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TRANSFORMING LIVES THROUGH DIABETES RESEARCH

HEARING

BEFORE THE

COMMITTEE ON HOMELAND SECURITY AND GOVERNMENTAL AFFAIRS UNITED STATES SENATE

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TRANSFORMING LIVES THROUGH DIABETES RESEARCH

WEDNESDAY, JUNE 22, 2011

U.S. SENATE,
COMMITTEE ON HOMELAND SECURITY
AND GOVERNMENTAL AFFAIRS,
Washington, DC.

The Committee met, pursuant to notice, at 1:34 p.m., in room SD–G50, Dirksen Senate Office Building, Hon. Joseph I. Lieberman, Chairman of the Committee, presiding.

Present: Senators Lieberman, Akaka, Pryor, Begich, Collins, Brown, Shaheen, and Lautenberg.

OPENING STATEMENT OF CHAIRMAN LIEBERMAN

Chairman LIEBERMAN. Good morning. The hearing will come to order. Thank you very much for being here. This is one of the afternoons and days that we look forward to, and I will say that the younger people here in front are much better behaved than the older people who usually fill this room, so I really appreciate it. [Laughter.]

As a point of personal privilege, I do want to note the presence of Secretary of War, Edwin Stanton, from the Lincoln cabinet—— [Laughter.]

Oh, no, that is Kevin Kline. [Laughter and applause.]

If you have not seen "The Conspirator," it is an extraordinary movie, and Mr. Kline is really brilliant in the role of Secretary of War Edwin Stanton, so I guess it is not a violation of our Senate ethics rules to plug a good movie of historical content. [Laughter.]

Today, as I have traditionally done, with good cause, I am going to turn the Chairman's gavel over to Senator Collins in recognition of her longstanding leadership on behalf of diabetes research, particularly for children, and her truly passionate advocacy for Federal support for that research. So without further adieu, I give the gavel to my dear friend and colleague, the great Senator from the State of Maine, Susan Collins.

[Applause.]

OPENING STATEMENT OF SENATOR COLLINS

Senator COLLINS [presiding]. Thank you. Thank you so much, Mr. Chairman. I am particularly grateful that you are allowing me to conduct this hearing. This issue is near and dear to my heart, and this actually represents the sixth hearing of the Children's Congress that I have had the privilege to conduct.

I very much appreciate the opportunity to hold this hearing to examine what is often the devastating impact that juvenile diabetes has had on an estimated 3 million American children and their families.

I also want particularly to welcome our distinguished witnesses and the more than 150 children who have traveled to Washington from every State in the country and from around the world to tell Congress exactly what it is like to have diabetes, just how serious it is, and why it is so important that we work together to fund the research necessary to find a cure. I want to give a special welcome to the delegate from Maine, 14-year-old Caroline Jacobs of Shapleigh, Maine. She will be testifying later.

I want to also recognize Senator Shaheen, who has joined us this afternoon, and I think Senator Lautenberg is coming, as well. Both of them have a longstanding commitment to issues affecting children with diabetes and their families. Senator Shaheen is also my co-chairman on the Senate Diabetes Caucus, and her daughter is the "Chair Mom" of this year's Children's Congress. So we are very delighted that she can join us, as well as our colleagues, Senator Akaka and Senator Brown. There will be others coming in and out today. Senators have so many different duties and obligations, but they care a lot about this issue and others will be dropping by, as well.

I do also want to acknowledge someone who is not able to be with us for the first time for the Children's Congress, and that is Mary Tyler Moore. I talked to Mary yesterday, and she sends all of her best wishes. She is recovering from some surgery. She is doing really well, and I know that we miss her, but she is here in spirit. And she is delighted that another famous American, Kevin Kline, is joining us today, so thank you, Mr. Kline, as well.

Diabetes is a life-long condition, and it is one that does not discriminate. It affects people of every age, race, and nationality. It is the leading cause of a lot of medical problems. Moreover, it is estimated that diabetes accounts for more than $174 billion of our Nation's annual health care costs and one out of three Medicare dollars. Medical costs for a child with type 1 diabetes are six times higher than the cost for a child without the disease. These statistics are overwhelming. But what really motivated me to devote so much energy and time to this issue was meeting with families whose lives have been forever changed by diabetes.

I will never forget, as a new Senator in 1997, meeting with a family whose son had diabetes. This was the first time I had really learned about type 1 diabetes, and this little boy looked up to me and said that he wished he could just take one day off from having diabetes, just one day, his birthday or Christmas. But, of course, those who have diabetes can never take a day off. But it does not mean that you cannot accomplish great things, and I am delighted to learn that many of you yesterday had the opportunity to meet with Supreme Court Justice Sonya Sotomayor and hear her personal story.

It is so important that you have traveled to Washington today to tell your stories. You put a human face on all of the statistics, and you help us focus on what Congress can do to better understand and ultimately find a cure for this terrible disease.

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In individuals with type 1 diabetes, the body's immune system attacks the pancreas and destroys the islet cells that produce insulin. An average child with diabetes will have to take more than 50,000 insulin shots in a lifetime. Of particular concern is the fact that the incidence rate of type 1 diabetes is increasing, particularly in children under the age of four. While the discovery of insulin was a landmark breakthrough in the treatment of diabetes, it is not a cure. People with type 1 diabetes face the constant threat of developing life-threatening complications and can face a reduction in their quality of life.

But thankfully, there is some good news. Since I founded the Senate Diabetes Caucus, funding for diabetes research has more than tripled and now it approaches more than $1 billion this year. As a consequence, we have seen some encouraging breakthroughs, and we are on the threshold of a number of important discoveries.

I talked today with several of you who have insulin pumps, for example. Advances in technology, like continuous glucose monitors, are helping people with diabetes control their blood glucose levels, which is key to preventing complications.

We are also moving closer to our goal of an artificial pancreas, which would revolutionize diabetes care. An artificial pancreas is an external device that people with type 1 diabetes could use to do what their bodies cannot, and that is automatically control both high and low blood sugar levels around the clock. This new technology has the potential to dramatically improve the health and quality of life for individuals with diabetes, and we are going to hear from Federal officials today who will tell us about the important clinical trials that are going on that are so promising. The Food and Drug Administration (FDA) has played a pivotal role in moving this research forward and making the artificial pancreas one of its Critical Path Initiatives.

We are making progress in the battle against diabetes, but this is no time to take our foot off the accelerator. We have two choices. We can sit back and continue to pay the bills and endure the suffering, or we can aggressively pursue a national strategy aimed at curing this disease.

And thanks to your efforts, thanks to your coming to Washington, there is increased understanding and support in Congress for diabetes research funding. Last year, we were able to pass legislation to extend the Special Diabetes Program for 2 additional years, and that program represents more than a third of our Federal commitment to diabetes research. As such, it is critical to our efforts to find better treatments, a means of prevention, and ultimately a cure.

So welcome to Washington. We are glad that you are here. Chairman Lieberman, thank you.

[Applause.]

Chairman LIEBERMAN. Thank you, Senator Collins, and really, what I want to say is "amen" to everything you said, so I will be brief.

I said at the beginning that I look forward to these hearings every session, and I do because they are so constructive. In a government in which, too often, too little happens that is constructive these days, this is a cause that unites people across party lines and

has enabled us, certainly in recent years, to come together to be supportive of diabetes research and to help facilitate some of the really miraculous advances that have occurred in dealing with diabetes in our time.

The fact that all you young people are here is the most important thing of all because you are the best advocates for this cause. First off, you show everybody how well you are doing, dealing with diabetes. But the second thing is you make us all want to make the investments that are necessary to make sure that we not only better treat diabetes, but really in your lifetime that we have a cure for diabetes.

It is with that sense of optimism that I am really honored to welcome you and all the other witnesses here today, and I thank Senator Collins.

Senator COLLINS. Thank you, Mr. Chairman. Senator Akaka.

OPENING STATEMENT OF SENATOR AKAKA

Senator AKAKA. Thank you very much, Senator Collins. I deem it an honor to join you here and to say thank you very much for chairing this important hearing again on type 1 diabetes and to share a commitment and really a passion in trying to move this along to improve the lives and quality of life for young people and people of our country.

I also want to welcome our distinguished panelists to this hearing who have been so committed to this issue. I also want to send a very special aloha to those Children's Congress delegates waiting to testify and those in the audience, all of you who are seated here. These are courageous young ambassadors who have traveled from all over the country and the world to educate us. They are here to share their stories of their own experiences, to bring a real human dimension to the policy debate. This shows how critical research and support is for diabetes and a hope for a cure.

Diabetes is a significant health problem in my home State of Hawaii, and it is an increasing challenge for our Nation. It is an issue that we will look at in the Indian Affairs Committee. It will be part of the minority health legislation that I plan to introduce. And it is the subject of the ongoing budget and regulatory policy debate.

In this context, I am proud to support the development of the artificial pancreas, and I will continue to support funding for research at the National Institutes of Health (NIH), which gives us the chance for better detection, better treatment, and the hope for a cure.

All the more reason that I am so pleased to see the children here every 2 years. They remind my colleagues and me about the struggle of living with type 1 diabetes and the importance of supporting diabetes research.

I would like to extend a special thanks to Aaron Tsuchitori, who traveled all the way from Honolulu with his mother to meet with me today. If you are sitting here, Aaron, please just hold your hand up. Oh, there you are. Yes. Thank you, Aaron, for coming all the way from Hawaii.

I look forward to continuing to work with all of you to improve the lives of individuals with diabetes. I am glad to be here with you and join you in this. Thank you very much.

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[Applause.]

Senator COLLINS. Thank you, Senator Akaka. Senator Brown.

OPENING STATEMENT OF SENATOR BROWN

Senator BROWN. Thank you, Madam Chairman and Senator Lieberman. It is good to see you all, and good to see a lot of the children here and their families coming out and supporting diabetes research. I have the honor of having met four young people from Massachusetts, Jackson Savage, Jordan Beals, Jonathan Beals, and Joshua Fish—I see some of them out there in the audience. They gave me a lot of good information. It is something that I have certainly been aware of and our families have been working on long before I got to Washington, so I want to thank you for your leadership in doing it.

I look forward to hearing all of our witnesses. I am going to be bouncing back and forth because of other hearings, but I look forward to staying for as long as I can. Thank you.

Senator COLLINS. Thank you, Senator Brown.

I mentioned that Senator Shaheen is the co-chairman with me of the Diabetes Caucus and has a special connection to this particular Congress, and we are delighted to have you here.

OPENING STATEMENT OF HON. JEANNE SHAHEEN, A U.S. SENATOR FROM THE STATE OF NEW HAMPSHIRE

Senator SHAHEEN. Thank you, Madam Chairman, and thank you to Senator Lieberman, to both of you, for holding this hearing today. I have a statement that I would like to submit for the record.[1]

Senator COLLINS. Without objection.

Senator SHAHEEN. I know we want to get to our panelists, so I just want to take a minute to introduce my granddaughter, Ellie, who is a delegate here with the Children's Congress—thank you—and her mother, Stephanie, and father, Craig, who are here, and they are co-chairing the Children's Congress this year. I also want to recognize Abigail Lore and her mother, Jeanine, who are from Merrimack, New Hampshire. Thank you both for being here, as well. And thank you to all of the families and all of the delegates who are here today.

I am very happy and proud to be able to join you in advocating for research for a cure for juvenile diabetes and also for moving forward as quickly as we can with the development of an artificial pancreas.

So again, thank you all very much for being here.

[Applause.]

Senator COLLINS. Thank you, Senator Shaheen.

Senator Lautenberg, we are delighted that you could join us again this year. I mentioned in my opening statement that you, too, have a personal connection to diabetes and have demonstrated tremendous leadership in this area.

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[1] The prepared statement of Senator Shaheen appears in the Appendix on page 40.

OPENING STATEMENT OF HON. FRANK R. LAUTENBERG, A U.S. SENATOR FROM THE STATE OF NEW JERSEY

Senator LAUTENBERG. I have a granddaughter, also, that I am fortunate enough to have who has diabetes. And I want to say thanks to the Chairman for inviting me here today. It is a personal issue for me, and I appreciate the chance to work with you, Senator Lieberman, but particularly with Senator Collins, our colleague from Maine. She has been so diligent, so persistent, so determined to help our country by making sure that those with diabetes can conduct their lives with a decent attitude and participation in all of the activities.

When my granddaughter was here during the Obama inauguration, I saw that she looked pale. I saw that she seemed tired, 12 years of age, and I said to my daughter, "Is there something wrong with Maddie?" And she said, "I do not think so, Dad, but some signs tell me we have to get her to a doctor." Therefore, they did that, and we visited her in the hospital a day after she got back to Florida, where she lived. She had her first treatment with insulin. She was bright. She was positive. She was hopeful. And I thought, all this devastation that came upon us when we learned that she had diabetes. And I can tell you, that granddaughter of mine is now on a soccer team that was running for the State championship in Florida. She is never too tired to take on an activity.

And she has been an inspiration to my life, just as all of you are an inspiration here. You do not know how much you do for us. You know that we try to do things for you, but you do more for us when we see your faces and we see your smiles and we see your parents, and we know that life is good for you and we are going to keep on working to make it better.

I thank our friends here and all of my colleagues for participating in this important hearing. Thank you, Senator Collins.

[Applause.]

Senator COLLINS. Thank you very much, Senator Lautenberg.

Senator Pryor, welcome.

OPENING STATEMENT OF SENATOR PRYOR

Senator PRYOR. Thank you, and thanks for having me. I think everybody understands this now, but if we do not get it, I want to make sure that everybody understands what a tremendous advocate you have in Senator Collins. Let us give her one more hand. She is great.

[Applause.]

Senator PRYOR. I really just want to say one more thing. I know that Davis Moore from Arkansas is here. Thank you for being here, and all of you who are wearing the blue shirts, you are making a difference. Thank you for coming to Washington, and thank you for fighting the good fight. It is certainly a fight worth fighting, and thank you for all the things you represent and all the great things you are going to accomplish. Thank you.

[Applause.]

Senator COLLINS. Thank you very much, Senator Pryor.

Leading off our first panel this morning is Academy Award winning actor and longtime Juvenile Diabetes Research Foundation (JDRF) advocate Kevin Kline. One of our country's finest film and

stage actors, as Senator Lieberman mentioned, Mr. Kline may have been virtually unrecognizable in his recent appearance as Edwin Stanton, the Secretary of War, in the movie, "The Conspirator," but he is no stranger to us. He testified before our Committee 10 years ago at our 2001 hearing, and I am delighted that he has made a return performance, an encore, I guess I will call it, because I look forward to hearing his perspective on the progress that has been made during the past decade and the road ahead.

So welcome. We are delighted to have you here.

TESTIMONY OF KEVIN KLINE,[1] CELEBRITY ADVOCATE CO-CHAIRMAN, JUVENILE DIABETES RESEARCH FOUNDATION

Mr. KLINE. Senator Collins, thank you. Senator Lieberman, thank you, and thank you for the nice mention of "The Conspirator," and my performance as a historical figure. Members of the Committee, thank you all for inviting me to appear today with this distinguished panel and amidst this collection of such remarkably poised, self-possessed, quiet, but ultimately very vocal delegates, I hope.

Ten years ago, as you mentioned, I had the honor of joining Mary Tyler Moore and the 100-plus delegates at the 2001 JDRF Children's Congress. Since then, I am happy to report that we have made remarkable progress in understanding this disease. We are many steps closer to a cure, and even as we are gathered here today, new tools are being developed to improve the day-to-day management of type 1 diabetes. But we still have a ways to go, which is why we are here now, not only championing the science, but pushing to accelerate programs.

Today, these great young delegates are getting the attention that they so richly deserve. But I would like to take a few moments to recognize all of the parents, siblings, and other special people that these young advocates have brought with them today. They know firsthand the challenges that we face as we shepherd our children and loved ones through life with the added burden of diabetes.

You see, when a child is first diagnosed with type 1 diabetes, the parents are thrust immediately into the additional roles of doctors, nurses, nutritionists, and even psychologists. They are on duty 24 hours a day, 7 days a week, 365 days a year, monitoring their child's blood sugar levels and physical activity, counting the carbohydrates in their meals and snacks, calculating insulin dosages, giving injections, as well as managing the emotional stresses which come from dealing with the daily rigors of this disease.

Each day, as I am sure these children will testify to, brings its own unique challenge to control blood sugar levels, even with the best of plans and the use of the latest technology. It is not unusual for parents to wake up routinely in the middle of the night to check their children's blood sugar to make sure it did not become too high or so low as to result in a seizure or a coma or worse. These blood sugar emergencies are all too common, and a number of parents here have had to call 911 to save their children's lives.

Many parents have become their children's advocates in the fight to cure diabetes by joining JDRF. As JDRF's National Walk Chair-

[1] The prepared statement of Mr. Kline appears in the Appendix on page 42.

person, I had the great pleasure of rallying people across the country to join the JDRF Walk to Cure Diabetes, and I am happy to report that thanks to the outpouring of enthusiastic support, we have raised millions of dollars with the walk. JDRF has put this money to work in a direct and efficient manner to support research for better treatments, prevention, and ultimately for a cure for type 1 diabetes.

The Federal Government has also played a critical role in the fight to cure diabetes, in particular with the strong bipartisan support for the Special Diabetes Program. I thank you, Senator Collins, for your leadership, and I thank your colleagues in the Senate and House who recognized the great return on investment from the Special Diabetes Program and who supported the 2-year $300 million extension this past December.

Together, JDRF and the Federal Government have made and will continue to make powerful partners in advancing research to cure, treat, and prevent type 1 diabetes.

Since I testified here before this panel 10 years ago, more than 40 of the genes have been discovered which put people at risk for type 1 diabetes. Numerous therapies to halt the autoimmune attack which causes type 1 diabetes are being tested in human clinical trials. New therapies have also been shown not only to halt the progression of diabetic eye disease, but also to improve the vision in those who already suffer from it. And finally, the artificial pancreas has gone from being merely a theory to a cutting-edge technology that has been shown in early trials to prevent dangerous low and high blood sugars.

Apart from finding a cure, the artificial pancreas represents a watershed moment in the management of diabetes and happens to also be a parent's dream come true. Imagine, if you will, going to bed at night without having to worry about dangerous nighttime high or low blood sugar levels, or knowing that your child will have a great day at school without the burden of pricking his or her fingers, counting carbohydrates, taking the right amount of insulin, and treating high and low blood sugars, or just getting so caught up in being a kid and forgetting to do some of these things and coming home from school dangerously ill. Best of all, imagine knowing that your child will live a long, productive life since these artificial pancreas technologies have the potential to keep him or her healthier longer, forestalling or completely circumventing the devastating complications until a cure is found.

I know the Food and Drug Administration has made the artificial pancreas a priority, and I commend Commissioner Margaret Hamburg for her leadership. But there is more that the FDA needs to do. Many of these children here today are, in fact, wearing the components of what will ultimately constitute an artificial pancreas, namely, insulin pumps that deliver insulin as well as continuous glucose monitors which give blood sugar readouts every few minutes. The challenge that we face now, however, is to get these devices, which do not yet work together automatically, to talk to each other and to control the blood sugar levels.

In other countries, there are devices now available that take the first step in this process, by automatically shutting off the insulin

pump when someone is going low. This is an important step and one that we need to take in the United States right now.

And we can do more than that. JDRF and federally funded research have, in hospital settings, tested artificial pancreas technologies that automatically turn insulin both on and off, and the results have been overwhelmingly positive. The next step is testing these artificial pancreas devices in real-world settings. To do this without delay, however, the FDA needs to provide clear and reasonable guidance. Many of the world's best diabetes researchers and leading clinician organizations have joined together with JDRF to propose artificial pancreas guidance to the FDA, and the majority of the Senate and the House have urged the FDA to give this proposal immediate consideration.

We now need the FDA to act. Parents who are up every night and worrying every day about their children simply cannot afford to wait any longer. It is past time for the artificial pancreas technologies to be tested in real-world settings. We urge, we implore the FDA to issue draft guidance for public comment on the artificial pancreas so that outpatient trials can begin and the oppressive burdens of type 1 diabetes can be lifted from millions of Americans as soon as possible.

Thank you for the opportunity to participate in the hearing today, and I would be pleased to answer any questions that I can.

[Applause.]

Senator COLLINS. Thank you very much for that excellent testimony, Mr. Kline.

Next, we will hear from Dr. Griffin Rodgers, who is the Director of the National Institute of Diabetes and Digestive and Kidney Diseases at NIH. He will bring us up to date on the advances in research, and I also hope that he will provide some examples of the research that is specifically supported by the Special Diabetes Program. Dr. Rodgers, welcome.

TESTIMONY OF GRIFFIN P. RODGERS, M.D.,[1] DIRECTOR, NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. RODGERS. Thank you very much. Mr. Chairman, Senator Collins, and Members of the Committee, as the Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), I thank you for the invitation to testify at this hearing on type 1 diabetes.

And on behalf of NIDDK and the other institutes and centers at NIH, I am pleased to report that we are vigorously pursuing research to prevent, treat, and ultimately cure type 1 diabetes and its complications. Through collaborative and coordinated research efforts with our partners, including the Juvenile Diabetes Research Foundation, and with the support of the Special Statutory Funding Program for Type 1 Diabetes Research, we are making critical steps toward these goals that I have outlined.

