SPEAKER 1: Hi and good afternoon. I'm keeping an eye to make sure we get the right set of slides up here. But it's my pleasure to introduce for CTSA Grand Rounds today Dr. Stephen Thibodeau. Dr. Thibodeau, we were just talking about, came on staff in 1987. So he's in his 25th year at Mayo, and even longer because he did a fellowship in clinical chemistry here after taking his PhD in biochemistry from the University of Washington in Seattle.

These days he's a consultant in the Department of Medical Genetics, the William H. Donner Professor of Medicine and a professor of laboratory medicine, and the co-director of the Molecular Genetics Laboratory. And we're excited to have him talking about the Center for Individualized Medicine in Biorepositories, the Mayo Clinic experience today. Dr. Thibodeau.

[APPLAUSE]

STEPHEN THIBODEAU: Well, thank you very much for inviting me today to tell you about what we're doing within the Center for Individualized Medicine and the Biorepositories program. And I really have to apologize right to begin with because this is really just going to be one big infomercial in terms of what we have and what we've done, what's available, what's available to the community at large. So part of this is really just to kind of one, tell what we've been doing, but also two, tell you about the resources that you have available to you for the sorts of things that we're doing.

So the talk I'd like to give, I'd like to give just a little bit of history and what the program is for the Center for Individualized Medicine. We'll talk about where the biorepositories program fits within CIM, a little bit about the background of that. We'll talk about the infrastructure of the biorepositories, as well as the collections, since we have multiple different components of what we're looking at. So if we take a look at the mission for the Center for Individualized Medicine, there was a slide earlier that kind of presented this.

But the Center for Individualized Medicine discovers and integrates the latest in genomics, molecular and clinical sciences into personalized care for each Mayo Clinic patient. It's an important aspect of when we look all of the programs within CIM, both research as well as the infrastructure programs, that it really is directed towards individualized medicine. Now, within CIM, there are five scientific programs that I've outlined here. There's pharmacogenetics, biomarker discovery, the clonomics, program, epigenomics, and microbiology.

Within each of these programs, there are a portfolio of a variety of different projects, a variety of different goals really all with the intent of getting as much of this information into clinical practice. That's the goal. The goal of CIM is a translational component, how do we really get the science into clinical care and clinical practices really as quickly as possible? Now, to support the scientific programs, we have five infrastructural programs-- biorepositories; the medical genome facility; informatics or information technology, the IT group; bioinformatics; bioethics; and our administration.

The program that I want to talk to you about today is our biorepositories program. But you can see the biorepositories program is really just one of the group of the programs that helps to support the CIM initiatives overall. But many of these programs really support initiatives throughout Mayo and throughout the institution. And the biorepositories program is one of those. The biorepositories program is not just for CIM, it really has been established to help all investigators at the institution in order to really accomplish what they need to accomplish.

So as you probably know, biorepositories, biospecimens is really not new. So in terms of what we're doing, I think we have some new things we're bringing to the institutions and some important things, but this is not new. Mayo Clinic has been collecting specimens really from the very beginning, surgical specimens in paraffin embedded material. We have a 100-year history and legacy of that material available to us for a variety of different projects.

There are literally hundreds of investigators who have collected material over the years, most of these being disease-specific. And for many of you that are affiliated with some of these research programs, you think about your own programs and your own diseases and how this fits in. So that part of what we've been looking at is, how do we take advantage of the history that we have and how do we really move into the next century in terms of what do we think that we're going to need in order to really accomplish what we need to do in the coming years and hasn't been sufficient?

And our feeling is that it hasn't been sufficient, that we really need to get to a different level in order for us to really be able to take advantage of the history, to take advantage of what we have, and to really help CIM and other investigators to really provide the resources and the work that they need to do. So the goal for the biorepositories program is to really develop a comprehensive plan for the collection, processing, storage, distribution, management, and usage of high quality clinically annotated specimens. Soup to nuts.

