UNITED STATES OF AMERICA

FOOD AND DRUG ADMINISTRATION

PATIENT-FOCUSED DRUG DEVELOPMENT FOR HEMOPHILIA A, HEMOPHILIA B, VON WILLEBRAND DISEASE AND OTHER HERITABLE BLEEDING DISORDERS: PUBLIC MEETING

Bethesda, Maryland

Monday,September 22, 2014

PARTICIPANTS:

Welcome:

DONNA LIPSCOMB
Office of Communication, Outreach and Development (OCOD) Center for Biologic Evaluation and Research (CBER) Food and Drug Administration

Opening Remarks:

GINETTE MICHAUD, M.D.
Deputy Director, Office of Blood Research and Review (OBRR) Center for Biologic Evaluation and Research (CBER) Food and Drug Administration

Overview of FDA's Patient-Focused Drug Development Initiative:

THERESA MULLIN, Ph.D.
Director, Office of Strategic Programs Center for Drug Evaluation and Research (CDER) Food and Drug Administration

Background on Heritable Bleeding Disorders:

STEPHANIE OMOKARO, M.D.
Medical Officer, DHCR Office of Blood Research and Review (OBRR) Center for Biologic Evaluation and Research (CBER) Food and Drug Administration

Overview of Discussion Format:

DONNA LIPSCOMB
Office of Communication, Outreach and Development (OCOD) Center for Biologic Evaluation and Research (CBER) Food and Drug Administration

Topic 1: The Effects of Your Bleeding Disorder That Matter Most to You

Topic 2: Patients' Perspectives on Current Approaches to Treatments

PARTICIPANTS (CONT'D):

Closing Remarks:

GINETTE MICHAUD, M.D.
Deputy Director, Office of Blood Research and Review (OBRR) Center for Biologic Evaluation and Research (CBER) Food and Drug Administration

Other FDA Panelists:

JONATHAN GOLDSMITH, M.D.

CHANGTING HAUDENSCHILD, M.D.

MENFO IMOISILI, M.D., MPH

DIANE MALONEY, J.D.

PAUL MINTZ, M.D.

NICOLE VERDUN, M.D.

Patient Panelists (AM):

DANIEL BOND

AMANDA HEISEY

MARK SKINNER

SONJI WILKES

Patient Panelists (PM):

JOSEPHINE DRONEY

DONALD GOLDMAN

KIMBERLY HAUGSTAD

DEBBIE PORTER

PARTICIPANTS (CONT'D):

BENJAMIN SHULDINER

MARK ZATYRKA

Other Participants:

LISA FAULCON, M.D.

SIMONE PORTER, M.D., MPH

KETAKI SINGH

GRAHAM THOMPSON

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P R O C E E D I N G S

MS. LIPSCOMB: All right. Good morning, everyone. After a bit of a delay, we're ready to get started, so if you're standing around, if you could get seated. So if you're standing around, if you could get seated.

I can't tell you how excited and happy we are to have you here today. My name is Donna Lipscomb, and I'm with the Center for Biologics Evaluation, Outreach, and Development here at CBER, and I'll be the facilitator for today's meeting.

I'm going to give my colleagues a chance to introduce themselves, but first I want to go over a few housekeeping rules for us today. We have several people on the Web as well as in the room, and we just want to welcome everybody, especially our Web participants. More and more of our meetings are happening virtually, and we're excited that we have an opportunity to share this information to people who couldn't make it. Your voice is important to us in this effort, and we

really are looking forward to hearing what you have to say.

I do want to let everyone know that this meeting is being recorded via the webcast and transcript, and it's going to be put up on our Web sometime after this meeting.

There are restrooms located, if you go out the door, turn right, go to the end of the hall and a little to the right. That's where they are. It's about as far away, so I would ask that you judge the distance when you're deciding when it's time to go. There's a drinking fountain down there as well, and you pass the kiosk. So for anyone who did not bring their lunch, when we break for lunch you'll be able to get a sandwich or some coffee from out there.

Feel free at any time to get up and move around. This is an informal meeting in that we want you to be comfortable. If you need to stretch, walk around, please do so.

And with that, I'm going to go ahead and ask my colleagues to introduce themselves.

DR. MICHAUD: Good morning, and welcome. My name is Ginette Michaud. I'm the deputy director of the Office of Blood, Research, and Review here in the Center for Biologics.

DR. OMOKARO: Good morning. Stephanie Omokaro, medical officer in the Office of Blood, Research, and Review, Division of Hematology Clinical Review.

DR. MINTZ: Good morning. I'm Paul Mintz. I'm director of the Division of Hematology Clinical Review in the Office of Blood, Research, and Review in CBER.

DR. GOLDSMITH: Good morning. I'm Jonathan Goldsmith. I'm the acting associate director of the Rare Diseases Program in the Office of New Drugs in the Center for Drugs, and I'm very glad to see some old friends.

DR. IMOISILI: I'm Menfo Imoisili. I'm a medical officer in the Office of Orphan Products Development, and I'm here to represent my office. And the person who was supposed to be here for us today is not here, so I'm representing him.

DR. VERDUN: Good morning. I'm Nicole Verdun. I'm from the Office of New Drugs in the NCEDR, the Center for Drug Evaluation and Research, and I'm a medical officer in the Division of Hematology Products.

MS. MALONEY: Good morning. I'm Diane Maloney, and I am the associate director for Policy in the Center for Biologics.

DR. JAIN: Good morning and welcome. I'm Nisha Jain. I'm chief of the Clinical Review branch in the Division of Hematology Clinical Review in the Office of Blood, Research, and Review.

MS. LIPSCOMB: Thank you. Well, what I'm going to do right now is kind of go over what our agenda for today is going to be like. First, I'm just going to give you a high-level overview, and my colleagues today are going to be giving a few presentations that set the context for why we are here. We're going to have opening remarks and we're going to hear about the actual initiative that brings us these patient-focused meetings,

background on the heritable bleeding disorders, and then I'm going to give you an overview of how the discussion format is going to go.

This is a bit different than a lot of public meetings we have. This is going to be more of a conversation between you and the FDA.

The two discussion topics that we'll be going over this morning will be disease symptoms and the impact that matter most to you, the patients. And this afternoon, we'll talk about the perspective on current approaches of treating the heritable bleeding disorders.

We also will have an opportunity to have open public comment. Now, if you're interested in saying something that's not in the venue of what we're questioning, if you want to go off-topic a little bit, I'm going to probably nudge you along and ask you to sign up for the docket. So out at the registration table is a sign-up list. There's room for about 15 people, and that's open to everyone -- patients, industry to speak -- and you'll have, depending on the number of people

that sign up, you'll have somewhere between two and three minutes to give your comments. But that is a first come, first serve, so when you get an opportunity, if you think there's something else you'd like to say that might be a little outside the scope or you just want to make sure your voice is heard, please go on outside and sign up for that part.

And then we'll have some closing remarks. So it's exciting to us. We're really glad to get started, and we're going to go ahead and let Ginette start for us.

DR. MICHAUD: Thank you, Donna. Good morning, everyone. And welcome. We're very excited to host this Patient-Focused Drug Development Meeting on hemophilia A, hemophilia B, von Willebrand disease, and other heritable bleeding disorders.

Our team has prepared extensively for this meeting so that patients and caregivers will have the opportunity to share with us your experience with a bleeding disorder, the symptoms

that are a part of your daily life, and the impacts of your disease. And we also want to hear your perspectives on current therapies and existing approaches to treating your disease.

This is an important conversation, and so we're very happy to see the large turnout. I believe that we have approximately the same number of participants on the webcast as we have here in the room. I do want to acknowledge the patients, your families and caregivers, and those who advocate on your behalf for your willingness to engage in today's conversation. And I do want to recognize the significant participation of healthcare professionals and representatives of the pharmaceutical industry. Your participation today shows your interest in directly hearing patients' perspectives and in listening to what patients have to say.

FDA is responsible for protecting the public health by ensuring the safety and efficacy of human drugs and biologic products. The Agency is also responsible for advancing public health,

and we do that by helping to speed innovations to make medicines more effective, safer, and perhaps even more affordable. While FDA does not itself develop new drugs or conduct clinical studies of new drugs, our role is to oversee and facilitate their development. Drug manufacturers and investigators obtain the information from -- I'm sorry, the authorization from FDA to study new drugs in patients, and once those studies are completed, manufacturers submit applications to FDA to obtain approval for marketing the new drugs.

Our intent today is to carefully gather your perspectives on heritable bleeding disorders and on currently available therapies. In sharing your perspectives, we'll hear directly from you, affected patients, your families and caregivers, and your advocates. This input, along with the comments that are submitted to FDA, will strengthen our understanding of bleeding disorders; in particular, the burden that these disorders place on patients and their families,

and the various ways that patients try to manage their disease, the side effects resulting from existing therapies, the ways in which current therapies do not fully meet patients' needs, and from the patients' perspective, how these therapies could be improved.

FDA will carefully consider your input when advising manufacturers on their drug development program for drugs or biologics intended to treat bleeding disorders, and your perspectives are also going to be considered when we assess products for marketing approval, and more specifically, in making an assessment of the benefits of a new drug versus its risks. In addition, the perspectives we hear today will be helpful more broadly in the drug development process, in helping to identify unmet needs or opportunities for developing new measures of effectiveness in clinical studies.

