7NIHUDPNEWS
Media Tele-Briefing

May 19, 2008
11:00 a.m. EST

Conference Facilitator: Good morning and welcome to the Undiagnosed Diseases Program press conference hosted by the National Institutes of Health. This press conference will last for 60 minutes.

There will be five primary speakers who will provide brief remarks, and then members of the media will be able to ask questions. To ask a question, you can press star and 1 on your touchtone phone to enter the queue. You may remove yourself from the queue at any time by simply pressing the pound key.

This call will be recorded, transcribed, and available on the Web sites of the NIH Office of Rare Diseases at rarediseases.info.nih.gov/undiagnosed, and the National Human Genome Research Institute at www.genome.gov.

Now it's my pleasure to turn the program over to your moderator, Larry Thompson, Chief of Communications at the National Human Genome Research Institute. Please continue.

Larry Thompson: Good morning everybody, this is Larry Thompson on behalf of the National Institutes of Health, Office of the Director, Office of Rare Diseases, the Clinical Center, and the National Human Genome Research Institute. I am

pleased to welcome you all to the news - all you news reporters who have joined us for this telebriefing. Additional material related to this announcement will be available on the Web sites of the Office of Rare Diseases and the National Human Genome Research Institute.

Our expert panel in the speaking order this morning will be the NIH Director, Dr. Elias Zerhouni, Dr. William Gahl, the Clinical Director of the National Human Genome Research Institute who will be managing this project or this program, Dr. Stephen Groft of the - who is the Director of the Office of Rare Diseases, and Dr. John Gallin, who is the Director of the NIH Clinical Center, which is the hospital here at NIH. And we have a speaker - a special speaker from the patient community, Amanda Young, who has been - had a difficult disease diagnosed here at the clinical center will be able to talk a little bit about what that experience is about.

But let me start by introducing Dr. Zerhouni who will give us some opening remarks. Dr. Zerhouni.

Elias Zerhouni: Thanks, Larry. I'm Elias Zerhouni, the Director of the National Institutes of Health based here in Bethesda, Maryland. I'm really pleased to help launch this great initiative of the Intramural Program of the NIH, and this will, in my view, could be very transformative because in my career as a physician, one of the observations I made over time is that physicians deal with about 6600 conditions and 6000 of these conditions are quite rare. And what I experienced in my life as a radiologist in practice is that often we were sent patients whose disease was undiagnosed. And so this problem is trying to address head on the issue of undiagnosed diseases - why is that.
First of all, many times what you will see is patients who have had a disease that was undiagnosed for years and yet the disease was known but rare, and therefore the skill set, if you will, that you would encounter in the community

would not be sufficient for a rapid diagnosis to be made. So you had a lot of anxiety, a lot of pain and suffering, and expenses that often were not necessary because the disease was already known.

So accessing a team of experts, as the experts we have here at NIH which is a unique combination -- there is no such combination around the world. We have over 1600 physicians all specialized in very, very - in great depth in the diseases that are of concern to them. So we thought that this would be a great advantage.

But then as science has evolved over the past few years, what has become quite obvious is that even common diseases have many subtypes. And what we are finding for example through the genomic research that we've done over the past few years is that even a common disease like diabetes, which is known today to have Type 1 and Type 2 – Type 1 for young children and Type 2, may actually - they have many, many different subtypes.

When I became NIH director, there was only one gene that was known to be involved in Type 2 diabetes. Today there are over 16 genes that we still do not understand - for example in diabetic patients why some respond well to treatment and some don't. So over time, I think what is emerging is this concept of personalized medicine where rare subtypes of a common disease also present a diagnostic challenge.

The third area where the NIH is - where we are interested is the emergence of new diseases. More and more, we are seeing in fact new manifestations of diseases, new causes for diseases, and diseases that are completely not understood at this point. So the idea of this program is to try to combine our many, many, many (main) years of knowledge here at the NIH and offer for the first time our combined, multi-disciplinary knowledge to launch this

Undiagnosed Disease Program here at the NIH to assist patients around the country and their doctors.

Because we believe that there is not only a service to be rendered, but also knowledge to be gained. And ultimately I think what we're facing right now is a complete change in the way medicine is going to be practiced. We're going to see patients earlier and earlier in the natural history of their disease, which makes it even more difficult to diagnose.