Now, before I highlight some of the exciting advances, I would like to acknowledge the important contribution of my fellow wit-

[1] The prepared statement of Dr. Rodgers appears in the Appendix on page 44.

nesses. Mary Tyler Moore, here in spirit, you continue to motivate us with your unwavering devotion to improve the lives of others with type 1 diabetes.

Kevin Kline, you tirelessly raise awareness of the disease and promote efforts toward a cure.

I am also pleased to share the table today with Dr. Zimliki, who will describe the complementary efforts of the FDA to advance the artificial pancreas.

I would also like to acknowledge the children, parents, and families who will testify and who sit in this room proudly representing their States and the many other Americans with type 1 diabetes. Many of you have participated in clinical trials to help improve diabetes care, not only for yourself, but for future generations. We are inspired by your dedicated efforts and your enthusiasm.

Now, research in type 1 diabetes has made a tremendous impact on the health and quality of life of people with this disease. I will reference three handouts during my testimony to illustrate these points, and these handouts are attached to the copies of my written testimony.[1]

On the first handout, a bar graph shows that the survival rate for people with type 1 diabetes has dramatically improved over time. For people diagnosed, for example, in the 1950s, represented by the blue bar on the far left side of the graph, only about 70 percent survived for 25 years with the disease. This number has dramatically increased to about 95 percent for people diagnosed in the 1970s, represented by the purple bars on the far right side of the graph. The outlook is even brighter for today's children, due to improvements in diabetes care and technologies. Still, the burden of living with diabetes, as my colleagues have mentioned, is enormous, and so it is critical to build on research progress to find ways to prevent and cure the disease.

On the second handout, you will see that even before type 1 diabetes becomes apparent, the immune systems of people who will develop the disease are destroying their insulin-producing beta cells, leading to a decrease in beta cell mass, and I will describe how the NIH is focusing our research on different stages of the disease progression.

Now, as indicated on the far left of this graph, understanding the causes of type 1 diabetes is essential to our preventing the onset of autoimmunity, a preclinical sign of the disease, and of the disease itself, and significant progress has been made in unraveling the genetic causes of type 1 diabetes. As was mentioned, just a few years ago, we only had three genes that we understood contributed to the risk of the disease. Today, due to the efforts of the Type 1 Diabetes Genetics Consortium and other researchers, nearly 50 genetic regions have been identified.

We know that there are likely factors that exist in the environment that interact with these genetics to turn disease risk into disease reality. And because the genetic risk for type 1 diabetes is now well characterized, we can identify those at risk and follow them, and this has allowed us to embark on a bold, long-term, systematic study to identify these environmental factors.

[1] The charts referenced by Dr. Rodgers appear in the Appendix on page 61.

This study, the Environmental Determinants of Diabetes in the Young (TEDDY), has enrolled over 8,600 newborns with high genetic risk for the disease, and we plan to follow them for 15 years. We will be collecting biological samples and information about their lives. Identification, for example, of an infectious agent that triggers this autoimmunity could lead to a vaccine to protect against this disorder. On the other hand, if we find that dietary factors protect from or contribute to the development of the disease, we can recommend changes to infant feeding practices. TEDDY may also shed light on other autoimmune diseases, like celiac disease.

The NIH also supports research in preclinical and early disease stages, as shown by the blue and red arrows. Today, blood tests can accurately identify relatives of people with type 1 diabetes who are at high or moderate risk of developing the disease within 5 years. This important advance has enabled Type 1 Diabetes TrialNet to launch clinical trials of promising prevention strategies to stop the autoimmune attack.

It is also important to identify ways to halt or reverse disease progression soon after onset to preserve any remaining beta cells. In collaboration with the Immune Tolerance Network, TrialNet is also conducting trials of promising therapies in newly diagnosed patients.

Now, the third handout continues along the spectrum of disease progression, and this next stage of the disease research, shown in green, focuses on people with established type 1 diabetes. A high priority for research at this stage is the development of new tools and technology to help people improve their blood glucose control because that can reduce disease complication by up to 70 percent. Certainly, an artificial pancreas to automatically link glucose monitoring with insulin delivery can make a positive impact on people's health and their quality of life. NIDDK is supporting innovations in technology critical to the development of an artificial pancreas. Working closely with our partners at the FDA, we are pursuing research to test artificial pancreas technology and ensure that it is safe and effective.

In recent advances, scientists developed and are testing a bi-hormonal closed-loop artificial pancreas, one that delivers not only insulin, but a counterbalancing hormone, glucagon, to more finely reproduce the activity of the human pancreas. In another recent study, researchers looked at overnight closed-loop insulin delivery following two different real-life dinner scenarios. Testing closed-loop technologies in real-life situations is really a key step toward moving this technology out of the clinic and into the real world.

A major goal of research at the next stage, shown in purple, is to investigate ways to replace the destroyed beta cells and restore beta cell function, and one approach to replace these cells is through islet transplantation, and the Clinical Islet Transplantation Consortium is conducting trials to study and to refine this therapeutic strategy. Scientists like those in the Beta Cell Biology Consortium are also pursuing strategies to replace islet cells by growing cells in the laboratory for transplantation into people or by expanding their remaining beta cells or by coaxing other types of cells in the pancreas to become beta cells.

Finally, until prevention or cure of type 1 diabetes is possible, research toward preventing, arresting, and reversing the complications of the disease is critically important, shown on the far right of that graph. Just recently, we saw the biggest advance in diabetes eye disease treatment in 25 years. A landmark study from the Diabetic Retinopathy Clinical Research Network found that patients who received a combination of a drug and standard laser therapy showed substantial vision improvement after 1 year. Advances like these in treating diabetic complications also benefit patients who have type 2 diabetes and are at risk of these complications, as well.

Hundreds of thousands of individuals have participated in research supported by the Special Diabetes Program. Remarkably, nearly 30 years after one pivotal trial study began, about 95 percent of the participants in this landmark trial, which showed that glucose control dramatically reduced type 1 diabetes complications, continue to participate in a follow-up study known as Epidemiology of Diabetes Interventions and Complications (EDIC), and as a result of their commitment, this long-term investment in research continues to identify ways to improve the health of people with diabetes.

I am grateful for the opportunity to share with you just a few examples of the many recent advances in ongoing research in type 1 diabetes. We continue to be inspired by the dedicated efforts of individuals affected by type 1 diabetes and by the organizations like JDRF that represent them. We look forward to continuing our partnership with JDRF and our sister Federal agencies on research to combat type 1 diabetes and its complications, and we will continue to be diligent in our fight against type 1 diabetes to help all the children here and the many Americans whom they represent today, and we will strive to improve their quality of life with the ultimate goal of curing this disease.

Thank you, Mr. Chairman and Senator Collins, for your leadership in calling for this hearing to continue to bring attention to the importance of type 1 diabetes research and for your continued support of NIH research. I will be pleased to answer any questions that you might have.

[Applause.]

Senator COLLINS. Thank you, Dr. Rodgers.

Our last witness on this panel, before we hear from the children, is Dr. Charles Zimliki. He is the Chairman of the Food and Drug Administration's Artificial Pancreas Critical Path Initiative. There is tremendous interest and excitement about this research and technology, and I look forward to hearing your statement.

TESTIMONY OF CHARLES ZIMLIKI, PH.D.,[1] CHAIRMAN, ARTIFICIAL PANCREAS CRITICAL PATH INITIATIVE, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. ZIMLIKI. Well, I share that excitement, as well. Madam Chairman and Members of the Committee, I am Dr. Chip Zimliki,

[1] The prepared statement of Dr. Zimliki appears in the Appendix on page 64.

Chairman of the Artificial Pancreas Critical Path Initiative, located within the Center for Devices and Radiological Health at the FDA.

I would like to thank the Committee for the opportunity to discuss the artificial pancreas system and what the FDA is doing to assist in the development of these critically needed and potentially life-changing devices. As a person living with type 1 diabetes, I am personally and professionally committed to seeing this important, novel medical device approved in the United States.

And I just want to go offline here and say, Mr. Kline, I fully support the proposal about issuing guidance, and I believe the FDA will submit guidance for all types of artificial pancreas systems before December of this year.

[Applause.]

Dr. ZIMLIKI. Diabetes is a disease that affects the entire family, especially when a child is diagnosed. I know this because I was diagnosed with diabetes when I was 13 years old. When I was diagnosed, the technology was a great deal different. They were just coming out with glucose meters, and it took much longer than it does today to obtain a blood glucose measurement. Technology has come a long way, and I am very grateful for that.

But even now, with today's technology, we still must prick our fingers to test our blood multiple times a day, and over time, it can really hurt. I am sure the children here can attest to that. We must also calculate insulin doses, administer necessary insulin via syringes or infusion pumps in order to lower blood glucose, and, as always, we have to be prepared for the inevitable lows and highs associated with diabetes. I admit, it is really tough being a diabetic.

While great strides have been made in diabetes management, current treatment is constant and pervades all aspects of a person's life, presenting a particularly arduous burden for children and their parents. An artificial pancreas system is an innovative device for treatment of type 1 diabetes that, once fully developed, will automatically monitor blood glucose and administer appropriate insulin doses. This life-changing technology will positively impact diabetic patients' health and quality of life.

As a person with diabetes, I am acutely aware of the benefits an artificial pancreas system will provide. I say "will" because I am highly optimistic that industry, researchers, and the FDA will bring this device to market. An artificial pancreas system will allow people with diabetes, especially children, to live active lives without the constant need to adjust glucose levels.

While I know the potential benefits are enormous, an artificial pancreas system is a significant risk device, meaning it presents a potential for serious risk to the health, safety, or welfare of the patient. If not properly designed, use of an artificial pancreas device in an outpatient setting can place patients at significant risk because the device controls the administration of insulin. As such, an Investigational Device Exemption (IDE) from the FDA is needed to allow the investigational device to be used in a clinical study.

Currently, the FDA has approved over 17 clinical studies for artificial pancreas systems at various levels of development, and we have seen promising results. The FDA is helping advance the development of an artificial pancreas system by prioritizing the re-

view of IDE studies, fostering discussion, shortening study and review times, and providing clear guidelines and a path to market for industry.

In 2007, the FDA created the Artificial Pancreas Critical Path Initiative, bringing together a multi-disciplinary group of scientists and clinicians from the FDA and NIH. One of the major goals of this initiative is to identify roadblocks and possible solutions to streamline the regulatory process. A shining example of this effort was how the FDA worked with the developer of a software program so that researchers working on an artificial pancreas system could test control algorithms and use the results in support of regulatory submissions. This important software tool enables researchers to quickly test artificial pancreas control algorithms and is accepted in place of costly and time-consuming animal studies. This effort saved investigators 6 months to a year in clinical study time and expedited the transition to human trials.

The FDA also encourages researchers to contact the agency early to discuss clinical study plans and get informal feedback that can improve their study designs and facilitate the review process. This quick, informal feedback can help investigators develop better and more complete study plans for the FDA review. When investigators submit their final study plan, the FDA gives these submissions the highest priority and works interactively with investigators to move them quickly and efficiently through the review process. Questions and research challenges are often quickly resolved, helping researchers start their study sooner.

The FDA guidance and industry standards help manufacturers and researchers understand the minimum requirements for making a device that is safe and effective. This helps them make the best use of resources and streamlines the regulatory review process. We agree with JDRF and others that guidance to industry is useful for product development.

On June 22, 2011, the FDA issued draft guidance that will help advance the development and approval of an artificial pancreas system to treat type 1 diabetes in the United States. This guidance document addresses an early version of an artificial pancreas system known as a Low Glucose Suspend (LGS) system. The LGS system can help reduce or lessen the severity of hypoglycemia by temporarily reducing or stopping delivery of insulin. Patients using this kind of system still must test their glucose levels on a regular basis with a glucose meter and give themselves insulin. The draft guidance provides recommendations for those planning to develop and submit for FDA approval an application for an LGS system.

The FDA is also seeking input from industry, researchers, and the clinical community on the draft LGS guidance. Specifically, the agency is interested in feedback about the types of clinical studies that should be conducted and what their target outcomes should be to demonstrate safety and effectiveness. Your input is also very welcome.

The FDA is also working on the second draft guidance, as I discussed. The FDA has been working with research communities, such as JDRF, to expedite this guidance, and we have promised the publication of the draft guidance by the end of this year.

Finally, the FDA is working with NIH and other interested parties in planning the next artificial pancreas workshop, which will focus on developing better technology for creation of a more accurate and reliable artificial pancreas system. This is the system that you can just put on and not worry about. I cannot wait for that day.

The FDA is fully committed to the development of an artificial pancreas to meet this critical health need. It is the goal of the agency to provide a clear pathway for manufacturers to provide people with diabetes with innovative, safe, and effective medical devices to treat their disease.

Madam Chairman, this concludes my formal remarks, and I will be pleased to answer any questions the Committee may have.

Senator COLLINS. Thank you, Dr. Zimliki.

[Applause.]

Senator COLLINS. Thank you so much for your testimony.

We are going to do a 6-minute round of questions so that we can get to the next panel. We could keep you here all day.

Dr. Zimliki, it is great news that you have given us today, and I saw the guidance on Monday about the draft guidance. In early May, 59 of us signed a letter that I spearheaded that encouraged the FDA to move forward with issuing guidance that would enable clinical trials for testing the artificial pancreas to move from an inpatient to an outpatient basis. Does this guidance help us along to achieve that goal of moving to the outpatient guidance?

Dr. ZIMLIKI. Yes, indeed, it does. This is the complete package guidance. This will help academicians start their investigations, get them approval for the clinical studies in the in-clinic, and it outlines what type of information the FDA needs to assure safety as we transition from the in-clinic to the outpatient settings.

Senator COLLINS. And on a related question for you, I have heard—and there are some delegates from Canada here today—that the Low Glucose Suspend system technology is available now in Canada and other parts of the world. Could you explain to us, and I am not trying to put you on the hot seat—well, maybe I am trying to put you on the hot seat—— [Laughter.]

But why is it not available here if it is available next door in Canada?

Dr. ZIMLIKI. Well, it is hard to draw comparisons across the various regulatory agencies around the world. The FDA has to operate within U.S. law, which states medical devices must be safe and effective.

I will give you an example. The European Union's law states that medical devices need to be safe and perform. That might not sound like a big difference, but there is a significant difference between the two, and I will use the Veo system as the example. This is going to be a long answer, I am sorry, Senator Collins.

The Veo system shuts off insulin when the continuing glucose monitoring (CGM) value is low. To evaluate the performance of that, all you need to do is show that the insulin pump shuts off when the sensor reads low. That is a perfect engineering question that can easily be tested on the bench side. The FDA agrees that type of performance is needed.

But what the FDA also needs for effectiveness is to know what happens to the patient when the pump actually turns off. That information is critical because it allows the prescribing clinician to look at the information that is provided in that clinical study and determine whether or not the patient can use this device beneficially.

With regard to the Veo system, I will say Medtronic and the FDA have been continually working together. The Aspire study is an ongoing study to provide sufficient safety data within the United States, and it is the hope of the FDA that this safety data will allow the transition to an outpatient setting and finally approval of that device.

Senator COLLINS. Thank you.

Dr. Rodgers, last year, Congress passed legislation extending the funding for the Special Diabetes Program through September 2013. How important is it for Congress to do multiple years as opposed to year-to-year renewals of funding? Does that have an impact on the kinds of studies that you can fund?

Dr. RODGERS. Well, Senator, we were very pleased to receive that multi-year renewal of the Special Diabetes Program through fiscal year 2013. The multi-year renewal greatly improves the planning process that goes on in NIDDK. For example, many clinical studies take multiple years to perform, and it would be very difficult, if not impossible, to start such a multi-year clinical trial without knowledge of whether the funds will exist in future years to continue those types of studies.

One area that we are absolutely looking at is to bring new people and new talent into this field. For example, in the artificial pancreas field, we have obviously very dedicated and talented clinicians and we have people in the device industry, but what needs to link them or, as my colleague Mr. Kline says, to actually get them to talk together are bioengineers. And so with this multi-year funding, we are trying to put in training efforts to bring bioengineers into this field, and training occurs over long time horizons, and therefore, multi-year funding is also critically important for them.

One final thing that I would say is that as we move toward the artificial pancreas, clearly, we would recognize that there might be some issues related to compliance, and so now we are trying to get people who have been previously engaged in behavioral science to tell us what particular challenges we might face, and we are trying to get them involved in research in diabetes. So training and bringing in new talent are critically important, and multi-year funding greatly assists in that regard.

Senator COLLINS. Thank you.

Mr. Kline, you mentioned in your statement that when there is a diagnosis of type 1 diabetes, it affects the whole family and involves the whole family. You also talked about the fact that there are different challenges at different ages. Could you, having lived with this for quite some time now, elaborate on the impact on the family and the challenges at different ages, from toddler to teenager?

Mr. KLINE. Well, it affects the entire family. It transforms the entire family, and it changes with age and the various vicissitudes

that the disease can go through. Suddenly, in the teenage years with the hormones being what they are, there are chaotic glucose levels.

Senator COLLINS. People are agreeing.

Mr. KLINE. And it is just a vast improvisation of figuring out how to react to this. Is this a real high number or is this the hormones? It is not unlike life that way, I guess, trying to find what is the absolute cause for any particular symptom.

But, obviously, when a child is diagnosed at 6 months, he cannot tell you that he is feeling low or feeling high. It is too horrible to imagine. It does get easier. All things being relative and given our human nature and our marvelous adaptability, we can adapt to a surprising number of things. Children get more and more used to it, get more and more on top of it, depending on the nature of the child. There are some type A personalities who are just all over their diabetes and are really in control of it, and there are others who are more in denial of it, who do not want to be bothered with it, who want those days of not having diabetes that you spoke of earlier, just one day, and sometimes they will just take that day, even though it is not an officially appointed day for such behavior. [Laughter.]

But they will take it upon themselves and havoc will be wreaked.

It gets easier and harder, but most of all, it does not stop. When your child gets older, goes off to college, you are still calling incessantly. You are still checking up. You are still worried. You are still making trips at strange hours of the night to deal with sudden insulin emergencies. It is moment to moment, hour by hour, day to day. It is ongoing, which is, I think, why JDRF wants to stress the urgency and the need to keep the research going and to get the artificial pancreas done because, I think, as these marvelous children can attest, tomorrow is going to be here sooner than we would like and we would like to have the artificial pancreas tomorrow, please, or yesterday, or today.

Senator COLLINS. Thank you. Senator Brown.

[Lights go out.]

Senator BROWN. That happens regularly with me. [Laughter.]

It is a conspiracy.

Mr. KLINE. I guess we have not paid our electric bill.

Senator COLLINS. You are not in Massachusetts, so I do not know why this happened.

Senator BROWN. It is following me everywhere.

Mr. KLINE. I asked for that. It is a very dramatic device called blackout. [Laughter.]

Senator COLLINS. That was very dramatic.

Mr. KLINE. Thank you.

[Laughter and applause.]

Mr. KLINE. That is what this button is.

Senator COLLINS. That was a good stage trick, Mr. Kline. [Laughter.]

Senator BROWN. That was perfect.

Mr. KLINE. How do you follow that?

Senator BROWN. Everyone is awake now. [Laughter.]

Mr. Kline, thank you very much for coming and offering your star power to a cause such as this. I think everybody I know has

some type of experience with diabetes, whether it is in their own family or with their friends, so we really would like to just thank you for taking time out of your schedule. I think we all respect your acting ability and what you also do with philanthropic causes, so thank you.

Dr. Zimliki, I have 225 medical device companies in Massachusetts. I visited Medtronic and others, and the biggest challenge is the fact that there is a tremendous amount of delay and inefficiency within the FDA. I have met with Commissioner Hamburg, and I will say that she recognizes that problem, and she is making great efforts to try to streamline, consolidate, and eliminate a lot of that duplication. The No. 1 issue I find in Massachusetts and as I travel throughout the country is you have a company that is trying to make a difference for people like this, and they are marching along with a checklist, and then in the middle of the checklist, they have to go back to square one at tremendous cost. And I look at those medical devices that are approved in Ireland and Canada, and our companies are saying to me, as their U.S. Senator, why are we not being approved here in Massachusetts and in the United States?

[Applause.]

Senator BROWN. So on the one hand, I have been very critical of the FDA and its delay because there needs to be consistency, stability, and certainty in the process for development and the ability to find cures.

On the other hand, I have also been very public in saying "thank you" to her and the agency for finally realizing that there is a problem and trying to fix it. So I wanted to let you know that, and I am wondering, how are you finding the new leadership and that new process? Is it moving along as expeditiously as you would like? It is a softball. [Laughter.]

Dr. ZIMLIKI. And I am due for promotion, too. [Laughter.]

Senator BROWN. Well, go for it.

Dr. ZIMLIKI. Absolutely. [Laughter.]

Yes, absolutely. We have new leadership, and Dr. Jeffrey Shuren has certainly said that there is room for improvement for the review process by increasing predictability, consistency, and transparency. There is an entire action plan in place regarding the improvements in the review process.