To date, FDA has held over 10 patient-focused drug development meetings on a variety of disorders, and thanks to the

participation of patients and caregivers, such as yourselves, as well as patient advocates, we have learned a great deal about the burden of disease and the gaps in current therapies. We urge you to participate fully in today's conversation, and we also invite you to submit any additional comments to the FDA docket.

I can't overemphasize the critical role of patients and caregivers in today's meeting. This is your meeting. We are here to listen to you -- patients, caregivers, and advocates -- because you have important information to convey and a very unique view on your life and how it's been altered by your bleeding disorder and the benefits and shortcomings of therapies as they exist today.

In closing, I want to thank my colleagues from the Center for Biologics Evaluation and Research for their efforts in preparing this meeting. This includes my colleagues from the Office of Blood, Research, and Review; the Office of Cell Tissue and Genetic

Therapies; and the Office of Communication Outreach, and Development. We are also grateful to our colleagues in the Center for Drug Evaluation and Research, for their very generous assistance in preparing for this meeting.

And so, in closing, I want to wish you a very successful and productive meeting. And I will return the microphone to Donna. Thank you very much.

MS. LIPSCOMB: Thank you. Theresa is going to talk to us next.

DR. MULLIN: Good morning. I'm Theresa Mullin, and I direct the Office of Strategic Programs in the Center for Drugs. And my office has been sort of coordinating this Patient-Focused Drug Development Initiative overall, and this meeting is one, as you were hearing from my CBER colleagues, this is one in a number of meetings. So I'm just going to take a few minutes to try to put a little context around this, and hopefully I won't be too repetitious. I realize some of the things I'm going to say Ginette has already said.

So hopefully that's okay.

But to begin with, we are trying -- and this effort is part of our broader effort in FDA to more systematically gather patients' perspectives on their disease and on the treatments that are currently available. We know that they have a very unique and critical perspective because a patient is the one who is suffering both the risks of any therapy and the benefits, and know what it's like to have the disease. So their views on how it feels to have the disease and what's working and not working about available treatments is obviously uniquely important in understanding that if we're going to be evaluating these treatments and looking at it in the context of things already on the market.

And so we see that input not only helping us get better insight to help inform drug development and advise sponsors who are developing new drugs, but even in reviewing drugs post-market once they're on the market. The perspective of patients, the severity of a condition and the

degree of unmet medical need very much perform what we call the clinical context in which we evaluate the risk versus benefit. The more severe a condition, for example, the more severe it is for the patients, the more perhaps life-threatening, the more willing patients often are to accept risks in exchange for some real benefit. And so we need to be very cognizant of that. That's really what needs to be informing our judgment of risk benefit, so that's why we think your perspective is quite necessary for us to really do a good job at doing premarket and post-market oversight of drugs.

And so this Patient-Focused Drug Development Initiative is one that we're doing as part of the Prescription Drug User Reauthorization. In 2012, we got some additional funds to help us to support and run these meetings, and we agreed to conduct at least 20 meetings over the course of five years. We're probably on track to do more than that. But in 20 different disease areas, the Center for Drugs is

committed to do at least 17 meetings; CBER is committed to do at least three such meetings in the areas that we oversee, the portfolio of diseases and products that we oversee. And these meetings give us that sort of systematic approach to trying to collect this information.

We had a public meeting and a process in September of 2012 on through October of 2012 to see what diseases we should consider. We put out some criteria. We received about 4,500 comments from the public about what diseases. We narrowed that down to a set in the first three years of diseases that I'll show you an overview of in a second. And we are now going through the process of identifying diseases for the last two years, 2016 and 2017 of this five- year reauthorization.

So here you see the diseases that we're covering in the first three years. And in bold and in blue, here we have today's meeting, hemophilia A, B, von Willebrand disease, and the other heritable bleeding disorders. And what you see over on the right is the remaining that we'll

try to be accomplishing within the next year basically.

Each of these meetings is tailored a little bit, but it's also consistent in terms of the questions we're asking. So there's some continuity across these meetings. Despite the fact the disease areas are different, we still ask some similar questions about what it feels like to live day-to-day with the disease, what are the biggest impacts the disease has on the patients' life and on their family, and so on. And then what their perspective is on what they're doing to treat the disease. But we also try to tailor these meetings, and the review divisions that are involved in reviewing the products may have specific questions or concerns. There may be questions about trials, people participating in trials, the kind of endpoints that matter to patients. And obviously, having you here provides a unique opportunity to ask you, you know, what do you think? Get your opinion about these things, and the review divisions find that to be very

helpful. So we have a combination of tailoring and then having some consistency across this as well.

The outreach that patient advocacy groups and patient groups help us with prior to these meetings is critical. We find that the more participation that we get, the richer the meeting, the more informative, and so it's wonderful, as Ginette was saying, to have the turnout today of people who are here in the room and also those who are able to participate on the Web.

And finally, what do we do with this information? Well, the most immediate product is a report that we call a Voice of the Patient Report. And in that report we try to very faithfully capture exactly the way patients tell us what they think and what they tell us and the way they say it in that report, both the face-to-face, what we hear in the room, and also what is provided by patients in the docket, and what we hear over the webcast. All of this input is brought into those reports and they serve as a

very valuable reference tool for the review division reviewers and any subsequent applications or information, questions they have in the disease area that we focused on in the meeting. It also, we think, will help spur further development interest in patient-reported outcome measures and maybe subsequent instrumentation that can further enrich clinical trials by bringing in a more systematic collection of that information about how the patient is feeling and functioning and the impact on their life in case a new treatment has a particular benefit in that area. We'd actually like to capture that information and have that be part of the application and the dossier of what we have.

And so with that I'll turn it over. You're going to hear now about the background of this disease. Thanks very much.

DR. OMOKARO: Good morning. Thank you again for your time and participation.

Today, I will be providing some background on heritable bleeding disorders. Some

of this information may not be new to you, but given that there are a number of different disorders represented here today, I will be highlighting the various heritable bleeding disorders.

I'll start with an overview of how the body normally stops or prevents bleeding. Then, I'll go into a background of the different disorders and talk about their symptoms and a little bit about treatment.

How a bleed stops normally involves the interactions between platelets and proteins in the blood called clotting factors. Platelets stick together and form a plug at the site of the injured blood vessel. Clotting factors then interact with platelets to form a glue or fibrin clot. This interaction holds the platelets in place and allows healing to occur at the site of injury while preventing blood from escaping the blood vessel.

Heritable bleeding disorders occur when normal clotting goes awry. These disorders are a

group that range from mild to life-threatening conditions and may be present lifelong. The underlying reasons that prevent normal clotting include problems with the platelet plug, such as in von Willebrand disease; defects in the fibrin clot because of low levels of clotting factors, such as in low factor VXIII or IX in hemophilia, as well as other factor deficiencies; excessive breakdown of a clot or fibrinolysis can also be an underlying reason, and this is seen in Alpha-Antiplasmin deficiency. Finally, fragile blood vessels can also lead to bleeding, as seen in hereditary hemorrhagic telangiectasia.

Now, let's move on to some of the more common disorders. Von Willebrand disease is the most common inherited bleeding disorder, affecting one in 100 people. However, more than 65 percent of these patients have no symptoms or have mild symptoms. It occurs equally in men and women and is due to reduced or abnormal production of Von Willebrand factor, which leads to problems in the platelet plug. Although bleeding may vary in

severity, there are some patients with very severe disease.

The second most common inherited bleeding disorder is hemophilia A, with one in 5,000 male births affected. Almost all patients are male because of its excellent inheritance pattern. Hemophilia A is due to low levels of factor VIII in the blood, which lead to abnormal clot formation. The lower the factor VIII level in the blood, the more severe the bleeding symptoms.

Hemophilia B is not as common as hemophilia A but it does have a similar X-linked inheritance pattern, with almost all patients being male. Hemophilia B is also known as Christmas Disease and affects one in 30,000 male births. Severe bleeding occurs due to low levels of Factor IX in the blood.

Now, let's talk a little about the rare bleeding disorders. Platelet disorders occur rarely in the general population with one in one million people being affected, such as in

Glanzmann thrombasthenia, Bernard-Soulier Syndrome, and even more rare in Gray Platelet Syndrome. Platelet disorders result either from not making enough platelets or from platelets not working properly. Although these patients have long bleeding times, they can also range from mild to severe disease.

Other examples of rare disorders include some that can be seen in a very limited number of families, such as Factor I deficiency or afibrinogenemia where over 200 cases have been reported. Other factor deficiencies, such as Factor V, VII, X, and XI are also rare.

So what are the signs and symptoms of heritable bleeding disorders? The symptoms are largely due to bleeding that may vary in severity, such as bleeding after circumcision or after having vaccinations, bruising or a collection of blood in the muscles and soft tissues, nosebleeds that are frequent or hard to stop, spontaneous bleeding that occur without any obvious cause, as well as bleeding following trauma or surgery.