Children for example - sometimes it takes a year or two to find out what exactly ails a young child. That we cannot afford anymore because by the time the time has passed, damage has been done. We need to preempt disease and this is where I think we will learn how to do that in this new unit of the NIH comprising of the - combining all the institutes' skill sets will be critical to this effort.

It will really usher the new era of personalized medicine. And will help us understand what I think is happening and that is that we are now reclassifying the diseases as we know them as well as understanding the rare diseases that many out there do not yet understand because of the complexity of the science that is required to understand them. No team - very few teams in the world can put those skills together and this is really what we are announcing today. This is a transforming initiative; this is something that we hope will advance science, but also reinforce the role of the NIH over the years, which has always been not just the National Institutes of Health, but the national institute of hope for many patients whose disease is undiagnosed.

So with that, I will let my colleagues from these institutes and centers - let you tell - tell you more about this exciting new program. And I'll turn it over I think to Bill Gahl at this point.

William Gahl: Thank you very much, Dr. Zerhouni. That was very expository.

As the Clinical Director for the National Human Genome Research Institute and the Director of the Intramural Program of the Office of Rare Diseases, and an advisor for a number of the organizations that are concerned with rare genetic diseases, I've been long aware of the need for an undiagnosed diseases program here at the NIH. Besides providing hope and information for the individuals, this program offers unique opportunities for discovery into human diseases.

So here are a couple of quick points. As doctors, we feel compassion for patients who have been without hope because they are sick and no one has been able to help them. For some, this program will offer real hope and maybe even relief. But as Dr. Zerhouni said, this is a research program and we won't be able to help everyone who seeks our care. The program's principle mission is the discovery of new diseases and variations of known diseases and many patients apply to this program will present with either known illnesses or problems that no one here is studying. For that reason, we've established a fairly stringent referral process to ensure that we have a reasonable chance of helping the patients who do come to Bethesda.

So as with all studies at the NIH Clinical Center, the avenue for participation in this Undiagnosed Diseases Program begins with referral from a patient's health-care provider. Patients will not be seen on a walk-in basis. The participants have to be referred by a physician or another health-care provider such as a nurse practitioner or a physician’s assistant in their own community into whose care the patients will return after they are seen at the NIH.

The referring physician will have to provide a medical summary and medical tests that point to some clue about what might be wrong with the patient. For

example, the patient might have an abnormal lab test, a mysterious x-ray finding, or a collection of symptoms that don't usually occur together. Such clues will give the NIH physicians a direction in which to pursue a diagnosis. Then invitation to participate will be based ultimately on the medical judgment of a board of medical reviewers here at the NIH. That board will have the final say about who is accepted into the program.

And we'll start this initiative slowly. The program is prepared to accept one or two patients per week and as many as 100 patients during the course of a year. If a patient is selected following physician referral and medical board review, he or she will be invited to visit the NIH Clinical Center and will be offered enrollment in a study for medical evaluation. The patient will have to provide consent for these investigations, but the care is free for the patient and the NIH will pay for travel and lodging.

Patients in the program will be evaluated at the NIH's hospital, the NIH Clinical Center, in Bethesda, Maryland, usually for about a week using the clinical center's unique combination of scientific and medical expertise and resources.

Dozens of NIH's senior attending physicians will consult on these cases. Their specialties include rheumatology, immunology, oncology, mental health, nephrology, hematology, ophthalmology, laboratory medicine, neurology, pain and palliative care, bone disorders, endocrinology, dermatology, primary immunodeficiency, dentistry, genetics, pathology, pulmonology, cardiology, internal medicine, pediatrics, and hepatology. If a diagnosis is determined, some treatment options will be explored but may not always be available. Individuals who are evaluated at NIH as part of this research program will be referred back to their own physician or health-care

provider so that follow up care is assured. And these cases will contribute to a catalog of descriptive conditions - a so-called phenotype atlas for the country.

As the experiences of the doctors working with these hardest of cases grow, the team attempts to develop a protocol to help other doctors work up a case that is resistant to diagnosis. NIH expects that this program will produce many scientific publications and probably inclusion of new information in some textbooks on diagnosis. Finally, some patients will be entered into existing clinical protocols attempting to produce new treatments.

Now to put the Undiagnosed Diseases Program in the context of some current related events, I'd like to hand it over to Dr. Groft. Steve.