My focus here today is about the artificial pancreas, and I am very happy and pleased to know that Dr. Hamburg and Dr. Shuren give me their fullest support, and we are going to make sure that this device gets approved. We are hopeful that this guidance improves transparency so that a company like you referenced does not go halfway through the development process and then have to start back at square one.

Senator BROWN. Right. Well, thank you. It is a tremendous job killer in my State and throughout the country.

I think you stated that you want a device that performs precisely, reliably, and individually as a unit. What steps are you taking to ensure the quality and safety of these systems in the clinical trials, specifically in your Phase II guidance?

Dr. ZIMLIKI. Just give me one second here.

Senator BROWN. You thought you were going to get easy questions.

Dr. ZIMLIKI. The Phase II guidance will adopt some of the information from JDRF. Now, granted, the Phase II guidance, which I will call the more advanced artificial pancreas guidance, is using some of the information that the clinical panel's recommendation by JDRF submitted to the FDA. It is a three-phased approach, and the idea would be to understand the device in the clinic, then transition into a more realistic version of home life except under mitigation or supervision, such as a diabetes camp. I am sure most of these people here have been to a diabetes camp, is that correct?

[Chorus of yes.]

Dr. ZIMLIKI. Thank you. I like it, too. Then the last phase would be the transition to the outpatient setting. That is consistent with the recommendations from the JDRF as well as most of the medical community.

The guidance is still under development, and we are going to be finalizing and publishing it in December of this year.

Senator BROWN. Dr. Rodgers, what is NIH's current role in supporting the FDA in this process in terms of how do you foresee NIH's role changing in the current months, and will you be facilitating the transition to clinical trials with the translational research?

Dr. RODGERS. Yes. Under the auspices of the Diabetes Mellitus Interagency Coordinating Committee, we regularly meet with not only our colleagues at the FDA, the Centers for Disease Control and Prevenion (CDC), and other Federal agencies, but other institutes within NIH that have a role to play in diabetes research. We work very closely with Dr. Zimliki and his colleagues in an Interagency Artificial Pancreas Working Group.

In fact, just a few months ago, we held a meeting in conjunction with the JDRF, and we are actually planning to have a follow-on meeting in the fall of this year to develop a working understanding of what are some of the challenges, what are the other groups that we need to bring into the question, particularly bioengineers, mathematicians, theoreticians, to try to assist us in moving more expeditiously along this pathway.

So we have an essential role. We have been working together very closely. This is not only with the FDA and the NIH, but the meeting in the fall of this year will also involve the JDRF, as well.

Senator BROWN. Very well. Madam Chairman, you surprise me more and more each day. I was not aware until this year that you were advocating for this cause, so thank you for that. Will there be an opportunity to submit questions to our panel members?

Senator COLLINS. Absolutely.

Senator BROWN. I just want to say, also, thank you to our panel and all the parents and children who came. It means a lot. I am going to be bouncing back and forth as I have done, so I will try to get back for the children. Thanks.

Senator COLLINS. Thank you. Senator Shaheen.

Senator SHAHEEN. Thank you, Madam Chairman, and thank you to all of our panelists this afternoon.

Dr. Zimliki, as you are aware, I share the frustration that both Senator Collins and Senator Brown have expressed about the pace

at which the FDA has moved on getting the guidance out on the artificial pancreas. I am pleased to hear you say that you expect that to happen by December, but I wonder if you could then outline what the next steps are once that happens, on the way to getting approval for the artificial pancreas.

Dr. ZIMLIKI. Can you clarify which artificial pancreas type system you are asking about?

Senator SHAHEEN. I know there are a number of those systems in development——

Dr. ZIMLIKI. Right.

Senator SHAHEEN [continuing]. And I am interested in seeing something that can be commercially available, on the market, that will be approved by the FDA and be safe and available to my family and all the families who are here. And I do not particularly care who the producer of that system is.

Dr. ZIMLIKI. I was just asking for clarification on the type. There are many types of artificial pancreas systems. We talk about the Veo system, which is a Low Glucose Suspend system. The agency believes that this is a type of artificial pancreas that should be on the market sooner than later.

Senator SHAHEEN. I appreciate that. I think for many of the people in this audience, they do not see that as the artificial pancreas that we are really hoping will be on the market. I agree, that is a step in the right direction, but as has been pointed out, that device is available on the market in other countries, and we would like to see not only that device available here, but to go to the next step, to have a continuous system available for people.

Dr. ZIMLIKI. Is the question that you would like to know the time line?

Senator SHAHEEN. I would like to know what steps the FDA sees that it is going to require in order to move forward. You said you expect to see draft guidance on that by December. So then what happens? I wonder if you could just outline the steps.

Dr. ZIMLIKI. The draft guidance is out for public comment for anywhere between 60 and 90 days, and we look forward to all the comments from the scientific community to help shape and modify that guidance in the hopes of making it final. It will become a guideline to an approval package.

Now, the timing and the ability to get a device approved depends on a lot of people. It really depends on the FDA being transparent and providing this guidance so that industry can follow it and actually conduct studies. That takes time, and it takes people like you out here in the blue shirts to volunteer and be part of these studies.

The process is that by probably mid-year or next year, the guidance will be finalized. Even when it is not finalized but published in December, industry can start developing their process in getting to an outpatient study and a pivotal study, which will lead to an approval.

In November 2010, I believe, one of the JDRF-sponsored investigators at our Artificial Pancreas Workshop estimated anywhere between 2013 and 2014 before getting to a pivotal study. There is a lot of information that needs to be built up to get to that final stage for product approval, and it is contingent on the research for

glucose sensing. We need better sensors. We absolutely need more reliable continuous glucose monitor sensors, and we need the research to really find out how to make that happen.

Senator SHAHEEN. Dr. Rodgers, you talked about the role that NIH has with the FDA. Can you talk about how NIH can be helpful in moving this process forward.

Dr. RODGERS. Well, Senator, in addition to working on a collaborative and coordinating basis, some of the vital research that Dr. Zimliki is mentioning is something that we see as our major contribution in moving the process forward and making it in fairly reliable and practical steps. Just recently, as I had mentioned, for example, in a closed-loop system, not only using insulin, but to try to more closely replicate what the pancreas does, scientists who we funded used two hormones, both insulin and the counter-regulatory hormone glucagon, to see whether one could get more precise blood glucose control over time. But again, these are done in a clinical setting.

Ultimately, for this to be effective in the real world, we have to try to replicate that to a great extent, and this is why the more recent studies are actually looking at two different meal scenarios, particularly at night, because that would be a critical step, if we could use this closed-loop system so that parents do not have to get up in the middle of the night to check their child's blood glucose. That would really be an enormous benefit. For example, these two scenarios, one was an eat-in scenario in which one ate a modest medium-sized meal to see how well the closed-loop system could look at the various levels of glucose control and how that occurred over the night setting. The second scenario was an eat-out, so you go out and replicate more of a larger meal that you would have if you were to go out dining and how well were you able to maintain that level of glucose control.

These are both very basic investigations that we are hoping to do, but then, in addition, the more practical, real-life scenarios, and moving this research forward from the clinic to the bedside.

Senator SHAHEEN. Thank you. Madam Chairman, my time is up, but I wonder if you would allow me to just ask Mr. Kline one question.

Senator COLLINS. Sure.

Senator SHAHEEN. Thank you very much, Mr. Kline, for being here and for being willing to testify on what we need to do. If you had one comment that you could leave with policymakers after today's hearing, what would it be? What would you like us to take away from this hearing?

Mr. KLINE. Well, I love the questions that you are posing because they are asking in simple language to explain what the steps are because so many things get lost along the way in the byzantine labyrinthine hallways of bureaucracy. I love that you are asking for a timetable and for really simple explanations of when this will happen and what needs to happen in order to get the artificial pancreas that will alleviate for these children and for type 1 diabetics around the world the constant burden of self-monitoring, something that will effectively work as a pancreas works and doles out the appropriate amounts of insulin and glucagon and takes the worry out of the constant vigilance that type 1 diabetics have to practice.

Senator SHAHEEN. Thank you. Thank you all very much.

Mr. KLINE. Thank you.

Senator COLLINS. Thank you. Senator Pryor.

Senator PRYOR. Thank you, Madam Chairman.

I would like to start with you, Dr. Zimliki. You have given us great news on the artificial pancreas. You have said some really positive, encouraging things about it, but another question that I do not think I have heard yet is will it be affordable for the average household? Tell us what you anticipate. What is your expectation on cost?

Dr. ZIMLIKI. I wish I could give you that answer. The FDA does not focus on cost. We work on getting the product approved. I will say that we are collaborating with the Centers for Medicare and Medicaid Services (CMS) for reimbursement, and the hope is that one day, not only will the study design I mentioned earlier provide approval for marketing within the United States, but also for CMS reimbursement.

Senator PRYOR. You mentioned that there are several models that may be headed to the marketplace?

Dr. ZIMLIKI. Several types of artificial pancreas systems? Yes.

Senator PRYOR. Do you anticipate that they will all be approximately the same cost, or will there be a big cost disparity?

Dr. ZIMLIKI. Again, I would have to defer to industry, which sets these prices. I apologize, but I cannot provide an answer to that question.

Senator PRYOR. So as part of your process, though, you do not really look at the cost?

Dr. ZIMLIKI. The FDA looks at the safety and effectiveness of the device.

Senator PRYOR. Well, we will have to work through the cost, maybe in another setting, but thank you for that answer.

Dr. Rodgers, let me ask you, if I may, how does the United States compare to other countries when it comes to diabetes research and treatment? Are we leading the world? Are we behind? How do we rank?

Dr. RODGERS. I think the research that is conducted in the United States really does lead the world. I think we can be proud of, in particular, NIH-sponsored research, as well as research that is sponsored by public groups. In diabetes, in particular, we are making great strides in understanding the genetic susceptibility.

As I mentioned, in type 1 diabetes, just a few years ago, we had three genes, now it is up to 50, and we know that among these 50, for example, there is a small number of genes that contribute a large amount of the genetic risk, and there is a large number of genes that have only a small component.

In this country, for the first time, and as a direct result of the Special Statutory Funding, we are beginning to see now that the incidence rate of this disease is increasing at an earlier age. We have to assume that over this period of time, it really is not the genes that are changing, but it is actually something in the environment. That is why it is critically important to undertake bold studies to determine what these factors are in the environment that are contributing to accentuating or initiating that autoimmune attack.

And this is why this TEDDY study that I reference in my comments really is going to provide us with a lot of information. Early on, we are using new technologies, for example, the human micro biome, in which we are looking at these samples that we are collecting from these children over time, and it is already giving us information about potential viruses, bacteria, or other agents that they are exposed to.

Although we are not focusing on type 2 diabetes, the story is quite similar. Just a few years ago, we just had a few number of genes. Now we are up to 60 or 70 genes that explain type 2 diabetes. We are seeing that understanding a lot more about type 1 diabetes is really contributing to prevention, potentially treatment, of type 2 diabetes, as well, which contributes to that $174 billion annual cost that Senator Collins referenced in her opening statement.

Senator PRYOR. So as we do research in the United States, we are sharing that with the world and others are benefiting from that research, as well?

Dr. RODGERS. Yes. Certainly, our investigators' work that is performed and funded through the NIH is made publicly available so that others can potentially mine the data and ask other promising questions. This is how one can really leverage the investments to get the greatest return on one's investment.

Senator PRYOR. And have we not designated a certain amount of funding or a percentage of funding to NIH specifically for diabetes research?

Dr. RODGERS. Well, obviously, the Special Statutory Funding is exclusively for that——

Senator PRYOR. Right.

Dr. RODGERS [continuing]. But over and above that, regularly appropriated funds also go to diabetes research.

Senator PRYOR. And you can see the results of that statutory funding?

Dr. RODGERS. Oh, absolutely. I just listed a few highlights to give you a glimpse of that. But over the period of time in which this funding has occurred, we have really advanced by leaps and bounds in understanding all steps of the progression of the disease.

Senator PRYOR. My impression is that the number of cases of diabetes has gone up in this country. Are you seeing that all around the world?

Dr. RODGERS. Of the number of cases of type 1 diabetes that have been followed, largely, the highest prevalence is in the Scandinavian countries. Finland, for example, has the highest incidence rate of the disease. The lowest incidence rate, by comparison, is in Venezuela. And so this clearly may be related to racial, ethnic differences, perhaps exposure in the environment to factors in diet, maybe sunlight exposure or other things.

But for the first time and as a direct result of the Special Statutory Funding, we have developed a program in collaboration with the CDC to begin to search for the incidence rate in certain sites around the country to determine whether our incidence rate is static or whether it is increasing, and we are beginning to see the same thing that is occurring over in the Scandinavian countries, that not only over time is the incidence rate increasing, but it is occurring at a much earlier age.

Senator PRYOR. And one last thing, if I may, Madam Chairman. We are seeing that same disparity geographically in this country. In Arkansas, we have a few counties where the incidence rate is over 10 percent, and that is not true in other counties. Is it more concentrated in the Southeastern part of the United States, is that fair to say?

Dr. RODGERS. I am unaware of any particular predilection for type 1 diabetes within the United States, but what I would say is that the Search for Diabetes in Youth Study (SEARCH), in conjunction with the CDC, is allowing us to begin to look at particular clusters where they may exist. When one sees the clustering of events, that has a high possibility, or at least opens the possibility, that there might be local environmental factors, and that is something that we are now poised to be able to look at as the CDC does for other types of clusters of disease.

Senator PRYOR. Thank you. Thank you, Madam Chairman.

Senator COLLINS. Thank you very much, Senator Pryor. Senator Begich, welcome.

OPENING STATEMENT OF SENATOR BEGICH

Senator BEGICH. Thank you very much, Madam Chairman. I know you have an important bill on the floor, so being here today is a great statement to the group that is here, so thank you for being here. I know Senator Lieberman also is on the floor. You are playing tag team, so thank you very much.

I want to make a statement, then I want to ask a couple questions, probably, if I could, to Dr. Zimliki.

First, I am pleased to be here and pleased to get the update on the current research and hear from so many folks and also from these young people. I have to tell you, you have been very patient for the entire presentation and discussion. We could take a lot of lessons from the young people who sit here so calm and collected, so thank you very much.

As Mr. Pryor just whispered, if only the Senate could do this, and I agree with him. [Laughter.]

We have come truly a long way in managing type 1 diabetes on a day-to-day basis. As a matter of fact, yesterday, I spent some time with two Alaskans, part of the Children's Congress, Hugo and Gus, who I think are right over there. We actually watched the Nationals and the Mariners—we are Seattle fans. We thought we were winning until the bottom of the ninth, and if anyone watched that game, it was a pretty exciting game. If you are going to go see a baseball game, that is the one that was well worth it. So we had a great chance to talk. They are nodding their heads "yes."

But we also had a chance to talk briefly, and we will talk again later today, but I know their attendance, and the attendance of their parents, Karen and Steve, and all the families and children who are here will help us understand better.

But it is exciting, and particularly exciting to see the development of the artificial pancreas that can truly transform lives, and I understand that we must continue to invest in the tools that help better manage the disease. I also know that we all really want and need to invest in research to help find a cure. To this end, we must

continue to forge the public-private partnerships and leverage funding to find a cure.

Diabetes is common and growing in the State that I represent, Alaska. In 2009, nearly 7 percent of Alaska's population had been diagnosed with diabetes. In 2007, the direct and indirect cost to our State was approximately $419 million. We can talk about the cost to the system, but when you look at the other impact, the human impact to families, the burden of the disease and what families have to do, it is significant.

This is why I am very glad to have so many people here today to deliver the impactful and memorable messages. I will tell you, 2 years ago, when I first got here, an Alaskan teenager came and visited me to advocate on behalf of the Special Diabetes Program, and she brought me a photo book of her life and what she has been doing to deal with type 1 diabetes, and it was very amazing because you can talk about it, but when you see the photos of her life unfold from day one and as she went through it, it was pretty impactful to me. It is a document and a booklet that I still keep in my office to remind me of the impact and the stories that are all around this issue.

Again, I want to thank the parents and the children who are here. Thank you for your advocacy.

To Dr. Zimliki, if I can ask a couple of quick questions. One, I want to follow up on your response to Senator Pryor, and that is you had mentioned the CMS reimbursement.

Dr. ZIMLIKI. Yes.

Senator BEGICH. You said you were working through that, and no disrespect, but when I have Federal folks in front of me, it is always, "soon," "maybe," "we are working on it," and I am going to ask you very specifically. You are working on it. What do you think the time table is for CMS to actually respond and resolve the issue of how it is going to be paid for?

Dr. ZIMLIKI. I cannot speak on behalf of CMS, but I can tell you that the first priority is to develop the appropriate clinical studies necessary for product approval and marketing within the United States. We have contacted our CMS affiliates, and we would like to make sure that the clinical study proposed can not only have the clinical data necessary for product approval, but also for reimbursement. We are hopeful that we can work with CMS to accomplish that.

We have also communicated with——

Senator BEGICH. Let me pause you there for a second.

Dr. ZIMLIKI. Yes.

Senator BEGICH. When do you think you will have that, because that is obviously in your control. You are having that discussion. So when do you think that will get some results so you can say, we have some partners. We are ready to roll.

Dr. ZIMLIKI. We need to finalize the draft guidance first, and then——

Senator BEGICH. So from December to when, then?

Dr. ZIMLIKI. Developing and publishing this guidance is not a trivial task.

Senator BEGICH. I understand.

Dr. ZIMLIKI. This is a huge, monumental effort that the agency is putting forward. I would like to say that we would have that information available at the same time of the publication of guidance, but I simply cannot guarantee that date. I apologize for that.

Senator BEGICH. No problem. Based on your experience for something of this magnitude, is it for CMS to say, yes, we can do this; it will be 2 or 3 years?

Dr. ZIMLIKI. I do not have the experience or the luxury of knowing how long that will take. I will talk to my Commissioner——

Senator BEGICH. Perfect. You went right to my next question——

Dr. ZIMLIKI [continuing]. And provide you with an answer.

Senator BEGICH. Great. And then maybe you could give me, from whomever would be the appropriate person at the FDA, experiences of the past and how long it took.

Dr. ZIMLIKI. Absolutely.

Senator BEGICH. I would think that would be important. I would appreciate that for the record.

The last thing, I will just ask very quickly, and then I apologize, I have to depart. How many clinical locations do you anticipate for the trials? Do you have a sense on that yet?

Dr. ZIMLIKI. No. It really depends on how quickly industry wants to do it and how much variability they want to introduce in their clinical study design. Certainly, it is more than one location, but it really is dependent. We have introduced enough flexibility to allow industry to dictate how many sites they would like to study and where they would like to study it.

Senator BEGICH. Great. Thank you very much, and I appreciate the comments, and I look forward to what you can put into the record. Thank you, Madam Chairman.

Senator COLLINS. Thank you very much.

I want to thank this panel of witnesses for excellent and highly encouraging testimony this morning. We will continue to work closely with all of you. Thank you.

[Applause.]

Senator COLLINS. Our next panel of witnesses consists of children who know firsthand the burdens of living with diabetes. Our witnesses are Caroline Jacobs from Maine; Jack Schmittlein from Connecticut; Kerry Morgan from Virginia; and Jonathan Platt from California. All of these children are JDRF Children's Congress delegates, and we are very happy to have them here today.

Caroline, since you are from my home State, you get to go first. [Laughter.]

TESTIMONY OF CAROLINE JACOBS,[1] DELEGATE FROM SHAPLEIGH, MAINE, JDRF CHILDREN'S CONGRESS

Ms. JACOBS. Good afternoon, Chairman Collins and Members of the Committee. Thank you for asking me to testify before you today.

My name is Caroline Jacobs. I am 14 years old. I am from the great State of Maine, where we say Maine is the way life should be. I am here as a Children's Congress delegate to talk about living

[1] The prepared statement of Ms. Jacobs appears in the Appendix on page 79.

with diabetes, the importance of technology for me and other children with diabetes, and my hope for a cure.

I was diagnosed with diabetes when I was 10 years old. It changed my life forever. With this disease, I must always think and be aware of how I am feeling, and I have had to grow up fast. I feel the burden on my friends and my family who are always worrying about me, always asking me questions about my blood sugar. So I am doing what I can to make a difference in finding a cure for juvenile diabetes.

I brought a "School Walk for a Cure" to my school, and this year is the third year for my family's walk team for the Walk for a Cure in Portland. I also make jewelry and bags to benefit JDRF. I do all of these things so we can continue research to find a cure for diabetes.

While we wait for a cure, I hope to see that more technologies are made available for children like me. One of the delegates here is from Canada and has a kind of insulin pump and continuous glucose monitoring system that protects against episodes of hypoglycemia when the patient is ignoring the dropping sugar levels. With this ability to stop insulin delivery when it detects a low blood sugar, this pump could lighten the burden and the worry for me and those around me. This technology is approved in Canada and other countries, but not here in the United States. It is hard for me to understand how a device like that can be available in a place just over the border from me.

