planning to go out for 2011 to keep this effort going since health of the oceans is a major initiative of the Obama Administration. But these efforts were co-funded with the National Science Foundation. So again, the idea that we're interested in partnering with different federal partners as possible.

We have a lot of interest in the whole, and I think we all do, in the growing epidemic of obesity in this country, which has environmental components. We know that certain early life exposures can lead to increased propensity for obesity later on. But we also know that obesity can be related to the built environment. You know, when all of us walk out of the door, right to our parked car, get in our car, drive to work, walk in the office, don't exercise, buy, you know, stop at McDonalds on the way in to have our fast food, that doesn't help our health as well. So we have some efforts looking at relationship there.

Autism is a major issue for us. I serve on the Interagency Autism Coordinating Committee, which was a Congressionally-mandated effort, which involves not only scientist, but advocates as well in the autism community. And it's been kind of, a little bit of a hard sell with

some of my fellow scientists to make them understand that Autism is more than just a genetic condition, but in fact, that there are environmental triggers or environmental progressors of autism. And what we're beginning to understand with autism is that whatever is triggering Autism is occurring very, very early because we used to say that you could identify children with Autism Spectrum Disorder at two years of age. Well, that age keeps dropping and now we're being able to, in certain cases, identify children as early as three months of age, or at least, begin to watch certain children with certain concerns. We know that, for example that there is a genetic component to autism. We know that if you had one child with autism or if you have a family history of Autism Spectrum Disorder, there is an increased risk that some -- another child in your family.

So we have a number of large epidemiology studies going on through our extramural program looking at these relationships. And we've just started recruiting 1,200 women, 1,200 mothers across the country who already have one autistic child, but are planning to have other children. And we are going to be following longitudinally these women and their families getting extensive, not only medical and biological histories, but environmental sampling, for example, as well, with the hope that this

will help elucidate some environmental triggers that are associated with autism. And we've got many, many other kinds of projects and programs going on in the extramural program.

So one of the things I wanted to talk about is the genes environment and health initiative which is a major cross NIH effort that we co-lead with the National Human Genome Research Institute. And there were two major parts of this. There's the exposure biology program and there's the human genetics program. Again, so we are the leads for the exposure biology program. And here we're looking at exposures, not only environmental chemical exposures but things like activity, things like, for example, a diet, things like psycho-social stress and addictive substances, as well.

And there are two parts to this exposure biology program. One is developing sensors for environmental exposures. So we all know that if you want to measure PM or certain VOCs, EPA has done a great job of developing backpacks that you can wear that will measure some of these things. It's a little hard to put a ten-pound backpack on a child, and many people find backpacks for example, difficult or obtrusive. So some of the efforts we've have here is, being developed very small, for example, deck of cards size kind of monitors that people

could wear. We have one that's been developed that picks up 40 different VOC's, for example.

In addition, there are necklaces that are being developed, that have in the necklace something, as you move, the necklace will record your activity. We have other things, for example, using cell phones to do dietary recall and -- or dietary measurements, what your eating. So, different kinds of approaches.

The other part of the exposure biology is not really looking at the issue of body burdens; that's something that CDC is focusing on with their national report card. But we're working at early markers of response. And again, trying to develop rapid and sensitive approaches to understand whether a biological response has been turned on.

Under the genetics part of the program that is lead by the Human Genome Institute, we're doing a lot of work here looking at things like G-WAH Studies, the deep sequencing of the entire genome, analyzing the data, trying to get extensive sequencing information and so on. And we're just at the point of starting to try to link these things together. Can we, for example from understanding exposures, can we find associations with certain genetic or, and I would argue, epigenetic changes as we go forward?

Breast cancer and the environment is another major extramural effort that we have. And this program is co-run with the National Cancer Institute. And in this case, we're trying to define how environmental agents affect the lifelong risk of breast cancer. Now this program has been in effect already for, I guess, six and a half years and we've just gone out with a re-competition to continue it for at least another five years. And at this point, the objective here is to identify potential windows of susceptibility, imply the genes in the environment, approaches where we're directly measuring exposure, diet, looking at the genetic polymorphism. We're trying to compare the animal models with people. We're also working very closely with the communities and developing educational messages to help informed lifestyle choices.

So some of the unique things about this breast cancer and the environment program is that in all the centers there are, basically -- they have to have, basically, three parts. They have to have a basic biology part. They have to have a human part, which involves both clinical and epidemiological studies. In fact, we recruited young girls starting at the age of seven, and these girls are being followed as they go through puberty with extensive biological and environmental sampling being

taken along the progress. And there has to be the community action part.

So that, in many of our, whether it's our children's centers or our breast cancer centers or where I talk about our partnerships in environmental public health, we require the involvement of community groups. Because the only way for us to do studies appropriately is get the communities involved, find out what concerns them, find out how they think they need to be approached. Otherwise, frankly, it's very hard to recruit subjects and get the information appropriately, so we have this very active program.