Stephen Groft: Okay, thank you very much Bill and thank you also for your willingness to initiate and lead this project as we start. I also want to thank Dr. Zerhouni and Dr. Gallin for giving us the opportunity to start this pilot project here at the clinical center. It is a very significant day that we begin the activity.

One of the most frequent questions and requests that we've received in the Office of Rare Diseases for the past several years relates to the requirement for initiating a study of individual diseases at the NIH Clinical Center. This protocol and this project will not do this directly, but may lead to other clinical trials, clinical studies eventually as more information is gained from the individual patients that enter this study here at the NIH.

The Office of Rare Disease coordinates research and information on rare diseases at the NIH and for the rare disease community. Just before this telebriefing for the media, we had a similar briefing to alert patient advocacy groups about the new Undiagnosed Diseases Program. We are fortunate to

have such a strong dialogue with many groups who are able to communicate the goals of this new program to their constituents.

We are also seeing an evolution of the role of the patient advocacy groups as funders and in some cases, major funders of research projects particularly for the rare disorders. So this evolution is occurring and it's occurring throughout the world as partnerships are being formed globally.

This day is also significant and this week for many reasons. The occasion for this program launch is coincident with a number of other events that are meaningful to the entire rare disease community. Included in this is the celebration of the 25th Anniversary of the Orphan Drug Act. It is also the 25th Anniversary of the establishment of the National Organization for Rare Disorders. This week starting tomorrow, there is a major conference, an international conference, on orphan diseases and orphan drugs that will be held in Washington in which we'll have representatives from over 22 countries that will join us to talk about the various needs and issues related to rare diseases.

There is a separate conference being held today on the Orphan Drug Act at 25 years - the retrospective and future that's being hosted the Food & Drug Administration and the Office of Orphan Product Development, and the Drug Information Association.

Our Genetic and Rare Diseases Information Center, funded by the National Human Genome Research Institute and the Office of Rare Diseases, reports that approximately 6.6% of inquiries that they received during the past three years were related to an undiagnosed disease. Also from a study done in 1988 with the National Commission on Orphan Diseases that approximately 50% of patients received a diagnosis in less than one year.

It took another 31% of the patients between one and five years to obtain a diagnosis and approximately 15% of the patients in this study reported that it required more than five years to obtain the diagnosis. And I think everyone can realize the number of specialists, the number of visits, and the number of clinics, and various trips that had to be made to obtain that diagnosis. So I think the significance of the program is quite understandable.

As I mentioned, all of the participants will be seen here at the NIH Clinical Center in Bethesda, Maryland. I'd like to ask Dr. John Gallin, Director of the NIH Clinical Center, to speak to us about this facility and the role the clinical center as it will be involved in the Undiagnosed Diseases Program. Dr. Gallin.

John Gallin: Thank you, Steve. And I also want to thank Dr. Zerhouni for his support in this exciting project and Dr. Gahl for helping to lead it.

Better health and health care for everyone depends on clinical research. Medical research is the sole mission of the NIH Clinical Center, guiding all of its activity for more than a half a century. The NIH Clinical Center, the nation's clinical research hospital, provides an extraordinary environment for excellence in both patient care and collaborative clinical investigation.

The clinical center is the largest hospital in the world totally dedicated to clinical research. Nearly 10,000 new patients come to the clinical center each year from across the country. Currently, more than 80,000 patients are participating as inpatients and outpatients in nearly 1500 clinical research studies conducted here, and about half of our patients have a rare disease. Some 1300 credentialed physicians, dentists, and doctor-prepared researchers along with more than 1000 nurses and allied health professionals work in the

clinical center. They care for patients as well as manage and monitor the clinical research studies.

About 140 specialized clinical teams made up of dozens of medical specialties see patients at the NIH Clinical Center. This new program will marshal a rich set of skills and expertise already at the clinical center to help patients with unusual medical conditions. Our patients are truly partnered in medical discovery.

Patients interested in participating in this research program need to discuss the option with their physician or health-care provider, such as a nurse practitioner or a physician's assistant. Information specialists at the clinical center's patient recruitment call center can provide more information about eligibility and what kinds of medical information referring physicians must submit for review by the program's medical team. The number to call is 1-866-444-8806. The program can also be accessed on the Web at http://rarediseases.info.nih.gov/undiagnosed.