Because I will be driving in the next 2 years, it would be important for me to have access to a technology that could help prevent my blood sugar from dropping. Having diabetes can make your blood glucose levels go too high or too low and make me feel sleepy or dizzy, confused, or have blurred vision, making it too dangerous to drive.

I would like Congress to encourage the FDA to move forward on next steps relating to the artificial pancreas, a combination of a continuous glucose monitor and an insulin pump with software that communicates between the two. The device will prevent highs and lows, especially at night when lows can be most dangerous. But it also would keep control of my sugars while I am driving, as well.

I hope we will not have to wait too long for this device. That way, I will no longer have to worry about others always worrying about me. More importantly, my family will feel less of the burden and my friends will not always have to adjust around me because of this disease, and I hope that this means I will have the opportunity to travel freely without worrying about this disease and enjoy the world and those who live on it. After all, is that not the way life should be?

Thank you, Members of the Committee, especially my home State Senator, Senator Collins.

[Applause.]

Senator COLLINS. Thank you. That was terrific. You sound like a pro.

Mr. Schmittlein, we are glad to hear from you next.

TESTIMONY OF JACK SCHMITTLEIN,[1] DELEGATE FROM AVON, CONNECTICUT, JDRF CHILDREN'S CONGRESS

Mr. SCHMITTLEIN. Thank you, Senator Collins, Senator Lieberman, and Members of the Committee for inviting me to testify. My name is Jack Schmittlein. I am 13 years old, and I have had juvenile diabetes for over 6 years.

On October 4, 2004, my life changed forever with my diagnosis. Instead of being a carefree kindergartner, I was faced with pricking my fingers 8 to 10 times a day, counting carbohydrates, and taking insulin shots. Managing diabetes is hard work that lasts 24 hours a day, every day.

Two years ago, my best friend, Peter, was diagnosed with type 1 diabetes. Before, he had been incredibly helpful in managing my disease, even keeping me company when I walked to the nurse's office to check my blood sugar. Peter and his family learned everything they could about diabetes so that I could come over to play at their house safely. Peter's diagnosis is just one more reason why I work to raise awareness about type 1 diabetes and one more reason why I am here today.

Important research to find a cure is happening all over the Nation, even at Yale University in my home State of Connecticut, to better understand the causes of type 1 diabetes and ways to prevent it.

I am grateful that Congress passed legislation to renew the Special Diabetes Program last year. This program is essential to helping find a cure for type 1 diabetes. The Special Diabetes Program has allowed for research that has led to the artificial pancreas. An artificial pancreas would help prevent my blood sugar from dropping and give me insulin if my blood sugar gets too high. Right now, I have to get up to check my blood sugar in the middle of the night, every night. It would make participating in activities I love a whole lot easier. I really enjoy playing basketball and football, but I often have to come out in the middle of a game to test my blood sugar. It would give me my life back so I can just feel like a kid again, not a kid with diabetes.

Despite this incredible technology, we need to do everything we can to find a cure. I am doing my part to help continue to push life-saving research forward. I have been a JDRF walk team captain for 4 years. I have organized a walk at my school to benefit JDRF. And I have also spoken about life with diabetes at two walks, a school assembly, and a Promise Ball fundraiser as a JDRF Youth Ambassador.

It is my hope that Congress will continue to support research at NIH, specifically the Special Diabetes Program. I really believe that we will find a cure for type 1 diabetes. The artificial pancreas is a promising result after strong investment in research.

I look forward to the day that I can say, "I used to have diabetes." Until that day, an artificial pancreas will greatly improve my daily life and the lives of other children who have type 1 diabetes. I know that Congress and JDRF are doing all that they can to make this possible for children like me. Just think, if we can improve the lives of millions of children and adults around the world,

[1] The prepared statement of Mr. Schmittlein appears in the Appendix on page 82.

why would we not? Research being conducted all over the country is bringing us closer to a cure, and the development of the artificial pancreas could keep us healthy while we wait for a cure.

Thank you, Senator Collins and Members of the Committee, for providing me the opportunity to give you a glimpse into what my life is like with diabetes. I look forward to answering any questions you may have.

[Applause.]

Senator COLLINS. Thank you, Mr. Schmittlein. You did a great job.

Ms. Morgan, we will hear from you next.

TESTIMONY OF KERRY MORGAN,[1] DELEGATE FROM GLEN ALLEN, VIRGINIA, JDRF CHILDREN'S CONGRESS

Ms. MORGAN. Good afternoon, Senator Collins, Senator Lieberman, and Members of the Committee. Thank you for inviting me to testify today.

I am Kerry Morgan from Glen Allen, Virginia, and I was diagnosed with diabetes 13 years ago, when I was 4 years old. Unfortunately, diabetes was not new to me when I was diagnosed. My older sister was diagnosed with the disease when she was four, too. Shortly after her diagnosis, I was enrolled in a clinical trial for first-degree relatives of people with type 1 diabetes to determine if they were at risk for developing the disease. On the trial, I received daily insulin injections in hopes to avoid or delay development of diabetes, but it did not work. Sometimes clinical trials do not. I was formally diagnosed with type 1 diabetes 1 year later.

Then, in what seemed like a flash, 10 years passed—10 years filled with thousands of insulin injections, finger sticks, tubing changes, endless carbohydrate counting, and worry. Ten years of toting around an awful green fannypack containing the vital necessities for everyday life. Even with my best efforts, I still have days with severe high and low blood sugars. My family and I hoped, just like the millions of people impacted by this disease do, for a better way to control this.

I was 14 when I enrolled in a clinical trial that was testing a continuous glucose monitoring system. This ingenious device, which I named "my little buddy," gave me instant knowledge of what my blood sugar was doing and where it was going. While on this trial, my A1c dropped from an 8 to a 7. This technology made living with the disease not only easier, but gave me hope that it was truly possible to manage diabetes better. It was not a cure, but it was more than I had before.

Living with diabetes is a daily struggle. It creates this cloud of fear and doubt. Thoughts of blood sugars and carbohydrates are always on my mind. I am constantly asking myself, am I OK? I always have to remember snacks and extra supplies to ensure that, in case of incident, I am covered because things can get scary quickly. I have had my pump stop working while out of town, unprompted by dropping it or submerging it in water. I do not just worry about now. I worry about my future. Diabetes never takes a break, so neither can I or my family.

[1] The prepared statement of Ms. Morgan appears in the Appendix on page 86.

Then last October, I enrolled in a clinical trial testing artificial pancreas technology. For 2 days, I was admitted into a hospital where they tested the closed-loop artificial pancreas system. After participating in clinical research since I was 3 years old, I can honestly say the closed-loop artificial pancreas trial was the most amazing experience of my life and holds so much promise for people living with this disease.

For 2 days, I had perfect control of my blood sugar levels. Two days of living with this technology provided me with the vision of what life could be like—life with far less complications, both short- and long-term. Creation of an artificial pancreas is within reach. I know it. I have been a part of it, and I will do all I can to get it into the hands of people living with diabetes, and I hope you will, too, so on the day the artificial pancreas is finally approved and released, people with this disease can say, "Diabetes? There is an app for that."

[Laughter and applause.]

Ms. MORGAN. Thank you, Members of the Committee, for all you do for those living with diabetes and working to make the artificial pancreas technology available to all those living with this disease.

Senator COLLINS. Thank you very much, Ms. Morgan, for great testimony.

[Applause.]

Senator COLLINS. Mr. Platt, you are up next.

TESTIMONY OF JONATHAN PLATT,[1] DELEGATE FROM TARZANA, CALIFORNIA, JDRF CHILDREN'S CONGRESS

Mr. PLATT. Good afternoon, Chairman Collins and other Members of the Committee. Thank you for inviting me to testify.

My name is Jonathan Platt. I am from Tarzana, California, a suburb of Los Angeles. I am 7 years old. I was diagnosed with juvenile diabetes at age 6. I had been losing weight, wetting the bed at night, and had extreme thirst. I was always very tired and emotional. My mom and dad thought I was adjusting to a new school and kindergarten. My blood sugar was over 650 when I was diagnosed with juvenile diabetes. I will never forget the day I was diagnosed. We found out later that the little red-headed girl who rode in the elevator with us was diagnosed with juvenile diabetes, also. That had never happened before in this doctor's office, two children diagnosed at the same time. I was thinking, how did I get this disease? I did not know what it was. I was very scared and nervous.

I am here as a Children's Congress delegate to tell you that I manage my disease, but I do not let it control my life. With this disease, I am able to swim, play basketball, and build Legos, but I am different. Unlike other children, I have to check my blood sugar 8 to 10 times a day. Everything I eat is measured and every carbohydrate counted. My blood sugar kit, juice, glucagon, and ketone strips go with me everywhere I go.

It is hard when I go to summer camp or do a sleepover or even go to a friend's house. Too much exercise or not eating all my food can be very dangerous. I think I am too young to have to worry about all this stuff.

[1] The prepared statement of Mr. Platt appears in the Appendix on page 89.

My parents have had to adjust their life because of my diabetes, but they say we all have it, not just me. Managing diabetes is a 24-hour job. We are doing our part to help find a cure by raising money for the JDRF Walk for a Cure. I am here to ask you to continue to do your part and fund research to find a cure.

A cure for diabetes means that I could go to any summer camp and have sleepovers whenever and wherever I want. It means I could be a regular kid again, and most of all, it would mean I would not have diabetes. Please help me make this possible. My life depends on it. Thank you.

Senator COLLINS. You did a great job.

[Applause.]

Senator COLLINS. I think this entire panel deserves another round of applause.

[Applause.]

Senator COLLINS. Now, I know that the children here have been sitting a very long time and that many of them could use a snack or water or need to test themselves, so I am going to ask the panel to each just ask one question, and then we will just wrap up the hearing because I know it has been a long afternoon, particularly for some of the younger delegates who are here.

First of all, thank you all for just wonderful testimony. You really have put a human face on what it is like to have diabetes, and that is far more powerful than statistics. You are the best advocates for funding for diabetes research that we could possibly have.

So, Caroline, my question is going to be for you. You were diagnosed in the summer, and you had some time with your family to get used to the idea of having diabetes and to learn what you needed to do in order to manage your disease. But I would like you to share with us what it was like when you went back to school in the fall.

Ms. JACOBS. Well, I was going to a new school at the time, so I was teaching my teachers how to deal with having a kid with diabetes and teaching my new friends how to count carbohydrates and all that stuff. Even at lunch, we would all try to figure out how many carbohydrates were in my food. I had a lot of support from friends, teachers, and my family, of course.

Senator COLLINS. I am sure that made a real difference.

Ms. JACOBS. Yes.

Senator COLLINS. Senator Begich referred to the scrapbook, and you gave me yours, and it is wonderful to go through it because I have learned so much more about the disease and about you. I want to thank you especially for being here, but I also want to thank all of our delegates.

Ms. JACOBS. Thank you very much.

Senator COLLINS. Senator Brown.

Senator BROWN. Thanks, Madam Chairman, again, for holding this hearing. Looking out there, I think I am at the Academy Awards. I see Mr. Kline right there, and then I come back to reality, and I see that we are here to discuss something very serious. Obviously, it affects everybody in this room. The wonderful part about being a U.S. Senator is, each day, you can learn and grow and you can understand new and different things, and if you do not

understand them, you obviously have an opportunity to actually find out the answers, which I find intellectually very stimulating.

Jonathan, I agree with you. You are too little to have to worry about this stuff. That being said, what has been the biggest challenge for you since you recently found out? What is the most difficult part of everything that you are going through right now?

Mr. PLATT. Well.

Senator BROWN. Is it keeping the daily requirements? Is it worrying about what happens if you do not do it right? I mean, what is the biggest challenge, do you think?

Well, you think about it for a minute. I am going to ask Mr. Schmittlein. What is your biggest challenge?

Mr. SCHMITTLEIN. Probably my biggest challenge with diabetes is at school, when all of my friends go to lunch, I have to always go to the nurse, and I have to bolus through my lunch, and sometimes, if we are in class and doing something fun, my blood sugar might be too low or too high, and so I will have to go down to the nurse and miss out on all the fun. So that is kind of hard for me because it is not fun to miss out on things you really want to do with your friends, so that is one of the things that is challenging for me.

Senator BROWN. Jonathan, you said earlier that your blood sugar was over 650, and I learned something today, that the average is 100 or below. I find that amazing that you were able to really function and now, obviously, address it. Have you thought of something that is challenging yet for you?

Mr. PLATT. Yes. Every time I feel low, there is no nurse at the school, and while in the library when there is something fun, if I feel low, I will have to go back to the class and check my blood sugar with the teachers.

Senator BROWN. So you are missing out on some things.

Mr. PLATT. Yes.

Senator BROWN. Well, thank you for that.

Thank you, Madam Chairman, for holding this hearing, and thank you, panelists.

Senator COLLINS. Thank you very much, Senator Brown.

Senator Shaheen.

Senator SHAHEEN. Thank you. Thank you all very much for your testimony. You are great advocates for the need to do more to address research.

Ms. Morgan, since you have not answered a question, my question is for you. We still have Dr. Zimliki and Dr. Rodgers here, and there has been a lot of discussion today about the artificial pancreas. Since you participated in one of those trials, is there anything that you would like to tell them about that trial that you hope they will bear in mind as they go back to the NIH and the FDA and continue work on trying to get an artificial pancreas that can be available to people?

Ms. MORGAN. The first thing I am going to say is it is awesome, so keep that in mind. And being on the artificial pancreas was so different than just living every day with diabetes because for that time, I did not have to worry. I did not have to think about it, and that was a new experience for me because I have had this disease since I was so young, I do not really know anything else. And so

not having to do that was such a weight off of my shoulders, and I think everyone here could use that. And so bear in mind that I think we need it and we need it soon, so keep working, keep funding, keep researching, and hopefully, it will be out soon.

Senator SHAHEEN. Thank you very much.

[Applause.]

Senator SHAHEEN. And thank you, Madam Chairman, for holding the hearing and for all of your work chairing the Diabetes Caucus. As we can see, it really is making a difference.

Senator COLLINS. Ms. Morgan, I really think that your final words sum up why we are here and what our purpose is. But I do want to take this opportunity to thank everyone for coming to this hearing, the wonderful witnesses that we had, the delegates who were chosen to testify, all of the delegates who are sitting in the well and around the room, and their families because diabetes truly is a disease that affects the entire family.

I want to thank the Juvenile Diabetes Research Foundation for working so closely with us. Mary Tyler Moore sent a letter and some testimony that we are going to put into the record, and we will have the record open for an additional 15 days in case anyone else has any words of wisdom for us or additional questions.[1]

But most of all, I want to thank the children who are here today. When you come to Washington and you meet with your Senators and Members of Congress, you make such a difference. It is because you are willing to come here and tell your personal stories that we have been successful in tripling the funding for research that goes for diabetes. And I know that with your help, we will one day soon have better treatments—the artificial pancreas that we have talked about today—but also, ultimately, the goal of all of us here, and that is a cure.

So I thank you all for coming to Washington, for being here with us, and for being such great advocates.

This hearing is now adjourned.

[Whereupon, at 3:32 p.m., the Committee was adjourned.]

[1] The letter and prepared statement of Ms. Moore appear in the Appendix on page 92.

APPENDIX

United States Senate
Committee on Homeland Security and Governmental Affairs
Chairman Joseph I. Lieberman, ID-Conn.

Opening Statement of Chairman Joseph Lieberman
"Transforming Lives Through Diabetes Research"
Homeland Security and Governmental Affairs Committee
June 22, 2011

I look forward to these hearings every session and I do because they are so constructive. In a city and government in which too often too little happens that's constructive these days, this is a cause that unites people across party lines and has enabled us certainly in recent years to come together to be supportive of diabetes research and to help facilitate some of the really miraculous advances that have occurred in dealing with diabetes in our time. The fact that you children--young people--are here is the most important thing of all, you are the best advocates of this cause and first off you show everybody how well you are doing dealing with diabetes. The second thing is you make us all want to make the investments that are necessary to make sure that we not only better treat diabetes but really in your lifetime that we have a cure for diabetes. It is with that sense of optimism that I am honored to welcome you and all the other witnesses today

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United States Senate
Committee on Homeland Security and Governmental Affairs
Senator Susan M. Collins

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Statement of
Senator Susan M. Collins

"Transforming Lives Through Diabetes Research"
Committee on Homeland Security and Governmental Affairs
June 22, 2011

I appreciate the opportunity to hold this hearing to examine the devastating impact that juvenile diabetes has had on an estimated three million American children and their families. This is the sixth Children's Congress that I have had the honor to chair, and I am particularly grateful to my good friend, the Chairman of the Committee, for turning the gavel over to me this afternoon.

I also want to welcome our distinguished witnesses and the more than 150 delegates to the Children's Congress who have traveled to Washington from every state in the country and from around the world to tell Congress what it's like to have diabetes, just how serious it is, and why it is so important that we fund the research necessary to find a cure.

I also want to give a special welcome to the delegate from Maine, 14-year old Caroline Jacobs of Shapleigh. Caroline will be speaking on our second panel this afternoon, and I am looking forward to her testimony.

As the founder and Co-Chair of the Senate Diabetes Caucus, I have learned a lot about this disease and the difficulties and heartbreak that it causes for so many American families as they await a cure. Diabetes is a life-long condition that does not discriminate. It affects people of every age, race and nationality. It is the leading cause of kidney failure, blindness in adults and amputations not related to injury.

Moreover, it is estimated that diabetes accounts for more than $174 billion of our nation's annual health care costs, and one out of three Medicare dollars. Medical costs for a child with type 1 diabetes are six times higher than the costs for a child without the disease, averaging $9,000 a year as compared to $1,500.

These statistics are overwhelming. But what really motivated me to devote so much energy to this issue was meeting more and more people – like our delegates today and their families – whose lives have been forever changed by diabetes. That is why it is so important that you all have traveled to Washington today to tell your stories. You put a human face on all the statistics. You help us to focus on what Congress can do to better understand and ultimately conquer this terrible disease.

The burden of diabetes is particularly heavy for children with type 1, or juvenile diabetes. Juvenile diabetes is the second most common chronic disease affecting children. Moreover, it is one that they never outgrow.

In individuals with type 1 diabetes, the body's immune system attacks the pancreas and destroys the islet cells that produce insulin. An average child with diabetes will have to take over 50,000 insulin shots in a

lifetime. Moreover, these injections must be carefully balanced with regular meals and daily exercise, and blood sugar levels must be closely monitored throughout their lives through frequent testing.

Of particular concern is the fact that the incidence of type 1 diabetes is increasing, particularly in children under the age of four. While the discovery of insulin was a landmark breakthrough in the treatment of diabetes, it is not a cure. People with type 1 diabetes face the constant threat of developing life-threatening complications, as well as a reduction in their quality of life.

Thankfully, there is good news for people with diabetes. Since I founded the Senate Diabetes Caucus, funding for diabetes research has more than tripled from $319 million in 1997 to more than a billion dollars this year. As a consequence, we have seen some encouraging breakthroughs in diabetes research, and we are on the threshold of a number of important new discoveries.

Advances in technology, like continuous glucose monitors, are helping patients control their blood glucose levels, which is key to preventing diabetes complications.

We are also moving closer to our goal of an artificial pancreas which would revolutionize diabetes care. The artificial pancreas is an external device that people with type 1 diabetes can use to do what their bodies cannot – automatically control both high and low blood sugar levels around the clock. It would link two existing technologies -- the insulin pump and the continuous glucose monitor – with sophisticated computer software to provide just the right amount of insulin at just the right time.

This new technology has the potential to dramatically improve the health and quality of life for individuals with diabetes. The Food and Drug Administration has so far played a pivotal role in moving research forward by approving clinical trials in hospital settings and making the artificial pancreas one of its Critical Path initiatives. I look forward to hearing more about what the agency is doing to advance this promising new technology.

While we are making progress in the battle against diabetes, this is no time to take our foot off the accelerator. We have two choices. We can sit back and continue to pay the bills and endure the suffering, or we can aggressively pursue a national strategy aimed at curing this terrible disease.

The good news is that there is strong support in Congress for diabetes research funding, thanks in no small part to the strong grass-roots support provided by JDRF volunteers. Last year, we were able to pass legislation to extend the Special Diabetes Program for two additional years through September of 2013. This critical program provides $150 million a year for juvenile diabetes research, over and above the regular appropriation for diabetes research at the National Institutes of Health.

The Special Diabetes Program represents more than a third of our federal commitment to diabetes research. As such, it is critical to our efforts to find better treatments, a means of prevention, and ultimately a cure for this terrible disease.

I am hopeful that this afternoon's hearing will help us to generate even more support to extend this important program far into the future.

Statement of Senator Daniel K. Akaka

Homeland Security and Governmental Affairs Committee hearing on "Transforming Lives Through Diabetes Research"

Wednesday, June 22, 2011, at 1:30 p.m.

Thank you, Senator Collins, mahalo for chairing this important hearing on Type 1 diabetes. I want to join you in welcoming our distinguished panelists who have been so committed to this issue. I also want to send a very special aloha to those Children's Congress delegates waiting to testify and those in the audience.

