

## **FDA-patient Dialogue on the Unmet Needs in Diabetes**

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Draft Transcript

### **Welcome – Opening Remarks**

**Dr. Helene Clayton-Jeter:** Welcome to the FDA patient dialogue on unmet needs in diabetes webcast. It's exciting to be here for the unprecedented interaction between the diabetes community and the FDA. Thank you so much for more than 7000 patients who responded to the recent questions from community surveys, as well as for the 1,000 people who are joining us today via webinar, and all of those on Twitter at #DOCasksFDA. What a way to start on this national diabetes awareness month with such a novel idea to bring the community together! Today we will hear from FDA leadership on what they do, then move into organizational perspectives with The diaTribe Foundation, JDRF, and ADA. Part of the discussion will be the two panels. One will be where I talk to patients and one where Kelly seated to my left will talk to FDA leadership. I will then discuss communication with FDA and conclude with the joint diaTribe Foundation wrap up.

What do we want to accomplish today? Primarily, we want to continue to open up the lines of communication between FDA and the patient community. We want to help the reviewers get a better sense of what it is like to live with diabetes, what is difficult for patients, and what patients need in terms of tools. Lastly, we hope this will be a pilot for potential future meetings at the FDA. With that, let's hand it over to Kelly Close, founder of The diaTribe Foundation, who will tell us how this got started.

**Kelly Close:** Thank you so much. It's wonderful to be here.

Thank you for the wonderful introduction. Let me give you a little bit of background on how this meeting germinated and how it got started. 18 months ago, I was lucky enough to hear the great FDA Commissioner, Dr. Margaret Hamburg, on a panel discussion. She is of course an engaging and amazing public leader. She helped lead the discussion on the fight against chronic and infectious disease on the BBC World Service's "The Forum" at the Aspen Institute. I'm listening to this with great intent as you can imagine, and she was there with cancer biotech leader Tony Coles (we hope the next time there is also a diabetes executive with her), and they were talking with the CDC Head Dr. Tom Frieden about chronic disease and infectious disease. As diabetes of course is the biggest health problem of our time, I was very interested to follow the dialogue. Directly after that, she was part of a fascinating and daunting conversation with public health journalist and thinker, Dr. Richard Besser and Mount Sinai CEO Dr. Ken Davis, who, as many know, is incredibly connected to diabetes. They got that conversation going on "What Will Healthcare Look Like in 25 Years?"

Of course, after listening to the ever so eloquent Dr. Hamburg, I went to speak to her about the problems in diabetes, how badly patients need help on so many fronts, and gave her some information on how patients think about problems on many different levels. Not skipping a beat, she asked me if I thought that diabetes patients would be interested in having a dialogue with the FDA and if we could come here and speak. I said of course I would! It would be amazing, and we have had great help in making this day happen. We worked hard trying to bring in different patient views and we know the perspectives of patients, partners and caregivers should be front and center as the FDA reviews the technologies we need.

We need this today more than ever. 5,000 people a day are diagnosed with diabetes, type 1 and type 2. Their voices are so important because we are facing the US spending \$250 billion a year on diabetes. It's still very important we think to bring in patients with many different perspectives and share with the FDA how diabetes affects daily lives, and what will make diabetes management better so that we can all impact public health in a positive way. Thank you so much for making this day happen. Today is a true landmark for patients and I'm excited for today's session. With over 7,000 people, responding to the survey and our panelists here today, we thank you so much for bringing together patient voices.

[Holding survey book.] This book has the summary along with just the answers to two of the questions. This is over 400 pages. We are excited for you to be able to hear these patients. This means the world to us. We also want to share big picture thoughts on what patients would most like to see with diabetes management with a video we've put together. With that, I think we are ready to roll.

[\[Patient Video\]](#)

### **The Role of the FDA in Diabetes**

**Dr. Helene Clayton-Jeter:** Thank you Kelly. I'm excited to have FDA leaders here to talk about all that they do and to get us all on one page. Some of the information that you will hear, you already know, but I hope you will appreciate and be patient. Now I am excited to start the role of the FDA in diabetes discussion. We will talk about what the FDA is and what it is not, what role they play in approving a drug or device, and more. Let's start here and bring Dr. Bull to the podium so she can enlighten us on her part in this piece of the FDA puzzle.

**Dr. Jonca Bull:** Good afternoon. Good morning to those on the West Coast and I want to say thank you to the organizers, colleagues in FDA and the Office of Health and Constituent Affairs for all that this program is doing on behalf of patients. I couldn't have been placed into a better spot because those powerful messages in the video resonate to our work.

I am the Director of the Office of Minority Health, which some people like to call the Office of Population Science, because you're looking in greater detail at who has the disease. We look at issues that have to do with demographics subgroups like sex, age, race and ethnicity. The basic question is: who are the patients that have diabetes? When we look at age-adjusted percentage of people 20 years and older with diagnosed diabetes by race, we see that there are different proportions of impact in the population. There is a disproportionate impact in subpopulations. When we look at the rate of cases of type 1 and type 2 diabetes amongst folks who are less than 20 years of age - this is our future. The news of this graph shows a moment in time, and does not convey that the numbers are increasing. When we look at population impact, and I have to point out that none of these go down to zero and that all groups are impacted, there is a differential population impact in subpopulations when you look at type 1 diabetes and when you look at type 2 diabetes.

In terms of unmet need, what we know is that the prevalence of adult diabetes is higher among Hispanics, non-Hispanic blacks, and those of other and mixed races other than Asian and non-Hispanic whites. The prevalence is higher in adults without college degrees and those with lower household incomes. What is the FDA doing? The review policy states that the database of the patients in the clinical trials submitted in a marketing application should reflect use in a diverse racial population, which reflects the likely patient mix.

In the findings of an FDA Safety and Innovation Act report, we looked at the trial composition, and we had a 67% white inclusion and only 2% black and African American and 31% Asian. We have to look at the same time that diabetes is a global problem and we need data globally, but also think about how does that reflect the patients that we take care of in the United States.

We also have greater input on the report. To highlight some of the concerns that we heard from patients and health professional groups, they cited that the proportion of some subpopulations are not consistent with the prevalence of the disease. They also cited that healthcare professionals and patients do not have sufficient demographic information to make well-informed treatment and diagnostic decisions.

We also heard from industry, and they highlighted a general lack of awareness about and limited physical access to clinical trials among some demographics. The needs of global development result in clinical trials with substantially different racial and ethnic representation in the United States and the question we have to ask is, when does the data matter in terms of looking at safety and efficacy?

In August of this year, the FDA posted an action plan, which was required under legislation to respond to the findings of the report. The deficiencies that we found and that the report highlights are three overarching priorities. The first one is to improve the completeness and quality of demographic subgroup data collection reporting and analysis. The second priority area is to identify barriers to subgroup enrollment in clinical trials and to employ strategies to encourage participation. The third one was to make demographic subgroup data more available and transparent.

Thank you for the opportunity to speak this morning and I look forward to the panel discussion.

**Dr. Courtney Lias:** My name is Courtney Lias and I am the Director of the Division of Chemistry and Toxicology here at FDA. Our division regulates devices used with diabetes like glucose meters, tests for hemoglobin, and artificial pancreas devices. I want to talk about a few things in what we do in regulating devices and a few points about some of the devices that we do regulate and questions that sometimes come up for patients.

I would like to talk about first: how does a new device get to the market? They are regulated by risk. Unlike a new drug, patients use things that go from the tongue depressor all the way to artificial hearts. You use the same regulatory paradigm for a tongue depressor and for an artificial pancreas. On the basis of the product, what is the right regulatory touch for that device? We have a classification where the highest risk devices are treated a lot like drugs, where there is premarket approval and full clinical trials to demonstrate safety and effectiveness.

Whereas in the lowest risk categories, the devices don't usually come to FDA before they go on the market and the manufacturer typically just tells FDA that they are going to make this product and make it under a good quality system and collect complaints. For example, diabetes devices fall across the spectrum and we have a lot of devices used by people with diabetes, including single use lancets, and they don't have to come to FDA before they go on to the market. We see products like the artificial pancreas device (which is a class III), which do have to go through clinical studies and review before going to market. Further, insulin pumps still come to the Agency as moderate risk class II devices and have a very well-defined pathway. That is how the new device gets to market, but we have other mechanisms to help as well.

For example, if an entity, company person, or inventor has a new product and wants to know, “How can I get my product to the market to patients?” we have a mechanism called the pre-submission process. It is free, and it’s where we talk about the new device, talk about how it works, and how we want to get it to market. It’s an interactive process where we can talk to them and give them help and advice, so when they come to us they can get the product on the market more smoothly.

Finally, we have a pathway to enable companies to get clinical trials going for devices that need them. For artificial pancreas devices, investigators and companies who are investigating can interact with us to get clinical studies approved. We look at whether they are safe and mitigation that the investigators have for patients, and go forward with those. With the submissions, we do make a concerted effort to be interactive with investigators or sponsors like companies and to make sure that the process can be as efficient as possible and people don’t get hung up on this unnecessary burden. For example, in the clinical study space, we’ve been able to get all the artificial pancreas devices approved within the first round of the last four years and that has accelerated the development process of devices to get to full course for patients in the near future. That is a little bit and a snippet of some of the things that we do in terms of the regulatory processes.

I would like to cover a few other topics briefly. In the survey there were comments about blood glucose meters and people wanting more accurate and reliable meters. We have draft guidances that we published in January that cover these topics – one for blood glucose meters for over-the-counter use by patients who have diabetes, and the other for blood glucose meters by health providers or people working in hospitals or long-term care facilities. These two documents propose premarket pathways the manufacturers use in the goal of creating policies that promote better, more accurate, but still accessible devices for patients and their healthcare providers. We try and solve challenges that we hear from patients and doctors about the use of devices in ways that we can do it in the premarket space. We want to give a big thank you to the patient community on these two guidance documents because this is one of the first guidance processes I have worked on where we had huge patient interaction. We had about 600 comments total on those two guidance documents and more than 400 of those comments were from patients. That helps us to understand what is important to you and make sure the policies that we end up with are in alignment with what you need and we are not going off in a direction that doesn’t help you get to the goals that you and your doctor have. We want to thank you for that and that is an area that is showing us that patient engagement can help us promote better policies.

On other ways that we engage with patients on new technologies, we have guidance documents that we have patient engagement on. One would be the mobile apps guidance, which a lot of patient groups did comment on, and that really helps us. In mobile applications for diabetes, it helps us understand, if I have a lot of devices I want to use, I want to be able to access the data from my phone or have one thing to interact with, and learning these things from a patient committee helps us create guidance documents. We need to understand how people use the devices that are put on the market, what the challenges are still in this that we need to solve together, and what type of things are going in the right direction. We want to thank you for that.

Finally, we do hear from the patient community when they don’t have things they need and they are crying out for pancreas devices, which are not yet approved here in the world. How do we get to that point where patients have access to those devices? That is important to us and we learned a lot from their engagement and communication.

Another thing we heard is with patients who may have other considerations for themselves and use test strips that have been previously owned. We want to raise the dangers that you might face if you were to purchase test strips that are not from the original source distributors. Test strips that are stored incorrectly, previously opened, or exposed to humidity can deteriorate performance and relying on these test strips can create dangerous situations. We caution people to purchase their supplies from reputable dealers. Finally, I would like to talk a little bit and put a little plug-in that we're having a public meeting on November 13. That meeting is meant to actually gather information from patients and healthcare providers in two specific areas. One is interoperability and we will discuss the issues on what it will take and what challenges exist for devices to communicate with each other so that we can get to the point where you can have different devices from multiple different manufacturers with communication that can be used together for the care you need. That is the first topic that will be discussed and the second one is how do healthcare and patient providers view bolus calculators. We want to understand how these products are to you so we can make sure the regulatory touch is the right one going forward for those products. That public meeting is here at FDA on November and I encourage you if you're interested to please attend. For the rest I look forward to the rest of the discussion and hearing from the patient panel. Thank you very much.