Along the way towards preparing for the launch of this program, various individuals came to mind - the young and the old who represent the personal aspect of the clinical research programs at NIH and now this Undiagnosed Diseases Program. One such patient, an extraordinary and courageous young woman who has joined us today to make this announcement, is Amanda Young.

Amanda Young will tell you the story of what it means to have an unknown diagnosis and what coming to the NIH has meant for her and for her family. Amanda.

Amanda Young: Thank you, Dr. Gallin. My name is Amanda Young and I'm 26 years old and live in Conyers, Georgia with my parents, Speed and Lisa Young, and my sister, Alex, who are all here with me today.

For most of my life, my parents searched for answers to my medical condition that left me vulnerable to life-threatening infections. No one could tell us why these horrible infections attacked my body over and over again. No one knew how to stop them because they didn't understand why I continued to get them.

My immune was as normal as anyone else's under a microscope except for one small thing - a continuously low white blood cell count. Even after years of trying, no one could give me a name or a reason of why my life was threatened time and time again. From the time I was 3-1/2 years old, I had had spinal meningitis three times, many seizures, and an abdominal abscess the size of a cantaloupe, just to name a few.

When I was 8, they had to amputate my leg. It started off as a scratch that I had gotten while playing, and overnight the scratch became infected, and as a precaution, I spent a week in the hospital. However, two weeks later, I was fighting to stay alive in the Intensive Care Unit. I had developed gas gangrene and a massive bacterial infection, and they were forced to amputate my leg and hip in the attempt to save my life. After this infection, my parents' search intensified as they became even more desperate and determined to find out what was wrong with me.

My family and I are able to be here today because of their search for answers that led us here to the clinical center and to Dr. John Gallin. My first visit was in 1990 when I was only 9 years old. Dr. Gallin made us a promise and he lived up to that promise. He told us that he would never give up on me and he never has. And on May 13, 2003, we received those magical words from Dr.

Gallin that we had been waiting 20 long years for. My disease finally had a name.

I want anyone who is searching for a diagnosis to be able to experience what my family did that day. It was incredible. All we've ever wanted was for my disease to have a name, for someone to tell me what was wrong, and Dr. Gallin did that for us.

I have an extremely rare genetic mutation. It's called the IRAK-4 deficiency. My body doesn't make a certain protein it needs to fight bacteria, therefore making me a target for life-threatening infections. I haven't had a major infection in several years, which is great. I have to pay close attention to what my body is telling me all the time. I can't let an infection sneak up on me since my body doesn't immediately recognize an infection.

I continue to come to the NIH throughout the year depending on my health or if Dr. Gallin needs me for more of his studies. Although my disease has a name now, we don't have a treatment or a cure. So I will continue to come here for my own studies and hopefully help further medical knowledge to help others at the same time. It is great to know that all that they have learned from me could possibly help someone else in this process. That is what this is all about is helping out each other. If what I've suffered through can somehow help someone else not have to suffer, I am so thankful.

The announcement today of the new Undiagnosed Diseases Program is like handing someone their life back. Everyone who is sick has to have hope to get better and with hope, they need help. Dr. Gallin gave us that hope so many years ago and today that same hope is being offered to people just like me all over this country. This is the most exciting news that anyone suffering with an unknown disease could hear - someone is going to try to help you.

Here at the NIH, they have the expertise and technology needed to study rare diseases like mine. In an odd sort of way, the NIH is like a home away from home for me, and I love Dr. Gallin from the bottom of my heart for all that he has done and continues to do for my family.

Thank you all so much for dedicating your time and efforts into this new project. You have not only given people a place to come for help, but you have also given us all a place to come for hope and I thank you all so much.

Larry Thompson: Thank you very much, Amanda. This is Larry Thompson again.

What I'd like you to do now is push star 1 and you can start queuing up for - to ask your questions. And while you're thinking of what you want to ask and getting in the queue, I want to remind everybody that if you don't have the background material or the press release or anything like that, you can call the Communications Office at the Genome Institute where operators are standing by. No, we have somebody standing by the phone at 301-402-0911. And we can send out along to you whatever it is that you need or else help interviews if that's also needed.

So let's start with our first question from Rob Roehr. Tell us where you're from, Rob.

Bob Roehr: Bob Roehr, BMJ. You've talked about in terms of national, I just wanted to know if this was also open to patients from overseas - from other countries or not.