We really want to be able to take a look at right from the beginning and how do we collect and process and store and manage all of what we have for not only within the CIM program, but for investigators as a whole? And the vision really is to create biorepositories. And when I talk about a biorepository, I talk about really a collection of information. It's not just the biospecimens.

So what we're looking at-- biospecimens, clinical information, and data that goes along with those specimens in order to create a collection of information that can be used. You can either use the clinical information or you can use the data, you can use the specimens, you can use it in different ways. So it just isn't the biospecimens, it's everything that surrounds that biospecimen that we're able to use. And so our goal is to create these sort of repositories of information that can be used and to help investigators create those biorepositories for their own research programs as well.

So within the program, we really have three key initiatives, three different components that I really want to step through to tell you what is it that we've done, what is it that we have available, and really what's available to you. And the three components that I want to talk about is the governance, what have we done as the oversight; the infrastructure for this, as well as the collections; how do we deal with each of these. So for each of these, I'm going to go through some of this a bit quickly.

But for governance, the main component for the governance is what's the group that oversees this program as a whole? It's represented by individuals from all three sites because the program that we have is a three-site initiative. We have a very active education/communication plan. And in part because we have our own Mayo Clinic biobank, which I'll tell you about, and within the Mayo Clinic biobank we have internal-external websites, we have newsletters, and we really want to be able to communicate to the community. And for us, the community as the participants, it's Mayo investigators, it's Rochester, it's the state, and it's national.

And we have a very broad base of individuals, or in terms of what we consider to be the community. A critical piece of the biorepositories program has been bioethics. We really could not have done all of what we've done without really having a very engaged ethics program, not only in terms of the infrastructure, but in terms of the collection that we have as well. I can't overemphasize how important this has been to us and how valuable it's been.

And I learned so much, I think, from the community advisory group as [INAUDIBLE]. So we've established and have worked with the community advisory group now for almost four to five years. We have a co-chair that's actively involved in all of the committee meetings that we have and they really have been there to address a lot of the social and ethical issues that revolve around via biorepositories and the collection of the material. And as a result, I think we've built some very robust sort of plans that now I think the institution of the IRB has begun to take in for looking at how to get appropriate consent or looking at the education material, returned results issues.

So a lot of issues I think that we've been able to address that I think have been helpful for the institution. The second component that I want to talk about is the infrastructure. And for us, the infrastructure is how do we get processed material and develop that? And so we really have two core labs that are responsible for this activity. The first is the Biospecimen Assessment and Processing Lab, what we call our BAP lab. The second is the Pathology Research Core, or the PRC, lab. And the BAP lab is responsible for all the pre-analytical processing; the collection of the material; [INAUDIBLE], extraction of DNA, RNA; the distributions; storage; and that sort of thing.

The Pathology Core deals primarily with tissue and tissue-based activities, looking at tissue microarrays, frozen sections, paraffin sections, immunohistochemistry, imaging, et cetera. And I'll talk about some of the services as we go through. It's important to emphasize here that we've established these capabilities and labs at really all three sites. Not all of the labs do the same things. Some labs have more capability than others, but we wanted to have a presence at all three sites in order to make sure that we cover all the material.

To give you a sense of the volume and the work that's being done, this is just for the BAP lab. And you can just scan down the services being offered, the number of cases, and the types of collections or the types of activities. So you can see that we're dealing with very big numbers. We have a large number of samples that come through the lab, on the order of 40,000 to 60,000 per year with lots of different processing. So there's a lot of activity there.

For the PRC lab, again here are the services offered here with the sectioning, imaging, microarrays, that sort of thing. And again, you can kind of get a sense from the numbers of the level of activity and the processing that that goes on. And again, the goal here was to establish central laboratories that could work with all investigators at the institution for all types of samples. We want to be able to do it easier, better, more cheaply than what people can do in their own labs to really help to funnel the activities so that we can provide really the best services possible for this.