**Dr. Helene Clayton-Jeter:** Before we go to the next speaker, as you can see, this is a rapid-fire dialogue and we won't have time for bathroom breaks. We will keep moving quickly and next I want to call Dr. Naomi Lowy from the Center for Drugs and Research.

**Dr. Naomi Lowy:** Good afternoon. I am Dr. Naomi Lowy. It's my pleasure to speak to you this afternoon about key issues related to the FDA and diabetes drugs. This is an overview of my brief talk and will first guide you through the FDA overall drug approval process from the first testing in humans to what happens after a drug is approved for marketing. I will describe the drug labeling process, which is a mystery, I believe, for many people, and touch on resources and how best to approach questions the patients have regarding a specific diabetes drug. First, the phases of drug approval are preclinical and clinical phases followed by a new drug application submission or NDA, a review of the NDA, and post-marketing phase. These are discussed in the next two slides. This infographic is available on the FDA website and summarizes the preclinical and clinical phases. You can follow along with number one, the development of the drug and testing. Once animal studies have been done, the applicant submits an investigational new drug or IND application, which outlines the proposal for initial testing in humans. The FDA reviews the IND application within 30 days to ensure human subjects are protected from unreasonable risks of harm and adequate informed consent is provided. We get into clinical trials on the right side of the infographic. The phases have increasing numbers of patients as they progress. At the end of phase 2, under number four, the FDA meets with the company to discuss the phase 3 studies being planned.

The second graphic summarizes the NDA review on the left side and post-marketing phase on the right side. This begins with another meeting of FDA in step number six and having the NDA submitted to the Agency. The application contains all the data about the drug in animals and humans as well about data how it is manufactured. The application is reviewed and at the end, the FDA conducts inspections of the facility where the drug will be manufactured, which is number 11 on the infographic. If the drug is approved, the post-marketing phase on the right

side begins, with safety information about the drug continuing to be collected in the phases. This is critical because clinical trials cannot predict all of the drug's effects.

Related to this concept of the importance of post-marketing surveillance, I would like to refer you to an FDA video that highlights Dr. John Jenkins. The video which may be found on the FDA website as well as on YouTube is entitled “FDA's role in Development, Testing and Monitoring of New Drugs.” There's a quote from the video that explains the post-approval program, and he says, “It is very important for people to understand that we don't know everything about new drugs at the time we approve them. If we waited until we knew everything you could possibly know then the wait would be too long and patients would be denied access to important new treatments.”

To give you an idea of how quickly the landscape of diabetes drugs is changing, this is a slide of drugs that were approved in 2014. Here I also included any weight management drugs approved in 2014. I do want to highlight an aspect of drug labels, which we also referred to as prescribing information. The proposed labels are actually sent by the applicant to FDA as part of the new drug application (NDA). The final label is a product of extensive negotiations between FDA and the applicant. It's important to note that new issues come up and can lead to modification of the label at any time after the approval of the drug. It can be company or FDA initiated but it's important to note that this can be a fluid process.

To show you what an actual label looks like, here is an example of a label for a recent diabetes drug, and this is the first page, the highlighted section of an actual 22-page label. In contrast to the label intended for healthcare providers, here is a list of FDA-approved patient labeling that, based on the safety profile of the drug, is also provided. These include medication guides, patient information, and instructions for use. Beyond these, patients today have many reliable resources for more information on diabetes care. The list here includes some of these, such as the National Diabetes Information Clearinghouse, PubMed Health, and the NIH drug information portal. Ultimately healthcare practitioners are the best resource and ideally patients should partner with their practitioner to personalize care to them.

I welcome questions – please send them to this e-mail address, and thank you very much for your attention.

**Dr. Helene Clayton-Jeter:** Next we have Dr. Patricia Beaston. She's also from the Center for Devices and Radiological Health.

**Dr. Patricia Beaston:** I am Dr. Patricia Beaston and a Medical Officer at CDRH, I spent my first seven of my 14 years at the FDA in the Center for Drugs. For a number of years, I've been at the FDA working on a number of diabetes projects and I will follow-up on Courtney's comment and tell you a little bit more about how we look at things from a clinical perspective. One of the things that comes up a lot, is that patients want to know about risk and benefit comparisons and how do we look at those - the risks of the studies versus the benefits of the knowledge that can be gained in the study.

Often the choice of deciding how benefits outweighing any perceived risk gets much more challenging because many times, and even in some of the studies with the patient first at it in the outpatient arena, it is important to understand that if the device fails, what are the

consequences of the failure and what happens? Not only to the patient which could be catastrophic, but what happened to other people around the patient at that time? Could the patient know that the device may have failed or was there a warning, and are the people around you also affected? If there's a problem with the device and this is what could happen, we try to understand what happens to the patient and the practitioners when that fails and we see if they've indicated and we feel that even if there is could be somewhat horrific – there is a chance to intervene in what was identified that it could be remedied, it does not preclude the device from going on the market. If not, we would have no ability to intervene or understand what's going on and make any change in the estimation of what potential benefit in the risk category would be. We really understand that patients want to have things and they want to have their own risk-benefit calculation, but it's important to consider that there are other people involved in this. Then there is the trade-off between convenience and inaccuracy in the ease-of-use. That could be where packages, where it could be convenient to do something faster or quicker if it's not as accurate as it could be, and you lose the ability to fine-tune as well as losing the therapeutic value of the device.

It also goes to the pumps. People don't want them swelling up in size but also want them to be doing much more, like the ability to detect the occlusion or the accuracy of the delivery, and you can change a number of things. So we do look at those things when we were looking at the balance, making things smaller and more convenient to doing what the therapeutic goal of the devices are.

The next point is we frequently hear is why a therapy is available on the market in Europe. I'm not unsympathetic, but I can tell you that the regulatory approach is very different in Europe compared to the US. With market information, the analysis for the majority of the devices are done in-house by a group of experts and we work together and have our designated specialty. And for European devices on the market, a lot of times they can say “We conform to whatever standard and we can check all the boxes,” and when they go on the market and if they require data, a lot of times it's not done by an FDA equivalent. They have what they call notified bodies. Different countries can have different notified bodies and even within the country they can have different notified bodies, and across the country some will agree to take information from others' notified bodies. So if every state did their own version of the FDA, and some of the topics would be the same, some answers would be different, and it would be hard to know if you bought something in one state versus another. The other thing is even though something can go on the market in Europe, many times, for the country to put it in their nationalized health system, it is required to have the same level of evidence of the FDA before they are willing to reimburse for it. And in Europe, they can take the drug off the market just as easily as they put it on. In the United States, there are laws that make taking products from the market more difficult because it requires negotiation and is mainly voluntary from the company.

Then there are two other points. The other is we do a lot with a combination products and many diabetes products are combination products in one way or another. Pens filled with insulin or other diabetes drugs, or pumps or other ways to deliver insulin or the characteristics of insulin have to be considered when you look at the software in the characteristics of the pump design. We are also looking at components of software that guide how different drugs are delivered, and they also send the control issues for how they are designed for patients and for healthcare providers to understand them. Finally if you're going to write a consumer report guide for diabetes, what would you like to know? If you went out and bought a glucose meter or pump, or some other diabetes product, how would you like to be able to make an informal choice for your product? Where do you think the resources are more reliable and which one is a

better bargain, and which one is more durable? If you can think about that that would be great input for us to take back.

I want to thank all my FDA colleagues sitting here and thank you for taking the time out and for lots of things going on in addition to this meeting.

### **Organizational Perspectives – The diaTribe Foundation**

**Dr. Helene Clayton-Jeter:** The next panel we have is on organizational perspectives. I would like for the presenter and patient to come up together.

The first presenter is Adam Brown from The diaTribe Foundation. Adam has a presentation so we will do that first and then he will enter into a discussion with the patient Francisco Estrada.

**Adam Brown:** Thank you so much to the FDA and everyone in the audience and everyone online for listening. It's an honor to be here on behalf of The diaTribe foundation. Personally, I have had type 1 for 13 years and I have had the opportunity to interact with many patients both online and off-line.

I want to talk about the complexity of issues that we believe are impacting patients. The first, which is that a 7% A1c is not a 7% and this is something we care strongly about. We know that A1c is a useful metric in terms of measuring a nice high-level overview of diabetes. However, it doesn't always tell you the full story of diabetes management. We hear an A1c of 7% is an average of 154 mg/dl. But as you can see on the slide, you can have vastly different diabetes management. You can spend a lot of time in range or almost no time in range and still have the same average A1c of 7%. And again that's not to say that A1C is not a good long-term outcome measure, but we want to get beyond that because it doesn't quite tell the full story. That is to say the time in range can be different even if they have the same number. When we look at pie charts of this, I think it puts it into perspective that we call these different breakdowns of time in range as the same A1c. This quote speaks to the challenges of someone with diabetes, because you're always walking a tight rope: "If I stand with one foot in a bucket of ice water and one foot in a bucket of boiling water, then on average I'm comfortable." To share a personal story from last night, I spent four hours with a blood glucose less than 70 mg/dl and I woke up around 40 mg/dl. A therapy that limits my overnight hypoglycemia will raise my A1c, and that is okay from patient perspective because it improves my quality of life because I don't get up in the middle of the night.

Diabetes is really easy if you don't eat, if you don't move, you get eight hours of sleep and you are never stressed. Especially on insulin therapy, it is so tough to do all of that. This is really what diabetes is like. There are more than 22 factors that affect our blood sugar every minute. I can have access to the best technology, the best doctors, the best everything, and be well educated and yet still I cannot manage all of the variables. Thinking about what patients are managing on a daily basis and trying to help take some of the variables out of the question would be beneficial. This is why you see so much stress in diabetes, because people who did everything right will still have blood sugar out of range, and it is so frustrating from a patient perspective. Because controlling all these variables is just so incredibly challenging.

We'd also like to see follow-up on areas of regulatory guidance, and on how the FDA advises sponsors. One we'd like to consider is creating a guidance for prediabetes, where there are 86 million Americans with prediabetes, but no pathway to get drugs to market. Also, having more type 1 therapies, particularly looking into type 2 drugs used in type 1, would benefit from a



guidance. For blood glucose monitoring, there is a trade-off between accuracy and convenience to a point, but beyond that there is not a marginal benefit of accuracy but there are huge trade-offs in terms of larger meters and meters and strips that take huge droplets. From a patient perspective, that matters. Appreciating the trade-off the companies will need to make is important. The last is cardiovascular outcome trials. We believe these trials delayed transformative therapies in a big way, cost billions of dollars, and enrolled hundreds of thousands of patients. We'd love to speak further with the FDA to re-examine the basis of those.

**Adam Brown:** Now I want to introduce Francisco, and we will have a short discussion about his experience living with type 2 diabetes. Francisco, tell me about yourself.

**Francisco Estrada:** My name is Francisco Estrada. I have had type 2 diabetes for five years. I formerly worked with the FAA for twenty-four and a half years and retired as the Chief of Staff in the Engineering Services Office under the NextGen Organization.

**Adam Brown:** How would you summarize your diabetes in two words?

**Francisco Estrada:** Two words I would use for it is "It stinks!" [Laughter]

**Adam Brown:** I know. I would love for you just to share when you were diagnosed, what your doctors were, what your diabetes management was like, how it all felt?