Bleeding can also be seen in the joints, and this can cause swelling, pain, or tightness, and often affects the knees, the elbows, and ankles. Heavy and frequent menstrual bleeding, as well as heavy bleeding after childbirth also occurs. One of the most serious symptoms is head bleeds or bleeding into the brain, and this can occur even after a simple bump to the head and requires emergency treatment. All of these symptoms are important to patients, and FDA recognized the need to explore them further so that they can be better accounted for in the drug development and review process.

There are multiple approaches to treatment. Avoidance of medications that can aggravate bleeding is important. Current therapies depend on the type of bleeding and the severity of bleeds, and may include platelet transfusions; fresh frozen plasma; cryoprecipitate; specific factor concentrates such as Factor VIII or Factor IX; desmopressin; as well as supportive treatments, such as hormone replacement therapies, pain medications, and clot

stabilizing medications. In terms of new treatments, gene therapy is being studied as a possible treatment for hemophilia.

There can be complications to treatment. One of the most serious complications is inhibitor development to factor concentrates. Inhibitors are antibodies that attack the clotting factor, causing bleeds to be more severe and making treatments less effective. Other serious complications include severe allergic reactions. Complications due to frequent intravenous infusions can also be seen and may lead to scarring of veins, which can lead to the requirement of implant catheter devices which have their own risks, as well as the risks of infections.

We are here today to listen to you. We encourage you to take this opportunity to provide FDA greater insight into your bleeding disorder. Thank you.

MS. LIPSCOMB: Well, before I get started on my overview of the discussion format,

it occurred to me as I was walking over to the Web table and looking at my colleagues that we do have some FDA colleagues who are assisting us that are sitting at the tables, and we have a couple of medical officers sitting at the Web to help answer questions. We have Lisa and Simone, Niketeh.

So let's go ahead and get started a little bit. First, an overview. Topic one. We're going to really ask our panelists, and then the question we're going to pose is, "What are the effects of your bleeding disorder?" And we're going to ask that you concentrate on those symptoms that you experience because of your conditions, and which of the one to three symptoms have the most impact on your life? And then we want you to concentrate on what are the specific activities that are important to you but you cannot do at all or as well as you would like? How has your condition and its symptoms changed over time? And what are your worries about our condition?

In the afternoon, we'll tackle the

question of what about current approaches to the treatment.

So what are you currently doing to treat your condition or its symptoms? And when we talk about that, we want you to also include how well are these treatments working for you? What are the significant advantages and disadvantages you found? What are the complications? How do they affect your daily life and how you go about your business of living? Has you treatment changed; why? What aspects of your condition are not improved? And then if you could also kind of think about what is an ideal treatment. If you could waive a wand and there's something perfect, what would you look for in an ideal treatment? And, finally, we'll talk about if you had the opportunity to participate in a clinical trial, say in experimental treatments, what would you consider? What would you consider? What would you have to think about in order to decide whether or not you were going to participate?

So, right now, as I continue going, I'm

going to ask my first set of panelists if they could start making their way up here to the table. We're going to ask them to give you a little bit of background on question one. And we're asking them to limit their stories and their experiences to five minutes of sharing. I recognize that these questions and this time limit is a constraint and it puts you in a box and it seems almost impossible; however, we do have a limited time today to kind of think about these questions. So what we really are going to do is try to focus on the questions that FAD can really think about and build on.

Now, if there is something that you really feel like you need to say and you don't have time, then I do want to again encourage you to sign up for the public comment period, or you'll be able to list your comments to the public docket. Once we hear from our patients, we're going to spread these questions out and I'm going to ask you your opinions and your experiences. And when we do this, I'm going to ask you to state

your name, and if you could, tell us what your disease is that you're talking about.

Now, on the other side is we are going to have some polling questions. So for our guests that are sitting at the table, there are these little clickers. They are not to order your lunch or to fling across the room to get my attention, although that's usually pretty effective. But when we have the polling questions come up, we'll test them out and you'll get to vote on some questions. So as a colleague of mine says, it will be very game showy and you'll get to pick your best answer. So we're looking for it.

People participating on the Web, you, too, will have an opportunity. The polling questions will come up on the screen, and you might have to scroll down if you don't see the answers that I'm mentioning, it but it's all there for you. What we will be doing is all comments, people on the Web, you'll also see little boxes where you can make comments. We'll actually incorporate your comments in our summary report.

Now, that leads us to sending us your comments. If you don't have time, if we don't get to you today, it's not because we didn't want to. Your experience is very important to us. We just have limited time. So you can send us your comments. If you have a friend that couldn't make it, they can send us their comments. If you have a friend that couldn't make it, they can send us their comments. If you're driving home on the beltway and the sun is no longer in your eyes and you're thinking, "Oh, I wish I said that," you can send it to the public docket. On the pages that you were given, you were given a handout of our slides today, you'll see that there's the website, which is www.regulations.gov. At the top corner there's a little button you're going to click that says "Comment now." It doesn't come with the music I would like. I would like it to have a drum roll, comment now, but that's your option to do. And we will also take those comments into consideration and put them in our summary report.

Again, now let's talk about the ground

rules for discussions. We encourage patients, caregivers, and advocates to contribute to the dialogue. We really want to hear what you have to say. FDA is here, but we've got our listening ears on, and we will ask you some questions, clarifying, finding out more about what your thinking is, but we're really not going to be able to answer very many, if any of your questions. So again, if there's a question that you have come up that we're unable to answer, you could put it -- we encourage you to put it to the docket. And we might not be able to respond to you, but at least we'll know what your questions are and it will help us inform how we go about our business.

The discussion is going to focus on symptoms and treatments. Like I said earlier, there's a lot of other things that we could talk about. However, this is what our focus is today. And so if we happen to get a little bit off topic, you'll see me kind of nudge you along back into what the purpose of the questions are.

The views today are personal opinions,

and we ask that you respect everyone's opinion. It might not be how you see a situation, but it's their reality. So we'll respect everyone's opinion and we'll really listen.

And then we want you to tell us how we're doing. How did this meeting go? Did it give you what you needed? At the end of the day there's going to be an evaluation survey and we really, really encourage you to fill that out. I can speak as someone who works in training, we really look at those and make changes on how we do things based on your input. So, please, do let us know how we are doing.

Again, the last time I'm going to mention this piece -- well, maybe after lunch if we're not filled -- we do have an open public comment period at the end of the day. This is the time where everyone gets an opportunity to speak. Prior to that, during the discussion period, we're really only going to be talking to our patients, our patient advocates, our family members, but the open public comment time is when everyone in the

room is free to come and speak to us. Again, if you could sign up out at the registration table, it is first come, first serve. I think we have about slots open, and depending on how many people are going to talk really will depend on how long you'll have to speak.

So with that, if we could -- everyone, if you could grab your clickers.

This is a demographic slide. Really, this is all very anonymous. We're not going to hold you to anything. It's not a scientific survey. We're just looking for some demographics to help us know who's in the room with us today.

And again, if I could get today's -- this morning's panelists, first panelists -- Sonji, Daniel, Mark, and Amanda to come on up while we're doing these.

I need my clicker. You guys can take your clickers. Here, let me give you some. We're going to get you clickers there. Great.

Okay. So our first question is where you live. Do you live inside our lovely area of

the metropolitan D.C. Area, the beautiful suburbs and our wonderful beltway? Do you live outside of our area and think why the heck do I have to go through this traffic to get here? Or are you international?

I did want to know. Ah. There we go. This is why I'm not really allowed to have the clicker usually. So, wow. Sixty-nine percent of you are outside of our area. How was that drive for you today? Was it great? What was it like on the Web?

MR. THOMPSON: About 85 percent outside the area.

MS. LIPSCOMB: Okay, thank you. All right. Our next question is which of the following best describes you: Do you have a heritable bleeding disorder? Are you a family member or caretaker of someone with a heritable bleeding disorder? Or do you work for a patient or advocacy organization?

Okay. The fun part on this thing is you get to see people voting, so that's what the green

things are.

And about 42 of you -- percent of you actually have a heritable bleeding disorder, with 30 percent of your family members. So welcome. We're so glad that you're here.

What was the percentage on the Web?

MR. THOMPSON: About half are advocates and the other half are equally split between patients and caregivers.

MS. LIPSCOMB: Great. Thank you. I think two of us are playing with the computer.

I'm going to put my -- I'm going to put the clicker down. It'll make it much more effective.

I think we have to go back one. There. Great. So if you don't see green and you've clicked once, try clicking one more time. Have you or your loved one been diagnosed with any of the following heritable bleeding disorders: Von Willebrand disease? Hemophilia A? C is hemophilia B. Other factor deficiencies? Platelets dysfunction?

Okay. Next slide. Great. Thanks. Oh, okay. Overwhelming in the room affected by hemophilia A.

MR. THOMPSON: And on the Web it's the same distribution.

MS. LIPSCOMB: Okay, great. Thank you. All right. What is your or your loved one's age?

If you're a patient caregiver, if you could be talking about the patient that you're taking care of.

A is 0 to 12, 13 to 16, 17 to 49. You can see in the pediatric ages we really kind of broke them down. 65 or older.

Okay. Can we have the results? Wow. It's quite a jump from the 0 to 12 to 17 to 49.

MR. THOMPSON: And on the Web it's very similar, although there are slightly more in the 50 to 65 category.