It's a very large group that we have. We have about 60 individuals, some very, very talented individuals who are really there to help. They're really there to help investigators and to help you with your research programs. And so it's clearly something that we're continuing to learn, looking at continuing to optimize and to improve the process. But I can tell you that for the lab, these individuals are here really to help and to really work with investigators and do the best that we can. And as I said, really a very talented group of individuals.

The current lab that we have is really kind of split amongst multiple different places. We have at least five different locations. We have about 15,000 square feet now for both the BAP and PRC lab, as well as the freezers that the BAP lab manages, in addition to some of the institutional freezer space. This has really caused some problems in having things distributed. And we've been for some time now trying to work with the institution to develop a more comprehensive plan to begin putting this together. And then just recently, that new plan was approved.

And so we now have 25,000 square feet that's been approved that will allow us now to consolidate all of the space that we have. So we're looking at consolidating all of the BAP-related activities, all the PRC-related activities, and all the freezer-related activities and really bringing that to a new facility that we hope will be really a state-of-the-art facility that, again, will be able to process and do pretty much anything that we need to and also to develop a very robust disaster plan. Because for all of you and for all of us that have been spending years and years and lots of money on these collections, this is really a very valuable resource that I think all of us will be using for many, many years.

So the space that we have is off-site a little bit in the warehouse. This is just to kind of give you a quick picture of the warehouse with kind of a preliminary plan that we've begun putting together that has the BAP and PRC lab in the middle, some administration, and where collections come in. We're incorporating robotically controlled freezers. We've just purchased one now that will have roughly 1.5 tube capability. So in the end, we will have robotically controlled freezers at all three sites and in total, we probably will have on the order of two to three million tube capability.

So we're really looking at how do we automate the entire process so that we can improve the quality, improve turnaround time, we can track what's going on, and that this material can be available to anybody at any time. So we've really spent a lot of time trying to develop the infrastructure in order to really help investigators across the institution. Now, part of that infrastructure is looking at IT so we also have an IT component. RLIMS is the computer base that the group works off of to track all of the specimens. And then we also look at getting data back so we have a data management system that we've also constructed in order to help with that as well.

So the third piece-- I know I'm kind of jumping here-- but the third piece I really want to spend some time on is the collections. Now, as I mentioned, biobanking isn't new to the institution. We've done lots and lots of biobanking with many different investigators. But when we started this project roughly five years ago, we really asked the question, what is it that we can do to help investigators in order for their biobanking needs? And so the infrastructure was one piece of that. But the other is that most investigators really in dealing with their own biorepositories are primarily collecting their disease group.

If I'm interesting cardiovascular disease or cancer, most of those collections have been based with the disease groups and not necessarily kind of any other group. So when we started this five years ago, really at the request and really with a considerable amount of support from Dr. Rizzo-- who just kind of stepped in-- that we looked and and said, what is it that we're not collecting as an institution could we help? And so what we ended up doing was saying what most people were not collecting were healthy control individuals.

So the Mayo Clinic biobank really kind of emanated from what is it that people were not doing and what is a collection that would benefit most individuals at the institution? And that was a controlled collection. So we really began looking at that as our starting point, but that led to really establishing an ongoing collection really at all three sites. We have the Mayo Clinic Biobank and our goal was 50,000 participants with the Mayo Clinic Biobank here in Rochester. We have a similar ongoing effort in Florida with 5,000 participants there. And then in Arizona, we're taking advantage and looking that as an opportunity for us to get into a minority group and looking at the Hispanic population within that area, recognizing that we really begin to really consider and look at minority groups in much more detail.

So what is the Mayo Clinic Biobank? So again, it's an initiative that was launched in 2007. The goal was to collect at that time 20,000-- we've expanded that to 50,000 participants-- but really to provide an institutional resource for all investigators at the institution. So this was fundamentally, in my mind, fundamentally different than what we have done as an institution in the past, maybe except from the paraffin. Because as you consider the biorepositories that might be out there, almost all of those are driven by either a single PI or a working group.