Larry Thompson: Dr. Gallin.

John Gallin: This is John Gallin. The answer to your question is that the NIH has a longstanding tradition of admitting patients from anywhere, but we only admit patients from abroad if the specific protocol and question that's being asked at NIH that we think can help that patient.

Most of the patients for this new program we expect will come from citizens and residents living in the United States. However, if there's a particularly compelling problem that this panel of 25 experts think we can help inform, then it is possible for a patient to come here. However, we will only pay transportation for such patients from a port of entry - that is once they arrive in the United States.

Perhaps Dr. Gahl would like to elaborate a little bit from the perspective of the person who will be running the program.

William Gahl: There's just one other issue and that is when medical records and a case is brought before this panel, the panel may decide that the case is not appropriate for the Undiagnosed Diseases Program. But there may be individual consultants whose area of expertise is related to that patient's case and they may want to bring a person from abroad for their own protocol.

Bob Roehr: Okay, great. Thank you.

Larry Thompson: I ask everybody to identify yourselves when you are speaking so that the reporters will know who to quote and quote them accurately. So let's go to Jennifer Couzin at Science Magazine and the rest of you start queuing up with your questions, please.

Jennifer Couzin: Hi, thanks for taking my question. I understand that patients with undiagnosed diseases are currently treated at the clinical center, and I was

wondering if you could tell me how many are treated now each year roughly and how that will change under the new program, which I understand can go up to about 100 a year.

John Gallin: We see about 10,000 new patients a year. And we currently follow over 80,000 patients, and roughly about half of those patients have a rare disease. So the net increase in the number of patients followed is not going to be huge.

But what is different is that this is the first time we're taking a formal multi-disciplinary approach so that every patient is going to really be looked at from the perspective of 25 senior attending physician scientists here who will consider the nature from a multi-system perspective of every problem.

Jennifer Couzin: And I'm sorry just to follow up. Then how is that different if someone contacts you now with an undiagnosed disease and you do accept them to the clinical center. How would their experience be different than it will be under the new program?

John Gallin: Currently, if a patient calls in, they are triaged to a specific institute and a specific program. So it's - I mean a specific protocol and a specific program, and the patient will be assessed there by one team. The difference is now they will be assessed by a large spectrum of teams.

Jennifer Couzin: Okay, thank you.

Larry Thompson: But actually isn't it - I'm sorry. Dr. Groft go ahead.

Stephen Groft: Okay. Jennifer, this is Steve Groft, the Office of Rare Diseases. And I think it's important to realize too that many of the rare disorders involve multiple organs and as Dr. Gallin mentioned, multiple systems as well that always

don't manifest symptoms at one particular time. So I think what we're trying to do is really to get a little bit better hold on what these symptoms and try to put all the pieces together with so many specialists involved that can look at all aspects of this disease that's being presented.

Jennifer Couzin: Okay, thank you.

Larry Thompson: Something you wanted to add? No.

John Gallin: Well the only thing to add is as Dr. Zerhouni pointed out to me - this is John Gallin. Right now, the great majority of the patients come to fit into one of the 1500 protocols. This new adventure will include patients who do not clearly fit into any protocol to see - and in some cases, we'll end up after seeing these patients probably creating new protocols that don't exist.

William Gahl: Yeah, this is Dr. Gahl. So really part of the thrust of this program is to make entry easier so that people in the community and physicians in the community don't have to find their own - the specialist who is interested. This program will triage for them just by making the call and sending in the records.

Larry Thompson: Plus you have a large group of docs who have already agreed to provide the cure for these folks coming in.

William Gahl: Exactly.

Larry Thompson: I'll remind everybody on the phone that if you want to ask a question, you need to push star 1 so that you can get in the queue. Right now, I don't have anybody in my queue, but let me ask you a question of - well before I do that, let me - that seemed to stimulate some. So let's go to Lauran Neergaard from The Associated Press. Lauran.

Lauran Neergaard: Hi, just a really quick question about the actual genetic mutation that Amanda Young had. Could you go back and say exactly what that was again, and spell it for us?

Amanda Young: I have the IRAK-4. It's I-R-A-K with the number 4.

Lauran Neergaard: Okay and...