**Francisco Estrada:** To me it was really a disaster. I had visited three different doctors in trying to get a diagnosis. They said I had metabolic syndrome or that I was prediabetic. I researched all of this, and the way I felt was terrible. I couldn't sleep. I would get up two or three times a night to urinate (sometimes even more) or to drink water. The job I held was stressful enough, and I felt a complete loss of energy. I felt tired and mentally exhausted most of the time. I kept gaining weight year after year. I couldn't lose it. So finally, my primary doctor said, "I think you're a diabetic." Besides starting me on metformin, my doctor said I needed to lose weight, but it's a lot easier said than done. I didn't lose the weight, even though I watched my diet and regularly went to the gym three or five times a week. My weight just kept on increasing. After I retired I set a primary goal for myself to get back in shape and to restore my health. I went back to the routine of exercising about five times a week in the gym. I watched what I ate, cut out drinks, and tried to relax as much as possible, but I wasn't getting ahead. It didn't make a difference! I finally got to the point where I said I would see if I could find something else out there and that's when I considered a gastric bypass. I heard a lot of things about it being helpful reducing weight, but I really wasn't ready to get cut. I decided to search for alternative "weight reduction" programs and I saw a program going through FDA trials where a doctor was testing a new alternative weight reduction device used in Europe. It is essentially a sleeve you put through your esophagus and it goes into your stomach. This was an alternative gastric bypass procedure that did not require surgery and could be done on an outpatient basis. I thought about it and contacted the doctor who was handling that study. Unfortunately, I didn't meet the requirements to participate in this program; however he did take my name and details in case something came up. About a week later, he passed my name off to the GRADE study and I became a participant of that study.

**Adam Brown:** What is it like being part of the GRADE study?

The GRADE study has been great for me. The GRADE study stands for Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study. It is a seven-year nationwide

study encompassing 5,000 patients. In Maryland, this NIH supported study is headed by Dr. Vanita Aroda at the MedStar Research Institute in Hyattsville and includes 150 participants. This program compares four FDA approved medications used to treat type 2 diabetes in combination with metformin. Its purpose is to see how well the different medication combinations control sugar levels and help determine the best treatment for type 2 diabetes.

**Adam Brown:** Great. Thank you.

### **Organizational Perspectives – JDRF**

**Dr. Aaron Kowalski:** My name is Dr. Aaron Kowalski, I am a scientist at the JDRF, and in addition I'm a person with type 1 diabetes. I'm pleased to be sitting here with Angie Platt, an incredible diabetes advocate and a mother of an 11-year-old son, Jonathan, who you saw was in one of the videos. I'm going to make some remarks and then have a dialogue with Angie.

Type 1 diabetes is insulin dependent due to an autoimmune attack. As many as 3 million Americans have type 1 diabetes, and 80 people a day are diagnosed. My brother was three when diagnosed, and I was 13, so it is very personal in our family. Type 1 used to be known as juvenile diabetes, but it can strike at any age, for children and adults, and we're going to hear from Angie about the challenges. It is not just personal diabetes. The family members are involved in taking insulin injections and other management – this is a balancing act to avoid highs and lows. It is a 24 hours a day, seven days a week, 365 day a year struggle. And despite tremendous efforts – and again Angie will say this much better than I can – highs and lows happen. Almost every day, and it can be life-threatening. So while insulin discovered in the early 1920s is a treatment, it is really not a cure, and doesn't prevent the possibility of the serious complications of diabetes such as eye disease, kidney disease, heart disease, or pregnancy complications. The JDRF has funded over a billion dollars in research over the years and our ultimate goal is to cure diabetes. But in the meantime, we need to help develop better treatments. Insulin, CGM devices, etc. have helped, but the majority of people do not meet the recommended ADA clinical guidelines for glycemic control. We need better therapies and we need the companies and FDA to work together, and the community to work together, to get there faster to ease the burden.

I can just say this as well dealing with diabetes myself that the time that you spend in the normal range makes a huge difference. What we know from data is that people spend just a fraction of the day in the normal glycemic range. We again need to do better. We know it A1C is superb to help us gauge how we are doing with control, but it is not the only metric. Adam said that very well. We need better tools to improve glycemic control but also to ease the burden of living with the disease. And we need to align as a community, industry, peers, FDA, and researchers to get there faster. There's still a huge unmet medical need. I'm going to turn to Angie because she's going to bring this home in terms of what this is really like to do day in and day out. Angie, I've been fortunate to visit with you and Jonathan. Why don't you talk about Jonathan and when he was diagnosed?

**Angie Platt:** Hello everyone. My name is Angie Platt, and I have a son Jonathan. He's 11-years-old and he was diagnosed with type 1 diabetes at the age of six. Jonathan was once a big kid, and now he's still a very thin kid. We as parents didn't notice the extreme weight loss, which was followed by extreme thirst and frequent urination, which turned into bed wetting. He was lethargic, and he had just started kindergarten. We had all of those telltale signs. So eventually it was suggested we get him tested for diabetes. We left his pediatrician's office and he was rushed to the emergency room with blood glucose of over 600.

**Dr. Aaron Kowalski:** Imagine...that's just shocking.

**Angie Platt:** My husband and I had never heard of type 1 diabetes. We'd heard of diabetes but we didn't think he would ever have diabetes. Because we didn't understand it at that time. I was in shock and confusion – that was the initial reaction that we had. Guilt too – we lived with guilt for a number of years. And hopelessness, really. We didn't know if Jonathan would ever have a normal life again. Luckily for us, when Jonathan was diagnosed, he spent one day in the hospital. It was a Monday afternoon. I remember that very clearly. October 12, 2009. We were sent home from the hospital on Tuesday, October 13, with a slew of supplies, mainly insulin, that we would administer to Jonathan to keep him alive. But if that same insulin was incorrectly dosed it could also kill him, so it was a really really heavy burden that we lived with and still live with to this day.

It is tough to talk about – to talk about his daily routine and when he takes the insulin, the devices he uses today and what that's like.

I take it for granted that people know what it is like to live with a type 1 diabetic child. But my day starts at 5:30 am, when I take Jonathan's blood sugar while he's still sleeping because that early morning blood sugar is critical. We try to have him wake up in range as often as possible. He wakes up each day and has the same breakfast every morning, but it is interesting because his blood sugar number at lunch can vary up by over 100 mg/dl. He can be low at lunch, normal, or high, and it is the same breakfast every single morning. That's followed by a lunch check, at school check, and if he has basketball practice we would check his blood sugar before and after. He gets checked at dinner, and his father and I for the past five years have checked Jonathan's blood sugar at 10:00 pm and at three AM. So overnight is really hard for us. It has been tough.

**Dr. Aaron Kowalski:** I've been doing this for 37 years and I still get choked up. Talk about your concerns and your fears you go through, and you do this day in and day out.

**Angie Platt:** Initially our concern was overnight lows, which we still are concerned about, but now our concerns are more about Jonathan's highs and lows each day. In a span of a day you can be 40 mg/dl and you could be 408 mg/dl, and like I said we test his blood sugar all the time. We watch what he eats, but he's a very active kid so I worry what highs and lows will do to his body over time and we worry about complications in the future.

**Dr. Aaron Kowalski:** What do you wish worked better and what can we do better as a community to help you guys?

**Angie Platt:** I will take you back to his initial diagnosis with type 1 diabetes – you are taking multiple injections a day of insulin. Jonathan was getting over 10 shots a day of insulin and not only is it the shot, it is the calculations. From morning breakfast, lunch, and dinner, there's a different insulin to carb ratio that must be calculated. There are corrections for highs that need to be calculated. It is a lot of work. It is a lot of math. It is a lot of tracking, and it is a lot of supplies. I remember four months after Jonathan's diagnosis, we said we were going to take a vacation. We packed all of our supplies – and with type 1 diabetes you pack extra supplies in case of emergencies. Being on vacation with a six-year-old, you want him to just be a six-year-old and have a popsicle and eat chicken nuggets and French fries. It was that four-month mark. I remember, it was an emotional break for me and I had to speak to our endocrinologist and say that I don't know how I could live like this anymore. I felt so bad because Jonathan was the

one with type 1 diabetes, but I'm telling his endocrinologist that I don't know if I can take this stress anymore. She said when to get back, and to see me, and he's going on an insulin pump, and that's going to make things much better. So my point is Jonathan went on the insulin pump and it changed our lives. Going on an insulin pump brought a whole new set of concerns, and glitches come up, but just easing the burden of calculating multiple injections a day made such a huge difference in our lives. I'm hopeful for more technology down the pipeline. Not having two devices, and the sensors not being quite as painful. I'm hopeful for so many things. That alone will ease the burden of living with type 1 diabetes.

I think there's a common perception out there in the community that people with diabetes are just not compliant, that they are just not doing it, and they are just not working hard enough. And what your hearing here is it's just an incredible amount of work, overwhelmingly so.

Jonathan he has two little brothers, Clarence and Sean are 15 months. I'm almost embarrassed but I have to be honest when I tell you that when I found out I was pregnant, my first thought was, "Will they have a type 1 as well?" And we don't know. They could or they could not have type 1 diabetes. We know that they probably are genetically predisposed. We don't know what the trigger is, so it is hard to avoid a trigger that you don't know. We are hopeful that if they do start to develop type 1 diabetes that we can slow down the onset, but we know we cannot stop the full-blown type 1 diabetes from coming. So I'm hopeful for prevention and that's why we love JDRF because they are working on a cure, better treatments, and also prevention. We are hopeful too with Jonathan that there will be better technology coming to the pipeline that will help make our lives easier for management and prevention as well.

**Dr. Aaron Kowalski:** Angie, you've been amazing. You are a true champion for people with diabetes and I think your message really molds with The diaTribe Foundation message that diabetes is more than just A1C. It is more than just glucose control. It impacts more than just the person with type 1 diabetes. My family did the New York City Marathon yesterday and it was for my parents, dealing with my brother and me growing up, so thank you for your comments.

**Dr. Helene Clayton-Jeter:** Thank you for your comments, and what a touching story. Now we will hear from the American Diabetes Association. We will hear from Dr. Maria Mupanomunda and her patients that will be a part of her presentation.

### **Organizational Perspectives – American Diabetes Association**

**Maria Mupanomunda:** I am Dr. Maria Mupanomunda, the Vice President of High Risk Programs and Health Disparities at the American Diabetes Association and here with me today I have Anna McCollister-Slipp and Rebecca Killion.

**Rebecca Killion:** I'm Rebecca Killion.

**Anna McCollister-Slipp:** I'm Anna McCollister-Slipp. I've had type 1 diabetes for 29 years and have all of the complications associated with that.

**Dr. Maria Mupanomunda:** The mission of the American Diabetes Association is to prevent and cure diabetes and to improve the lives of all people affected by diabetes. The burden is huge. There are 29 million people in the United States with diabetes. 8.1 million of those are undiagnosed. An additional 86 million people have prediabetes.

Despite improvements in care, diabetes remains the leading cause of blindness and end stage renal disease. And despite improvements in therapies, many patients are not meeting their glycemic goals. We know hypoglycemia as a limiting factor in the fight against hyperglycemia. Our position is very clear. We have made a commitment to the outcomes that are of importance to patients and to talk about unmet patient needs, recognizing that they vary from patient to patient and from circumstance to circumstance.

We know that to some degree, having A1c lowered with less hypoglycemia or weight gain and a favorable side effect profile is ideal. Quality of life is equally important, and today we have two of the best advocates. I do want to give them a lot of time to talk about the day-to-day challenges of living with diabetes and some of the compromises that they have to make. And they will talk to us about why they have to make some of those compromises. I will start with Rebecca. What are the compromises you have to make personally with diabetes and why?