So I just mentioned the partnerships in environmental public health. And this is our umbrella program which incorporates all of our outreach efforts to community groups, whether it's environmental justice, whether it's the breast cancer groups, whether it's our core centers and the groups, for example, within there. But we're trying to strategically coordinate and integrate the initiatives that we have to involve the communities and science as in environmental public health research.

And we're really, part of the efforts here, is how do we communicate to people better? We all know risk communication, not only is it very difficult to do it appropriately, but it's really a science that needs some

more input. So we're trying to help improve that science. And we're trying to create and provide materials which increase our awareness and literacy of environmental health risks. And again, we're all in the advancing environmental public health.

Now, I want to switch and talk a little bit of Superfund program, which again, is part of our extramural effort. Again, funding coming from a different place than everything else. But this is really two parts. We have the Superfund research program. And the objective of that program is to detect hazardous substances in the environment, to look at the potential risk of those substances in human health, and to develop basic biological chemical and physical methods to reduce the toxicity of hazardous science, substances. This is the program, which actually has an application. This is where we were trying to solve problems. This is where we are working with EPA very closely to try to find out what are your issues that are given Superfund site. What are your concerns?

We've been very successful at working with the regional Superfund risk managers. The Office Solid Waste and Emergency Response (OSWER) or Office of Superfund Remediation and Technology Innovation (OSRTI) seems to be a little less knowledgeable about how the work that we're

doing under this program has actually informed the decision making that has gone on at some of their Superfund sites. And we're working very hard to try to improve that, but we've actually done technology development. Sometimes coming up with very, very simple technology, like if you want to keep down the amount of metal dust at an abandoned mine site from being distributed by the winds, you plant some appropriate ground cover and that will help keep the metal down. So that's, for example, been a very simple success story.

The other -- and that, the Superfund research program is about a 50 million dollar program. Our worker training program is about a 30 million dollar program. And in the worker training program, we've trained over two million workers over the last 20 years to do hazardous waste cleanup of an emergency response across the country. So, for example, you know, there was that horrendous tidal wave that hit Samoa last summer. We had just, actually, sent -- a team had actually been there training the chiefs in June. And I think that might have helped reduce the loss of life in that area because people were prepared to deal with an emergency.

So, again this is a grants program where we create state-of-the-art training materials; actually, they train different handlers and responders and waste cleanup

workers. And it's integrated with the National Response, we work very closely again with parts of EPA, parts of OSHA, other organizations here, as well as, for example, the labor unions. For example, the International Union of Fire Fighters. So again, the relationship here between the NIH Superfund program is integrated with EPA, and I already mentioned that, and also with ATSDR, as well.

So how do we protect the health of people living near Superfund sites? We're working on defining the biological mechanisms, we have actually developed mediation tools and we train our workers.

We're currently in the process of developing or updating the strategic plan for Superfund. We're trying to achieve a better understand of the route of exposure, the effects and the prevention so that we can help contribute to reducing uncertainty of risk, and help decision making.

Now I want to switch briefly to talk about the National Toxicology program, which I also already mentioned, is an interagency program. This was established by Secretary of Health and Welfare back in 1978, Joe Califano, to coordinated toxicology research, actually across the federal government and it was headquartered here at NIEHS. We conduct research on many nominations, we've tested thousands of different agents in

different kinds of toxicology studies, and we communicate the results through technical publications and peer-reviewed papers and so on, and we also conduct a lot of analysis activities. For example, we are legislatively mandated to report, to prepare something called a report on carcinogens where we actually list what chemicals are known to be human carcinogens, what chemicals are likely to be human carcinogens. Things that are not known or likely are not listed. We are currently working, hoping to get out this year the 12th report on carcinogens.

We also have, for example, the Center for the Evaluation of Risked Human Reproduction known as CERHR. This program is currently under some evaluation. This is the group for example that did the evaluation of thylates a number of years ago, about a year and half ago released a report on BPA, which has had a major effect demonstrating some concern for a number of health effects at BPA. But we're realizing that there are more things than just reproductive and developmental health that we're concerned about, and so we are going to be expanding the scope of some of the reviews that we do there.

We are also the home for ICVAM which is the Interagency Committee for the Validation of Alternative Test Methods. ICVAM really doesn't validate; it evaluates and, in fact, this is a 15 -- it's a committee composed of

representatives from 15 different government agencies, each agency has one representative on the central committee. And NICEATM is, is our group that basically shepherds the ICVAM process through. We have actually evaluated -- ICVAM has evaluated over 27 different alternative tests, several of which are now being used by different regulatory agencies.

So, as a briefly said before that, you know, NIH, CDC, and FDA are the agencies that make up the National Toxicology Program, and largely it's NIEHS and its NIOSH as the part of CDC, although there is a lot of work with NCEH as well, and it's largely NCTR as FDA, although again, there is a lot of work going on with other parts of FDA as well.