MS. LIPSCOMB: Okay. And we do have 16 and 19 percent in the older.

Well, excellent. We're glad to have everybody here.

Let's go to the next question. Okay, this is an easy one. You're not going to get much time on this. Slow. Okay, what do we have there? It's kind of overwhelming there. 94 percent of us are male. What on the Web?

MR. THOMPSON: 70 percent male and 30 percent female.

MS. LIPSCOMB: Great. Thank you. So this question really gets to how severe has your bleeding disorder been in the last year in that it had you go to the hospital. So how often have you or your loved one had to go to the hospital or emergency room because of the bleeding disorder? Either none in the past year, one to two times, three to five, six to 10, or more than 10 times.

We're split in the room between one to two times and none, with 3 percent of you more than 10 times. So I can't even imagine what that must be like.

How is it on the Web?

MR. THOMPSON: On the Web we have 44 percent, none; 22, one to two; 16, three to five;

and 16, six to 10.

MS. LIPSCOMB: Thank you. Okay. All right. Well, thank you for that background. That really gives us some information that frames our discussion. I wanted to make sure I turned off that so we didn't hear that buzzing that drives people crazy. So the first question that our panelists are going to speak about are the disease symptoms and the daily impacts that matter most to them as patients.

So we're going to ask Sonji. Oh, yes. I'm sorry. Touch the red button and it'll light up for us.

MS. WILKES: Hello. My name is Sonji Wilkes, and I am from Englewood, Colorado. I have mild hemophilia. But today I want to tell you about my 11-year-old son, Thomas.

Thomas has severe hemophilia A, and he has been fighting an inhibitor since he was about seven months old. He also has asthma and an acquired immune deficiency and needs IVIG treatments every four weeks. While his bleeding

episodes have been numerous and frightening, the most challenging impacts for him and my entire family are situations that influence his quality of life beyond just his clinical conditions.

Venous access is our number one concern. Because he infuses factor concentrate daily for his immune tolerance, good venous access is paramount. When he bleeds and needs multiple infusions per day, the need for access is even more critical. As an infant, he had a Broviac catheter. Eventually, the Broviacs succumb to the wear and tear of repeated use. We made the decision to implant a PORT-A-CATH. Little did we know that it would be the first of five ports to date, along with multiple PICC lines. Thomas's veins are hard to stick on a regular basis, and he has a repeated history of compartment syndromes after peripheral infusions by medical professionals. It is uncertain whether if he will require another port or even if his body will hold up to another insertion, not to mention the bleeding and infection risk involved with the

surgical placement. It's a terrifying place to live to have the very medication that can save his life in your hands and not know if you're going to be able to infuse it because of venous access issues.

Chronic and acute pain management has also been a significant challenge for Thomas. Repeated joint bleeds into his left ankle have miraculously caused very little visible damage, but he consistently complains of soreness there and in other areas of his body. He recently said to me as we were standing in the grocery store, "Mommy, my body is like that of an old man's. I'm just sore all the time." He is 11.

He does not tolerate most opiates or narcotics, and the side effects often make him harder to manage medically. In 2013, we tried a combination of a transdermal opiate patch and an anti-nausea drug during a particularly nasty shoulder bleed. Despite my insistence for weaning, Thomas continued on these patches for three months, two months past the worst of the

acute pain. He became dependent on the patches. The suffering my then 10-year-old son had to go through during the withdrawals for such powerful, yet mildly effective drugs was something I would never wish on my worst enemy.

Like most boys, Thomas has a competitive spirit, but because of his physical limitations, most sports are off limits. He started swim lessons at an early age, and in the summer of 2011, swam with a neighborhood swim team. He excelled, and even qualified for the All-Stars meet, and we continued with a year-round team, but he spent much of 2011- 2013 sidelined as he battled port infections and significant bleeds in his iliopsoas and quad muscles. Last summer, he returned to the pool but found he didn't have the stamina or speed that he once had. Despite sadness about not being able to do what he loves on the level that he'd like to participate at, he continued to have fun with his peers.

Thomas misses an average of 20 school days per year. During the past year, he missed an

entire trimester due to the shoulder bleed and the resulting dependency on pain medications. Our school district worked with us to provide a homebound teacher, but she was only with him for two hours a day and he soon fell behind. Even after he had recovered enough to attend school, he had to remain home one day a week for us to retain eligibility for the homebound teacher.

Through sheer determination, Thomas was able to move on to the sixth grade this year. His father and I, distraught over him being unable to attend school, bought, at our own expense, a robot that travels from class to class, enabling him to replicate himself from a distant location so that he can interact with his peers and teachers as if he was physically present at school.

Hemophilia hasn't gotten easier over time for us. The bleeds, pain, and line infections still happen despite all of our preventative efforts. As a family, we've just become more skilled in coping. We've made multiple attempts at immune suppression therapy to

eradicate his inhibitor, but simply cannot sustain a zero-Bethesda unit.

From the time Thomas was born, we've tried to prevent bleeding management to minimize joint damage. I didn't want Thomas relying on a wheelchair. Limited mobility has become less of a worry though as I see Thomas adapt when he needs to, but he root cause of that limited mobility, whether or not his factor concentrate will work and address a bleed to minimize that damage is what worries me the most. Bleeding management of an inhibitor patient is staggering. Currently, we only have two products to choose from to control bleeding, and only one product approved for prophylaxis. Every time a bleed happens, I never know, and I hold my breath to see if it's going to work and if the bleed is going to stop.

It's scary, and I never know if it's going to take one treatment or multiple infusions over the course of a week or weeks. I worry that my child might literally lose life or limb, and I only have a limited range of medical interventions

to help him. There is worry over the affordability of the drugs available to him. There's worry over the access to his medical team and if my insurance company will allow me to utilize their expertise. There is worry over his mental and emotional condition. There is enough worry to feel an ocean, but I will meet that worry with advocacy and empowerment so that my child can live his best life despite any limitations.

Thank you for the opportunity to share our experiences today.

MS. LIPSCOMB: Thank you so much. Dan? If you could hit your red button. Thank you.

MR. BOND: Hello, my name is Dan Bond. I'm a 60- year-old engineer with severe hemophilia B. I've spent my career making things go faster, so I hope this is brief.

I've had a total of six joint replacements -- both knees, both elbows, one ankle, and one hip. Technically, only five were due to bleeding. The hip replacement was after a fall down stairs going to breakfast at an NHF

lobbying event here in D.C. a few years ago. I blamed the smell of the bacon.

I've also had a total of five revisions in my replaced elbows. Joint replacements are like getting a new kitchen. Revisions are like unclogging a sink. Both are good to do but one is far more rewarding.

The surgery cut through the muscles and left me with very little strength in my triceps, making it exceptionally difficult for me to turn wrenches. In addition to the limited strength -- there's only a one- eighth diameter pin connecting the two parts of my elbow. The first elbow repair surgery was to replace that pin after I bent it opening a jar. I have to be very careful using what little strength I have.

My first job in high school was as a deckhand on a Caribbean charter sailboat that was spending the offseason in Galveston. It seemed like a great life. I dreamed of living on a boat, sailing around the world. Never mind the idea of infusing fresh, frozen plasma in the middle of the

Atlantic. It seemed like a good idea to a 19-year-old. As my ankles degraded with joint disease, it became clear that I couldn't walk on a pitching deck. I haven't sailed in over 40 years.

In college, I discovered bicycle racing. I trained in Houston with national championship riders, serving mostly as traffic for them to pass. After my elbow replacements, it became too difficult and dangerous for me to ride and expose the fragile implants to a crash. I haven't ridden a bike in over 20 years.

As an engineer, I enjoy building things. It's grown increasingly difficult for me to do that. It's frustrating to know that I could unstick a bolt and not hurt myself if I could just get a longer wrench to fit. Working under a car is out because I can't reach overhead. With my replaced knees, kneeling is out. Pretty much all I have left is telling other people what to do. It's fun in its own right, but not as satisfying as doing it myself.

Sixty years is a long time with this

disease. There was a history of hemophilia in my family, so there was a relative in the delivery room ready to give me a direct transfusion. Fortunately, it wasn't needed. I've seen treatment progress from that to dried plasma, to fractionated plasma, to plasma concentrates, to recombinant clotting factor, to long-lasting factors.

In 2002, I was subject for a gene therapy trial. With each leap, the condition became easier to manage, but of all of these advances, the most life changing was going from being hospitalized for treatment to self-infusion. I began self-infusions with fresh, frozen plasma in 1975. Factor concentrates, 3,000 IU vials, easy reconstitution are all lovely improvements, but they pale next to the change from hospital-based administration to self-infusion. The freedom allowed by self-infusion made pretty much everything I've done possible. It gave me the ability to travel, to get an education, and to do what I enjoy.

Like 10,000 of the 20,000 people with hemophilia who were alive in the '80s, I contracted HIV as a result of infusing plasma concentrates contaminated with the virus. Thousands of them died, but thanks to early and consistent treatment, and no small amount of luck, my HIV is undectable. Hepatitis C now kills more people with hemophilia than HIV now, but last year I became one of the lucky few who spontaneously cleared the hepatitis C.