These are the courageous young ambassadors who have traveled from all over the country and the world to educate us. They are here to share their stories of their own experiences. They bring a real human dimension to the policy debate. This shows how critical research and support is for diabetes and a hope for a cure.

Diabetes is a significant health problem in my home state of Hawaii, and it is an increasing challenge for the nation. Diabetes is an issue that we will look at in the Indian Affairs Committee, and it will be a part of the minority health legislation that I plan to introduce. It is the subject of the ongoing budget and regulatory policy debate. In this context, I am proud to support the development of the artificial pancreas.

I will continue to support funding for research at the National Institutes for Health, which gives us the chance for better detection, better treatment, and the hope for a cure. All the more reason that I am so pleased to see the children here every two years. They remind my colleagues and me about the struggle of living with Type 1 diabetes, and the importance of supporting diabetes research.

Finally, I wouuld like to extend a special thanks to Aaron Tsuchitori, who travelled from Honolulu with his mom to meet with me today. I look forward to continuing to work with all of you to improve the lives of individuals with diabetes.

Thank you.

Homeland Security and Governmental Affairs Committee Hearing:
"Transforming Lives through Diabetes Research"
June 22, 2011

Opening Remarks Senator Scott Brown

Thank you, Mr. Chairman for holding this hearing today in conjunction with the Juvenile Diabetes Research Foundation's (JDRF) 2011 Children's Congress. On numerous occasions, I have taken the time to meet with MA constituents, patient-advocates and researchers to learn more about the daily challenges in the diabetes community, but also of the important research efforts, that I am very proud of, happening in the Commonwealth. The numbers are certainly convincing—diabetes continues to be an important health issue, with nearly 26 million people diagnosed in the United States and in Massachusetts approximately 360,000 residents or about 6.8 percent of the population diagnosed with diabetes.

Among chronic diseases, diabetes is one of the costliest. One in every three Medicare dollars is spent treating people with diabetes and in 2007, diabetes accounted for $174 billion in health costs for the U.S. In Massachusetts alone, the indirect cost of diabetes care was roughly $4.32 billion dollars in 2007. And with the numbers of people living with diabetes increasing, we know that the health care costs will continue to grow. In this tough economic climate, I think that the numbers supporting NIH and preventative health research investments demonstrate the cost effectiveness of research. That is why, along with several of my colleagues here today, I remain committed to support robust funding for the National Institutes of Health.

Earlier today, I enjoyed the opportunity to meet with the four impressive children from Massachusetts participating in this year's Congress. They took the time to share their personal stories and describe the struggles they face on a daily basis. With their stories in mind and the FDA's recent release of the artificial pancreas draft guidance, it's great we have Dr. Zimliki and Dr. Rodgers with us because I believe this is an important step forward in improving the lives of all children living with Type 1 diabetes. Like many of the people here today, diabetes has touched both my family and friends. Therefore, I will continue to support the diabetes research and treatment efforts of the Juvenile Diabetes Research Foundation, the NIH, and Children's Hospital in Boston to improve the lives of those living with diabetes.

Senator Shaheen
Opening Remarks
Committee on Homeland Security and Governmental Affairs
"Transforming Lives through Diabetes Research"
June 22, 2011

Good afternoon. It is a pleasure to be invited to join you here today. I want to thank Senator Lieberman, Senator Collins and the Committee on Homeland Security and Governmental Affairs for holding this important hearing. It is critical that we bring more attention to diabetes research and the development of technologies, like the artificial pancreas, that will improve the life of those with the disease.

I especially want to thank Senator Collins for her leadership on this issue. I am pleased to be the co-chair of the Senate Diabetes Caucus. I know that we both share an interest in finding a cure to diabetes and in investing in promising diabetes research.

I am especially pleased to be able to join my colleagues to welcome JDRF's 2011 Children's Congress to Capitol Hill. As many of you know, this disease is personal for me: my granddaughter, Elle, was diagnosed four years ago with type 1 diabetes. She is here today as part of the New Hampshire Children's Congress delegation with her mother and my daughter, Stefany, as well as her father, Craig. I am also so pleased to welcome another delegate participant from New Hampshire, Abigail Lore, from Merrimack and her mother, Jeanine.

I have long been an advocate for investing more research dollars to find a cure for diabetes and to expedite the development of the artificial pancreas. Diabetes- which includes type 1, type 2 and gestational diabetes—is one of the most costly chronic diseases. Last year, the United States spent $175 in medical costs related to the disease. The disease puts an incredible toll on patients across the country, our health care system and our economy. If we can find a cure or curb the growth of diabetes we will save our health system money.

But more importantly, research is needed because of the personal toll that diabetes has on families in New Hampshire and across the country. The emotional and financial pressures for families who are managing the disease are significant. Daily routines for those families include regular blood sugar tests and insulin injections. Diabetic patients must monitor every meal, other medications that are taken and the amount that they exercise. Those families

also must deal with the complexities of health insurance coverage and keep abreast of doctor appointments and the most recent scientific advancement in treatment of the disease.

Researchers across the country are working hard to advance type 1 diabetes studies, and we must not let it slow down. The Special Diabetes Program holds promise to continue the research that can lead to new therapies and treatment. And I hope that through the research that is going on all over the country, we will soon be able to develop the artificial pancreas, which has the potential to change the lives of millions of type 1 diabetics.

I thank all the advocates joining us today for their hard work in sharing their story about life with diabetes. And I thank JDRF for their hard work advocating for research funding and pushing for the development of new treatments and therapies that will change the lives of those with the disease.

I look forward to hearing from our panelists today to learn more about their life with the disease, and the promise that diabetes research holds.

Testimony of

Mr. Kevin Kline
Actor and JDRF Celebrity Advocate Co-Chair

Senator Collins, Senator Lieberman, and Members of the Committee, thank you for inviting me to appear before you today with such a distinguished panel and with such remarkable kids.

Ten years ago, I had the honor of joining Mary Tyler Moore and the 100 plus delegates at the 2001 JDRF Children's Congress. Since then, we have made remarkable progress in understanding type 1 diabetes. We are many steps closer to a cure and new tools are being developed to improve the day-to-day management of this disease. But we still have work to do and I thank you for sticking with us to get the job done.

Today, these great delegates are getting all of the attention, as they well deserve. But I'd also like to recognize all of the moms, dads and other special people these kids brought with them today. When a child is diagnosed with type 1 diabetes, parents must take on additional roles immediately as doctors, nurses, nutritionists, teachers and even psychologists. They are on duty, 24/7, 365 days a year, monitoring their child's blood sugars, counting the carbohydrates in food, calculating insulin dosages, educating others about their child's diabetes, and managing the emotions from dealing with the daily rigors of the disease. Each day brings its own special challenge to control blood sugar levels, even with the best of plans and use of the latest technology.

And with each exciting new stage that children with type 1 diabetes reach – whether it be starting kindergarten, going to summer camp, learning to drive or going off to college – there is a mom, dad or loved one looking over their shoulder worrying about their safety. Many of these parents have become advocates so that one day their child won't have to deal with diabetes anymore. They, like me, joined JDRF and the fight to cure diabetes.

As JDRF's National Walk Chairperson, I had the great pleasure of telling people to lace up their shoes and walk – one foot in front of the other, walking the walk to raise money to find a cure for type 1 diabetes. We have raised a lot of money with the Walk to Cure Diabetes, and JDRF has put this money to excellent use. The federal government has also played a critical role in the fight to cure diabetes, in particular with the strong bipartisan support for the Special Diabetes Program. I thank you, Senator Collins, for your leadership, and thank your colleagues who recognized the great return on the investment from the Special Diabetes Program and supported the two-year, $300 million extension last December.

Together JDRF and the federal government for years have made and will continue to make terrific partners in advancing research to cure, treat and prevent type 1 diabetes. Since I testified before this panel ten years ago, more than 40 of the genes have been discovered which put people at risk for type 1 diabetes. Multiple therapies to halt the autoimmune attack which causes type 1 diabetes have been tested in human clinical trials. New therapies have been shown to not only halt the progression of diabetic eye disease but to improve vision in those who have it. And the artificial pancreas has gone from being a theory to a technology that has been shown in early trials to prevent dangerous low and high blood sugars.

Aside from a cure, the artificial pancreas is a parent's dream. Imagine going to bed at night without having to worry about dangerous nighttime high or low blood sugar levels that could result in a seizure, or a coma – or worse. Or knowing that your child will have a great day at school without the burden of poking his or her fingers, counting carbohydrates, taking the right amount of insulin, and treating high and low blood sugars – or forgetting to do all that and coming home from school dangerously ill. Or sending your child off into the world as an adult, without having to worry about who will look after him or her all of the time. Best of all, knowing that your child will live a long, productive life since these artificial pancreas technologies have the potential to keep him or her healthier, longer, until a cure is found.

I know the Food and Drug Administration (FDA) has made the artificial pancreas a priority, and I commend the agency for that. But there is more the FDA needs to do. Many of these children here today are wearing the components of an artificial pancreas – insulin pumps that deliver insulin and continuous glucose monitors which give sugar readouts every few minutes. The challenge, however, is that these devices don't yet work together to automatically control their blood sugar levels. In other countries, there are devices available that take the first step, by automatically shutting off the insulin pump when someone is low. This is an important first step we need in the United States now.

But we can do more than that. JDRF and federally funded research have, in hospital settings, tested artificial pancreas technologies that automatically turn insulin both on and off – and the results have been amazing. The next step is testing these artificial pancreas devices in real-world settings. To do this without delay, however, the FDA needs to provide clear and reasonable guidance. Many of the world's best diabetes researchers and leading clinician organizations have joined together with JDRF to propose artificial pancreas guidance to the FDA. And the majority of the Senate and the House have urged the FDA to give this proposal immediate consideration. Now we need the FDA to act.

Parents who are up every night and worrying every day about their children simply cannot afford to wait any longer. It is past time for artificial pancreas technologies to be tested in real world settings. We urge the FDA to issue draft guidance for public comment on the artificial pancreas so outpatient trials can begin and the burdens of type 1 diabetes can be lifted from millions of Americans as soon as possible.

Thank you for the opportunity to participate in this hearing today. I would be pleased to answer any questions you may have.

Testimony of Griffin Rodgers, M.D.

Director, National Institute of Diabetes and Digestive and Kidney Diseases

Committee on Homeland Security and Governmental Affairs

June 22, 2011

Chairman Lieberman, Senator Collins, and Members of the Committee, as Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), I thank you for your invitation to testify at this hearing on type 1 diabetes. On behalf of the NIDDK and the other Institutes and Centers of the National Institutes of Health (NIH) within the U.S. Department of Health and Human Services (HHS), I am pleased to report that we are vigorously pursuing research on type 1 diabetes and its complications. For each of the past several years, NIH has invested over $1 billion in diabetes research. This investment is complemented by the support and efforts of our research partners—academic institutions around the U.S., HHS' U.S. Food and Drug Administration (FDA) and Centers for Disease Control and Prevention (CDC), and patient-advocacy groups—with whom we share the goals of preventing, treating, and ultimately curing type 1 diabetes. Through collaborative and coordinated research efforts, we are making critical strides toward these goals. Today, I will highlight recent advances and future opportunities in type 1 diabetes research, including research supported by the *Special Statutory Funding Program for Type 1 Diabetes Research* (*Special Diabetes Program*).

Type 1 diabetes strikes mainly in childhood and adolescence. It is an autoimmune disease, in which the body's own immune system attacks and destroys the insulin-producing beta cells found in clusters called islets within the pancreas. To survive, people with type 1 diabetes require daily administration of insulin in the form of injections or via an insulin pump. They must monitor their food intake and physical activity in order to manage their blood glucose levels. Even with continuous and vigilant management, patients are still susceptible to developing serious, long-term complications that can damage the eyes, kidneys, nerves, heart, and other organs. The disease greatly affects the quality of life of people with type 1 diabetes

and their families. Furthermore, we now know that type 1 diabetes diagnoses are on the rise, and that the disease is occurring in children at younger ages than before, often appearing during infancy.

IMPROVING THE OUTLOOK FOR PEOPLE WITH TYPE 1 DIABETES

Research in type 1 diabetes has made a tremendous impact on the health and quality of life of people with the disease. NIDDK's landmark Diabetes Control and Complications Trial (DCCT) demonstrated that intensive blood glucose control, beginning as soon as possible after diagnosis, can prevent or delay diabetic complications of the eyes, kidneys, nerves, and heart. The DCCT concluded in 1993, but its follow-up study, the Epidemiology of Diabetes Interventions and Complications (EDIC), continued to follow participants to determine the long-term effects of prior intensive versus conventional blood glucose control. In a recent report, the researchers compared overall rates of eye, kidney, and cardiovascular complications in DCCT/EDIC participants. After an average of 30 years with type 1 diabetes, participants in the DCCT/EDIC intensive control group had lower complication rates than participants in the conventional control group. Improved control over a 6 year average study time yielded health benefits that last for decades. Since the study began in 1983, the prognosis for people with longstanding type 1 diabetes has greatly improved due to major improvements in glucose monitoring and insulin delivery. This progress has accelerated in the past decade. For example, several continuous glucose monitoring devices now approved by the FDA give real-time information for tracking and trending of glucose levels, helping people with type 1 diabetes supplement the management of their blood glucose to help control their disease. Because of these insights and improvements in diabetes care and therapy, people with type 1 diabetes are

living longer, healthier lives than ever before and experiencing lower rates of disease complications. For example, only about 70% of people diagnosed with type 1 diabetes in the 1950's survived for 25 years with the disease compared to about 95% for those diagnosed in the 1970's. Indeed, the Joslin Diabetes Center in Boston, Massachusetts, has a Medalist Program that recognizes individuals who have lived with type 1 diabetes for 25, 50, and 75 years with a special award to commemorate their dedication to lifelong diabetes management. Just last month Joslin awarded one of these medals to a man on his 90th birthday—the first American known to live 85 years or longer with type 1 diabetes. These inspiring accomplishments don't stop with a medal; many of the 50-year medalists have volunteered to participate in an NIDDK-funded study to identify factors that protect from the development of eye and kidney disease. It's exciting to report that through research, the outlook for people with type 1 diabetes continues to improve.

Still, the burden of living with diabetes is enormous, so it is critical to build on research progress to find ways to prevent and cure the disease. For example, advances in research have led to blood tests that can now predict the risk of developing the disease in relatives of people with type 1 diabetes. Building on this knowledge, we are now able to launch clinical trials to test new prevention strategies. Until prevention and cure are possible, improved outcomes will depend on improving devices to monitor and control blood glucose levels. Advances in continuous glucose monitoring are expected to help people of all ages. To build on these developments, research on how to best help people use new technologies is key toward moving this treatment strategy into practical use.

Pursuit of the research goals to prevent, treat, and cure the disease involves partnerships among scientists—with diverse backgrounds and expertise from many academic institutions— as well as partnerships among many of the Institutes and Centers of the NIH, the FDA, the CDC,

and patient-advocacy groups. Patient-advocacy groups, like the Juvenile Diabetes Research Foundation International, are instrumental in facilitating and in contributing support to many of these collaborative research endeavors. By complementing research efforts supported by the NIH and CDC, patient-advocacy groups are key partners in our battle against type 1 diabetes. Without question, the most important partners in these efforts are people with or at-risk for type 1 diabetes who volunteer and participate in clinical research. Their commitment to help improve diabetes care, not only for themselves but for future generations, inspires us. The clinical research we conduct would not be possible without their enthusiastic participation and dedication.

Research to prevent, treat, and ultimately cure type 1 diabetes requires a multi-pronged approach. The NIH focuses on research at all the stages of the disease: to prevent the onset of autoimmunity; to stop the autoimmune attack once it has begun; to preserve beta cells early in the course of the disease; to improve glucose control in people with established diabetes; to restore beta cell function in people who have significant beta cell loss; and to prevent, arrest, and reverse complications. Through this multifaceted strategy, we can achieve a comprehensive understanding of the disease process, and form a foundation for future advances in treatment, prevention, and approaches to a cure. I would now like to share with you some of the exciting progress that has been made in type 1 diabetes research.

UNDERSTANDING THE CAUSES OF TYPE 1 DIABETES TO PREVENT ONSET OF AUTOIMMUNITY

Type 1 diabetes is caused by a complex combination of genetic and environmental factors that lead to the development of "autoimmunity"—a preclinical sign of type 1 diabetes.

Understanding the causes of the disease is essential toward preventing onset of autoimmunity and type 1 diabetes and curing the disease. Just a few years ago, only three genes involved in development of type 1 diabetes were known. Today, as a result of efforts from the NIDDK-led Type 1 Diabetes Genetics Consortium (T1DGC) and other researchers, nearly 50 genetic regions are known that influence risk for type 1 diabetes. This group of researchers came together to collect information and DNA samples from families with type 1 diabetes to identify common genetic risk variants as well as the rare risk variants. The Consortium has collected over 38,000 DNA samples, and continues to add to our understanding of the genetic influences of the disease. NIDDK is also supporting efforts to pinpoint the specific, causal genetic variants among the identified genetic regions, as well as critical studies to determine how identified variants influence risk of developing the disease. These variants, as well as studies of their functions, may lead to targets for therapeutic and prevention strategies, potentially in a personalized manner.

Importantly, we know that not every person with high genetic risk goes on to develop type 1 diabetes, indicating that there is a factor—or factors—in the environment that interact with the genetic risk. Studies also show that the number of people diagnosed each year with type 1 diabetes is on the rise; increasing environmental exposures might account for these trends in diagnosis of type 1 diabetes. Determining the environmental factor or factors is critical to understand the disease process and to develop prevention strategies. For example, if research determines that a virus is involved, a vaccine to protect against the virus could be developed. Or, if a dietary factor is involved, a dietary intervention could be designed. Toward identification of environmental triggers, the NIDDK supports a bold, long-term initiative known as The Environmental Determinants of Diabetes in the Young, or TEDDY. TEDDY researchers are

following newborns until they are 15 years of age, and recently completed enrollment of over 8,600 after screening over 425,000 newborns to identify infants at high genetic risk to develop type 1 diabetes. For a decade and a half, investigators—aided by devoted parents—will regularly collect information about the child's diet, illnesses, vaccinations, allergies, and other life experiences. Biological samples are being collected as well and will be used for studies to identify early markers of the disease. Importantly, children enrolled in the study are now developing autoimmunity and type 1 diabetes at the predicted rates, indicating that the study is on track and poised to make a major contribution to type 1 diabetes research.

This achievement represents tremendous progress toward amassing the largest set of data and samples in the world on newborns at risk for autoimmunity and type 1 diabetes. To ensure that we learn as much as possible from these samples and maximize our investment in TEDDY, samples from the study will be made widely available to researchers. Already TEDDY investigators are using newly developed technologies emerging from the NIH Human Microbiome Project to study the microbiomes of these children to determine whether viral or bacterial-based treatments could be used to prevent the disease. Importantly, the benefits of TEDDY are expected to extend more broadly to include people with celiac disease, a digestive disorder caused by autoimmunity directed at gluten proteins in wheat and other grains. Celiac disease and type 1 diabetes share some genetic susceptibility factors, and many people have both diseases.

While TEDDY is a prospective, long-term investment to find the environmental causes of type 1 diabetes, scientists in The Trial to Reduce IDDM [insulin dependent diabetes mellitus] in the Genetically at Risk (TRIGR), led by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), are testing whether a dietary intervention can reduce

the risk of diabetes-associated autoimmunity or type 1 diabetes. A small pilot study, conducted by the Finnish arm of this trial, recently reported the promising finding that children who received the intervention had fewer diabetes-associated autoantibodies than children who did not receive it. Prevention strategies will also be informed by knowledge of who is developing diabetes. The CDC-led Search for Diabetes in Youth (SEARCH) is providing important information on the number of U.S. children in certain areas with diabetes, the rates of development of childhood diabetes, and whether these rates and the clinical course of diabetes in children and youth are changing over time. By building on critical SEARCH findings, researchers may be able to design interventions that can prevent or delay disease onset in at-risk individuals and interventions to reduce risk for complications of diabetes.

TESTING STRATEGIES TO STOP THE AUTOIMMUNE ATTACK AND PRESERVE BETA CELLS

Simple blood tests for the presence of preclinical markers of type 1 diabetes can now accurately predict the risk that relatives of people with type 1 diabetes will develop the disease within 5 years. This important advance means that people can now be screened for risk of type 1 diabetes. In the future, this could lead to identifying people who may be most able to benefit from a prevention strategy. Today, toward that goal, it means that people with high risk identified by screening are eligible for trials to test promising prevention strategies. For example, NIDDK's Type 1 Diabetes TrialNet is an international clinical research network focused on prevention in individuals at risk for type 1 diabetes and is currently conducting trials of potential prevention agents.