**Rebecca Killion:** I have to make compromises because I have diabetes. I wouldn't need to do these things if it wasn't a literal matter of life and death. A little bit more about my background: I'm an adult onset diabetic and I was diagnosed at the age of 38. I was training for a marathon and I'd been on my long training runs and I was running up into people's yards to drink out of their hoses. And I was going to get arrested doing this but I really was thirsty. I made all sorts of excuses as to why that was. The thing I did not want to admit, although I had it in the back of my mind, is that this is not normal – this is something else. I tell the story to my husband – this is part of the compromises and how it affects people other than the person actually with diabetes. I remember getting ready for work one day and I finally decided I was going to say it out loud, and when you say it out loud it is real. So to my husband, I said, "I think I have diabetes," and he said, "No, you are fine." I just exploded on him because it took so much for me to say that. Of course in his desire to be supportive and comforting he was diminishing it – "Of course, you are fine." I'm not fine. So I guess that when you think about that, the first compromise, and the compromises I make every day and I will make every day for the rest of my life, is the fact that on the day that I acknowledged it and was diagnosed, I lost a lot of my independence. For somebody like me who is nothing if not the captain of her own ship, that was really difficult. It's still a struggle, and the loss of control is very humbling. I was first diagnosed as type 2, but that was later diagnosed with type 1 after I had an incident of very severe ketoacidosis. But as I started out on my journey as a diabetic, the first thing I realized is that I'm dependent on a drug. Very difficult. I convinced my doctor that I was going to be the patient that was cured from diabetes through sheer force of will...that didn't work out so well. So I started on multiple therapies. That was my second realization, that this is something I have to do every day for the rest of my life if I intended to actually have a life.

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### **Patient Perspectives**

**Dr. Helene Clayton-Jeter:** Welcome patient panelists – I am very excited for the opportunity to get to speak with you today on patient perspectives.

[Transcript missing for this portion]

First, I'm interested to hear your thoughts on better trial participation. Trials help the FDA better understand the safety and effectiveness of drugs and devices before they are put on the market. Have you ever participated in a trial and what was your experience like? How can we increase trial participation and increase diversity?

**Cherise Shockley:** As you said, we need to be very creative in working together as patients and also organizations.

**Dr. Helene Clayton-Jeter:** As Dr. Bull mentioned in her presentation, we are looking at clinical trial participation, especially in the minority population. And that's something we're mandated to look into. So we're in the implementation phase now. So I'm looking forward to see what's produced from this Congressional mandate.

**Manny Hernandez:** I myself have not, but shortly after being diagnosed I signed up my son on Trialnet, which I think is something that everybody with type 1 diabetes should do to help advance the science in understanding the condition.

Now as a Hispanic, but for some of the very same reasons, I see the need for a lot more diversity, I was pretty shocked to see some of the data in the Advisory Committee as well. There is severe shortage of data for minorities, which is like whoah, we need to fix that!

Now, I think sometimes we think of diversity as something that is addressed through language, or being multilingual for that matter. But it's truly about being multi-cultural, so there is the model of using health promotoras as an example of really getting creative in terms of reaching out and engaging patients.

One thing that came up in a conversation about clinical trials a while back was this is a trend thing now with food trucks. They're everywhere and they really meet people where they are instead of expecting everyone to go to where we're waiting for them. So I was wondering if we could do something about it, and have trial trucks/trial buses.

**Rebecca Killion:** I actually have participated in multiple studies and trials. And I have to say I do it because I feel it's a duty to do it. I know it's very important and I know that I have benefitted from others who have gone before me and have died. I have to tell you it is an unbelievably difficult undertaking. It is egregiously burdensome in terms of time and effort, and I understand because I worked for a law firm. I understand why these things get very, very complicated.

But you need to make it easier for people. You can get the information out there and make it easier for people to know what's available so people could handle it well. But for the participants in it if you want to maintain people from the beginning to the end of the studies that are not just dropping out because they have complications but because it's incredibly burdensome, you need to make it easier for patients to participate and to streamline.

**Dr. Helene Clayton-Jeter:** Is there something you want to add?

**Adam Brown:** Yeah. Just to add one little thing, I also have not participated in a trial. So I do think it speaks volumes that three of the four speakers on this question have not, which I think speaks at how hard it is as a patient to know what trials are out there. Clinical trials are profoundly, profoundly not patient friendly. It's hard to find trials. The trials aren't updated frequently. Even patients who are in the know and who are also in the media, they don't find out about trials.

And often, you don't qualify for them. Your A1c might be too low. You might not meet the inclusion criteria. So I love that the FDA wants to do studies and gather data. And it's so critical

for making sure the devices are safe and effective as well as drugs. But trials ask a lot of patients and of companies. And I think that's something critical that we need to keep in mind.

And just to touch on the risk question real quick, I think those of us who are type 1 or anyone with type 2, we have enough drugs on board to kill us at every minute. And that's a really big risk we that we as patients take every day.

And one of the biggest errors that patients make is in carb counting. And you ask diabetes educators how many carbs are in this and they get it wrong every time. Not even the experts can figure it out. So I think appreciating the risks that the patients take every day just because we're on insulin therapy is really important.

**Francisco Estrada:** Just wanted to comment. The reason I'm here today talking to you about my experience is because I was lucky enough to have stumbled in to do a clinical trial. I talked to a doctor who told me I was ineligible for it. A week later, he had a call from another doctor and said, "Hey, would you be willing to participate in my trial?" Now, there has to be a better way of finding out what's out there.

**Dr. Helene Clayton-Jeter:** Well, thank you. Anna?

**Anna McCollister-Slipp:** I also want to say someone like me who takes so many medications usually is screened out of them. So I think it would be really helpful to have a clinical trial designed for actual patient populations. So many of the trials screen people like me out.

**Dr. Helene Clayton-Jeter:** And you'll probably hear more on this later on in the discussion session with the FDA when Dr. Jonca Bull speaks.

I think we've talked a lot about A1c. So let's go to this question. If you want to write a consumer report on diabetes, I think my colleague, Dr. Patricia Beaston, talked a little bit about this. What would you include in this? Specifically, what information do you want that you cannot find or that you lack access to?

For example, accuracy of medication to their grade, inclusions, what would you write in your consumer report if you can do that? So who wants to tackle this first? Okay, Adam, go ahead.

**Adam Brown:** I think this is a really cool idea. Unfortunately, I feel that most patients just don't look at package inserts. They don't look at labeling information. The print is small. It's hard to unfold the map that is packaging labels. When we test new products at *diaTribe*, we apply this test. Can I set this up without an instruction manual?

Because that's how easy products should be, right? We all live in a world of iPhones and iPads. And we can pull it out of a box and turn it on. And a 5-year old could get it up and running. And that's how our medical devices should be. They should be that easy. And I think it's really hard from a patient perspective to expect people to read through 300-page manuals because none of us want to spend more time on diabetes. We're doing it 24 hours a day.

So the most we're going to read is a one page guide, a one page quickstart. The most we're going to look is scroll through an app that has a quickstart guide, just because we spend so much time on diabetes. And if I have a problem with my pump, I mean I forget how to unlock my Animas pump, I Google "unlock Animas pump". I get to the Animas page. I find the two

buttons I have to press which I always forget and that's what I do. So when I have problems I don't go to the instruction manual, which is very tedious. I just Google the problem.

**Brian Cohen:** So in terms of a patient, it is often difficult to know and select from different products. So if you look at all different meters, I mean there's not a way for us as patients to know how to compare which are the best meters, which gives errors when we use them, which is more accurate, or which is more convenient.

We need information as a consumer in order to be able to select between these different products. And I'm not saying that this has to be consumer reports line up. But we have to be able to differentiate between products, and the information we have doesn't help.'

**Dr. Helene Clayton-Jeter:** You've heard the presentations earlier so keep that in mind, and also I want you to keep in mind that cost and reimbursement and the practice of medicine are outside of our regulatory purview. So while keeping all these things in mind, I want you to ask the question: "What is one message you would like to leave with FDA?"

**Rebecca Killion:** I think about it a lot. I mean, I have great respect for the FDA, but what I would like the overarching message to be is we are all in this together. A point you made earlier is that we rely on the FDA to help us ensure that we don't have fraudulent products; that they meet the claims that they say they will, etc. But again we, as patients and caregivers, are an enormous source of passion and perspective. And I know that that is here at the FDA as well. I hate the word synergy. Let's call it proportional to fire. Together, we will achieve so, so much more.

**Howard Lee:** Thank you for making it possible for us to come and share our thoughts. We have to reach diabetes in the same level as other diseases, especially cancer, because it is just as impactful and it is just as dangerous as cancer, and therefore we need to have a greater emphasis on how we get to being able to effectively treat this for future generations. So thank you very much for what you are doing.

**Cherise Shockley:** People ask me, 'How are you doing?' and I'll respond, "Oh I'm doing fine." And if you take look at me, I look like I'm fine, but I'm not. There are 30 million people in America just like me. Please move with urgency when approving tools and devices, so you [FDA] can help improve the quality of life of myself and the 30 million others like me."

**Manny Hernandez:** Can I say something real quick? I will be brief. Don't hate me for this please, I know reimbursement may not seem to be the mission of FDA, but here's a thought that I'd like to leave – At the end of the day, what good is a product or a drug if we don't have access to it after it hits the market? I was super inspired when I heard Dr. Courtney Lias speak a few weeks ago about how there's a creative and intentional movement towards looking at the economic studies as well as safety and efficacy analysis, so by the time a drug moves through the pipeline, it's closer to reimbursement reality. I would love to see more of that. I would love to see agencies and payers becoming more involved, because at the end of the day it's great moving these products through, but it's also critical that they be accessible.

One final thing, which I know that those who cannot watch now are very passionate about, that I want to bring forth again that we need stronger enforcement to make sure any noncompliant



product out there absolutely does not fall in the hands of patients. We talked about it a lot. Thank you so much for having us today.

**Angie Platt:** I would love to leave you guys with this comment, as a caregiver and a parent of a type 1 diabetic: Two summers ago, my son Jonathan went away to a diabetic summer camp. And it was the first time in years that my husband and I actually got to miss our son – just miss him as a person, because we weren't monitoring his diabetes for 24 hours a day. I'm so thankful for the FDA for keeping us safe, I truly am. And as technologies and treatments come through the pipeline, I'd like you all to remember that A1c is important, but just as important is keeping families together, and keeping families happy, and keeping marriages together. The ripple effect of living type 1 diabetes, it affects all of those aspects of a family – not just A1c.

**Helene Clayton-Jeter:** I was going to have a second part to my question and it was exactly where you left off – not just A1c. Because I want this question aimed at raising the consciousness of the medical reviewers. What are your thoughts on A1c as the way to evaluate diabetes management. As we think about approving safe and effective biologics, what should be captured from the patient perspective?

I want you to have in the back of your mind – you're trying to raise the consciousness of the medical reviewer. As the medical reviewers are reviewing these products, what would you want them to hear?

**Rubin Scott:** What I would actually want the FDA to know is that in the community, people are fed up. They're tired of being sick and tired. We need to get information in a way that we can understand it, so that there aren't as many complications. People I work with don't want to go to the doctors – they don't want to hear the words, "You're diabetic," or, "You're prediabetic," or even, "You have to take a daily shot." People ask me everyday how I do it, and I say, "Well, I have to live with it if I want to live." That's just what I want to say, and I appreciate being here and thank you for hearing our voices.

**Helene Clayton-Jeter:** Thank you. I think we probably have exhausted you guys, right?

**Patient Panelists:** No.

[Laughter]

**Helene Clayton-Jeter:** Does anybody want to comment on my last question? You may at this time. Anna?

**Anna McCollister Slipp:** You heard me talk about it already so I won't belabor it too much, but just in terms of any things that are important -- we now have pretty accurate glucose monitors. Measuring time in range I think is a particularly helpful potential alternative measure. But also beyond time and range, quality of life is also absolutely critical. Additionally, non-glucose related hormones that are effected by diabetes – there are a variety of satiety hormones that are impacted. We have very significant increases in eating disorders, particularly in girls and adolescents with type 1 diabetes. My fear is that there are so many treatments that could be advanced that aren't being advanced. Because if you're a pharmaceutical company and deciding which drug to license, you ask yourself, 'Am I going to

make a drug that impacts A1c, or do I want to license a drug that perhaps has a more difficult FDA regulatory pathway ahead?’ And you go with the safer bet, and as a result we’re living without potential cures that could be advanced in clinical trials.