This collection was really meant to be an institutional collection, so this is the institution that's invested the resources in order to provide this. There there's an oversight group in a group that manages it, but this collection is really meant to be there for everybody. So my first message in my infomercial here is that this repository is for you. We will not have been successful in creating this repository if it's not being used. So we're really looking for individuals, all the PIs, individuals at the institution to be able to use it for the types of studies that you want to use it, and I'll tell you a bit more about what those capabilities are.

But the informed consent is an open consent. Each study that uses it-- so it's a registry, so we expect that people who want to use it will have their own IRB project. We're consented to use the specimens in virtually any type of study. We can have access to medical records over time, we have access to additional specimens over time, we are able to go to these individuals over time. And all of the data, and we'll get into this, comes back to the biorepository. So this is pretty much complete in terms of what you might want.

The target population is they have to be a Mayo Clinic patient and we were generally looking for healthy individuals. And so we're targeting those areas of the clinic that generally have healthy individuals-- family medicine, community medicine, looking at the Kasson Clinic, the Northwest Clinic. So generally, where we're getting our well checks or kind of the quick checks coming in and out. But the goal was to get Mayo Clinic patients so we'd have access to medical records in a generally healthy population.

As I said, the consent allows for specimen and data, allows for past and future access, allows for future contact, and with a certificate of confidentiality. The biobank, we know who the individuals are so we clearly have access to kind of identifiers. But when specimens are given out, they're basically given out in an anonymous fashion. So you have your study, you indicate the type of sample you want, the amount of sample you want, the clinical records. We'll pull that for you, create a data set, and provide that to you.

So we are working very hard at trying to make sure that we protect the participants in the biobank as much as possible, given what they're participating in, and we're acting as an honest broker in between to make sure that we look at the best interests of the participants, as well as the interest of the institution and investigators. In addition to access to the medical records, we have provided a health questionnaire. So for some of you who might have participated, so this is number two of my infomercial, anybody here who wants to be a member of the Mayo Clinic Biobank-- some of you might be-- please, we have lots of different places where you can become a participant and we're always looking for more individuals for this.

We have given a 50-page questionnaire, family history, that again, we take a look at demographics, general health, quality of life, et cetera for these. So we have a lot of additional information that we've obtained from these individuals. From individuals we collect a variety of different sample types. We have EDTA tubes, from the EDTA we get DNA. We'll have buffy coat, we have plasma, we have serum, we have sodium citrate plasma, and for a subset we've collected material in order to get slow frozen cells so that we can do EBV transformation or use the cells directly.

So again, we have a broad range of biospecimens that are available for use by investigators. We have extracted some medical record information, as I highlight here, just so that we have some baseline information. But otherwise, what we do is we access the medical records. So anytime, individuals need information then we will just go into the medical records, pull up the information that's required for the study, and then pull that together. So we're not trying to duplicate information, we are really just taking advantage of all the existing databases that might be out there.

So as of really the beginning of 2013, where are we at? Our goal is 50,000, we're almost at 30,000 participants now that we have collected. And you can see the distribution here of the number of female versus male. Slightly more female within the group. And with the age distribution. So the age distribution is what you might expect it to be, given the population that we're dealing with here at Mayo. So we're always looking for younger participants in order to even that out a bit, but we do have a broad range of age groups that we're looking at.

The area that we recruit from is, again, generally from a five-state area. It's interesting that almost 40% of the participants are from Olmsted County. And that's important for us, in part because we are also trying to tie this with the Rochester Epidemiology Project. So the the REP has been an ongoing study for many, many years. And so this allows us now to kind of couple other existing projects at Mayo and take advantage of the number of different infrastructures that we have.

And you can see the distribution in terms of Minnesota and/or kind of the surrounding states. But generally, within southeast Minnesota, a significant part of that within Olmsted County. With the 30,000 participants, we can now begin looking at data to see what sort of things are we seeing within this population? So what we've listed here are the 10 most common prevalent diseases by self-report. And you can see that the most common is hyperlipidemia, then hypertension, et cetera.