John Gallin: And this is a protein in a pathway we call the toll-like receptor pathway, which are - a pathway that recognizes infectious diseases and patterns of infectious diseases and is critical for initiating an immune response to these infections. And Amanda lacks a key protein in the pathway that causes the signaling to occur.

And both her parents carry the gene, but they each have a different form of mutation. So Amanda has something called a compound heterozygote where she received the gene from her mom and her dad and sort of got a double dose of misinformation and that's what caused her disease.

Her sister is well clinically, but she too carries the same gene that her mom carries.

Larry Thompson: But a normal version from her dad?

John Gallin: But a normal version from her dad, so she's completely healthy.

Elias Zerhouni: Lauran, this is Dr. Zerhouni. Let me make the point also that at the time Amanda developed her condition, the existence of toll-like receptors, and their role in immunity was not known at the time. So it’s the discovery of the toll

receptors later then connected the thought in Dr. Gallin's team's work with Amanda's potential disease.

And this system of toll receptors is really related to what we call innate immunity. This is what the human species has inherited over the evolution to defend itself against infections, which as opposed to adaptive immunity where you get exposed like a vaccine. And once you're exposed to the agent, then you develop an immunity for it. So the toll receptors were a discovery that occurred after the onset of the relationship between Dr. Gallin and Mrs. Young.

John Gallin: That's correct. They were actually described in the fruit fly first and then now they're recognized to be very important in all mammal species in addition to the fruit fly.

Stephen Groft: And this is Steve Groft, and I think that's what we're seeing in so many of the rare disorders that as more and more, the basic research that is conducted and supported, we are getting that translation into the clinical picture and it's something that years ago we didn't have quite an emphasis on the rare diseases.

And the research would go so far and then stop and now we're seeing this translation into the clinical aspects of the patient. And knowledge is increasing tremendously with so many of these rare disorders and it's occurring on a global basis, not just here in the United States. But the partnerships, the research partnerships and the partnerships with the patient groups are getting rather extensive and very, very useful as far as supporting research.

William Gahl: Yeah, this is Dr. Gahl. I think this program is going to be an illustration of that too because it doesn't go just one way - that is research to translational and patient care. It also goes patients being seen and enlightening us with respect to what the basic defect is, and what's going on in terms of the physiology and the cell biology. So we expect this program to contribute to that too.

Larry Thompson: Okay. Okay, Lauran?

Lauran Neergaard: Thank you.

Larry Thompson: Great. Let's go to Bridget Kuehn -- I think is how you pronounce your last name -- from JAMA Medical News.

Bridget Kuehn: Hi, I want to just make sure - kind of clarify what exactly the program entails. If a patient has an undiagnosed disease, their doctor would refer them and then their case would be looked at by the panel. Is the panel going to diagnose them or just decide if they are qualified? And then if they do get referred to a protocol, what kinds of protocols would those be?

Larry Thompson: Dr. Gahl.

William Gahl: Well, the panel will review the case and decide if it's eligible to come to the NIH and be a part of this program.

Bridget Kuehn: Okay.

William Gahl: After that, the goal would be to make a diagnosis, but that goal cannot always be achieved. So sometimes this will be just a - let's say the foremost

evaluation that can be performed by a multi-disciplinary group of individuals who can do the clinical research upon it.

Bridget Kuehn: Okay.

William Gahl: And the last part was...

Bridget Kuehn: And if they are referred to a protocol...

William Gahl: Right.

Bridget Kuehn: I mean can you give an example of what a protocol might constitute for this program.

William Gahl: Right. So on this board of consultants are 25 or so individuals who each have their own protocols in their own area of expertise. One of them is expected to take the lead on this, so a patient may be referred to that protocol and enrolled in that protocol and then others will - other consultants will serve to help come to a diagnosis. As a default, they can come to a protocol that's entitled inborn errors of metabolism and then basically my service will care for that patient.

John Gallin: But I'd like to add that every patient will get an evaluation, and if it turns out that a patient does not seem to fit into a protocol that's at NIH, the physician and the patient will get feedback. And so this will be information added to the patient and to the primary care team about what we think might be done, or directions to follow, or what kind of care to pursue.

Bridget Kuehn: Okay.

Larry Thompson: That was Dr. Gallin and Dr. Gahl would like to add...

Stephen Groft: This is Steve Groft. Sorry.

Larry Thompson: I mean - I'm sorry.