In addition to preventing the disease, it is important to identify ways to halt or reverse disease progression after onset. This could result in preservation or restoration of a person's insulin-producing capacity. Results from clinical trials have suggested that preserving remaining beta cell function in people with type 1 diabetes can have dramatic, long-term health benefits. Toward this goal, TrialNet also conducts trials testing therapies in newly diagnosed patients, frequently in collaboration with the National Institute of Allergy and Infectious Diseases' (NIAID) Immune Tolerance Network (ITN). Several agents have now been proven effective in slowing the progress of type 1 diabetes and preserving beta cell function, but these effects wane over time. The next step will be trials of combinations of agents that are individually effective to determine if the beta cell preservation can be extended when the agents are used concurrently. Collectively, TrialNet and ITN have 8 ongoing trials testing therapies in newly diagnosed people. One trial, a collaboration between TrialNet and the NICHD-led Diabetes Research in Children Network, is testing whether intensive blood glucose control upon diagnosis can preserve the ability of a person's pancreas to produce some of its own insulin. This trial employs a "closed-loop" system—a continuous glucose monitor linked to an insulin pump—in the hospital within a week of diagnosis. Patients are then sent home with an insulin pump and a continuous glucose monitor to use as part of the trial for the next 2 years, and investigators will determine whether this approach is able to delay progression of the disease.

DEVELOPING AN ARTIFICAL PANCREAS TO IMPROVE GLUCOSE CONTROL

A high priority for research is the development of new tools and technologies to improve the ability of people with type 1 diabetes to more precisely control their blood glucose levels. An artificial pancreas, based on mechanical devices requires, at a minimum, three basic

components: a continuous blood glucose sensor, an insulin delivery system, and a way to link the two in a loop. Such a system would automatically turn the measurement of blood glucose levels into a practical, precise, and "real-time" insulin-dosing system. Importantly, artificial pancreas technology could help people safely achieve the tight blood glucose control associated with preventing or delaying life-threatening disease complications. Thus, this technology has high potential to have a positive impact on patients' health and quality of life, alleviate an enormous amount of patient burden, and improve long-term health outcomes. Working closely with our partners at FDA, we are pursuing research to develop the artificial pancreas and ensure that these technologies are safe and effective for people with type 1 diabetes. I'm pleased to share with you some of the progress that has been recently made in this area.

An important question has been whether all the data provided by these technologies can actually help people achieve better blood glucose control. A recent study demonstrated that automated, real-time feedback of blood glucose control, glucose variability, and risk of dangerously low blood glucose levels resulted in improvements in long-term glucose control and reduction in episodes of low blood glucose levels. Research like this—to understand how to best help people take advantage of these technologies—is vital to improving the health of all people with type 1 diabetes.

In an exciting technical advance, investigators reported promising results from tests of a bi-hormonal closed-loop artificial pancreas, one that delivers both insulin and another hormone—glucagon—to more finely reproduce the activity of the human pancreas. This innovative strategy was developed by a bioengineer who, upon learning that his infant son had developed type 1 diabetes, switched his research focus to type 1 diabetes. In another recent report, researchers looked at overnight closed-loop insulin delivery in people with type 1

diabetes following two different real-life scenarios. In one, people had an "eating in" meal that mimicked a night of eating a medium-sized meal at home. In the other scenario, people had an "eating out" meal—a larger meal at a later hour. In both scenarios, a closed-loop system was able to improve glucose control and reduce the risk of dangerous drops in blood glucose levels overnight. Testing the closed-loop system technology in real situations that people find themselves in daily is critical to its development, and this advance marks a step toward moving closed-loop systems outside the clinic. This study used continuous glucose monitors that were derived from an NIDDK grant to a small business, highlighting the importance of fostering small business innovation in this field.

Our partners in industry are critical to the growing momentum toward an artificial pancreas. In addition to NIDDK small business grants that laid the groundwork for continuous glucose monitors, another company, SmartCells, Inc., who also received support from NIDDK small business grants, made substantial progress in preclinical development of a new formulation of insulin in which insulin release is automatically responsive to fluctuating blood glucose levels. This product—called SmartInsulin—has the potential to lower the risk of low blood glucose and improve glycemic control. Merck & Co, Inc. recently acquired SmartCells, placing this novel technology in a position to be developed to its fullest potential. NIDDK continues to stimulate and support innovative research on technologies that may lead to the development of the artificial pancreas through solicitations to the small business community. In addition, based on input from a recent meeting of scientific experts, NIDDK will support partnerships between diabetes researchers and bioengineers to promote training and career development in this exciting and emerging field. Through the development of these unique partnerships, we hope to

recruit more bioengineers into diabetes research and create many more success stories in the future.

RESTORING BETA CELL FUNCTION

Although insulin therapy is life-saving, it is not a cure. Therefore, a major goal of type 1 diabetes research is to vigorously investigate ways to replace beta cells destroyed by the disease and restore beta cell function. One strategy for replacing beta cells is islet transplantation. Clinical trials are ongoing to study and refine islet transplantation technology. The Clinical Islet Transplantation Consortium (CIT), jointly led by NIDDK and NIAID, has launched 7 studies to find methods that have higher success rates and fewer risks. To date, 363 participants have enrolled in these trials in North America, 66 of whom have received a transplant as part of these trials, and the investigators have begun the long-term follow-up protocol for these patients. Outcomes with islet transplantation continue to improve, and may ultimately lead to more widespread use of this treatment strategy for individuals with type 1 diabetes.

Investigators are also pursuing novel strategies to replace islets without the need for donor pancreata and toxic anti-rejection drugs. Basic research has increased the understanding of how pancreatic cell types develop, the events involved in development and regeneration of the pancreas, and the factors required for normal function and development of the beta cells. This knowledge is essential for the goals of growing beta cells in the laboratory for transplantation into people and coaxing other cells in the body to become beta cells—thus eliminating the need for transplantation all together. Research in this field has been accelerated by the NIDDK-led Beta Cell Biology Consortium (BCBC), a unique, team-based approach to solve the challenges of developing cell replacement therapy. Exciting advances from the BCBC continue to bring the

field closer to this goal. It is through studies in the BCBC that a key factor necessary for making the insulin-producing beta cells—a factor called Rfx6—was identified. Researchers now know that they will have to ensure that Rfx6 is present in order to successfully generate beta cells from precursor cell types in the laboratory. Another group of BCBC investigators discovered that by increasing the levels of a protein called Pax4 they could coax established alpha cells—another pancreatic cell type—into becoming beta cells in mice. Other BCBC scientists observed spontaneous conversion of alpha cells to beta cells in adult mice that were engineered to lack beta cells. These discoveries—of a critical factor for beta cell development, and that adult pancreatic cells have the potential to convert to beta cells—generate a fuller picture of pancreatic development and plasticity and may pave the way toward new cell-based therapies for diabetes.

PREVENTING, ARRESTING, AND REVERSING COMPLICATIONS

Persistent elevation of blood glucose levels, despite insulin therapy, slowly damages the body's organs and can lead to life-threatening diabetes complications. Until prevention or cure of type 1 diabetes is possible, intensified research toward preventing and treating the complications of the disease is critically important. Diabetes has multiple effects on blood vessels. While a paucity of small blood vessels contributes to poor wound healing in people with diabetes, in the eye, diabetes leads to excessive new blood vessel formation. Basic research on the growth of new blood vessels led to the discovery of a key regulator of blood vessel growth. Because tumors require a blood supply for growth, a drug that inhibits this regulator, and thus new blood vessel growth, emerged from research on cancer and is now an FDA-approved treatment for metastatic colon and lung cancer. These important advances from basic and clinical research set the stage for the biggest advance in diabetic retinopathy, a devastating eye

disease, in 25 years. Investigators in the National Eye Institute-led Diabetic Retinopathy Clinical Research Network (DRCR.net) compared a version of the cancer drug—ranibizumab—in combination with the standard therapy—laser treatment—to laser therapy alone for the treatment of diabetic macular edema, a swelling in the eye that often accompanies and aggravates diabetic retinopathy.

The results from this landmark comparative effectiveness trial demonstrated that the combination therapy was substantially better than laser therapy alone at treating diabetic macular edema. Nearly half of the patients who received the combination treatment showed a substantial improvement in vision after 1 year, compared to 28 percent receiving only laser treatments. As a result, in the future, this class of drugs could become the new standard of care for diabetic macular edema. The DRCR.net continues to test new therapies for the full spectrum of people with diabetic eye disease to treat this debilitating complication of diabetes.

The Diabetes Control and Complications Trial (DCCT), which provided dramatic evidence that type 1 diabetes-related complications of the kidneys, eyes, and nerves can be prevented or greatly delayed through intensive blood glucose control, continues to yield important, life-saving data through the follow-on EDIC study. Comprehensive and meticulous data collection of DCCT/EDIC participants for more than 25 years, with participation rates of about 95 percent, has created an unparalleled resource of individuals with type 1 diabetes that is ideal for study of the clinical course of diabetes and its complications and for the validation of endpoints that can facilitate future drug development. For example, using genetic data from DCCT/EDIC participants, researchers recently identified a gene region associated with regulating blood glucose levels. Understanding how a person's genetics influences blood

glucose control is important for personalizing therapy to provide the optimal care to each individual.

Cardiovascular disease is increased up to 10-fold in people with type 1 diabetes and contributes to reduced life expectancy. EDIC investigators also pioneered use of new noninvasive diagnostic tools, such as ultrasound, to measure the thickness of the carotid artery in people with type 1 diabetes. This allowed them to investigate the long-term effects of intensive blood glucose control on the progression of atherosclerosis, and show that early initiation and continued maintenance of intensive blood glucose control can slow progression of atherosclerosis. By validating new analytical tools for early detection of cardiovascular disease before events occur, the results of EDIC are paving the way for future trials that are smaller, shorter in duration, and less expensive to conduct. This long-term investment in research has and continues to pay major dividends, resulting in improvements in the health of people with diabetes.

EMERGING OPPORTUNITIES IN TYPE 1 DIABETES RESEARCH

Recruiting talented new researchers with different areas of expertise to type 1 diabetes research is critical to our goals to prevent, treat, and cure the disease. Management of diabetes in children is particularly arduous and requires an exceptional level of effort from the children, their families, and their health care providers. These extraordinary clinical care demands make it challenging for pediatric endocrinologists involved in diabetes care to also pursue research careers. Moreover, there is a long process of training and career development before a new independent investigator is ready to obtain grant support and lead a research laboratory. Through support from the *Special Diabetes Program,* a cadre of pediatricians specializing in

childhood diabetes received such training and career development. I'm pleased to report that a recent evaluation of this program showed that, of the 28 pediatric endocrinologists who received training under the program, 27 of them—96 percent—remain in academic science. Many of them have also successfully competed for independent funding to conduct research. The success of this program led NIDDK to recently issue a solicitation announcement for the next round of the program, and also plan to develop similar programs in other fields, such as bioengineering and behavioral research.

These scientists will be well poised to take advantage of emerging scientific opportunities, such as those identified in the recently released Diabetes Research Strategic Plan, spearheaded by the NIDDK. This Plan will serve as a scientific guidepost to NIH, other federal agencies, and to the investigative and lay community by identifying compelling opportunities for research on diabetes and its complications. The Plan addresses research advances, key questions, and extraordinary opportunities in 10 major diabetes research areas, and reflects the efforts of the scientific community, patient-advocacy groups, and Federal staff. In addition, NIDDK recently solicited input from experts from outside the NIH on ideas for the use of funds resulting from the recent extension of the *Special Diabetes Program*. This meeting served as a critical source of input for NIH to ensure the most scientifically productive use of the funds.

Finally, I am pleased to report that NIDDK also recently released an Evaluation Report on the *Special Diabetes Program.* Analysis of projects supported by the funds from 1998 through 2010 revealed that over 2,500 publications, nearly 40 patents, and countless scientific resources have resulted from projects supported by the *Special Diabetes Program.* The *Program* has fostered clinical research as well as stimulated recruitment of new investigators to the field

of type 1 diabetes research. Research supported by the *Program* has resulted in important scientific advances and benefits to the health and quality of life of people with type 1 diabetes.

CONCLUDING REMARKS

I am grateful for the opportunity to share with you today these few examples of recent advances and ongoing research efforts in type 1 diabetes research. We continue to be inspired by the dedicated efforts of individuals affected by type 1 diabetes, and by organizations that represent them. We look forward to continuing to partner with these organizations and our sister Federal agencies on research efforts to combat type 1 diabetes and its complications. We are grateful for the full range of support that NIH has received for type 1 diabetes research. We will continue to be diligent in our fight against diabetes to help all the children at this hearing and the many other Americans whom they represent here today. Improving their quality of life—with the ultimate goal of curing their disease—is the driving force behind our efforts.

Thank you Mr. Chairman, Senator Collins, and Members of the Committee for your attention. I will be pleased to answer any questions you may have.

People with Type 1 Diabetes
Are Living Longer, Healthier Lives
Patients alive 25 years after diagnosis
100%
95%
90%
85%
80%
75%
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1950-1959
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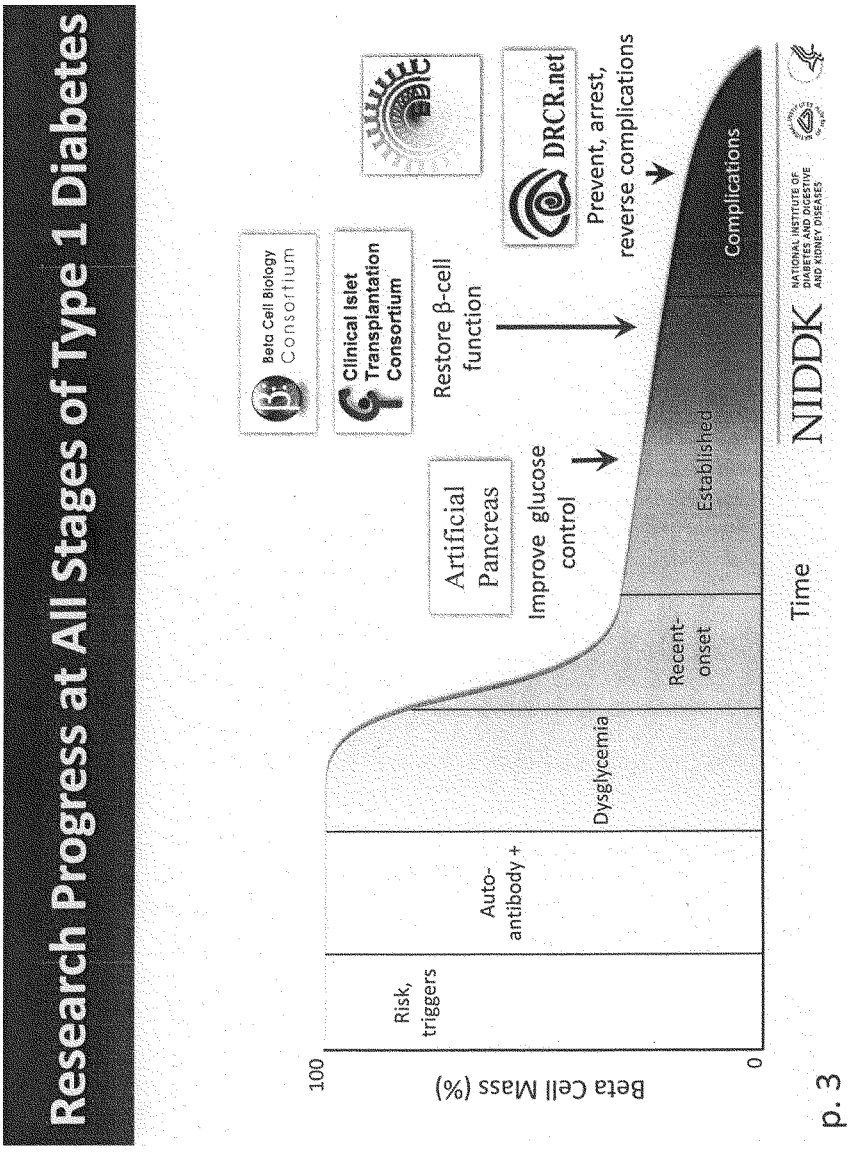
Diagnosed between...
NIDDK
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES
Adapted from Diabetes 55: 1463-1469, 2006.
p. 1


Research Progress at All Stages of Type 1 Diabetes
Beta Cell Biology Consortium
Clinical Islet Transplantation Consortium
Restore β-cell function
Artificial Pancreas
Improve glucose control
DRCR.net
Prevent, arrest, reverse complications
Beta Cell Mass (%)
100
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Risk, triggers
Auto-antibody +
Dysglycemia
Recent-onset
Established
Complications
Time
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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

STATEMENT
OF
CHARLES ZIMLIKI, Ph.D.,
CHAIR, ARTIFICIAL PANCREAS CRITICAL PATH INITIATIVE
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

COMMITTEE ON HOMELAND SECURITY AND GOVERNMENTAL AFFAIRS

UNITED STATES SENATE

"TRANSFORMING LIVES THROUGH DIABETES RESEARCH"

JUNE 22, 2011

INTRODUCTION

Mr. Chairman and Members of the Committee, I am Dr. Charles Zimliki, Chair, Artificial Pancreas Critical Path Initiative, located within the Center for Devices and Radiological Health (CDRH) at the Food and Drug Administration (FDA or the Agency). I would like to thank the Committee for the opportunity to discuss the artificial pancreas system and what FDA is doing to assist in the development of these critically needed and potentially life-changing devices. As a person living with type 1 diabetes, I am personally, as well as professionally, committed to seeing this important novel medical product come to market.

Diabetes is a lifelong disease for which there is not yet a cure, and which can lead to serious complications such as blindness, kidney disease, and nerve damage. FDA is committed to continuing its work with the Juvenile Diabetes Research Foundation (JDRF), other federal agencies, researchers, academia, and many other interested parties to facilitate the development of these important devices. In particular, FDA applauds the work of the JDRF Artificial Pancreas Project, which brings together JDRF and academic and business partners to speed the development and approval of automated systems for people with type 1 diabetes.

On Monday, June 20, 2011, FDA took an important step toward advancing the development of an artificial pancreas system by issuing a draft guidance that outlines Agency expectations for engineering testing and clinical trials for a first-generation

artificial pancreas system, called a Low Glucose Suspend System. I will discuss the importance of this document later in my testimony.

FDA Regulatory Authorities for Medical Devices

A medical device, as defined by federal law, encompasses several thousand types of health products, from simple articles, such as tongue depressors and heating pads, to cutting-edge and complex devices, such as implantable defibrillators and robotic equipment for minimally invasive surgery.

The Medical Device Amendments of 1976 to the Federal Food, Drug, and Cosmetic Act (FD&C Act or the Act) gave FDA specific authority to regulate the safety and effectiveness of medical devices. Medical devices are assigned to one of three regulatory classes based on risk.

Class I, General Controls, is the lowest risk category of devices and includes items such as adhesive bandages. These devices are subject to the General Controls of the Act, which include establishment registration and device listing, compliance with current Good Manufacturing Practice (cGMP), and labeling, recordkeeping, and reporting requirements.

Class II, Special Controls, is a medium-risk category of devices and includes devices such as intravenous catheters and powered wheelchairs. They are subject to the General Controls of the Act as well as Special Controls, which may include special labeling

requirements, mandatory performance standards, and post-market surveillance, in order to ensure device safety and effectiveness.

Class III is the highest risk category of devices and includes devices such as heart valves and coronary stents. These devices are subject to the General Controls of the Act, plus approval prior to marketing of a premarket approval application (PMA) containing scientific evidence of the device's safety and effectiveness.

Background on Diabetes

As you know, Diabetes Mellitus is a chronic, debilitating disease affecting every organ system. Type 1 diabetes usually strikes children and young adults, although disease onset can occur at any age. This form of diabetes is an autoimmune disease in which the pancreas stops functioning effectively.

The pancreas secretes several hormones, including insulin and glucagon, as well as digestive enzymes that help break down food. Insulin helps cells in the body take up glucose (sugar) from the blood to use for energy, which lowers blood glucose levels. Glucagon causes the liver to release stored glucose, which raises blood glucose levels.

Diabetes occurs when the pancreas cannot produce any or enough insulin to regulate blood glucose. People with diabetes can keep blood glucose from getting too high or too low through regular injections of insulin and occasional injections of glucagon. It is critical for diabetes patients to regulate their blood glucose in order to lower the risk of

long-term diabetes complications such as blindness, kidney failure, and cardiovascular disease.

Diabetes is a disease that affects the entire family, especially when a child is diagnosed. When managing type 1 diabetes, patients must vigilantly test blood glucose multiple times per day via finger sticks and a glucose meter. They must calculate insulin doses, administer necessary insulin in the arm, leg, or stomach with a needle or insulin infusion pump to lower blood glucose, and safely dispose of used syringes. Glucagon injection kits should be readily available in any setting to treat severely low blood glucose in an emergency. Some patients benefit from additional monitoring with a continuous glucose monitoring (CGM) system. Diabetes management is constant and pervades all aspects of a person's life, presenting a particularly arduous burden for children and their parents.

Overview of an Artificial Pancreas System

An artificial pancreas system is an innovative device for treatment of type 1 diabetes which, once fully developed, will automatically monitor blood glucose and administer appropriate insulin doses. This life-changing technology will positively impact diabetic patients' health and quality of life and improve long-term health outcomes. As a person with diabetes, I am acutely aware of the benefits an artificial pancreas system will provide. An artificial pancreas system will allow people with diabetes, especially children, to live active lives without the constant need to adjust glucose levels—a constant reminder of the dangers caused by this disease.