So it's interesting, now we can begin looking at the different distribution of conditions that we have within the group. Even though we've targeted healthy population, we've not targeted disease population. But clearly, individuals will have-- none of us are normal, I don't know what normal is. And so we take all the sorts of the normal biology that we all have and we can begin seeing now how that normal biology begins influencing what we're doing.

The five most common cancers that we have, the first is skin cancer, which is not too surprising; and then the other is prostate, 5%; breast, 4%; melanoma, 3%; and colon cancer. We expect that over time, individuals will be developing disease so we can actually follow these patients over time. So although we can identify these as generally healthy and use them as controls for other studies, they will develop disease that we can take advantage of.

So within the group, we've also developed principles of the use of the biobank, and I've alluded to some of those. But the first is that all of the projects that use biobank are really going to have their own separate IRB. So we have approval as a registry. We have approval that patients can be used. So for anybody who wishes to use the biobank, then basically they have their own study, their own IRB approved protocol. And what's relevant there is that the consent is just waived. We already have the consent to do the work so you don't need to reconsent these patients.

It's basically that we have access so you basically just define your study and get that IRB approved. We're looking for peer review. We want to make sure that the studies are appropriate for the sorts of things that we. We do have an access committee, and the access committee will review what we have as well. Samples, we only give samples that are required for the study. I'm really chintzy, and anybody in terms of kind of annoying these projects I've been involved in-- I see Carla back there-- and so everybody knows that we're only going to give you the amount of DNA, in part because we've spent so much money in directing this.

We want it to be used so we're really pushing very much not for the material to be used, but we don't want it sitting in someone's freezer. We don't want to say, OK, here give me x number of micrograms and then it's just going to sit there for the next 20 years. We really want the material used. So we want people to consider this and think about this and make believe that this freezer were in your lab. If it were in your lab, you would take what you would need, do the study, and then obviously leave it there.

Well, think about it this way, take what you need and when you need some more, come back to our freezer and tell us what you need and we'll give you some material at that point. And we want to make good use for that. So we will evaluate, what is it that you're doing and then decide the amount that's appropriate and try to give you the amount that we feel that will give you what you need but at the same time not waste a lot of material in the process for this.

For the high end users, for those individuals that we know will come back repeatedly for material and/or I come in I said, jeez, my study, I'm going to need a control group and I want that control group for the next 10 years. How do I know that I'll be able to get material over that period of time? And what we've said is that if we know that you're a high end user and we know that you're going to be able to use this material, then we will flag that sample, at least 30% of that sample, so that we know that you will have material available to you for the course of the life of that study, however long that study might be.

We're going to hold it for you, we're going to keep it so that you just come back. You need it, you come back and we know that we'll have it flagged. So we're trying to give investigators the confidence that this isn't going to go away, we're not going to change our mind. And we want to encourage people to use it so that if it's only a one-time use or if I need it for the next 10 years, we will work with investigators to do what we need to do in order to make sure that people have access to the material of what we're looking at.

So one of the requirements, though, is that we want the data back. So if you have a study and you do a study, then we don't want the results of your case control analysis of the case or your final results. What we're really interested in is give us the raw data of the samples that you've used for the controls. So if you've done G-WAS, or if you've done sequencing or if you've done whatever protein-based analysis, we're now getting that back from investigators with the idea that now the biobank really has access to that data so that if future investigators want to have genotyping data and we already have it, then we can just go in and mine the genotyping data, rather than giving you other samples.

So that's part of the repository idea is that we want medical record data, we want the biospecimens but we want data. And so now we are already beginning to build that data. We have whole exome sequencing data on almost 100 individuals, we have G-WAS data on over 2,000 individuals and that data now is being used in multiple different ways. And so we don't have to keep on giving out DNA anymore, we just give out the data and we give out the data repeatedly for what we're looking at. So it's another way of kind of managing these biorepositories as we look forward so that we can make maximum use of the information that we want.