Stephen Groft: That's okay. I think it's important to note also, Bridget, that you know the referrals can also come in from your nurse practitioners and physician's assistants or other health-care providers that have access to the patient and are able to compile a summary, as well as other specialists.

I think this is not something that's just puzzling to the family practice or the internists, but many times the individual specialists just don't know where to turn either. And so I think that's part of the significance of this is that we're going to accept the summaries from any of the groups that I just mentioned.

Larry Thompson: Dr. Zerhouni.

Elias Zerhouni: Dr. Zerhouni. I just want to stress the fact that the reason we're doing this now is because of the advances that have been made over the past five years at the fundamental level.

We have many more molecular markers that we discovered, the significance of which is not always understood. It's clear that with the new techniques that have been developed in proteomics and genomics, very few teams in the world have the combination of these new tools to be able to study them in the context of diseases that haven't yet been diagnosed properly.

So I think that's the significance of this effort. For the first time, we're going to combine the tools that came out of the labs -- like Dr. Gallin was saying toll receptors discovered in Drosophila -- to human disease. And that bridge

could not be really crossed 10 or 15 years ago because we didn't have the tools.

Larry Thompson: Okay, let's go back to Bob at British Medical Journal. Bob?

Bob Roehr: You said the first year or so you would have - probably deal with about 100 patients or so. Is there any plan to expand beyond that? And what are, you know, some of the barriers that you have to expanding?

Larry Thompson: This is Bill Gahl.

William Gahl: Yes, we'll actually receive a lot more records than 100. About 100 will come to the NIH as our patients. And yes, there will be plans to expand. We hope if this program is, you know, is well received - and we think it is well received. So yes, but we don't know the exact types of patients that we'll be seeing either. So I think that that will in part determine whether or not we expand.

John Gallin: But we do have capacity for a substantial expansion and it really depends on how much interest and how much value we think this adds to the research programs.

Larry Thompson: That was Dr. Gallin. Anybody else? Okay, Jennifer Couzin again at Science Magazine. A follow-up question?

Jennifer Couzin: Yeah, I just have two very quick questions. One was in terms of the funding. This is now about $280,000 in funding. Is that per year or total? And then I just wanted to clarify this is potentially open to patients outside of the U.S. in certain circumstances.

Larry Thompson: Dr. Groft, do you want to take the first one and Dr. Gallin then.

Stephen Groft: Yeah, this is Steve. I'll take the first part. And yes, the total amount is approximately $280,000 from our office - the Office of Rare Diseases. But I think it's important to realize that - and that is per year for approximately three staff members - two nurse practitioners and a scheduler or assistant.

But I think it's important to understand too that we're receiving services both from Dr. Gahl and the National Human Genome Research Institute, and all the other institutes that are providing services or personnel and the intellectual power that comes with it. We're the beneficiaries of an unbelievable system here at the NIH as many of you are familiar. But with the rare diseases, it's particularly significant to be able to pull all these people together at one point to look at individual patients and records to come to some conclusion.

John - Dr. Gallin can comment on the other part maybe.

John Gallin: Well, for sure the leveraging of all the resources in the intramural program - the clinical resources, which are probably in excess of $900 million a year to make this happen is really what's driving this and the enthusiasm of all the folks.

What was the second part?

Larry Thompson: Yeah Jennifer, what was part two of.

Jennifer Couzin: Oh, I'm sorry. I know you addressed this already, but I was still a little confused. Is this open to people outside of the U.S.?

John Gallin: Yes, people from outside the United States can apply, but we don't expect that many of them will actually be accepted. But if they have a compelling problem, they certainly will be included, but the travel for them will only be from the port of entry to the United States. We will not be able to travel them from their home country.

Jennifer Couzin: Okay.

Larry Thompson: Dr. Groft.

Stephen Groft: And Jennifer, this is Steve again. The enthusiasm and support from those who are in the fellowship training here has been phenomenal. I think they are all extremely interested in this. And again, I can't tell you the number of scientists who - they start looking at rare disorders because no one else is looking at them. So whatever we can do to build up that interest, and concern, and research will be beneficial to all the rare diseases as we continue to grow.

Larry Thompson: Okay, great. So let's move on to Jeannie Baumann from BNA.