With my diseases under control, my biggest worry is about the social contract that keeps me alive. In my 60 years, I've cost the citizens of this country well over $20 million in inflation adjusted dollars. My insurance this year has paid out $191,000, and this was a year with no unusual procedures or surgeries. And so when I say I owe a great debt, it's not just a metaphor.

Hopefully, my experience is worth some fraction of that. I'm also trying to pay it back by volunteering for Phase I and Phase 2 trials,

including the gene therapy trial, which has recently led to some real successes. I'm also on product advisory boards, scientific advisory boards, as well as the board of my local chapter.

We often say that the bleeding disorders community is like a big family. And like any parent, I'm just trying to make things a little better for the next generation. Thank you.

MS. LIPSCOMB: Thank you, Dan, so much. Mark?

MR. SKINNER: So good morning. And thank you very much for the opportunity to be here and present today.

I want to share with you a little bit about my life and what it means to me to be normal in terms of what I would aspire to. Like Dan, I was born at a time when treatment did not exist. My early treatment was fresh frozen plasma and whole blood. I live with severe hemophilia today, as well as all the comorbidities that came over the course of time. The promise of better treatment and a better life that arose from the

clotting factor concentrates that were developed in the 1960s did lead to my acquiring all of the hepatitises -- A, B, and C -- which fortunately within the last year I cleared because of the advances of the new drugs. But I also, over the course of time, have had nine joint surgeries. I've had both of my knees replaced, both of my ankles fused, surgery on my elbows, and am facing the prospect of a shoulder replacement because of the chronic joint disease.

And so though enormous progress has been made, it hasn't been without its challenges. And life is certainly far from normal for me today. Three years ago, as an adult, I started secondary prophylaxis, which for me was life- changing, but my annual factor bill exceeds $600,000 a year for my medication costs because I'm one of those unfortunate individuals who happens to have a shorter than typical half- life, and to control the residual bleeding and swelling that occurs, I require frequent infusions and infuse every other day.

So as we think about what is normal, I'd very much appreciate this focus and shift to thinking about what is important to the patient in the patient-centric approach. Historically, when we thought about normal, and we've talked about normal, for me as a child, normal was achieving a normal lifespan, a normal adulthood. As a child, I was expected to live into my early 30s, and I think for many of us, we're still stuck in a definition of normal. Normal is surviving a normal life that everybody else has. And to me, normal is so much more than just a life expectancy. My goal isn't to survive, but my goal is to actually have a high quality of life. And as we think about the dimensions that mean a normal quality of life, it is going to be very much individualized. We've really moved from that generation of treating the disease to the opportunity now to treat the individual, and thinking about what are those life goals, those aspirations, and what are the things the individual wants.

So, for me, the new criteria should be more than lifespan. It should be more than factor levels in terms of treating to a clinical number. But it really should be working with the patients to think about -- and the individuals and the families -- to think about what's required for me as an individual to have a normal work and career life. Throughout my life, I was forced to make a number of career decisions from what I wanted to do to what I was able to do because of my bleeding disorder. As a young man, and as a law student, I was very interested in going into the Foreign Service. My hemophilia was an exclusion because I couldn't accept a posting anywhere around the world because I lived with a rare genetic disease and I needed to have treatment. I was forced to make decisions on where I was going to locate and have my career because I knew with the complications -- not only the hemophilia, but the HIV and the viral infections -- that I needed to be near a major medical center. I grew up in rural Kansas. I grew up four hours from my

treatment center and was forced to spend a lot of time in a car in a very painful situation waiting to get to the nearest access for treatment. I know that exists for many of my friends and colleagues around the world today.

I think of a normal family and a normal social life. For me, a normal family life seems somewhat inconceivable because of the prospect of HIV and the ability to plan ahead. So those opportunities, although I have a wonderful life now, certainly were challenging, and I expect at a different level the social and family life issues face young children today.

I think of normal activity in sport. Very similar to Dan, within the last 20 years, I gave up riding a bike. It was just too painful. It was too difficult. And even recently, one of my favorite activities, swimming, is very problematic because of the problems in my shoulder. I do maintain a relatively active life, but the sports and the activities in which I can engage, despite being on prophylaxis, are still

limited because of my disease.

So within the current treatment paradigm, I would say that we really haven't yet achieved normal. And my desire for normal is to lead a comparable life to someone who is not affected with a bleeding disorder. I think to realize that goal, I do think that we need to shift our clinical focus and to build the outcome around outcomes that are important to patients, not just relevant clinical endpoints, so that I don't have to make decisions about my life goals related to the disease, but that I know that the drugs are being developed to help me make decisions about my life goals that are actually important to me as an individual.

While it's important to me not to bleed and to have no bleeds in life, an annual bleed rate of zero is really not much more than a numeric value if it doesn't mean that I can have the quality of life. So I would encourage you to begin to think about and use your influence as the FDA to help bring that needed change, to bring

those qualitative aspects of what normal means to patients, and not necessarily treating to a lab value or chasing a numeric value of zero bleeds. If we have that holistic approach, and it may be challenging, I think we will all be better off. Thank you.

MS. LIPSCOMB: Thank you. Amanda?

MS. HEISEY: Hello. My name is Amanda Heisey. I'm from Elizabethtown, Pennsylvania, and I'm here today, hemophilia has been a part of my life since I was born. My older brother had severe hemophilia A with an inhibitor. He contributed HIV and hepatitis from blood products in the 1980s, and he suffered from chronic joint pain and joint damage. My four-year-old son now suffers from the same diagnosis. He has severe hemophilia A with an inhibitor.

We have faced many challenges over the years. One of the most difficult symptoms to deal with is the joint pain during bleeding episodes. When my four-year-old son has bleeding into his knees or ankles, he is unable to walk. It is

always a challenge to watch -- I'm sorry. I don't think I can read this.

MR. SKINNER: Would you like me to read it for you?

MS. WILKES: When my four-year-old son has bleeding into his knees or ankles, he is unable to walk. It is always a challenge to watch your young son in pain. There is little pain medication available that we feel comfortable giving him because we do not feel comfortable giving him narcotics.

During and after bleeding episodes, we are concerned with the damage into his joints. The acute bleed is difficult to manage; however, the chronic joint damage is always a concern. Every bleed puts him at risk for chronic joint damage. We are concerned for his future. We do not want him to experience arthritis. I have seen this with my brother who had chronic joint damage.

My son is unable to participate in many physical activities due to hemophilia. He is unable to participate in sports due to the risk of

injury. Although he is young and is not ready for many sports, this is difficult because he has an older brother who does not have hemophilia. Is older brother plays hockey and baseball. Many times he says he will play hockey when he is older. This is an issue we struggle with as parents because it is difficult to explain to a young boy why he cannot play a sport.

During bleeding episodes, he is placed on what the physicians calls "couch rest." This is exactly what it sounds like. He sits on the couch and rests. He cannot participate in any activities during his bleeds. He rests on the couch and watches TV. We even have to carry him to the bathroom. During these events, we usually have to cancel any family activities that were previously planned. The bleeds often lead to multiple treatments. Because of the multiple treatments, I, myself, often have to miss work as I am his primary caregiver.

One activity that we have always counted on for Payton was swimming. He has not always

been able to participate due to his port. He has an implanted port for his daily treatments, but because of the port, he is at risk for an infection. Infection could lead to an additional surgery which would be risky. We do what we can to protect him from infection. He is not allowed to swim in bodies of water such as ponds or oceans due to the risk of bacterial infection. Our children ask to go to the beach and we avoid it to avoid the risk of infection. He is also not supposed to swim in a public pool within 24 hours of accessing his port. This poses a problem when we access him daily.

Our son has experienced changes with hemophilia over the past four years. Our son was diagnosed with hemophilia one week after he was born. When he was 10 months old, he was diagnosed with an inhibitor. At that moment, it was like he was diagnosed with a new disease. We would have to take bypassing agent instead of Factor VIII he needed. We struggled with his inhibitor increasing until he was 18 months old. At that

time, he started on a daily factor treatment of Factor VIII to attempt to tolerize the inhibitor. He has been on that treatment for over three years and has not tolerized at this time.

There are periods of time when the Factor VIII seems to help and work well, during which time he has no bleeding episodes. However, since March 2014, he has experienced many bleeds into his knee joints and recently had an ankle bleed. At those times, he has increased pain and is unable to walk. Our biggest concern currently is his inhibitor status. I am concerned that the inhibitor will not completely go away and that we will continue daily treatments. I am concerned because of the fluctuation of the inhibitor and the ability for the Factor VIII to be effective. If the inhibitor increases again, he will be at risk for more bleeds, which will eventually lead to joint damage.

MS. HEISEY: I'm sorry about that. I just wanted to say I probably should have went first because when they started talking I started

thinking of all the things he wasn't going to be able to do.

MS. LIPSCOMB: Amanda, thank you so much for sharing your story and your son's story.

I think that everyone up here on our panel deserves a round of applause. Thank you so much for sharing.

(Applause)

MS. LIPSCOMB: Which leads us now -- how many of you -- oh, usually I sing when a microphone comes on. I was forbidden to do that. Come back at lunchtime and I probably will.

How many of you heard your stories in any of these -- by a show of hands, heard your stories?