Then finally in terms of final comments, we are your allies and assets. I’m a DC person, I understand what an ugly environment we all live in and we as patients want to support you in your desire to innovate and to drive forward. So please reach out to us. And there are lots more behind me who would be happy to join. We are your asset, so let us be that asset.

**Helene Clayton-Jeter:** Thank you, Anna. I think that’s a great way to wrap up this panel session. Kelly Close will be moderating the next session with the FDA. I want to thank you for joining us today and I will see you around after the meeting.

My FDA colleagues can come up again and join us. I will turn this session over to Kelly Close.

### **FDA Perspectives**

**Kelly Close:** Thank you to the folks out there for helping us. I think we’re having a few technical problems, so people if you can help tweet and help record things, that’d be awesome. It has been really, really wonderful to hear so many patient views, and we thank the FDA so much for helping bring patient voices to the agency. We really do understand how incredibly under resourced the agency is. You are public servants – you’re heroes, in our eyes – for all you are trying to do and make happen, and we are really excited to get to be here and talk to you a little bit more. We will try to do a really quick introduction - please tell us your name again. We haven’t met all of you – please very briefly describe your job title, what you like the most about your job, and the biggest challenge. And we’re going to try to do these in 60 seconds each. Thank you, Dr. Lias, for starting us off.

**Dr. Courtney Lias:** My name is Courtney Lias. I’m the director of the Division of Chemistry and Toxicology Devices. And we regulate the diagnostic devices for diabetes. I think one of the things that I like the most about my job—I’ve been here for about 11 years working in this group—is that I get to learn new things every day. And learning new things really helps me not only do my job better, but also to help promote effective public health as well.

**Dr. Naomi Lowy: Hi.** My name is Naomi Lowy and I’m currently a medical officer with Professional Affairs and Stakeholders Engagement. I have worked in the Division of Metabolism and Endocrinology Products for seven years. My favorite part of working here is working with an intelligent, powerful, and very creative team of physicians and scientists who all love being here. I love working here at FDA. I would say the most challenging part is the fact that working here, people are waiting for a magic wand for treating diabetes. We all want that magic wand. Nothing would make us happier than a company finding that and bringing it to us, and we want to approve drugs that are safe and effective. Thank you.

**Dr. Stayce Beck:** My name is Stayce Beck and I’m the branch chief for the Diabetes Diagnostic Devices group. I’ve been at the FDA for six years and working on diabetes for four years. And my favorite part about working with diabetes, I would say, is working with patients and patient advocacy groups and academics and companies to really try to work together to come up with solutions to help manage diabetes.

**Dr. Patricia Beason:** My name is Patricia Beason. I’m a medical officer in CDRH Office of Device Evaluation. What I like the most about my job is to see new technology and to help

companies and investigators problem solve to sometimes take something that wasn't going to be successful and make it successful and help move ahead. What I find the hardest thing to do is that it's hard to balance a lot of the time with what companies are willing to do, and what patients want to do. There is a fair amount of internal political pressure and to have all those balls in the air, trying to make a balance sometimes doesn't always come out in the way that you would hope it to come out.

**Dr. Jonca Bull:** Hello, I am Jonca Bull. I served as a member of the Office of the Commissioner staff and I'm the principal advisor online and director of the Office of Minority Health, which is a relatively young office. It was mandated under the Affordable Care Act so we will be celebrating our fifth anniversary in 2015. What I like most about FDA is that both from the standpoint of scale and scope, the impact of what you do here can be so profound. I think we also have the opportunity to be the voice for things that aren't getting done, and to bring a human face to issues such as unmet needs. It's interesting because I think over the past five years, we did a very cursory look back at recent approvals in diabetes and there's been a lot of new approvals in diabetes. But we are still here talking about unmet needs and things are not where they need to be. So we can be waving the flag saying look at all these new products that are on the markets, but at the same time have we really addressed the fundamental problems that patients face on a day-to-day basis? I think that's why these kinds of meetings and hearing your voices is so critical. I want to thank you all so much for being here and I think to me the big takeaway is that this is just the start of an ongoing dialogue. One that's already taken place, but hopefully in a much more strengthened way as we go forth. I've been amazed at the people we've heard from today about the patient perspective. And I think this is a huge step. I think something has to be this game changing, but will certainly add a deeper dimension to our internal deliberations and our interface on the public's behalf with regulated industry.

**Kelly Close:** Thank you so much for the responses and especially the last one. Really acknowledging that it does go beyond all of the approvals we are seeing, especially on the drug side, and how fast technology is moving is absolutely unprecedented. That's amazing for patients to see and we do have to come together as a broader community to make sure that we are impacting all the pieces that go together. This is so we can take our medicines well, so that we can get into the trials, so that we can move all of these things forward. So we can also understand more broadly how the rest of this sector needs help from all of us and also probably much beyond all of us as well. Getting many other agencies involved and probably many other foundations as well, etc.

I wanted to just say – it was great to put together this survey that had amazing learning for even all of us patients who sat there and were reading it last night. And again this was just two of the open-ended questions. But one of the things that really hit home to me getting this was that we are not at goal and we're the ones taking the surveys. You know, if we're not at goal and we have access to the surveys, are online, etc., that's not a good thing at all. I think that if you look at the complications that people are enduring, especially depression, this is also something we absolutely need to and can address. I think you also just need to think about the serious negative impact on many daily activities – and we heard a lot about that today. I like that we've been able to bring those patient voices to you so that you know what makes it harder to be successful in managing our diabetes. We all know that as drugs and devices become easier for us to adhere to as patients, this will have a big impact on public spending and this is a massive societal problem of course that we all need to address, so that we can get more of the funds away from treating people with very serious complications and more toward prevention - prevention of complications and prevention of diabetes.

Courtney, you did hear a lot about people thinking about A1c not being the only measure, and I was wondering if you could talk little bit about that because your area has so taken the lead; getting this as part of the guidance for the artificial pancreas was so amazing for so many patients and I was wondering if you could talk about that a little more broadly and how that could be more universal at FDA?

**Dr. Courtney Lias:** Sure. The artificial pancreas guidance articulates that companies and device developers should talk to FDA about what endpoints they propose that make sense for that device they are making. Devices are made for different purposes and maybe the endpoint makes more sense in one case and less in another case. There's not really a one-size-fits-all study design or endpoint for all diabetes products. So that really articulates the way we think about a lot of device studies and the way that we talk to companies. We really wanted to communicate that we are open to hearing what the goal of the device is and how patients will benefit, because at the end of the day the decision we're making is assisting a device to be put on the market. Do the benefits outweigh the risks? There are a lot of different types of benefits that patients can see from a device and lowering of A1c is not really one, and the point that Adam made - that someone with low A1c may actually become safer with a higher A1c if they suffer from a lot of hypoglycemia. And it was really an attempt to show that we're open to that discussion. I think that steadily this is something that we want to make sure that people are aware they can talk to us about.

**Kelly Close:** Thank you. The leadership you've shown on this front I know has been really heartwarming to patients because ironically some of the therapies and technologies that reduce hypoglycemia can potentially increase A1c, not reduce it. I think sometimes when we go to Advisory Panel meetings and so forth, there is not as much notice about it, and it would be really nice for people to understand variability better, especially since we know we can measure it. Would you say that there's input and engagement from the diabetes community that would be helpful and convey that? Is there anything else you can use from us?

**Dr. Courtney Lias:** The type of input we're hearing today is helpful. The type of things people can really help us understand are other benefits, like the benefits of preventing hypoglycemia at night has become very clear to us. Things that are maybe not related to A1c but have huge benefits either for caretakers or the patient.

**Kelly Close:** We're going to keep moving quickly. We are going to talk about the scale of that more. That was interesting how patients conveyed the huge risks that they take on every day in an obviously very heterogeneous patient population. I wonder, is there room for FDA you think to have some patients take on more risk if they want to? I think many patients as we heard do feel they are walking a tightrope every day and already taking a lot of risks. Just wondering how you would feel, big picture, about the FDA engaging in diabetes to meet about the tolerance for risk when it comes to better diabetes treatments? You could comment on this broadly. I think we have thought about if you have incredible hypoglycemic unawareness like I do, I am more eager to take on more risk than someone else who may not be who is more recently diagnosed. Maybe you might think that there is a lot of risk with a certain insulin. I would love to hear some comments on that broadly?

**Dr. Naomi Lowy:** I also want to thank all of the patient advocates that spoke. As a clinical reviewer who has been stuck in the data of some of these clinical trials, it is really refreshing to hear your stories and it is really powerful, so thank you very much for that. Along those lines, I think engaging patients in general is always a good idea from CDER and CDRH perspective. We're always looking for ways to enhance the conversation, and one of those ways is to

understand patient tolerance for risk. And we will work with the Office of Health and Constituent Affairs to make sure that those concerns are addressed in a complete and timely fashion. Yes, that's something that I think we would definitely be open to.

**Kelly Close:** What about the idea of conditional approvals? We think your job is so hard because it feels like you want things to be zero risk and there's no way that things can be zero risk. We attempt to make it that way, but can we help you at all? Again, I think the differences in patients makes it hard to approve therapies for all people with diabetes, so in terms of exploring conditional approvals as a way to get things out there, it sounds like there might be more openness to that?

**Dr. Patricia Beaston:** I just wanted to clarify, conditional approval doesn't mean that it goes on the market, then it can come back off. Conditional approval means that if they meet certain requirements - like we think you pretty much have everything answered and we could approve it on the condition that you can answer this one last thing. It is not like the European version where they can put something on the market for one, two, three years and then if it is not coming up the way they like, they will take it back off the market. We don't have a regulatory pathway to do that.

**Kelly Close:** Yes, I might not have the lingo right on a quote unquote "approvable". Just the idea that it might be approved for a certain segment of patients. It is just that we feel like it is a really hard job to do things like one-size-fits-all or all type 2 patients or all type 1 patients. Maybe you could look at segment of patients that has a lot of hypoglycemic unawareness, or maybe it is people with a lot of complications, I don't know. I'm trying to engage in conversation about how we can be creative.

**Dr. Jonca Bull:** I think we have to be careful from a definitional standpoint on how we will use the word "conditional approval," because in our world, largely when there's a limited clinical database for the approval, I think actually we call it an "accelerated approval," it is conditioned on the sponsor getting additional data for the trial. So they get their approval, but then there's more data that they have, which is different. Someone brought up an extremely important point, that's when we start to get things complicated. That's what is happening in Europe and what's happening here. We are really talking very different regulatory pathways.

**Kelly Close:** We totally get that. It's interesting. Take Tresiba, which is available in Europe but it is not available here. I understand there are differences in how the regulatory roles were made. It might be interesting to think about if it could be used in type 1 versus type 2. It's not so much about Tresiba itself, but it is delaying iDegLira, which is an amazing transformational drug and it is available in Europe. I don't want to get us caught up in one product, but just to say I don't know if at the Advisory Committee meetings if the people who are advising FDA who are out there who are not involved in drug development always realize what can happen when things don't move forward at all. I don't want to get us caught up in the lingo, but go ahead, Dr. Lias.

**Dr. Courtney Lias:** It's important for us to always realize that people who are on the Advisory Committee or patients don't always realize our definitions of the pathways that might exist. I do want to clarify that Devices does not have authority over things like "conditional approvals."