While the potential benefits are enormous, an artificial pancreas system is considered a significant-risk device, meaning it presents a potential for serious risk to the health, safety, or welfare of a patient. If not properly designed, use of an artificial pancreas device in an outpatient setting can place patients at significant risk because the device controls the administration of insulin without the oversight of health care professionals. As such, an investigational device exemption (IDE) from FDA and Institutional Review Board (IRB) approval are needed to allow the investigational device to be used in a clinical study. These are necessary in order to protect the rights and safety of human subjects while collecting the data needed to establish the safety and effectiveness of the device in a PMA. All clinical evaluations of investigational devices, unless exempt, must have an approved IDE before the study is initiated. FDA has approved 17 IDEs for clinical studies of artificial pancreas systems at various levels of development. To date, FDA has not approved a PMA for an artificial pancreas system indicated for outpatient use.

At the current level of technological development, the artificial pancreas system consists of three devices already familiar to many people with type 1 diabetes: a blood glucose measuring device (such as a glucose meter); a CGM system, which is a sensor placed under the patient's skin that measures the glucose in the fluid around the cells and sends information to a receiver; and an insulin infusion pump, which delivers controlled amounts of insulin into subcutaneous tissue to lower the concentration of glucose in the blood. These three devices are commonly found in sensor-augmented insulin pump systems. What distinguishes an artificial pancreas from a sensor-augmented insulin

pump system is a computer-controlled algorithm (controller) that communicates between the CGM and infusion pump. It communicates by receiving information from the CGM and performing a series of mathematical calculations that result in an automatic and appropriate insulin dose from the infusion pump. It is critical to the health of people with diabetes that these components perform precisely and reliably, individually, and as a unit.

As noted, FDA has approved 17 IDEs for research on three types of artificial pancreas systems, all in various stages of development. These systems differ in how the insulin pump acts on readings from the CGM system and the level of autonomy with which they manage patients' glucose levels. They are the Low Glucose Suspend (LGS) System, the Treat-to-Range System, and the Treat-to-Target System.

Our guidance, released on Monday, June 20, 2011, entitled "Draft Guidance for Industry and the Food and Drug Administration Staff: The Content of Investigational Device Exemption (IDE) and Premarket Approval (PMA) Applications for Low Glucose Suspend Device Systems," deals specifically with the LGS type of artificial pancreas system and, once finalized, will provide guidance on information that should be submitted to FDA to facilitate marketing of this basic type of artificial pancreas. An LGS system helps eliminate, or reduce the severity of, a dangerous drop in blood glucose levels by temporarily suspending insulin delivery when glucose levels approach a low threshold. This kind of system serves as a potential back up when a patient is unable to respond to a hypoglycemic (low blood sugar) event. Patients using this system will still

need to actively manage their blood glucose levels by periodically checking those levels with a glucose meter and self-correcting their blood glucose levels with insulin.

A treat-to-range system reduces the likelihood of a hypoglycemic event or a hyperglycemic event (when blood glucose is dangerously high) by adjusting insulin dosing if a person's glucose level approaches low or high thresholds. Patients using this system also will still need to check blood glucose levels with a glucose meter and give themselves insulin or eat to maintain control of glucose levels.

A treat-to-target system sets target glucose levels and tries to achieve these levels at all times. This system would be fully automated and require no interaction from the user, except for calibration of the CGM system.

A fully functioning artificial pancreas system, such as the treat-to-target system, will not only monitor glucose levels in the body but will also automatically adjust the delivery of insulin to reduce high blood glucose levels and minimize the incidence of low blood glucose with little or no input from the patient.

The Challenges of a Fully Functioning Artificial Pancreas System

Recreating the precise and dynamic glucose regulation function of a healthy pancreas is a challenging task. This task is further complicated by the numerous behavioral and biological factors that impact diabetes management, and by the current limitations of the devices that are the components of the artificial pancreas.

Current FDA-approved or cleared diabetes management devices have dramatically changed the quality of life for people with type 1 diabetes. While these devices are safe and effective for their individual uses, none is intended to be used alone and all require significant management by the patient. FDA has not yet reviewed their safety and effectiveness as one, closed-loop system designed to perform all functions required for blood glucose management consistently and precisely, with minimal management by the patient. Researchers have made significant progress toward combining these devices into a more dynamic system, and FDA will continue to prioritize this development; however, more research is needed.

Continuous Glucose Monitors

CGMs incorporate sensors that measure glucose levels in the fluid around cells. These glucose levels may differ from the level of glucose circulating in the blood. FDA has not approved CGM values alone as a way to determine insulin dosing. Also, CGM sensors can build up organic matter on their surfaces once they are inserted under the skin. This organic matter can impact the effectiveness of the sensors, leading to inaccurate readings or outright failure of the sensors. More research and advances in sensor technology will help CGM systems more accurately and quickly measure blood glucose and resist build up.

Blood Glucose Monitoring Devices

Blood glucose monitoring devices (such as glucose meters) are used to calibrate CGMs. A more accurate blood glucose monitor provides for a more accurate CGM. Blood glucose monitor readings can be influenced by various factors, such as when a patient is sick, taking other medication, or simply dehydrated. Research to improve the readings of blood glucose monitoring devices can sharpen the accuracy of the overall artificial pancreas system.

Infusion Pumps

FDA has identified problems with the mechanical components and software of many insulin infusion pumps. These problems have led to improper insulin dosing and compromised patient safety. These known problems with infusion pump software present challenges to creating the computer programs to connect insulin infusion pumps and CGMs in an artificial pancreas. The Agency is taking steps to bring safer infusion pumps to market, but more research and innovation to improve the overall safety and effectiveness of the pumps would benefit any artificial pancreas system.

Insulin

FDA must also consider the limitations of insulin delivered by artificial pancreas systems. The insulin currently used in artificial pancreas systems can take hours to completely absorb, and the absorption rates can vary, among patients as well as within the same patient throughout the day. Creating a control algorithm that allows the CGM

to take both factors into account is difficult. The development of faster-acting insulin would help artificial pancreas systems better calculate insulin doses.

FDA's Role

FDA is helping advance the development of an artificial pancreas system by prioritizing the review of research protocol studies, fostering discussion, shortening study and review times, and providing clear guidelines and a path to market for industry.

The Critical Path Initiative (CPI) is FDA's national strategy to drive innovation in the scientific processes through which medical products are developed, evaluated, and manufactured. In 2007, FDA created the Artificial Pancreas Critical Path Initiative, bringing together a multi-disciplinary group of scientists and clinicians from FDA's three medical product centers (the Artificial Pancreas System Review team) and the National Institutes of Health (NIH). These scientists share knowledge in order to facilitate the transition of devices from research to marketing approval. One of the major goals of this initiative is to identify roadblocks and possible solutions to streamline the regulatory process. Many of FDA's efforts, some of which are described below, are unique to the development of an artificial pancreas system.

Collaboration with Researchers and Other Stakeholders

Many stakeholders play a role in the development of an artificial pancreas system—researchers, clinicians, medical device designers, and manufacturers. FDA has worked to encourage the collaboration of these stakeholders so that an artificial pancreas system can

be brought to patients more quickly. FDA and JDRF have worked together on our shared goal of facilitating the development of artificial pancreas systems. In July 2008, FDA, JDRF, and NIH co-sponsored a public workshop that focused on state-of-the-art research and development of an artificial pancreas. The workshop provided stakeholders with a forum for information sharing to accelerate the development of an artificial pancreas. As a result, JDRF and FDA supported investigators in the creation of a theoretical model of glucose and insulin metabolism allowing quick evaluation of various control algorithms as a substitute for animal testing. Use of this time and money-saving tool expedited the transition from bench-top to bedside testing.

Additionally, in November 2010, FDA co-sponsored a second public meeting with NIH to discuss the clinical development plan for transitioning from clinical trials in the hospital to the outpatient setting. These interactions with stakeholders resulted in the development of the artificial pancreas guidance released on Monday.

FDA continues to share with researchers and other stakeholders what we have learned from pre- and post-market reviews about the performance of artificial pancreas components. For example, FDA has worked to obtain permission from specific manufacturers of component devices to provide certain researchers with confidential information that may help further their research. Enabling a better understanding of the challenges of combining the component devices into a system in which patients can entrust their health and their very lives is critical for product development.

Rapid Response to Preliminary Study Plans

FDA encourages researchers to contact the Agency early to discuss clinical study plans and get informal feedback that can improve their study designs and facilitate the review process. FDA responds within two weeks to investigators seeking preliminary feedback on their artificial pancreas system study plans. This quick, informal feedback can help investigators develop better and more complete study plans for FDA review.

Interactive Review of Investigational Device Exemption (IDE) Study Plans

When investigators submit their final study plans for FDA review, the Artificial Pancreas System Review Team gives these submissions the highest priority and works interactively with investigators to move them quickly and efficiently through the review process. Questions and research challenges are often resolved during the first round of review, helping researchers start their studies sooner.

Guidance and Standards for Researchers and Industry

FDA guidance and industry standards help manufacturers and researchers understand the minimum requirements for making a device that is safe and effective. This helps them make the best use of resources and streamlines the regulatory review process.

As mentioned earlier, on June 20, 2011, FDA issued a "Draft Guidance for Industry and the Food and Drug Administration Staff: The Content of Investigational Device Exemption (IDE) and Premarket Approval (PMA) Applications for Low Glucose Suspend Device Systems." This guidance outlines the minimum safety and effectiveness

information recommended for product approval, contains an IDE submission template detailing critical information, and provides a clear and predicable regulatory path for manufacturers seeking to market an LGS system. It was developed with considerable input from industry, researchers, and other stakeholders and provides manufacturers with information that could bring a first-generation artificial pancreas system to market.

FDA is asking for public feedback on the LGS guidance. In addition, FDA will be reaching out to the medical communities that work with people with diabetes to obtain feedback regarding the proposed guidance. Based upon the feedback, FDA will update the guidance accordingly.

FDA has continued to pursue all types of artificial pancreas systems and will be proposing another guidance to address the safety and effectiveness testing for the other more advanced autonomous artificial pancreas systems not covered in the first guidance. To expedite the second guidance, FDA has been working with research communities such as JDRF. Their knowledge and understanding of diabetes and diabetes research have significantly accelerated the development of the second guidance. FDA expects to complete this guidance by the end of 2011.

In addition, FDA is working with NIH and other interested parties in developing the next artificial pancreas workshop, which will focus on developing better technology for the creation of a more accurate and reliable artificial pancreas system.

CONCLUSION

FDA is fully committed to the development of an artificial pancreas to meet this critical health need. It is the goal of the Agency to provide a clear pathway for manufacturers to provide people with diabetes with innovative, safe and effective medical devices to treat their disease. Mr. Chairman, this concludes my formal remarks. I will be pleased to answer any questions the Committee may have.

Testimony of Caroline Jacobs

Age 14, JDRF Children's Congress Delegate from Shapleigh, Maine

At the Hearing entitled:

"Transforming Lives Through Diabetes Research"

Wednesday, June 22, 2011, 1:30 p.m.

Before the

Senate Committee on

Homeland Security and Governmental Affairs

G-50 Dirksen Senate Office Building

Washington, D.C.

Good Afternoon, Chairwoman Collins and Members of the Committee. Thank you for asking me to testify before you today.

My name is Caroline Jacobs, and I am 14 years old. I am from the great state of Maine, where we say Maine is the way life should be.

I am here as a Children's Congress delegate to talk about living with diabetes, the importance of technology for me and other kids with diabetes, and my hope for a cure.

I was diagnosed with diabetes when I was 10 years old; it changed my life forever. With this disease, I must always think and be aware of how I am feeling and I have had to grow up fast. I feel the burden on my family and my friends who are always worrying about me – always asking me questions about my blood sugar.

So, I am doing what I can to make a difference in finding a cure for juvenile diabetes. I brought a *School Walk for a Cure* to my school, and this year is the 3rd year for my family's walk team for the Walk for a Cure in Portland. I also make jewelry and bags to benefit JDRF. I do all of these things so we can continue research to find a cure for diabetes.

While we wait for a cure, I hope to see that more technologies are made available for kids like me. One of the delegates here is from Canada and has the kind of insulin pump/continuous glucose monitoring system that protects against episodes of hypoglycemia when the patient is ignoring the dropping sugar levels.

With its ability to stop insulin delivery when it detects a low blood sugar, this pump could lighten the burden and the worry for me and those around me. This technology is approved in Canada and other countries, but not here in the United States. It is hard for me to understand how a device like that can be available in a place just over the border from me.

Because I will be driving in the next two years, it would be important for me to have access to a technology that could help prevent my blood from dropping. Having diabetes can make your blood glucose levels go too high or too low and can make me feel sleepy or dizzy, confused or have blurred vision making it too dangerous to drive.

I would like Congress to encourage the FDA to move forward on next steps relating to the artificial pancreas, a combination of a continuous glucose monitor and an insulin pump with software that communicates between the two. The device will prevent highs and lows, especially at night when lows can be most dangerous, but it also would keep control of my sugars while I am driving as well. I hope we will not have to wait too long for this device.

That way, I will no longer have to worry about others always worrying about me. More importantly, my family will feel less of the burden, and my friends won't always have to adjust around me because of this disease.

And I hope this means that I will have the opportunity to travel freely without worrying about this disease, and enjoy the world and those who live on it. After all, isn't that the way life should be?

Thank you, Members of the Committee, especially my home state senator, Senator Collins.

Testimony of Jack Schmittlein

Age 13, JDRF Children's Congress Delegate from Avon, Connecticut

At the Hearing entitled:

"Transforming Lives Through Diabetes Research"

Wednesday, June 22, 2011, 1:30 p.m.

Before the

Senate Committee on

Homeland Security and Governmental Affairs

G-50 Dirksen Senate Office Building

Washington, D.C.

Thank you, Senator Collins, Senator Lieberman, and Members of the Committee for inviting me to testify. My name is Jack Schmittlein. I am 13 years old, and I have had juvenile diabetes for over six years.

On October 4, 2004, my life changed forever with my diagnosis. Instead of being a carefree kindergartner, I was faced with pricking my fingers 8-10 times a day, counting carbs, and taking insulin shots. Managing diabetes is hard work that lasts 24 hours a day, every day.

Two years ago, my best friend Peter was diagnosed with type 1 diabetes. Before, he had been incredibly helpful in managing my disease, even keeping me company when I walk to the nurse's office to check my blood sugar. Peter and his family learned everything they could about diabetes so I could come over to play at their house safely. Peter's diagnosis is just one more reason why I work to raise awareness about type 1, and one more reason why I am here today.

Important research to find a cure is happening all over the nation, even at Yale University in my home state of Connecticut, to better understand the causes of type 1 diabetes and ways to prevent it. I am grateful that Congress passed legislation to renew the Special Diabetes Program last year. This program is central to helping to find a cure for type 1 diabetes.

The Special Diabetes Program has allowed for research that has led to the artificial pancreas. An artificial pancreas would help prevent my blood sugar from dropping and give me insulin if my blood sugar gets too high.

Right now, I have to get up to check my blood sugar in the middle of the night every night. It would make participating in activities that I love a whole lot easier. I really enjoy playing basketball and football, but I often have to come out in the middle of the game to test my blood sugar. It would give me my life back so I can just feel like a kid again... not a kid with diabetes!

Despite this incredible technology, we need to do everything we can to find a cure. I am doing my part to help continue to push life-saving research forward. I have been a JDRF Walk Team Captain for four years, have organized a walk at my school to benefit JDRF and have also spoken about life with diabetes at two Walks, a school assembly, and a Promise Ball fundraiser as a JDRF Youth Ambassador.

It is my hope that Congress will continue to support research at NIH, specifically the Special Diabetes Program. I really believe that we will find a cure for type 1 diabetes. The artificial pancreas is a promising result after strong investment in research.

I look forward to the day that I can say "I used to have diabetes." Until that day, an artificial pancreas will greatly improve my daily life, and the lives of other kids who have type 1 diabetes. I know that Congress and JDRF are doing all that they can to make this possible for kids like me.

Just think: if we could improve the lives of millions of children and adults around the world, why wouldn't we?

Research being conducted all over the country is bringing us closer to a cure, and the development of the artificial pancreas could help keep us healthy while we wait for a cure.

Thank you, Chairwoman Collins and Members of the Committee, for providing me the opportunity to give you a glimpse into what my life is like with diabetes. I look forward to answering any questions you may have.

Testimony of Kerry Morgan

Age 17, JDRF Children's Congress Delegate from Glen Allen, Virginia

At the Hearing entitled:

"Transforming Lives Through Diabetes Research"

Wednesday, June 22, 2011, 1:30 p.m.

Before the

Senate Committee on

Homeland Security and Governmental Affairs

G-50 Dirksen Senate Office Building

Washington, D.C.

Good afternoon, Senator Collins, Senator Lieberman, and Members of the Committee. Thank you for inviting me to testify today. I am Kerry Morgan from Glen Allen, Virginia and I was diagnosed with diabetes thirteen years ago, when I was four years old.

Unfortunately, diabetes wasn't new to me when I was diagnosed. My older sister was diagnosed with the disease when she was four. Shortly after her diagnosis, I was enrolled in a clinical trial for first-degree relatives of people with type 1 to determine if they were at risk for developing the disease. On the trial, I received daily insulin injections in hopes to avoid or delay development of diabetes.

It didn't work. Sometimes clinical trials don't. I was formally diagnosed with type 1 diabetes one year later.

Then in what seemed like a flash, ten years passed. Ten years filled with thousands of insulin injections, finger sticks, tubing changes, endless carbohydrate counting and worry. Ten years of toting around an awful green fanny pack containing the vital necessities for everyday life. Even with my best efforts I still have days with severe high and low blood sugars. My family and I hoped, just like the millions of those impacted with this disease do, for a better way to control this.

I was 14 when I enrolled in a clinical trial that was testing a continuous glucose monitoring system. This ingenious device, which I named "my little buddy", gave me instant knowledge of what my blood sugar was doing, and where it was going. While on this trial my A1c dropped from an 8 to a 7. This technology made living with the disease not only easier, but gave me hope that it was TRULY possible to manage diabetes better.

It wasn't a cure, but it was more than I had before.

Living with diabetes is a daily struggle. It creates this cloud of fear and doubt. Thoughts of blood sugars and carbs are always on my mind. I'm constantly asking myself, "Am I *okay*?" I always have to remember snacks and extra supplies to ensure that, in case of incident, I'm covered because things can get scary quickly. I've had my pump stop working while out of town, unprompted by dropping it or submerging it in water.

I don't just worry about it now, I worry about my future. Diabetes never takes a break, so, neither can I or my family.

Then, last October, I enrolled in a clinical trial testing artificial pancreas technology. For two days, I was admitted into a hospital where they tested the closed loop artificial pancreas system. After participating in clinical research since I was three years old, I can honestly say the closed loop artificial pancreas trial was the most amazing experience of my entire life and holds so much promise for people living with this disease.

For two days, I had perfect control of my blood sugar levels. Two days of living with this technology provided me with a vision of what life could be like: Life with FAR LESS fear of complications both short and long term. Creation of an artificial pancreas is within reach, I know it, I've been a part of it, and I will do all I can to get it into the hands of people living with diabetes, and I hope you will too.

So, on the day the artificial pancreas is finally approved and released, people with this disease can say, "Diabetes: There's an APP for that."

Thank you, Members of the Committee, for all you do for those living with diabetes, and working to make the artificial pancreas technology available to all those living with this disease.

Testimony of Jonathan Platt

Age 7, JDRF Children's Congress Delegate

from Tarzana, California

At the Hearing entitled:

"Transforming Lives Through Diabetes Research"

Wednesday, June 22, 2011, 1:30 p.m.

Before the Senate Committee on

Homeland Security and Governmental Affairs

G-50 Dirksen Senate Office Building

Washington, D.C.

Hello, Chairwoman Collins and other Members of the Committee.

Thank you for inviting me to testify. My name is Jonathan Platt. I am from Tarzana, California, a suburb of Los Angeles. I am seven years old.

I was diagnosed with juvenile diabetes at age 6. I had been losing weight, wetting the bed at night and had extreme thirst. I was always tired and very emotional. My Mom and Dad thought I was just adjusting to a new school and kindergarten. My blood sugar was over 650 when I was diagnosed with juvenile diabetes.

I will never forget the day I was diagnosed with juvenile diabetes. We found out later that the little red headed girl who rode up in the elevator with us was diagnosed with juvenile diabetes also. That had never happened before at this doctor's office, two kids diagnosed at the same time. I was thinking how did I get this disease. I didn't know what it was. I was very scared and nervous.

I am here as a Children's Congress delegate to tell you that I manage my disease, but I do not let it control my life. With this disease, I am able to swim, play basketball, and build legos. But I am different.

Unlike other kids, I have to check my sugar 8 to 10 times a day. Everything I eat is measured and every carbohydrate counted. My blood sugar kit, juice, glucagon and ketone strips go with me everywhere I go.