The access to the biobank is really pretty easy. We have a website. You can go on the website and we have a form. You get together with the access committee, we review what you want. And we have refused a couple of studies, but the vast majority of studies we approved because our goal is to have people use it for what we're looking at. So there's a number of different ways for us to take a look at this. Part of the access group, one of the things I wanted to mention is that when we look at the access group, we have multiple people sitting around the table.

So around the table are really kind of the director of this, and Janet Olson and Jim Sirhan are the individuals who are primarily responsible for the biobank. But we will take a look at the study to make sure that we've got the study information, but we also have the statistics group there to make sure that we can mine whatever data that we need to mine; we have someone from the BAP lab to make sure that we know how much DNA; we have a genetic counselor there because we're interested in return of results, what kind of results are we going to be getting. Because one of the issues that we had agreed to with our participants is that if there's any clinically relevant information that is actionable, we will return those results to participants.

So we have worked out a process for doing that which I'll share with you and that process now, in fact, has been incorporated as part of the IRB for other protocols. So we've been able to use kind of our group to help with that process. We have lots of different types of studies that can be used as case control, cross-sectional, time trend, prospective cohort, nested case control, cost/health service. So we're looking at this as being a very broad repository that can be used in as many different types of studies for as many different investigators as possible.

As I've mentioned, we have a large number of users. Right now we have about 57 PIs who have been approved to use for roughly over 40,000 samples within the biobank. I've listed a few of those studies here. The different types of studies for that first group are the case control studies, many of these being cancer-related, and the number of specimens that each of these investigators are using. And for some of these investigators, we're looking this is a long-term investment for what we're looking at.

So the strengths of the biobank is that it's embedded in a clinical practice. This There are many different biobanks outside of Mayo. There are clearly some biobanks that are much larger outside of Mayo. But I think what's unique to what we're doing is that this biobank is completely embedded in our clinical practice in terms of having access to all of the other infrastructure and information that we have. So it really takes advantage of kind of our general medical practice and our patient population that we have in really making a cost-effective way to collect.

For many of these instances within a community, we are looking at individuals that have long-term. So we haven't refused anybody, but clearly we're more interested in individuals that live in the area that use Mayo Clinic as their primary health care system so that we have a long history of the medical records for this. As I mentioned, we have a very active ethics and community program which has been really quite valuable to us. And again, we can now begin interfacing with multiple other projects, REP is an example, that are also working like with the Mayo Genetic Consortium kind of within the group at Mayo as well.

Coming back to the communications stuff, we have-- as I mentioned-- two websites now. We have an internal and an external website. So all you have to do is Google Mayo Clinic biobank and if you want to see, it will actually be one of the top hits. The external one is really geared towards participants. But one of sort of the policy decisions that we made very early on, which I think has really served us very well over the years, was that we were going to be completely transparent.

Virtually everything that we have done is on the website. Our consent form is on the website, all of our education materials are on the website, the questionnaire is on the website, our IRB protocol is on the website so that anybody who wishes to know what we've done, how we've done it, and what we've learned can really just get on the website to see. I see that's served us well because we were all concerned initially about creating this type of resource, especially how it might be viewed within the community, both the local community as well as the national community or the state community.

And overall, it's really been received quite well. We never put it out there to advertise or to kind of brag about what we're doing, but overall I think more and more articles are coming out where individuals are kind of pointing towards Mayo as being kind of a leader in terms of how to set these things up and what to do. So in that sense, I think it's really helped us considerably in what we're doing. We have two newsletters over the course of the year. All of the newsletters are on the web, so if you want to get a sense of what we're doing then we're all out there.

The internal website is really geared towards the Mayo community and primarily for investigators so that if you need to get on and see what we've done or how to do it, then everything is there as well. We have letters that we put as example letters for NIH grants, we've put the background sections up for NIH grants. So we try to set things up that for investigators in terms of what they need or how to get access and how to get the material, then it really should be pretty complete. And if not, we have contact names, so just give us a call and then basically, we can help you through the process of looking at this.