We have put out two draft guidance documents that try to get at the same things. One is the pre-post market guidance document. It proposes that FDA would try and shift in a way that is

still safe for patients, some of the requirements into the post market phase and try to advance and promote the availability of new devices on the market. The other is an expedited access PMA draft guidance which is meant to talk about the regulatory pathway where companies can comment if they have a novel device for an unmet need or a new modification of a device that does something different, that FDA can work very closely with companies to try and speed up that pathway to get to market for those devices. There are a couple of tools that we proposed to try and get that I think are talking about.

**Kelly Close:** Thank you so much. I wonder if you and Dr. Beck – we've been really impressed with how FDA has been using big data and we've especially been seeing that on the device side. I wonder if you could talk little bit about that? You worked with the T1D Exchange to better understand the prevalence of hypoglycemia. I know you worked with Medtronic and CareLink database to examine how people are using devices in the real world. I know as patients we often feel like the randomized control trials – I've done a lot of trials, you know, you feel a lot of love – and it's not really like the real world necessarily. But if you look at big data and ways things are happening the real world, can you talk about this benefit?

**Dr. Stayce Beck:** Sure. We've been able to use things like that Type 1 diabetes exchange, as well as other tools. One of the ways that CDRH diabetes diagnostic group has been able to use big data and form some of the clinical studies that we have investigators do – so they've been able to use things like that type 1 data exchange, as well as some of the data sets that the companies are using to collect that real-world data to get some baseline epidemiological data. That helps us to be able to pick the right populations to do some of these studies and to help us to get some of the different endpoints, and to even minimize the number of patients that are going to be in study so that we can shift some of that premarket burden to post market so devices can get out there more quickly. It is been invaluable for us and has really given us, like you said, real world information because when you're doing clinical studies it is sometimes an idolized world and we don't really get to see certain events. We want to protect the patients' safety, but it gives us a chance to see what happens out there.

**Kelly Close:** There were so many comments I think from the patients earlier about wanting to make sure that we are broadening access to clinical trials, and we would love to know how you think patients could help do that because we obviously know your advising sponsors and it is not something you have control under either, but we would love to get more people very focused on this massive problem of not having all the right representation in trials – it is really big problem.

**Stayce Beck:** Yes, I think the workshops like these today will give us some important insights into some of the different things that people are facing and that was one of the things I took away from the patient comments sharing how clinical trials are 1) hard to get into and 2) when you are in, them how difficult they are. So I think when we review different IDEs to clinical trials, we are looking at patient safety and making sure that the studies aren't going to really cause any untoward problems. I think most of the things that I heard, and what I want to take away, is to see if there are different ways to perform the studies that can reduce the burden on the people that are participating. A lot of times we just want to get as much information as possible out of the study so I think that it is a very important point that I would like to consider in the future when we are looking at these studies – to try to incorporate things into the study that will reduce the burden.

**Jonca Bull:** One of the things that we've tried to encourage companies to do even in some of their early trials is – you really don't want to enroll people with a lot of conditions because it is hard to figure out if there's a problem, and is it related to the new treatment or is it related to the underlying myriad of issues? On the other hand, it doesn't seem reasonable to do this group and do the next group, so with some of the companies we proposed where you start with that patient group, and as you see that you have some understanding of the effectiveness of the device or drug and the safety, and were there any safety issues that you can cause that you didn't quite understand. And now can you open it to the next group of patients as that first group is going through. If they need a certain timeline and a number of patients, then you can expand the enrollment to be more inclusive of another population and then as you get some more experience with them, then you can continue to expand. In a sense, you are stacking the population. Not requiring three or whatever trials sequentially, but you are building them up, and it also allows you to look at the data in the way that it acknowledges that is the way you did it. But that takes planning both on the side of the reviewing team and from the company willing to do this and to plan ahead. So it can be done, but it takes more forethought in making it happen.

**Jonca Bull:** Can I add to that something that came up earlier in the discussion? It had to do with how exclusions and inclusion criteria are built into clinical trials and that we are trying to take a much more thoughtful look as to who are the patients likely to use the drug when it goes into the marketing mix – if it is a patient who has a comorbid condition, and what comorbidities that we would expect the likely patient to have. We need that information, so we are trying to have more reality-based trials within the limits alluded to in terms of trying not to have so much noise in the trial that you cannot discern safety and efficacy adequately for the drug under study, but also to take into account the reality check on how this drug is actually going to be used in real people.

**Kelly Close:** Yes and no - patients would be so happy to hear that because we do understand the importance of the randomized control, but again, like seeing what is in real life to be interacting with the drugs and technology, that's how we are going to be able to do a better job of taking care of ourselves and again, that's how we are going to be able to impact public health really successfully.

So there are a couple of things - we have one piece of good news, which is that we are back online and we actually got permission to go for an extra 15 minutes after this panel. We're going to ask our patients to come up again and we're going to ask you what is the one message that you will like to leave with FDA today because all of that wasn't able to be captured. I guess we've got about 10 minutes left here.

One of the questions that you have spoken to a little bit are things that you've learned today, which is so heartwarming to us and probably a question that we'll end with is what you think you learned from patients. That would be great because I think the online community and off-line community would all love to hear about that. I was also just going to ask in a little bit if you can just say a bit more about the hardest part of your job, and what do you most wish that you could change about your job that would make it easier, as I think it is really important for all of us to also understand the constraints.

**Dr. Courtney Lias:** I think one of the difficulties is that we want to be transparent and have a lot of open conversations with all stakeholders, and yet we are constrained in some ways by the laws we operate under that require confidentiality about our interactions with companies. So a lot of times there are a lot of rumors out there we are not able to dispel and there's a lot of

information out there we are not able to engage on. That's challenging, so we have to find better ways and also we can find creative ways to still have that conversation and still try and make those points and that's rewarding.

**Dr. Naomi Lowy:** Getting into the question of what I have learned here today – it's from patients. We don't often get to hear this, but we got the data from the clip with us, and we don't often get to really hear what it was all like to be in the clinical trial and I think that was a really powerful point. Number one, hearing that it is difficult to even find some of these clinical trials is frustrating to hear because we do need everyone's participation in these trials. Everyone counts. And hearing about how difficult it is to go through the process of the clinical trial, which I don't know if that is the case for everyone. I think some people who are in a clinical trial are being taken care of very, very well so I don't know if that's universally everyone's experience.

**Kelly Close:** I agree in fact on some of that. I'm sure there's a big continuum about how a lot of people experience trials, so it's good to hear different experiences about that.

**Dr. Naomi Lowy:** Then maybe the big takeaway for me was the frustration we heard from patients on how they work so hard to do so well in managing their diabetes, and have not been able to necessarily translate that great goal for themselves into great results.

**Dr. Stayce Beck:** So one of the things that I find to be a challenge is actually what I find to be one of my favorite things, which is really balancing patient needs with the regulatory framework and some the technology limitations that are out there. But as Courtney said, that's actually also part of the most exciting part, which is to try to come up with innovative ways to work together to ensure that everyone's needs are met. One of the things that I learned today that was really powerful to me was the labeling. That is the way that we are able to communicate with patients, so we do a review of the device and we look at the benefits and risks, and then we try to get that conveyed to patients through that labeling. So I think you've given me a challenge which is to go home and try to think of other innovative ways to get that information to users and the way that they are actually going to use it. Some of that is a regulation. We do have to have certain elements in the labeling and that's the regulation that I think there might be some other ways we can get that information out.

**Dr. Patricia Beaston:** I like my job. It is very challenging, and like I said before, it gives an opportunity to help get things to the market that patients can really use and benefit from. I think one of the biggest challenges is what Courtney alluded to, is that the confidentiality goes one way and the company's go out and they say the FDA didn't do this, the FDA didn't review that. The patient groups get upset with us. We cannot say the company actually didn't collect the data correctly. We cannot really give you the reasons why we decided not to do something because there is confidentiality.

**Kelly Close:** We totally get that there's confidentiality. But the more the patient advocates understand and the more of the details that you can share is a good thing. We are seeing more transparency. We are happy about that.

**Dr. Patricia Beaston:** But that's a bit frustrating. So when you are sitting somewhere and somebody mis-quotes what I said, and you really cannot stand up and say that's not exactly the case. The other frustrating thing coming from drugs is that drugs have really good labeling. If you want to find information on a drug, you can go on the Internet and you can find anything you want to know about what's in that labeling for the drug. You can do the same for a PMA



device, or Class III device that gets approved. The labeling rules are quite different from the 510(k), the other devices that don't require a PMA. This goes back to if you're going to write a consumer reports guide. So for these 510(k) devices, what is the information if you wanted to go shopping, that you would want if you had a little chart or graph or whatever that had to be filled in by the companies? What information do you want them to have to make available to you before you even choose to buy something, so you can have an informed decision. This is one of my frustrating things, which is to try to make sure that that information is always accessible to patients.

**Kelly Close:** It is hard, adding value for each patient. All of the patients in the world have a common diagnosis and then their lives are all really different, so there's not going to be one-size-fits-all. But I think there are a lot of interesting things that the diabetes community is excited to get back to on that front.

**Dr. Patricia Beaston:** I just wanted to give you an example. If I took a bunch of people in the room who were using insulin pumps, pretty much the majority of them cannot tell me the time it takes for their occlusion alarm to go off, or the rate it will deliver 20 units of insulin. For different pumps it is amazingly different, but everybody assumes the devices are all the same. And part of the goal for labeling the information is for patients to really understand the device, and I'm sorry the manuals are really big, but sometimes if you don't understand that information you cannot make the best choice in how to use that device.

**Dr. Jonca Bull:** I think it is always important to have these kind of independent dialogues with the end-users. I think we really have to be clinical outcomes focused, because you can have control of the metabolic measure or measures more tied to A1c and not actually tie into the patient's big picture. Are we having the kinds of positive long-term impacts and outcomes we want to see? Are we preventing neuropathy? Are we slowing the course of some of the more critical complications of what it means to be a diabetic? So I think having these conversations aside from when we are camped out at the table with regulated industry is just a really important added dimension for us at the FDA, because ultimately our mission is about protecting the quality of public health. We act as an advocate, as a surrogate, on behalf of the American public in assessing data so that you can have confidence in those labels, confidence when you are using the device with the medication, and that's the critical role that FDA plays.

Most of everything we've talked about today is about control of diabetes, not cure. I think we also have to have aspirational goals in this space as well. In terms of where we would like to be, not just that we are getting more choices and the different classes of drugs that we have now, but that we are actually moving toward things that are game changing.

**Kelly Close:** Yes, absolutely. I love hearing the goal for us all to think in a really aspirational way, because we are all older longer. When I was diagnosed, I was definitely going to die 15, 20 years sooner than all of my peers, and that's not actually true anymore. The great Trevor Orchard has shown us this data in type 1, that this statistic has narrowed incredibly and in type 2 it also has narrowed incredibly. And everyone is staying older longer and we want to be approaching it in healthy way, not creating care for the elderly that will be even more unsustainable for the public health system. I'm so grateful to hear you challenge us all in that way, Jonca. There's a couple of more device question specifically because we have Dr. Beck and Dr. Lias here. One of the things that we are hearing from patients is concerns about blood glucose monitoring accuracy. We know that patients talk a lot about wanting greater accuracy, and obviously we have to do our part in learning how to better count carbs and washing our hands and all of that stuff. But how do you guys think about it, because I guess that we don't

always realize as patients maybe there's guidance that the accuracy is so hard and maybe that meters will have to be bigger or need a bigger drop of blood, or longer testing time. Patients also probably would complain about that and it also might affect adherence to what we are supposed to be doing. Can you talk a little bit about how you juggle those things and what the decisions were like?

**Dr. Courtney Lias:** Sure. We think about those things a lot when we are putting out things like our draft guidance document. We don't want patients to have to deal with longer testing time, bigger drops of blood, or things like that. We made an assessment based on our conversations with people from the industry on the likelihood of those types of things happening with our proposals. We also are lucky in that we've got specific feedback from industry on what we believe they can or cannot do. All indications are they are not going to revert to longer testing time. Yes, I think that's a tactical maneuver.