Jeannie Baumann: Hi. Yes, I was just wondering. I know you probably can't give an exact time, but how long a patient can expect to wait between the time that they get the physician referral to actually getting into the protocol and how long that time lapse would be.

Larry Thompson: Dr. Gahl.

William Gahl: Yes, thank you. When we receive inquiries, we expect to send back a postcard and some notification to the families right off that we've received it or that something is missing. But once we have the whole package together,

we expect that within about six weeks the board of consultants reviewing these cases will reach a decision.

Jeannie Baumann: Oh, okay. Thank you.

Larry Thompson: Okay, let's go to the next question. Mark McCarthy at Medical Device.

Mark McCarthy: Medical Device Daily actually.

Larry Thompson: Sorry, I can only see part of the - but thank you. Go ahead.

Mark McCarthy: One of the things that occurs to the causal observer is that NIH could find itself pretty overwhelmed with applications especially in a nation with 300 million. At some point if NIH is forced to try to prioritize, will the mortality question or speed of mortality take precedence over, you know, perhaps a wider - a disease that's more widely distributed or perhaps not as lethal? I mean how will NIH go about deciding which cases to prioritize?

Larry Thompson: Dr. Gahl.

William Gahl: Well you know I'm sure that when the board of consultants looks at these individual cases that that will be one of the considerations that they look at. But remember, the main point of this is to try to be able to help people and therefore, we need to have some sort of a clue to pursue and some reasonable expectation of benefiting the individual or the family.

And secondly, the purpose of this is to acquire new research knowledge. And you know eminent death is one of the criteria for the first of those two issues, but not for the second. So I think it will all go in the mix and there will be

some consideration of the issue you raised, but actually, I don't think it will be paramount.

Larry Thompson: Okay, I don't have any other questions in the queue right at the moment. If anybody has one, put one in quick or we could - anybody have any final comments that they would like to make here.

And the only question actually that I still had was for Amanda. What was it like to actually come here to the clinical center and receive care here? And we also have Amanda's mother here. Lisa is also here, and she could give us a little bit of a sense of what it's like to be a mom with a small, young child who is sick that you have no idea what's wrong.

So Amanda, what's it like? And then Lisa if you could just comment on what it's like to come here.

Amanda Young: I believe it's unlike any other hospital that I've ever been to. Before I came here, I was going to hospitals all over the south and trying to figure out what was wrong with me and just being turned away time and time again saying, "We don't know what's wrong with you. You're further than medical technology. You'll have to come back later. And go home and live a normal life," and it was so hard to hear that. So trying to find a hospital that would actually stick with me was - and finding the NIH - was amazing.

And coming here is completely different. The bedside manner here is wonderful compared to doctors at home at least. And I love my doctors at home, but it's just - it - I'm glad to know that there's a place that will not give up trying to find out what's wrong with you. If you go other places and everybody gives up, it's so disheartening. And I love coming here. I love it here.

Lisa: You know, we've had - we had one medical facility tells us at one point, "Your daughter's body is further advanced than medicine. Take her home and live your life as well as she can." And you would politely say, "Thank you," and you'd go on and you'd start your search again because as a parent, you cannot give up. And when you come here, that hope is renewed again. And to find people who - this is all that they do is they try to research and help.

And realizing as a parent that if they accept you hopefully their knowledge and what they gain throughout their knowledge is going to help other people. I think it's invaluable to know that things that they may study through (Mandy) or through the genetics testing that they do with my husband and our other daughter and myself could potentially help other people. I think it's invaluable to everyone out there. Not even the people who may be sick, but who may eventually have children or grandchildren who are suffering. And it's just a place that we feel very fortunate when Mandy was 9 to have found and we've just grown to love it here.

It's not always easy to come. It's absolutely a job to take care of a sick child. It's not an easy thing as a parent and we dedicated our lives. We always tried to say, "It's not Mandy's disease, it's our family's lives." And we hope that through what we've helped her through that we've been able to do that. But it's not easy and it takes dedication and it takes time, and the fortunate thing here is we feel like as much as we've given, it's been given back to us double.

Larry Thompson: Final comments gentlemen, ladies? I have no other questions in the queue so I guess we'll bring this telebriefing to a close. And if there's - if reporters have any other questions, you can always reach us at the Communications Office at 301-402-0911, and we'll be happy to help you out. So thank you all for participating and we'll bring this to a close.

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