So the community advisory board, as I mentioned, has been really I think one of the key aspects of what we're doing. I know through the CTSA, there's been a community group and there's been a lot of overlap between the two. But this has really been something that's been actually really very enjoyable for me but I've really learned a lot. So the CAB was really developed to guide the biobank activities to begin with. So right from the beginning, we wanted to have input on the consent, our educational material, and a lot of the issues that resolved, and they really helped us step through this process.

So they advise us on the management and operation. We have a very active group right now. As I said, the co-chair is part of our group. They help review policies governing-- they don't make policy, they don't vote on these policies, they're an advisory group to what we're doing. They evaluate all of our material-- all of the education material, all of our correspondents that we might do. So they help us kind of go through that process. And really, they help us cull through some of the more complex problems.

When we set up the biobank, we also came in with the idea that we would not be able to predict what the future would be like, that we wouldn't be able to identify all of the issues and problems. So we did our best to try to identify and to work with and do as much as we could, but we tried to establish a process that said, look, things are going to change. We don't know how they're going to change. Let's make sure that we have a process in place that as things change, we can adapt and change and kind of incorporate. And the community advisory board has been part of that process.

They've been in that group that has helped guide what we've done over the years and when things become complex, how do we kind of navigate those complexities. And one of those, for example, has been the return of results. We said that we would begin returning results to participants if we found clinically important information. That's a very easy thing to say, and but it's a very, very difficult thing to do. And so we said, yeah, we can do that. And we kind of did a lot to begin with and then actually, as you get into it, it's like this is really a much more complex.

And so we've really been spending the last five years dealing with that level of complexity. And just to give you an-- for that kind of one topic, this really goes back to 2007 when we first started putting this together and putting it in the consent. Because when you have the consent, at least for us, we wanted to make sure that the consent reflected what we were going to do. So every sentence that you put in there, you have to think about, OK, well now how am I going to do that?

But we had nothing in place so we had to kind of look ahead and say, what would we do and how would we do it? And it really took us two years. It took us two years to set up the biobank. People were getting frustrated because actually, we were given funding to set up the biobank, but we weren't collecting anything. But it took us two years to set up the biobank because it took us two years to set up the consent process, and the community advisory, and kind of try to deal with all the informed consent issues, the return of results issues.

And every time we thought that we were there, you'd put something down and you'd say, OK, we don't know how to do this. So we had to spend some time in trying to figure that out. Now, again, although it took us some time, I think it has served us very well. Because although it took us two years to do that, I think we really set the stage and we really anticipated a lot of things. Now, we really then clutched samples very quickly. Once we had things in place, we were able to collect 20,000 samples in three years so we met our goal.

But that really kind of at that stage at the beginning. But you can see that even though we began those discussions in 2007, over the years as we began now getting closer to actually having to give return results back, we started engaging the community and the community advisory board a little more. So we had multiple meetings with them, we had national meetings looking at what was happening nationally, we presented to the IRB and legal and really tried to work something out and in the end then worked out a process that we as a group were comfortable with, the community advisory group was comfortable with, the IRB was comfortable with in terms of what we had.

And that, in fact, now I think is the template that the IRB is using for return of results issues in general for the institution. So the first part of what we look at when we have a return of results is that we convene an expert panel. We don't have all the expertise within our group. And we really wanted to make sure that when we returned results, and this is what we said, that we wanted to set a high bar. We were not interested just providing return of results and people not knowing what to do with them. And so we really want to make sure that there was a very high bar, that we would only be returning results when we really thought that-- again, that's easy to say, very difficult to do.

So we wanted to make sure that we had important health implications, that the associated risks were both established and substantial, that the findings could be actionable that one could do something with it as we looked at that. So in the end, we tried to define that and then we would have a panel. So this is kind of the process that we worked out just as an example of one of the issues. So in this case, this is the flow path that we've now defined that is now in place.