**Kelly Close:** I think we worry about what patients do as well. Of course there are some enforcement problems. I think for us, we do want to make sure that the products are ones that the patients can and will use, and that adherence is good.

**Dr. Courtney Lias:** That's the reason the criteria that we proposed on over-the-counter guidance is different than the criteria proposed on the healthcare guidance, because we are taking into account the capability that manufacturers have to make larger lot sizes. And they just aren't capable yet of doing that in over-the-counter market with the types of sizes and lot they have to make. The healthcare market share is so much lower and a number of steps they make is so much lower that the types of manufacturing changes that they would have to make are feasible in that area to do that.

**Kelly Close:** That's great. Thank you very much. I think it is been amazing year to see how patients through patient advocacy groups, the ADA and JDRF, the Helmsley Charitable Trust – there've been many more patient groups coming to give their opinions and we are really gratified that you have listened. It is amazing to sit in mid-August to hear Dr. John Jenkins of the Office of New Drugs to say it may be time to revisit the basis of cardiovascular studies for diabetes drugs. And things change, you get new information and all that, so we are very happy to see some of these things potentially looking to change. To end, what do you all envision as a best-case scenario for the diabetes community engagement with the FDA going out of this meeting?

**Dr. Courtney Lias:** What I've experienced over the past year and half, as we have really been engaging more with the patient community, is the amazement and the amount that we can help each other. There are certain initiatives that we want that maybe patients also want, that the industry may be hesitant to do. But they want to please the patient population, so working together we can actually get things moved forward and that's been very gratifying, so I would like to continue to try and make sure that we communicate so that patients and FDA are on the same page as much as possible, so we can work together to move policy forward.

**Dr. Naomi Lowy:** I think that having periodic meetings such as these as general topics are very helpful, and then I think beyond that having patients meet with the specific center divisions that regulate the devices or drugs are helpful for both ways for patients to express their concerns and their needs as well as for the divisions to get a sense of what they can do for patients.

**Kelly Close:** Thank you. I think patients would love to be able to meet with reviewers and work more from there. Thank you.

**Dr. Stayce Beck:** We've been working over the past year to attend a lot of different meetings with a lot of the people in the room, including patients, and to get to hear perspectives and have some really good conversations about the needs that they have that we're not meeting. So I think that I'd like to continue to do that. I think we had really good success. Courtney brought up early with the guidance where we got over 400 patient comments which really, we talked to a few people, Kelly and others, to get out that word and issued a challenge. I think a lot of people did, and they gave us a really good perspective that we often don't get to see and helps us with forwarding the guidance.

**Kelly Close:** We as patient advocates, many of us like Strip Safely – the amount of time and effort that patients are using and this is not their day job, so it is really great to hear that that was helpful. Thank you.

**Dr. Patricia Beaston:** I'm in the fortunate position where I'm actually honored to be able to see patients at Walter Reed once a week, so I take care of diabetic patients pretty regularly. I have diabetes communicators that I work with. I think one of the things that would really benefit the FDA and patient advocacy groups is if they can work on giving better access to their physicians. Ones that have to care for them and the time and resources that they need to better help you better make choices and to better support you in the choices that you want to make. Because when I talk to my colleagues who are not in the same privileged position, they need to have the time or resources to give you the care that they really would like to give you, so if you can advocate for them to have better opportunities, that would be a good thing.

**Kelly Close:** We would love to be able to do that. We are really so aware that so many of our doctors and nurses, that it is a labor of love and the fact that they spend more time with us or to help us figure out the analytics is a major problem that advocates really do want to help with.

**Dr. Jonca Bull:** I think most of it has already been said in terms of how valuable this type of engagement is, because ultimately it is about what the patient experiences. That the health care providers have the information that they need to make an informed decision in your care. I think we also know that we are not there yet in terms of optimal treatment of diabetes. I think if there's anything I'm taking from this session, it is just how many gaps there are. How challenging it is on a day-to-day basis, hour by hour basis to be a diabetic and the burden that a diabetic lives with. I have family members that are diabetic, so I'm well aware of many of the day to day challenges, the meal to meal challenges, the activity challenges that are part of living with diabetes. I think to the extent that the work that we do here in the FDA in regard to therapeutics, how we can know where things are not optimum. Because one of the things that I've learned in almost 20 years as a regulator is that a lot of just putting the energy out there about unmet needs can almost be magical in terms of driving better choices, because the oil does go to the squeaky wheel, as that old saying goes, so I think this is important. I think accountability for us as a public health agency working with regulated industry is a critical way that patients interface with FDA because you keep us honest. You help us in terms of our role in working on your behalf to ensure that products are safe and effective and also that we are keeping a very open and robust dialogue around the things that still need to be done.

**Kelly Close:** To all of the doctors, thank you so incredibly much for getting the voice of patients and multiple parts of the regulatory process. What we would like to do now is we've got a bonus extra 20 minutes or so, and we're going to bring patients back up to hear what their

one piece of advice would be with their closing comments to FDA. Then we will have closing comments from the FDA and The diaTribe Foundation. Thank you so incredibly much for having such an open, honest and candid dialogue.

### **Patient Panelists Return**

**Kelly Close:** I think we would like to ask RJ to start. So we've got a few moments left with FDA – can you talk about one thing that you would like to leave with the group?

**RJ Scott:** The thing that I would really like to leave with the FDA is that the communities that are small – a lot of them are unaware or uninformed, so my biggest thing is to let them know that there is a voice and that if you do have something to say, that it will be heard and will be addressed. Like I said before, I was really sick and tired of the whole situation about being diabetic because you don't know one day to the next. If this drug works for me will it work for the next person? Then I have a lot of other drugs that I take. What kind of complications and what will it do to me if I commingle them together? That's my biggest concern. Thank you.

**Adam Brown:** Thanks, Reuben. I just want to salute you guys, Courtney and Stayce for staying here. We know you have a hard job. It's so hard and I think it is easy for us to talk about all of the challenges because we face them every day, but you guys have a harder job and we want to help make it easier. Please talk to us. We want to help.

**Francisco Estrada:** I would like to voice that also. Yes, you do have a hard job and I think there is hope for everyone here. For me, it has been a very educational experience being here today. I didn't realize how complex diabetes was. I still consider myself a neophyte but we are here to help and we'd like to see this happen again. Hopefully next year.

**Brian Cohen:** I want to echo what's been said. I feel grateful to have the FDA have our back. But I'd also like to say that as patients, I think we have a responsibility to try and help out so I've encouraged the FDA to try and work with the patient community to do a better job with the post marketing surveillance to actually engage patients more actively and effectively in the MedWatch program. To label things so that patients know that they can report side effects and maybe there's an opportunity for patients to help provide information on the actual effectiveness of drugs and treatments out in the wild.

**Dr. Aaron Kowalski:** So I'm wearing my patient hat here. My final comments are to reiterate just how hard living with diabetes is. I think of myself as a pretty active and involved person in this community and a scientist. I've been working in the field for long time. 37 years in our family and in the past 24 hours my blood sugar has been spent at about 400 and below 55. And it is real. When I think about the incredible research that's coming along, I commend Courtney and your team for the incredible leadership that you've shown to think beyond A1c and the different outcomes like hypoglycemia and time in target. I think JDRF and the community, as we look towards encapsulated islets and smart insulin, incredible advances that we're funding, to see CDER thinking about these outcomes as well will be very, very important because there's no doubt that we need better treatments.

**Angie Platt:** One of the comments that was made on the earlier panel was about the users of pumps and how we may not know how quickly insulin is dosed. I don't know all the technical information about how a pump works but I know that it has changed the quality of our life drastically. I'm looking forward to the technology that's coming through the pipeline because I know that's going to help us tremendously as well. As my family consists of three boys, my son

has type 1, and two who thank god, don't have type 1 yet, so prevention is also really something important that you could take a look at as well. And thank you so much for having us here today.

**Anna McCollister-Slipp:** To reiterate some of my previous points, several of us talk about the critical importance of getting away from the somewhat myopic focus on A1c as the be-all end-all measure. I won't belabor that but I would like to encourage FDA to consider the complexity of this disease. It is time in range, it is glucose control, but it is also the multi hormonal impact that happens with diabetes and the fact that as regulators you have the ability to encourage companies to think more expansively about it. I think it is a huge opportunity for all of us. Then finally again, as the DC person on the panel, this is an incredibly ugly political environment. We are your biggest assets. We are here to support what you guys are doing. The work that Courtney and Stayce have done has been incredible, as well as other people. I'd love to see the same type of enthusiasm in CDER and I'd love to see the people in CDER realize what an asset the patient community can be in supporting their efforts to work with companies to create drugs and get drugs through the process that are better than the ones that we currently have.

**Manny Hernandez:** It is hard to add a lot to what other panelists have said but I will point two things out. First, I have also heard about some of the challenges and frustrations that you guys encounter as well, because obviously you are passionate about what you do just like we all are here. So not only in terms of addressing some of the things that we are hoping to see evolve, do let us know how we can push in other directions as well. For example, we ask for more enforcement and surveillance, but this requires resources, so maybe we should be advocating for that as well to make sure you will be able to do jobs that we are asking you to do more of. You are not alone. We are in this together and I'm incredibly, as the rest of my panelists and friends are, thankful to you for having us here. As a recent citizen it is incredible, an incredible honor, to be here today. We started taking pictures up front!

**Cherise Shockley:** I guess it is weird because we just said this a few minutes ago. We look like we are okay, but we are not. There are millions of people in America just like me. Please move with urgency in approving tools, devices, and medication that will improve the quality of life for myself and the other millions of people living with diabetes.

**Dr. Helene Clayton-Jeter:** I want to thank you again. I'm sorry for the technical difficulties but I guess this is our transition into my presentation, which is going to be very brief because I really felt like the rest of why we are here today is because of you and I want to thank you all for participating. And then after my presentation, Kelly Close and I will adjourn.

**Kelly Close:** Thank you so much for making this happen and for the leadership that you've shown in the office.

### **Communicating with the FDA**

**Dr. Helene Clayton-Jeter:** Stakeholder engagement with the Office of Health and Constituent Affairs – this is the office which I work out of. I'm the Director of the Cardiovascular and Endocrine Liaison Program, and of course you know my name is Dr. Helene Clayton-Jeter.

So what I want to do today is go back over some of the things you've heard and reemphasize some things about the FDA. I want you to look at the common misconceptions. FDA does not

develop drugs. FDA does not test drugs in clinical trials. FDA does not regulate the practice of medicine. I want to make sure we heard that loud and clear today and we are all on the same page.

The slides will be available via CVENT and posted online after the webcast, so I'm not going to go through all the slides, but I thought it was important to put things in like how patients gain access to drugs. We'll take a look at that later. But what's more important for me to talk about is the FDA patient participation milestones. The Office of Health and Constituent Affairs actually came about in the '80s - in 1988, as a matter of fact, as a response to the outcry of the HIV/AIDS epidemic. After that, we added other programs to our office. So we started basically as the Office of AIDS and Special Health Issues, then changed to just the Office of Special Health Issues. Recently, we underwent another name change and now it is called the Office of Health and Constituent Affairs.

The office was established to work with patient advocates focusing mostly on HIV/AIDS and the HIV/AIDS community. In 1990, the cancer patient advocates were recruited into the patient representative program and the program did expand to include patients and caregivers of serious and life-threatening diseases.