Let's hear one or two of those. Let's try to take a conversation from someone. Who would like to --

MS. GATES: Good morning. My name is Carletha Gates, and all of us have so many similar stories. I am a carrier. My father, Roosevelt Green, had severe hemophilia A he passed away in

1997 from HIV that he contracted from a blood product.

I'm the oldest of three girls in my family. We're all carriers. We all have two sons a piece, and I also have two daughters. They're all severe hemophilia A. All the stories are the same. What has impacted our family the most -- well, as far as an improvement, my father had all the joint diseases, when through cryoprecipitate, treating at the hospital, five hours away from the hospital. But with my generation, my sons, they do have the privilege of treating at home on prophylaxis. My oldest son, who is 25- years-old, does have a bit of joint issues because that was before the days they started doing prophylactic treatment, but my 19-year-old, he has no joint issues. He's able to treat with prophylaxis. He has access.

And what's most important is blood safety, making sure the blood supply remains safe so that the treatments remain safe. That's the most important to me. My son, he was six years

old when my father passed, and he knew that he had hemophilia. He knew he had HIV. He goes, "Mommy, am I going to die from hemophilia?" I said, "No, baby. Hemophilia didn't kill your father -- your grandfather -- it was the HIV. You're going to live a much better life because the treatments are getting better." And later on as he got older he said, "Mommy, you were right." He's able to do everything most of his peers, except for basketball, but that got better as he got older. We steered him into golf and swimming. So that's changed over time.

But what worries me the most -- I appreciate you guys having this because you need to hear it from our perspectives. We're not the ones that are going to develop future treatments, but we're the ones that are going to have to deal with the future treatments, what that brings. And my son told me to send this message. He wants to take a pill. He does not want to infuse intravenously. Develop a pill that he can maybe take once a week. Like, if you have a headache,

you take an ibuprofen or aspirin or whatever. Well, he doesn't take aspirin, but something simple. That would make it even better for their quality of life.

I could go on. It would take me eight hours of nonstop talking to tell you some of the stories and issues that we've gone through, but I think you're going to get a pretty good snippet of it. But I thank you for having this meeting. It means a lot to our community.

MS. LIPSCOMB: Well, thank you very much for that. We will be talking more about treatment this afternoon. So thank you. Did anyone have an experience that's different than what we heard? Okay. Did you want -- okay. Thank you.

MS. CESTA: Hi, I'm Jeanette, and I have von Willebrand disease, and my three teenagers do. And although there's clearly many similarities between the different bleeding disorders in our community, I think the experience of having VWD definitely has some differences between the experience of hemophilia and the challenges can be

a little bit different. I think part of it comes in having knowledge of our disease. I think that's something that impacts myself and my family a lot in terms of the journey we have taken personally over the years in getting more informed and understanding our disease state and understanding our treatment possibilities and how it affects our life.

And when you talk about von Willebrand disease, I think there's always an issue, kind of, of validation sometimes. And when I look at those numbers that you put up in the beginning about how many are symptomatic, I question that because I think of the times my family has gone to the ER, we've been infused, we've had these events, and it's never documented on our records. And so, also thinking about the number of people in my extended family who clearly have bleeding symptoms who have not been diagnosed. So I just think there's, you know, we've had internal bleeds spontaneously. We've had muscle bleeds, joint bleeds. You know, menorrhagia has been a huge

impact on my life and now I have two teenage daughters who are facing the same issues. And better treatment options but still it's years of struggle in trying to find what works.

MS. LIPSCOMB: Well, thank you for that. Christopher?

MR. TEMPLIN: I wanted to comment. Mark, I'm glad you commented on the quality of life. I think more emphasis needs to be put on quality of life outcomes. I think sometimes you might look at the majority of the community and everybody's doing great, but there are those folks that fall through the cracks and have issues with their joints that choose them to be able to unattain that quality of life. Maybe you have a desire to ride a bike through Central Park or something and you can't do that.

And I was glad to see Sonji say that she had hemophilia. I have hemophilia, and I have a three-year-old daughter who has a diagnosis of hemophilia B. So I wish maybe the FDA goes back and redoes some pamphlets or publications to try

to get rid of that male-only distinction. It's just a pain in the neck when you have to fight with the doctors to make them believe that yes, this is really a legitimate diagnosis. I'm not a good patient myself when a doctor comes in and asks how long I've had hemophilia, so I'm definitely not a good patient when my child is there being treated, and I usually end up getting hauled off by security. So having the FDA put some bona fide information, because maybe my daughter has two defective Xs, maybe she only has one. I don't know. But I know she has a diagnosis of hemophilia B. So regardless of the genetics, I go by factor level, factor activity. And it is low enough to make her have hemophilia B.

MS. LIPSCOMB: Thank you. Thank you. Do we have any comments from the Web?

DR. FAULCON: Our Web participants basically have shared the same comments that we've heard here in the audience, and that is that they feel that there's a need to redefine what's normal

for patients with bleeding disorders, and in particular, hemophilia. And they also have commented on the effects of developing an inhibitor later on in treatment and how that has changed their quality of life.

MS. LIPSCOMB: Okay. Thank you. Does the panel have any questions that they'd like to ask at this point? Christopher, does your daughter have any bleeding episodes?

MR. TEMPLIN: Yes. Yes. Yes, she injured herself at her daycare in a door and had to be treated then. And she busted her gums falling. She fell and bit her lip. So she's been treated a few times.

MS. LIPSCOMB: Okay. Thank you. Yes?

MS. WILKES: I would share that I did not no. We had no family history of hemophilia in our family, so I was 26 years old before I knew that I was a carrier, and that was with Thomas's circumcision. And as soon as the symptoms were starting to be described I knew. But further testing did prove. And 10 years ago, as a woman,

I had to fight for treatment. That tide is turning but it depends on where you live on how well that treatment is for women with bleeding disorders. And I do think we need to talk about redefining those definitions because it should be based on your factor activity level, not on your genetics.

MS. LIPSCOMB: Thank you. Thank you very much. Okay.

MS. CHADD: I just -- I wanted to add to that as well. I am a symptomatic carrier if you looked at my genetic sequencing, but my factor levels go as low as 12 percent, which makes me qualify as having mild hemophilia. This is my son and he's moderate to severe hemophilia and on prophylaxis. I have a 45-year-old brother as well that deals with comorbidity issues as well.

But I'm heading into another major surgery, as a matter of fact, a week from today, and had a major surgery last December to have a tumor removed. And it was a fight for me to get the physicians to listen and say you're female but

you're a carrier of hemophilia. You can't be affected by hemophilia. And so it really took a lot of lab work for them to see it and actually believe it because of the fact that they needed that lab level to actually qualify that for their thought process. So it really -- taking that labeling off of that and allowing it to be less of a stigma of a full male disorder would definitely be beneficial because I have a daughter. I have two beautiful nieces. My mother as well is a symptomatic carrier. So it is definitely an ongoing battle for the women of the hemophilia community to get the treatment that they need, although it's getting better for us with our sons and our brothers and our fathers.

MS. LIPSCOMB: Thank you. Thank you so much for that.

I still see a few hands up. We're going to take one more question or comment and then we're going to move on to a couple of other questions that I think will elaborate more.

MR. LONG: I'd like to point something

out. We keep referencing factor percentages or numbers. They are very important and they can drive physicians to pay more attention. But a good example, I'm 3 percent. I have relatively few issues. I have a niece who is a symptomatic carrier. She's 25 percent. She has many more issues. And so doctors need to take into account not only the percent of your factor but all of the other clinical manifestations that you have because each of us is unique as well as having similarities.

MS. LIPSCOMB: Thank you for that. Can we have the next slide, please? I'm sorry. Back to polling. I know it's like our favorite part of the day. Which of the symptoms currently has the most significant impact on you or your loved one's life? (a) Joint damage or pain; (b) heavy menstrual bleeding; (c) bleeding in the muscles and soft tissues; (d) bleeding in the head; (e) anxiety and depression.

We recognize that you probably want to put your top two or three. Unfortunately, the

clickers that I have only let you pick one, so.

Okay. So most joint damage, 67 percent leads. I suspect that those numbers will be just -- not different but there'd be a little more skewing -- less skewing if we got to do two or three.

What about on the Web? What do we have there?

MR. THOMPSON: On the Web, 54 percent, joint damage; 18 percent, heavy menstrual bleeding; 9 percent, bleeding in the muscles; and 27 percent for anxiety or depression.

MS. LIPSCOMB: Okay. How many times in the past year did you or your last one experience a bleed? Zero to four times, 5 to 11 times, 12 to 23 times, 24 times or more? This is within the last year.

Okay. Wow. I can't even imagine that. So 50 percent of you have 5 to 11 times. What about on the web?

MR. THOMPSON: Twenty percent for 0 to 4, 40 percent for 5 to 11, 27 percent for 12 to

23, and 9 percent for more than 24.

MS. LIPSCOMB: Right. And in the room we have 17 percent at 24 times or more.

What we want to do now is discuss in more detail how your bleeding disorders have affected you and your health on an average day. So let's talk about joint pain. I believe that the number was 67 percent in the room and on the Web 54. Thank you.

So overwhelming -- can we get the next slide, please? Thank you. And the next one?