So at the time that a project is set up, we ask right then at the beginning of the project, are we going to have return of results issues as an issue over the course of this project? And if the answer is yes, then we work with the investigator right then before the study even begins to work out the process for what we're doing. And that's why we have a genetic counselor as part of that committee. So it's the genetic counselor that works with that group and sets up.

So at the end of the study when we have these issues that come up, we already know what we're going to do, the path has already been set, and we've already made the decisions before we even start from what we're looking at. At the time that we have them and have to make the decision, we get that expert panel together. And it's the expert panel that goes through and really decides, should these results be returned or not? And if no, then we're done, and if yes, then that defines the rest of the path.

So if yes, we are going to return results, then what we do is we send a letter to the participant. And in that letter, we basically ask whether or not we [INAUDIBLE] tell them that we have information on a recent study that they were selected to participate on and that we have return results. We try to be very careful in that initial letter not to say anything about what the results are or what the study is in detail, just a little bit of information, and basically ask, do they want to have return results or not, yes or no?

And so we are giving them the option. So we always give the patient or the participant the option to participate. If no, then we're done. If yes, they wish to participate, then basically we have a follow-up meeting with a genetic counselor. And the genetic counselor will review with them what the project was, what the implications of the project are, what the implications of the results are that they might be getting so that they have more information and they can make a more informed decision about whether or not they want to get the results or not.

So again, at the end of that session, we will ask the question again do they want to have return of results or not now that they've been more informed about what the study is and what's going on. So some people at that point say, thanks, no. Now I understand what it is, I don't think that I need to know. And others might say yes. So if they say yes, then we will set up a second meeting. So this gives them time to think about it again.

And so at that time in the second meeting, we'll have a second opportunity to meet with a genetic counselor and then the genetic counselor will go through and do a more routine counseling sort of session where they will provide the returned results at that point and then provide the results offer whatever follow-up tests might be important or could be done and have recommendations as to what they could be doing and whether it's a positive or negative result as we take a look at these. So we've kind of worked out a process for that, which again, I think overall has-- we've already gone through the process now one time on a very small project so it's a good learning project for us.

And again, that whole process, I think, has worked very well. But it provides a framework, I think, that we and other investigators can use in terms of how we deal with some of these issues. So the last slide that I have for you, given the time, is really the infrastructure. It's part of what we've done over the past five years. You can see that we've built a lot of infrastructure around our collections. We have risk questionnaire information now that we've built, we have our processing labs, the BAP lab, the PRC lab, we have other IT sort of [INAUDIBLE] and the IT group, we have a communication plan, we have a bioethics plan, we have patient registries that we've built.

And so as we've built all of these, the infrastructure around a collection, we are now in the process of how do we migrate that or duplicate that for other repositories? So the idea is, how can we help other investigators to do these sorts of things? So everything that I've described for the biobank been built from the beginning in a way that can be replicated to work with other investigators. So for patient registries, for example, we've already built four or five other patient registry sort of IT systems to help other investigators to do what we've done.

Our ethics group has worked with other groups now to kind of take advantage of the lessons learned and what we've done and to build informed consents and/or the return of results issues and that sort of thing. So again, what we're trying to do is to build a broader infrastructure within the institution so one, we can provide the infrastructure to process specimens and store and manage specimens; that we can help investigators the collection and the consent forms so that individual investigators and individual groups can do what they need to do and to do it best and we can provide some infrastructure around that and then what we can do the best in terms of helping to define what we're doing at our end. So I'll end with this in terms of this is a very large group.

If we take a look at all the individuals on the infrastructure side, all of the individuals on the collection side, now really incorporating individuals really at all three sites and really helping to provide a system that really is across the foundation and really there to really help investigators throughout the institution what you need to do for your studies, in addition to helping the Center for Individualized Medicine. So I will stop there.

[APPLAUSE]