In 1991 the first patient representative served on an antiviral drug Advisory Committee for HIV. In 1996, patient representatives received voting privileges as members of FDA Advisory Committees and cast votes on therapies related to cancer. I know that all isn't equal in the Center for Devices as far as voting, but we do have a presence there as well. In 2001, the FDA expanded the role of patient representatives to serve as consultants to the medical product review division, to gain the patient's view early in the medical product development process and to provide patient advocates an opportunity to take part in FDA's decision making at meetings between the FDA and product sponsors, which are also called developers. In 2011, FDA created the patient network, and also in 2011, the program that I now manage and direct - the Cardiovascular and Endocrinology Liaison Program (CELP) was established. In 2012, as part of the reauthorization of the PDUFA V - FDASIA section 1137 came into effect, which my office is responsible for. Basically, section 1137 requires the incorporation of the patient perspective into FDA decision-making in a more robust manner than what we had been doing. In 2013, FDASIA 1137 required the establishment of workgroups which are currently developing procedures for its' implementation across the agency. So we have CBER, CDER and the CDRH all sitting at the table to come up with these procedures. There's also the FDASIA 607 work group, which my colleague Dr. Jonca Bull referred to, and her office is responsible for the implementation of that as well and they are developing procedures for the implementation.

The next slide talks about stakeholder engagement and the picture down to the right is a picture of me engaging patient representatives at one of our annual patient representative workshops. That's the role of the people in my office. We engage with patients, health professionals, patient advocacy organizations, health professional organizations, and now our role has expanded and we include consumers, industry, and tribal nations in that as well. My focus though, is mostly on patients and health professionals.

So if you look at the patient liaison program, which is in my office, you'll see that we have a patient network, a patient representative program that falls under that, and then we also have a health professional liaison program in our office. You will see that in my program I have it listed under both programmatic categories, the patient and the health professional, because those are my audiences.

Then you should look at the bottom of the slide where we have legislation, public comment and public meetings, and the MedWatch program listed. The MedWatch program is a voluntary adverse event reporting program and that's out of our office as well. I wanted to give a little history on the FDA patient network because that was established in 2011 and all of the conditions or other programs dealing with diseases fall under this program – HIV/AIDS, cancer, and your cardiovascular and endocrine liaison program does fall under this. That's where we held our inaugural last chat with Strip Safely, which was the result of a patient query, specifically Bennett Dunlap, alerting us to the fact that patients did not understand the glucose monitoring guidance documents that were going out. So in my liaison role, I connected with the Center for Devices and we had our first live chat and it was posted on the patient network. I want to say we did not have technical difficulties at that time so that's interesting. We found a different route this time and we will see about that, but it was really a well-attended live chat, and we look forward to doing more of those in the future. The FDA patient representative program, as I stated in the previous slide, was established in early 1990s and since its inception it has grown significantly to extend the representation of patients on a lot of advisory committees beyond the antiviral committee that you saw. Next, I will talk about the Cardiovascular and Endocrine Liaison Program. The slide gives you the purpose of the program. Basically it serves as the liaison between FDA and the cardiovascular-endocrine health professional and patient communities. It encourages and supports active participation and informs FDA regulatory policies, advancing the safety and effectiveness of medical products that treat diabetes, hypertension, heart disease and obesity. We also promote healthy dietary nutritional practices. We cannot forget that because that's a part of each disease I have addressed above.

This is a screenshot of the patient network webpage – I'm not going to spend a lot of time on this, but this is a webpage that was designed just for patients. This is for one-stop shopping where you can get everything you need within the FDA that really pertains to a patient. We have a newsletter that goes out where you can get information on clinical trials, patient representative programs, and then all of the programs that we have as far as diseases like HIV/AIDS or diabetes can be found through this page as well. This slide shows the patient representative program, and this is a picture, I think from last year, of the most recent patient representative workshop. We actually train the patient representatives on what they can expect when they come to Advisory Committee meetings. We spend about a day and a half doing that. This tells us who qualifies as a patient representative. I'm so honored to have two patient representatives who have joined us today as a part of the patient panel. They are Anna McCollister-Slipp and Rebecca Killion. They are SPGs, or special government employees and they bring your patient voice to meetings and to consultations as needed.

This slide is up because I thought it was very important to show that the FDA doesn't just listen to the patient voice when we sponsor meetings, but we also listen when meetings are sponsored by stakeholders. You probably are familiar with FDASIA, the FDA Safe and Innovation Act, which congressionally mandates us to hold patient focused drug development meetings. FDA puts out a list of diseases/conditions for each two-year timeframe. We now have the draft list out for 2014 to 2017. I wanted you to know that the FDA is interested in non-FDA sponsored patient focused drug development meetings. I wanted to give an example of a very successful meeting, which can be replicated in any disease or condition area.

The Parent Project Muscular Dystrophy meeting on Duchenne's muscular dystrophy was held in December 2013. After that meeting, the meeting organizers took all the comments and information from this meeting and they proposed a guidance to the FDA, specifically to the

Center for Drugs Evaluation and Research. It has been submitted to the FDA, and the FDA actually is considering potentially adopting what's in that guidance. I look at this as no different from any other organized patient advocacy function and I think that this is a template that maybe other patient advocacy groups may want to follow. I will have links to all of this information on CVENT as well after the meeting so you can get more information there.

Public comment and public meetings – how else can you get involved? This is also tied back to stakeholder engagement and what we do. What I wanted to do was give you one example of a meeting coming up on December 5, 2014. Basically, we submitted a Federal Register notice to let the public know that we are holding a meeting on December 5, 2014. My FDA colleagues alluded to this earlier and so did Kelly Close. When we put out a Federal Register notice, you can go on the regulations.gov web page and sign what we call a docket, and place your comments there. This example is of one of the preferred focus meeting topics out of the provider list of proposed conditions, and so I think this is important for you to know what we do as far as trying to get information out and you can have input even if you cannot physically attend the public meeting. You always can comment on the open public docket. My next example is of a public workshop coming up on November 13 that was also mentioned earlier. That public workshop will be on November 13 and we will talk about software used in diabetes management. This is open to patients, health professionals, industry, and researchers. Basically we are looking at interoperability issues. We want to hear about them and I think this is a great way that we get information out and you can come in and give us information that will help us to better do our job.

MedWatch is also a program in my office. MedWatch is a voluntary reporting of adverse events. I'm going to put up a couple of ways that you can get that information in to us and what we are trying to do to make it a simpler and less complicated process. MedWatch is the FDA's safety information and adverse event reporting program. Through FDA MedWatch, patients, caregivers, consumers, and healthcare professionals can report serious adverse events. You can submit the completed form, which is called form 3500, to the FDA MedWatch system, either online, by fax, or by telephone.

I want to spend a little time on this and this is really the end of my presentation, because I think it is important. We need to know when something is happening, but I guess a lot of times when I'm out talking to patients, they're like "How do I know this is something you really should report to the FDA?" So I want to give you reasons, some questions, and answers. Why report to MedWatch? The FDA is interested in cases where the potential for harm exists. Such reports help FDA identify and better understand the risks associated with medical products. Not all products have clinical data trials before clearance to market, as we heard earlier. We have limitations of clinical trials to identify safety signals before marketing. A number of patients tested may be too small to detect something serious or rare problems, and you know clinical trials are relatively brief. So what should you report? You should report any event that is fatal, is life-threatening, or life altering. These are the types of things we want to hear about because without the data, we cannot approach the issue and try to resolve it. You should also report things that have the potential for harm or close calls. You should report something that causes a birth defect or requires prolonged hospitalization, is permanently disabling, or requires intervention to prevent permanent impairment or damage.

Who could report? I'm going to repeat that again - *anyone* with a serious problem can report to MedWatch. Patients, physicians, pharmacists, nurses, business-owners, you name it. You all can, and should be, reporting to the MedWatch program. What is my role and what is the Office of Health and Constituent Affairs? We are your bridge. We look at our office as the



bridge from FDA to external stakeholders and the bridge from external stakeholders to the FDA. We are the bridge connecting you guys. So we are bringing the information in and the queries in that you want us to hear about, and we'll take the information out on what medical reviewers are working on, or what different offices want to get out to you. That's what we do. That concludes my presentation so now let's get to the wrap-up. It was quick and dirty, but I hope you got something out of it.

### **Wrap-up**

**Kelly Close:** Absolutely. I'm going to share the podium here. The diabetes community has broken the system again, and there are so many people signing on the system that it literally has not been able to handle it. We are taking really good notes at The diaTribe Foundation, so we thank everybody for continuing to tweet this. It is a statement as well that so many are out there. So many sisters and brothers out there, partners, caregivers, everyone wants to hear what's going on here and what you have made happen. We are going to wrap it up just by putting a couple of quick slides up, and just to say, this has been really a tremendous afternoon here in Maryland. The fact that there have been so many people that are interested in what's happening I think is a really great thing and I think the fact that we heard from FDA that they want so much more patient input is absolutely fantastic.

**Dr. Helene Clayton-Jeter:** I want to thank my colleagues at FDA so much, and to so many patient advocates for participating today. I think we've gotten great perspective on the challenges patients face and how reviewers can keep those in mind as they think about new drugs and devices. As for wrap up and next steps, we're excited about where FDA can take this information, and take this transformative pilot discussion. I'm going to hand it over to Kelly on our collective hopes and dreams for where we go from here. I know Kelly has alluded to this and we've had a tremendous afternoon. We shut down streaming and we are capping off a major year for patient advocacy. These slides are self-explanatory.

**Kelly Close:** We are going to flip through this, but this has been amazing leadership by so many people. The fact that Manny couldn't join the Afrezza discussion and yet has so many things to say about how insulin is a really dangerous drug and there needs to be more alternatives – that was amazing, and look at what you made happen there – him talking to all of the reviewers. We loved that and that could never have happened without you and that is unprecedented at a review meeting at FDA.

Let's go to the next one. Again, obesity is such a cornerstone problem for so many people with diabetes, not just type 2, but many people with type 1 as well. The fact that so many patient advocates could come speak at this one was absolutely essential. We see today that we had so incredibly much patient input. We don't know what to say. It has been a very, very big deal for us to be able to be thankful to FDA. You are right for all of your colleagues for allowing so many voices. So what's the plan? What are the next apps?

**Dr. Helene Clayton-Jeter:** I'm saying those slides and the things we have accomplished - external patient advocacy, as a moderator of the novel March live chat, and then the internal patient advocacy with securing Manny's remote access. I just asked the question and they said "We will give it a try." Then to the open public session of the Afrezza Advisory Committee meeting, where we had a huge, huge patient line-up. So the FDA has stepped up on stakeholder engagement with the diabetes community and I look forward to more opportunities to come.

**Kelly Close:** So we are going to talk about some of the plans on the last slide. So you want us to participate, and you don't want to make it only open to patients who can come to Washington, so thank you for making it possible to do this by webcast, by videos, etc. And maybe even making more time at some of the meetings for patient voice would be fantastic. We would love to see, as Anna and others alluded to, more conversations like this and more with the drug leadership.

**Dr. Helene Clayton-Jeter:** I think I liked this meeting because it was a 10,000 feet high look at diabetes and now the next meeting with the Center for Drugs, a more specific and in-the-weeds meeting will be possible for they now know what to expect. I look forward to this as the next step.

**Kelly Close:** It was great to hear really a lot of openness to discussion on more patient centered study outcomes building on the time in zone for the artificial pancreas trials that the drug side has really pioneered. And then discussion to re-examine cardiovascular outcome trial guidance, this is really important because the FDA is advising all of the companies on how to spend hundreds of millions of dollars on these trials. And it is going here, it is not going to other parts of research, so we were very happy at that meeting where the ADA and the patient groups advocated for that. And continuing the conversation off-line as well as online.

**Dr. Helene Clayton-Jeter:** So the FDA would like to say thank you and The diaTribe Foundation would like to say thank you. We thank you for joining us today and we hope all of us are a bit wiser and more informed and better educated because of this webinar. Thank you so much.

**Kelly Close:** Yes. We want to share responsibility and join in a more collaborative and actual partnership between patients and the FDA. Thank you very much.