It is hard when I go to summer camp, do a sleep over or even go to a friend's house. Too much exercise or not eating all my food can be very dangerous. I think I am too young to have to worry about all this stuff!

My parents have had to adjust their life because of my diabetes, but they say we all have it, not just me. Managing diabetes is a 24 hour job. We are doing our part to help find a cure by raising money for the JDRF Walk. I am here to ask you to continue to do your part and fund research to find a cure.

A cure for diabetes means that I could go to any summer camp and have sleepovers whenever and wherever I want. It means I could be a regular kid again. Most of all, it would mean I would not have diabetes.

Please help me make this possible. My life depends on it.

Thank you.

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JDRF Juvenile Diabetes Research Foundation International

dedicated to finding a cure

Mary Tyler Moore
International Chairman

Dear Senator Collins,

I am so sorry that I can't be with you for this year's Children's Congress. I ask that my testimony be included in the hearing record as I feel so strongly about the need for a continued federal commitment to diabetes research and the need to remove roadblocks that are delaying the availability of exciting new therapies in the United States.

I appreciate your tremendous leadership and strong support for all of JDRF's issues, and thank you and Senator Lieberman for holding this important hearing to help increase the public's awareness of the seriousness of type 1 diabetes and the burden it places on our health care system.

I look forward to our next Children's Congress and being with you in 2013.

Warmest regards,

Mary Tyler Moore

Mary Tyler Moore
JDRF International Chairman

Testimony of

Ms. Mary Tyler Moore
International Chairman, Juvenile Diabetes Research Foundation

At the Hearing Entitled

"Transforming Lives Through Diabetes Research"

Wednesday, June 22, 2011, 1:30 p.m.

Before the

Senate Committee on Homeland Security and Governmental Affairs

Senator Collins, Senator Lieberman and Members of the Committee, thank you for welcoming us and for providing us the opportunity to discuss an issue so near and dear to our hearts – finding new treatments and a cure for type 1 diabetes and its complications. Joining me today are over 150 children and teenagers from across the United States and seven other nations, all delegates to the JDRF's Children's Congress. I am honored to be among them as JDRF's International Chairman and perhaps oldest delegate. I am inspired every day by these young people, by their resilience and determination and sense of humor in coping with diabetes, which gives me new strength to face my own day-to-day challenges of life with the disease.

I am here before you today to say we are making progress but need to act urgently to remove barriers that are delaying the advancement of new therapies to people with diabetes. Since I first appeared before you at the 2001 Children's Congress, we have moved diabetes science from mice to men, thanks to your tremendous leadership and the public-private investment in research. We are especially grateful to Senator Collins, Senator Lieberman, and the other Senators on this panel for your strong support for last year's renewal of the Special Diabetes Program, which comprises 35 percent of the federal type 1 diabetes research budget. But I implore you not to rest, because we are not there yet. Each of the children here is counting on you to continue your support of this critical research and to address the barriers that must be overcome to realize the promise of our research efforts.

We have progress to report, which I know Dr. Rodgers will discuss in a moment. I would like to highlight two recent developments that I find particularly exciting:

- Now, for the first time, we can improve vision damaged by diabetes, which is the leading cause of adult onset blindness. A major research study funded by the National Institutes of Health and JDRF found that nearly half of the people receiving the new therapy improved their vision by at least two lines on the eye chart. This important breakthrough could help millions of Americans with diabetes maintain the ability to read, drive, and stay in the workforce, preventing significant government costs. This therapy was recently approved for use in Europe and is expected to be submitted shortly for review by the Food and Drug Administration for use in diabetic eye disease.

- At the same time, studies have shown that artificial pancreas devices can significantly reduce out of control blood sugars which cause devastating complications from diabetes. One study found an artificial pancreas could double the amount of time children and teenagers spend in target glucose ranges, reducing dangerous high and low blood sugars. And an artificial pancreas could also play a big role in reducing the financial burden that diabetes places on our Medicare system – a new analysis commissioned by JDRF shows that use of an artificial pancreas by working age people could save Medicare nearly $2 billion over the next 25 years.

I am pleased that these new developments will help the children here today avoid many of the emotional and physical burdens that I face after more than 40 years with the disease. Diabetes has taken its toll on my vision – I can no longer see well enough to drive, navigating a dark backstage can be a challenge, and let me just say I've had a mishap or two worthy of Dick Van Dyke! I have also experienced dangerously low blood sugars at a variety of inopportune times,

and have required my dear husband Dr. S. Robert Levine to rescue me from unconsciousness on a number of occasions.

To help the children here today and the millions of other Americans with type 1 diabetes, we need to remove roadblocks delaying the availability of new therapies here in the U.S. We need immediate action by the FDA to ensure the artificial pancreas can move to the next stage of testing – if not, this promising technology could be delayed for years and available overseas long before it is available in the U.S., as some technologies already are. I know that if I had had an artificial pancreas 40 years ago, I would likely not be facing such a heavy burden of complications as I do today. Please, take action now so the children here today will have the opportunity that I did not, an opportunity for a life free from the many daily burdens of diabetes. We urgently need your help.

Thank you. I am delighted to answer any questions you may have.

Post-Hearing Questions for the Record
Submitted to Dr. Griffin P. Rodgers
From Senator Scott P. Brown

"Transforming Lives Through Diabetes Research"
June 22, 2011

Mr. Brown: What is the NIH's current role in supporting the FDA in this process? How do you foresee this role changing in the coming months? Will you be facilitating the transition to clinical trials with translational research?

Dr. Rodgers: The NIH and FDA are working closely together to accelerate development of an artificial pancreas. Under the auspices of the Diabetes Mellitus Interagency Coordinating Committee, we regularly meet with our colleagues at FDA, CDC, and other Federal agencies to coordinate our efforts to combat diabetes. Through the Interagency Artificial Pancreas Working Group, NIH and FDA have jointly sponsored workshops on an artificial pancreas, including a public workshop in November 2010 focused on the clinical and safety expectations for artificial pancreas systems. Defining these expectations is key to getting the systems appropriately tested in research settings and ultimately approved for use outside the clinic. To continue this momentum, planning is under way for a joint NIH-FDA-JDRF workshop on technology innovation for artificial pancreas systems.

The NIH supports scientifically meritorious research to overcome scientific barriers to the development of this technology and to address issues important to FDA regulatory approval. For example, grants supported by the Special Diabetes Program have been awarded by NIDDK to small businesses to develop innovative technologies that may advance progress toward an artificial pancreas. Through support of clinical research, the NIH addresses questions about how a given therapeutic approach or technology, like an artificial pancreas, may be more (or less) beneficial to patients. Already, artificial pancreas systems are being tested under closely monitored conditions in NIH-supported research, and, in some cases, FDA authorization is required for the researchers to perform these studies.

To identify the most promising diabetes research opportunities, the NIDDK recently published a Diabetes Research Strategic Plan that includes a chapter focused on emerging research opportunities in the development of an artificial pancreas. Because many of the current barriers and emerging opportunities relate to engineering, with the recent renewal of the Special Diabetes Program, NIDDK plans to support training for bioengineers to encourage them to pursue research on an artificial pancreas. The NIH will continue to support research toward the development of an artificial pancreas and to test these systems in clinical trials, and work with FDA to make the artificial pancreas a reality.

Mr. Brown: As you mention in your testimony, testing the closed-loop system in real world situations is critical to its development. Do you have any plans for specific research studies to test this system for the unique needs of children?

Dr. Rodgers: The NIH recognizes the need to test technologies specifically in children as they will have unique challenges to its use. In addition, the NIDDK's landmark Diabetes Control and Complications Trial showed that good blood glucose control, as soon as possible following diagnosis, reduced the risk of complications over subsequent decades. Therefore, it is important to help children achieve good blood glucose control early in their lives.

Toward this goal, the Special Diabetes Program has supported a number of clinical studies in children. These include studies using continuous glucose monitoring technologies—a component of an artificial pancreas—specifically in children. These studies showed that physical activity during the day increased a child's risk of hypoglycemia at night. These findings point to the importance of adjusting a child's diabetes management regimen on active days. The NIDDK currently supports several studies testing artificial pancreas technologies which include children. Additional studies—like that of the bi-hormonal closed-loop system I mentioned in my testimony—plan to include children later.

With the recent renewal of the Special Diabetes Program, the NIDDK also plans to support research to improve treatment adherence in children, adolescents, and young adults with type 1 diabetes. This includes testing behavioral approaches to enhance utilization of continuous glucose monitoring and, ultimately, an artificial pancreas in children. Such research could provide important insights to help children to best take advantage of new technologies like an artificial pancreas.

Mr. Brown: After hearing Dr. Zimliki's updates, it is promising to hear of the significant progress on the development of this technology. However, he also suggests that considerable research still needs to be done. Is the basic scientific research on par with this technology development and in a good place to continue to support this progress or is the science lagging behind?

Dr. Rodgers: Basic scientific research is on par with the technology development and in a good place to continue to support this progress. NIH-supported scientific research is driving the development of technology toward an artificial pancreas. For example, the Special Diabetes Program supports research conducted by small businesses to develop innovative technologies toward an artificial pancreas.

While researchers develop new technologies, it is also important to move forward and build on the currently available technology. For example, research supported by the Special Diabetes Program contributed to the development of all three FDA-approved continuous glucose monitors. Such monitors are a component of artificial pancreas systems currently being tested. In another example, a key aspect of closing the loop between glucose sensing and insulin delivery in a mechanical artificial pancreas is the development of algorithms. These sophisticated computer programs interpret continuous glucose sensor data and instruct the insulin pump to deliver the proper amount of insulin. NIDDK-supported research led to the development of algorithms currently being tested in clinical trials of mechanical closed-loop systems.

Just as current artificial pancreas approaches being tested are using continuous glucose monitors generated in previous decades with NIDDK support, strategies being developed now will lead to improved artificial pancreas systems in the future. Research toward a bio-artificial pancreas—one that includes replacement of the beta cells lost in type 1 diabetes with transplanted, bioengineered tissue—is being conducted by scientists, including those in the NIDDK-led and Special Diabetes Program-supported Beta Cell Biology Consortium.

The NIH will continue to support meritorious research toward an artificial pancreas, balancing these two goals: to improve current technologies that may contribute to today's artificial pancreas, including glucose sensors, computer models, insulin formulations, and

insulin delivery systems; and to develop the next generation of technologies to lead to tomorrow's artificial pancreas.

Mr. Brown: I think we can all agree that in addition to the personal and families struggles with diabetes, the financial burden of diabetes is serious. With annual costs for diabetes in the United States at roughly $174 billion, these numbers are troubling, and during this difficult fiscal climate, we need to be dedicating resources and efforts to try to reduce these costs. From a financial perspective, what could we anticipate from the introduction of such a device?

Dr. Rodgers: An artificial pancreas would enable easier and more appropriately adjusted delivery of insulin in response to minute-to-minute changes in blood glucose levels. This could improve insulin treatment and care for people with diabetes, and could help people to achieve good blood glucose control. Blood glucose control is important because the landmark NIDDK-supported Diabetes Control and Complications Trial demonstrated that intensive control, beginning as soon as possible after diagnosis, can prevent or delay diabetes complications. Researchers from this trial estimated that implementation of intensive insulin management in the entire U.S. type 1 diabetic population could save 920,000 years of sight; 691,000 years free from end-stage renal disease; 678,000 years free from amputation; and 611,000 years of life.[1] These complications of the eyes, kidneys, nerves, and heart are costly to treat, and contribute to the $174 billion annual cost of diabetes. Therefore, an artificial pancreas could help reduce the economic burden of diabetes in the U.S. by helping people with diabetes delay or prevent diabetic complications.

In addition, the risk of abnormally low blood glucose, or hypoglycemia, is a major barrier to the intensive blood glucose control that has been demonstrated to reduce the risk of complications. Severe hypoglycemia can lead to seizures, comas, and even death. Ambulatory services, emergency room visits, and in-patient hospitalizations for severe hypoglycemia can contribute to the cost of diabetes. By balancing insulin needs and administration more precisely, an artificial pancreas could reduce hypoglycemic events and thereby reduce health care costs associated with severe hypoglycemic episodes.

Indirect costs such as lost workplace productivity for parents of children with diabetes are also included in the $174 billion estimate. An artificial pancreas would allow parents to care for their child without compromising workplace productivity and their own well-being.

[1] [1] The DCCT Research Group. Lifetime benefits and costs of intensive therapy as practiced in the diabetes control and complications trial. JAMA 276: 1409-1415, 1996":

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

The Honorable Joseph I. Lieberman
Chairman
Committee on Homeland Security and Governmental Affairs
United States Senate
Washington, D.C. 20510-6250

AUG 05 2011

Dear Mr. Chairman:

Thank you for providing the opportunity for the Food and Drug Administration (FDA or the Agency) to testify at the June 22, 2011, hearing entitled "Transforming Lives Through Diabetes Research" before the Committee on Homeland Security and Governmental Affairs. This letter provides responses for the record to questions submitted by Senator Scott Brown provided to FDA in your letter dated July 7, 2011. We have restated the questions in bold, followed by our responses.

Thank you again for contacting us concerning this matter. If you have further questions, please let us know.

Sincerely,

Michele Mital

for Jeanne Ireland
Assistant Commissioner
for Legislation

The Honorable Scott Brown

1) **It is good to hear that the development of this breakthrough technology is a priority for the FDA; however, I think we can all agree that there is much work still to be done. What I continue to hear from Massachusetts is that there continues to be a lot of uncertainty for manufacturers and the private sector hindering development efforts. Since we already have three working devices, in the market, that now need to be fully integrated along with new software developed, I feel it is critical that we do not create any additional hurdles to manufacturers and industry to stifle this development and innovation. Do you envision the artificial pancreas being regulated as a combination device or a medical device? Is unnecessary regulatory burden prohibiting this technology from coming to the market?**

Recreating the precise and dynamic glucose-regulating function of a healthy pancreas is a challenging task. This task is further complicated by the numerous behavioral and biologic factors that impact diabetes management, and by the current limitations of the devices that are components of the artificial pancreas system. Current FDA-approved or cleared diabetes management devices used as intended have dramatically changed the quality of life for people with type 1 diabetes. While FDA has determined these products to be safe and effective in their individual uses, these devices have not yet been proven safe and effective working together in a closed-loop system. Researchers have made significant progress toward combining these devices into a more dynamic system, but more research in glucose sensors and blood glucose monitoring devices, infusion pumps, insulin, and glucagon is needed. For example, glucose sensors often build up organic matter on their surfaces (biofouling) once they are inserted under the skin. Biofouling could potentially impact the effectiveness of the sensors, which may lead to inaccurate readings or cause sensors to stop working. More research and advances in sensor technology will help glucose monitoring systems more accurately and quickly measure blood glucose levels and resist biofouling.

Getting a safe and effective artificial pancreas system to people with type 1 diabetes is a top FDA priority. The Agency will continue to work with all interested stakeholders to facilitate the development of an artificial pancreas system. FDA efforts to advance product development include: prioritizing the review of research protocol studies, setting performance and safety standards, fostering discussions between patient advocacy groups, other federal agencies, researchers, and academia, sponsoring public forums, finding ways to shorten study and review time, and providing clear guidelines and a path to market for industry.

More information about FDA efforts in facilitating the development of a safe and effective artificial pancreas system is available at *http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/HomeHealthandConsumer/ConsumerProducts/ArtificialPancreas/default.htm.*

FDA anticipates regulating artificial pancreas systems as medical devices.

2) **I am proud of the continued efforts of our diabetes patient-advocacy community, medical device industry and researchers in Massachusetts, and as the FDA moves**

forward collecting input on your recently released guidance, I would hope that you will be reaching out to our respected medical community—do you have any specific plans to do so?

Many stakeholders, including patient-advocacy groups, researchers, clinicians, medical device designers, and manufacturers, play a role in the development of an artificial pancreas system. FDA has worked to encourage the collaboration of these stakeholders so that an artificial pancreas system can be brought to patients more quickly. FDA has held or co-hosted several public meetings designed to include the perspectives of all interested stakeholders. Examples include:

- July 2008 – Toward an Artificial Pancreas (FDA/National Institutes of Health (NIH)/Juvenile Diabetes Research Foundation (JDRF) Workshop)
- March 2010 – Public Meeting: Blood Glucose Meters
- March 2010 – Advisory Committee Meeting – Insulin pump failures
- May 2010 – Public Meeting: Infusion Pump Workshop
- October 2010 – Association for the Advancement of Medical Instrumentation/FDA Infusion Device Summit
- November 2010 – FDA-NIH Public Workshop – Clinical Development of an Artificial Pancreas

FDA is in the process of planning a second FDA/NIH/JDRF workshop for later in 2011 which will focus on developing better technology for the creation of a more accurate and reliable artificial pancreas system.

In addition, the "Draft Guidance for Industry and the Food and Drug Administration Staff: The Content of Investigational Device Exemption (IDE) and Premarket Approval (PMA) Applications for Low Glucose Suspend Device Systems," issued on June 20, 2011, was developed with considerable input from industry, researchers, and the clinical community. The Agency is asking for public feedback before finalizing the guidance.

As part of the outreach for the low glucose suspend (LGS) draft guidance, FDA specifically targeted health care professional groups, alerting them to the availability of the draft guidance and requesting their input. The targeted provider groups include the Diabetes Technology Society, the American Association of Clinical Endocrinologists, the American Diabetes Association, the Endocrine Society, the JDRF, the National Institutes of Health, the Endocrine Nurses Society, and the American Association of Diabetes Educators.

FDA will continue to collaborate with the medical community and other stakeholders. The Agency will seek public input on forthcoming guidance for the development of an artificial pancreas system and continue our efforts to prioritize and expedite clinical research in this area.

3) **What I hear most often in talking with folks living with diabetes across Massachusetts especially adolescents, are the challenges of managing their daily glucose levels. As children and teenagers spend significant time outside of their**

homes, while in school or engaged in extracurricular activities or for young adults in college, who are living on their own, away from their families, and eating in dining halls without their parents' supervision. You allude to some of the behavioral and biological factors that impact developing this technology, but can you address some of the particular factors you have identified for youth or any plans to address these factors through continued research and development efforts?

It is critical for diabetes patients to regulate their blood glucose to lower the risk of long-term diabetes complications such as blindness, kidney failure, and cardiovascular disease. One of the critical elements in developing an artificial pancreas system for the pediatric population is ensuring safe and effective use of this device in real-world scenarios, such as those you have described. In addition, addressing the impact of human factors, such as user interface, logic of operation, labels, instructions, and the ability to hold up to the rigors of being an active child or young adult, in developing an artificial pancreas system for pediatric use, are important considerations. FDA will address human factors in the next guidance document for manufacturers developing a more sophisticated artificial pancreas systems, such as the treat-to-target or treat-to-range systems. A treat-to-range system reduces the likelihood of a hypoglycemic event or a hyperglycemic event (when blood glucose is dangerously high) by adjusting insulin dosing only if a person's glucose level approaches the low or high glucose thresholds. Patients using this system will still need to check blood glucose levels with a glucose meter and give themselves insulin to maintain control of glucose levels. A treat-to-target system sets target glucose levels and tries to achieve these levels at all times. It would be fully automated and require no interaction from the user, except for calibration of the continuous glucose monitoring system.

4) **As you describe in your testimony, we need to find a device that performs "precisely and reliably, individually, and as a unit." I recognize that first generation models of this nascent technology raise some concerns particularly related to issues of patient safety. What steps are you taking to ensure quality and safety of these systems and the clinical trials, specifically in your phase II guidance?**

One of the critical aspects of the guidance currently under development for the more advanced treat-to-target or treat-to-range systems will be based, in part, on comments received to the predecessor guidance. A fully functioning artificial pancreas system will not only monitor glucose levels in the body but also, automatically will adjust the delivery of insulin to reduce high blood glucose levels and minimize the incidence of low blood glucose with little or no input from the patient. Since these more advanced systems are intended to require such minimal patient input, FDA also will address safe use of these more advanced systems in real-world scenarios. However, the second guidance is still in development and is expected to publish in December 2011.

5) **I realize that asking about the expected timeline continues to be the million dollar question, but can you predict any of the potential setbacks or delays moving forward with this process?**

Issuance of the LGS draft guidance in June was an important step toward advancing the development of a fully automated artificial pancreas system. This draft guidance, and the forthcoming draft guidance for treat-to-range and treat-to-target systems, will provide researchers and manufacturers with additional clarity on the Agency's expectations.

FDA believes that an approvable LGS system could be developed with existing technology. However, improving the accuracy of continuous glucose monitors so that they can be used to determine insulin dosing, not just blood glucose tracking and trending, could rapidly accelerate research and move LGS systems into the final stage clinical studies needed for approval.

For more sophisticated artificial pancreas systems that could provide more accurate glucose control, such as the treat-to-range and the treat-to-target systems, more research is necessary in the following areas: glucose sensors and blood glucose monitoring devices, infusion pumps, insulin, and glucagon. FDA recently has published the technical challenges in developing an artificial pancreas system at the following link *http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/HomeHealthandConsumer/ConsumerProducts/ArtificialPancreas/ucm259567.htm*.