Never mind. Clearly, this is what I want. Let's talk about joint pain specifically and damage. Does anyone want to share with us some specific examples of how joint damage has impacted your life?

Thank you.

MR. ANTELL: Sure. I'm Mark Antell, moderate hemophilia A. Ankle problems. I've got this arthropathies -- I've had the arthropathies that go with hemophilia, but probably the -- I'm most severely affected in my ankles. I don't know

that pain is so much the problem as it is incapacity, the difficulties in walking, because pain is something that I think most of us have learned to walk through if we can, maybe with factors so that we can do it, but the problem is that the joint itself becomes weakened, dysfunctional, and a bad ankle leads to all sorts of problems, both -- it leads to problems in the hips and the knees as well. And it also, I think, makes you a little more liable for falls. So again, I'd say pain is not so much the problem as dysfunction.

MS. LIPSCOMB: Okay.

MR. THOMPSON: Quick note is please hold the microphones close to your mouth when you speak because that is how the Web participants can hear you. Thank you.

MS. LIPSCOMB: Okay, thank you. Mark?

MR. SKINNER: Yeah. I think pain is an interesting concept in hemophilia. I think we develop a threshold and a tolerance for pain very early in life, and we don't quite appreciate what

normal is without pain. And I think as a result -- and there's been a lot of community research done that pain is really vastly under-recognized within the community, and pain is vastly undertreated. And our care systems are not set up to do it. I judge pain by do I want to get up off the couch and walk and refill my coffee cup? Because it hurts too much just to walk across the room. Now, fortunately, much of that has been resolved in my lower extremities, so getting my second cup of coffee isn't what causes me pain because I can walk now, but reaching for something on the top shelf or doing other kinds of activities, there is a persistent level of pain. So when I get the little smiley faces every time I go in to my doctor's office about what do you think today, it's sort of relative to what? So we don't have a good system to actually even understand what the level of pain is because it doesn't take into account it's something chronic from the beginning and we don't know the difference. But I think the data tells you that

it is there, and it's under-recognized, and it's undertreated.

MS. LIPSCOMB: Okay. Thank you. Back there. Thank you.

MR. CURTIS: So I have severe Factor VIII deficiency, and I have plenty of joint pain. But the studies that I've been doing on quality of life in the U.S., you give these guys these visual analog skills to try and measure how much, you know, how they're doing, and they almost always put in something like an eight. And you look at them and they're pretty crippled up and they can't hardly walk and you ask them, "How the hell are you an eight?" You know? And they say, "Well, I'm better than him." You know. So it's kind of within the community that that's our frame of reference. Right? And so I believe that a lot of the data may not really be reflective of the amount of pain each of these individuals is seeing.

MS. LIPSCOMB: Thank you. Thank you. I'm going to ask that the operator queue up the

phone. I think we'll take a call from the phone. But while we're waiting for that.

MR. MONES: I'm Glenn Mones. I'm an advocate and I direct the New York City Hemophilia Chapter.

Anecdotally, I think that pain as a driver of adherence is a bigger factor than most people normally account for. I think that the connection between, you know, infusing appropriately and relieving pain is more powerful than a lot of people realize and needs to be considered. And in speaking with many families, you know, what is it that, you know, is the reminder it's time to infuse? It's not I'm going to sustain long-term damage. Sometimes it is. You know, or that's what I'm supposed to do or that's what my doctor said to do. It's pain.

MS. LIPSCOMB: Thank you. Operator, do we have our phone call yet? Maybe not yet. We'll go on.

MR. TEMPLIN: Hi, Chris Templin here. One of the issues that I found in my personal life

is I didn't want to complain about the pain because I didn't want to be looked at as a woos or a sissy because I'm a big guy, and how can a big guy like me be in pain? But, and I found in the community that I really didn't know where to go to ask because I didn't want to get on the big heavy duty drugs and be zonked out, and I didn't want to go to the pain clinic to be looked at as a drug seeker or a drug user because, there again, I don't look like I'm in pain because the pain is so subjective, you know. Markedly, we build tolerance to it and a threshold to the pain. And I was very fortunate my mom was a nurse who worked at the VA Hospital, and the VA did a lot of research on pain because they get a lot of people that are hurt and in a lot of pain. I really had to research to find the pain medications to take and I chose methadone as my pain medication, but I get that whole stigma that comes with going to the drug store each month to get that drug. And any time I ever wind up at a doctor's office to write that on the form that that's what I take, and any

time I have to, you know, disclose on any government forms what medication I take, it's a stigma. "Oh, my goodness. You're on drugs." I have a commercial driver's license, so that's actually a disqualification for me to be able to drive because I'm on methadone. But I drive anyway. Don't tell the DOT. But it's just that whole stigma. I'm not a recovering addict. I'm just somebody who is trying to take of some pain and do it in the best way possible to not have to compound the situation of having to go through withdrawal. And my heart is with you, Sonji, for your child, because I can imagine that's horrible.

MS. LIPSCOMB: Thank you. Do we have comments from the web?

DR. PORTER: We had a comment from Justin, who talks about the joint damage that makes -- he describes joint damage as making the disorder visible to the world, not only in that there's pain in limiting mobility but now that there's judgment from others who see him.

And I guess we can maybe potentially ask

others in the room whether or not they've experienced similar stigmata related to joint damage potentially.

MS. LIPSCOMB: Okay. A show of hands? Anyone else who's had that same experience? Anyone want to talk about it?

MR. BRAYSHAW: Hi, my name is Paul Brayshaw. Severe hemophilia B, Factor IX deficient.

A lot of the similar experiences I've faced, I guess some of the ones, the stigma associated with having limping or other inability to walk normally, I guess, was a way -- it was one of the ways I was exposed to the world, especially in grade school or high school. I think that if I was on crutches and didn't have a cast or some sort of a wrap, I think I was always called a faker and I'd probably get pushed around for that alone. And those are the kinds of things that extend through life. Even parking in a disabled parking space, I think people look at you like, oh, you don't have any apparent disability. You

know, there's no wheelchair or whatever. And I guess maybe it's something that I experience just from people looking, but I think it's also, you know, you can face comments or other types of stigma associated that I guess just gets underreported and it's just part of the day-to-day effects of the pain.

MS. LIPSCOMB: Okay.

MS. WILKES: I wanted to circle back to pain for just a minute because most of our hospitalizations over the last three, four years have not been because of the bleed; it's been because of the pain. And ultimately, treatment of the pain has snowballed in such that the side effects from the drugs, pain drugs, and vomiting and low heart rate and sedation often become more of a problem than the bleed itself. I mean, I have literally said to an attending doctor, "Just send me home. I can do the infusion. You're making this worse." And after our experience this past fall, I mean, we are at that stage now where he doesn't want pain medication. And that's hard

as a mom to watch because you know that that damage is happening and you want to protect your child. That's your whole job in life, is to protect your child.

So yes, there is pain. Have we come far enough in addressing that pain, especially in pediatrics? Absolutely not. And there is stigma, Paul. I was totally fearful of Thomas going to school in a wheelchair. We're very lucky. We're at a fantastic school. Those kids rally around him and take care of him, but we have had some bullying instances where kids have thrown stuff at him in a wheelchair. And it's tough. It's really tough.

MS. LIPSCOMB: Operator, do we have any phone calls?

OPERATOR: We do have a call in the queue. If you would like to ask a question or make a comment, please press star. Thank you.

I'm showing no comments at this time.

MS. LIPSCOMB: Thank you. Okay. So in what we've discussed and in what we've spoken,

does anybody have a story that they feel that's a little different that they want to -- and I use the word "story," and I apologize. I don't mean it as if, you know, what's your experience is really what we're saying, that we haven't talked about?

Okay. Do my colleagues have any questions they'd like to ask anyone?

No? Okay. All right. In serious bleeding our numbers were -- do you have that question? What was the number?

DR. JAIN: Thirty percent.

MS. LIPSCOMB: Thirty percent? Okay. What about that? I'm sorry. I'm trying to read my notes and I apologize for this. What about serious bleeding? Does anyone have --

Oh, thank you. I thought we couldn't go back to that. So as you can see, the various different bleeds there come up to 21 percent in that. Does anyone have an experience with serious bleeding that they'd like to share? Outside? Okay.

MR. BRAYSHAW: Hi, Paul Brayshaw again. I can share an experience from college. I was actually away at school, about an hour away from home, and I had a hand bleed, a right hand bleed, which is my dominant hand. And I was taking factor, as I would with most bleeds. Growing up I was mostly on-demand. And at this episode I was just doing the same. You know, had the pain and felt like I would just start with a regular dose, and that was fine, except then it didn't go away. So I took another injection, maybe two more. And I ended up not having the bleed resolved, and so I ended up in the emergency room, and I ended up having to have a carpal tunnel release because it was such a significant bleed. It turns out that the medication I was prescribed was for Factor VIII deficiency, not Factor IX. So fortunately, I was able to work through the injury and have full motion of my hand, but it was kind of a significant bleeding episode that was just a mistake from the pharmacist dispensing.

MS. LIPSCOMB: Okay.

MR. PEZZILLO: My name is Rich. I have moderate hemophilia.