So, so there are some new and renewed areas of emphasis for the NTP. Again, we're trying to improve the coordination across the federal government. We're working on developing new methods for efficient toxicological assessments. We're increasing the understanding of exposure response relationships and issues of dosimetry.

Another thing is we are trying to integrate the results from data rich techniques with a traditional tox data. And we are very involved with EPA and with the National Human Genome Research Institute with tox 21. Much of this was in response to the NRC report of 2007,

the need to move in to more high throughput kinds of screening. The NCCT program and ToxCast is part of this tox 21 effort. This involves high throughput robotic testing. So far there are at least four hundred different assays which are being run. There are over a thousand chemicals that have already been run through. The data is starting to be analyzed. We're expected to run through over ten thousand different compounds. I think what we're going to get out of this testing is at this point of this rapid screening is not definitive answers about how toxic and what are the doses related, but it is going to help prioritize the needs for further testing with certain chemicals.

So there's kind of a conceptual shift going on for environmental health sciences. The old approach is that chemicals act by overwhelming the body's defenses by brute force at very high exposure doses. The newer approaches I would say is that chemicals can act like hormones and drugs and disrupt the control of development and function at low doses to which the average person is exposed. We're redefining what we mean by low dose. I mean, when I talk about low dose, I talk about a dose that relevant for what is in people. That's to me is the definition of a low dose.

We also are focusing on sensitive windows of

exposure. You know, I have to say that NTP may have the two-year gold standard bioassay by taking, you know, adult animals and exposing them for two years and asking whether it causes cancer. What we've missed the critical windows. The most critical times of during development. So in fact, NTP is now -- has now begun that all of our rat studies are starting with parinatal exposure. So, that in fact, we capture those sensitive windows. And then we're also looking at the developmental basis of chronic disease, and this we believe is related to the whole epigenetics area.

There is a problem that makes all of this difficult. Almost all of our work in the past has focused on a single agent exposure. Nobody is exposed to a single agent. Nobody is unexposed. There is no such thing as a real control. It's very hard to know how many agents are going to influence the effects of a given exposure. And that's true both in space and time. So, concurrent exposure can cause one response, sequential exposure can result in another kind of response. And we have to begin to try to link exposure and disease based upon multiple exposures, which not only include environmental chemicals, but involve, for example, diet. We now know, for example, that a fatty diet completely can lead to a completely different response than a healthy diet.

We're looking at things like nanosafety and the whole issue of nano-materials. I mean, industry and medicine haven't waited. You know we're all -- if you're a woman you're busy smearing nano-particles on your face every morning with your cosmetics. We're busy putting nano-sunscreens on our kids every day. I know remediation at least for some drinking water, maybe not drinking water, but ground water is being used, you know, putting in zero fail on iron and other nano-materials to clean up iron. There are all kinds of medicines now that are actually being delivered as nano-particles. We know next to nothing about the safety of these nano-materials. We can make certain predictions, if we have nano particles that have reactive species on their surface. And in fact, and they are persistent. I certainly don't want to be around them very much. But we have a major effort, and some of this is coordinated through a cross agency task force, EPA has a major nano-effort, we have a major nano-effort, so did other parts of the federal government. But we are currently spending about, in FY 10, we are spending almost 30 million dollars on the issue of nanosafety research.

Another area that we are involved in and much of this is coordinated with EPA. In fact, we co-chair with EPA the new Global Change Research Program Health Effects

Committee which is under OSTP. And we have kind of taken the lead within NIH for the issues of climate change on health. We're working with Fogarty Center, heading a trans-NIH work group and we have lead an interagency group to develop a white paper which is looking at what are the health research needs related to climate change and, in fact, that's at the point of just about final sign off by multiple federal agencies including EPA has been extensively involved in developing this paper and getting out.

We've also had White House State held debriefings that we co-ran with EPA and we recently released a series of papers in Lancet which were really important because it was the first time that anybody focused on not how much is it going to cost to mitigate climate change, but we focused on what are the health benefits of mitigating climate change? You know, if we can get rid, or if we can reduce the amount of, you know, black carbon, if we can reduce the amount of ozone, we can have tremendous health benefits very quickly.

We are currently, we're working with Fogarty Center, we have some challenge grants under the stimulus package in this area and others, and we're continuing to integrate some of this with the effect of Ocean and Health.

So there has been a new vision in the past year for NIEHS and NTP. First of all, the strong desire to partner with our sister institutes and other federal agencies including EPA. Health and the environment is our priority. We're looking at new issues and new technologies. We realize that we need, not only the best individual science, but in many cases we need team science to address the complex diseases and complex environmental impacts, and we have to really continue to integrate across research disciplines and with all our partners. And whatever we do, we need to make sure that we communicate it so that it has an impact on human health protection. So thanks to all of you.

(End of audio)