And when you talk about stories that are different, I formed an inhibitor at age 18. So usually you hear inhibitors at a younger age. And growing up I had pretty much no symptoms. You know, my father epitomized -- my mom and dad epitomized RICE -- rest, ice, compression, elevation. It was when I had my wisdom teeth out and I went to a non-HTC where the hematologist didn't know how to control the bleeding. So I was exposed to a large quantity of Factor VIII and I formed this inhibitor. So I went from managed care to unmanaged care. And during that time, for about 10 years before I was tolerized, I went from everything from neuropathy on my left-hand side, to joint damage, to forming a clot, to frequent infusions. And I think, you know, the big thing is that we don't talk about, especially for me, is forming a clot. No one had ever mentioned that someone with hemophilia can form a clot. I had a port in my biceps area and I was on crutches, and

because I was not using the crutches the correct way, and because I was on large doses of clotting factor, I woke up in the middle of the night and my whole arm was blue and swollen. And I think that's something as patients, it's not talked about. It's almost taboo, that having hemophilia means excessive bleeding. It doesn't mean that you have a tendency or you're at risk for clots. And I think there needs to be more education about that because, especially for those with inhibitors, you're using high doses of clotting factor. And still now, even though the clot has resolved itself, I went a year on Lovenox, so I'm infusing twice a day clotting factor, and then I'm sticking a needle inside of, you know, subcu into my stomach, thinning the blood at the same time. So, you know, for a 25-year-old at the time, it's really difficult to manage.

So I think when you ask the question, kind of bleeds that kind of stand out, during the time with the inhibitor I was on an airplane and the seatbelt was a little tight around my waist

and there was some turbulence. I ended up bleeding, you know, into my abdominal area. And that's something again that growing up, I know the inhibitor is a different story, but you don't think about these things. So education about this could really be good.

MS. LIPSCOMB: Thank you. That's really important for us to hear.

I saw some other hands up.

MS. PORTER: Hi. My name is Debbie Porter. I just wanted to follow up on a little bit of what Rich was saying as to we, too, had a very bad experience with blood clots from the bypassing agents. And I'm actually talking this afternoon, so you'll get to hear a little bit more about that. But I'm pretty active with the inhibitor community in hemophilia, and that is becoming more and more common. And I really think it is something that we really need to think about.

My son, actually, almost died from a blood clot. He has lost both of his subclavian

veins. He has no more circulation from his head back to his heart. He spent three months in intensive care growing new veins. And this is something we don't think about and it's very serious. And I do think that the risks with the bypassing agents are significantly contributing to that.

The other thing that we don't really have up there when we're talking about severe bleeds is kidney bleeding. And for us, that has been recently our most serious bleeds. And the hardest to control because, again, you're trying to treat but you don't want to clot. I mean, if you clot in the urinary system, you have a big problem. So, again, we're having this constant balancing between trying to treat a bleed and trying not to clot.

MS. LIPSCOMB: Thank you. Okay.

MR. ZATYRKA: Hi. My name is Mark Zatyrka. I have severe hemophilia A. And I just wanted to point out that it's not really just serious bleeds that this community faces as well.

I was talking to another individual with hemophilia recently and we were kind of talking about our most embarrassing bleeds, and like Rich said, you know, with a seatbelt on an airplane, my friend was opening a pickle jar and got a serious bleed in his wrist. And a couple years back, just from sitting with my legs crossed for too long, I got an awful bleed in my ankle and I couldn't walk for like two weeks. So it doesn't always take an extremely serious trauma to create a bleed that can really affect your quality of life. So I just wanted to make that point that, you know, it can be little things as well that can trigger a bleed that really has an impact on your life as well.

MS. LIPSCOMB: Okay. Mark?

MR. SKINNER: I agree with that. I have my doorman open my pickles and olives now because -- although they make electric jar openers.

I think the definition of what is a bleed is something that, you know, we're talking about severe bleeds, but there's also bleeds at the other end of the scale that we haven't talked

about. So some refer to them as micro hemorrhages or micro bleeds. And the definition of bleeds that both the FDA uses in terms of its clinical trials and what we're asked when we go into the clinic tend to be those kinds of things that actually manifest themselves as pain, warmth, swelling, tingling, something that you actually have a clinical or a visual sensation for. I think what we don't know is there may be a whole series of things that go on before we know them and have a cumulative effect.

I mentioned earlier that I am contemplating a shoulder replacement surgery. I have never had a known trauma or bleed in my shoulder. But if you look at it on X- ray, it's as shot as any of my other joints. So undoubtedly, something has gone on in that shoulder that has caused the joint destruction. And maybe it's a series of micro bleeds, but I think the definitions, when we talk about a bleed, we can't just assume those things that are seen. We all run into that trouble even when we go into

the emergency rooms. If they don't see blood, they don't think that you're bleeding. And so you go to the end of the line. And there's a whole educational problem there. But we shouldn't be thinking about just severe bleeds. We need to be thinking about treatment that actually manages those bleeds that aren't recognized that might have a cumulative effect as well.

MS. LIPSCOMB: Okay. Thank you. Thank you.

MR. SHULDINER: Good morning, everybody. My name is Ben Shuldiner, and sadly, you're going to have to listen to me later on, so I'll try to keep this brief now.

You know, Mark Zatyrka brings up an interesting question about what is a bleed. I have a really shot left elbow. It hurts most of the time. Is it bleeding? I have no idea. I know it hurts. Maybe it's bleeding sometime. Maybe it's not. Maybe it's the arthritis. Maybe it's just joint damage. And I think a lot of us, you know, because pain is a constant thing for us

and because we have target joints and because we are suffering through all sorts of other issues, it's sometimes unclear is it an actual acute bleed that is currently going on or is it just that, you know, we have really bad joints and so it hurts more today than it did yesterday. And so it's had. Like, even when the question was asked, you know, previously, how many bleeds have you had this year? I don't know. It really depends on your definition, and so I appreciate this idea that it's about managing pain, managing joint damage. You know, and if we could ever have a conversation about things like making elbow replacement better, ankle replacement better, those two are really bad joints throughout the community, and the replacement there is not as good as it really could be. And that's something, though it's not hemophilia per se, it's very important to the community.

MS. LIPSCOMB: Okay. Thank you. I saw your hand.

MR. GOLDMAN: Hi. My name is Don

Goldman. I'm a person with severe hemophilia. I'll be on the panel this afternoon, so I won't go into that. But I just want to tell a very quick story.

Back in the early 1960s, in those days my medical insurance would not pay for disease-related emergency room treatment. If it was a disease, it wasn't covered, like if you had a cold or if you had asthma or anything else like that. So if you go there and the reason that you're there is you're bleeding because of hemophilia, there's no coverage. So I decided -- I talked to my doctors and I said, "Well, don't call it hemophilia. Call it a micro trauma." And all of a sudden they said, "That sounds like a good idea." And we called it a micro trauma and they covered it. And later on that term began to be used in the orthopedic and physical therapy community and none of them really understood that it really all derived from insurance company jargon in the first place.

I have a question I want to ask

everybody just to raise your hands, if you would, with respect to the issue of pain and joint damage. How many of the people here, either them or their loved ones, have used some kind or some form of analgesic painkiller within the past week?

I don't know -- how many have not? I mean, personally, if it weren't for Percocet, I would be very unhappy. It's a very good thing to get to sleep at night if need be, and sometimes during the day it's necessary to continue.

MS. LIPSCOMB: Well, thank you. We had like a two to everybody else kind of ratio there.

One more and then we're going to go to the phone after this next speaker.

MS. CHADD: I just wanted to bring also to the room and to the discussion today, having friends with children with mild or moderate hemophilia and having not heard some of that represented today as much, when talking about serious bleeding or episodic treatment versus prophylactic treatment, a lot of times people affected by hemophilia that have moderate or mild

hemophilia that are treating episodically are not treated aggressively enough. And so a bleed that could have been handled very quickly and could have been resolved very quickly actually turns into something that's very serious because of trying to be less aggressive with the therapy and trying in an effort to use less factor and those means. I have two personal friends who have adult children now that due to spontaneous cerebral bleeds or brain bleeds are now deficient in their adulthood, and it's something that could have been avoided had they been treated a lot more aggressively. So I just wanted to put that bleeds that may start small generally have the opportunity to become quite a larger scale and not just in the hemophilia side of it but impacting the mental capacity of our people.

MS. LIPSCOMB: Thank you. Operator, do we have someone on the line?

OPERATOR: I'm not showing any comments at this time.

MS. LIPSCOMB: Okay. Do we have any

comments from the Web?

DR. FAULCON: One of our Web participants with von Willebrand disease commented on how severe or heavy menses have impacted the quality of her life, specifically causing a lot of anemia and iron deficiency. We had another comment regarding the diagnosis of symptomatic carrier versus mild or moderate hemophilia just by factor levels, and wanting to just make the comment that females who are carriers also have symptoms, also experience bleeding episodes.

And our last comment was from a person with actually a pretty rare bleeding disorder, who commented that most of her serious bleeds are related to internal organs. So she's had an experience with diverticulitis and a significant GI bleed that has impacted her life.

MR. THOMPSON: And we do have one person on the phone actually, so if, Operator, you want to open him up.

Operator?

OPERATOR: Yes, we do have a question or

a comment in the queue from Justin. Your line is now open.

JUSTIN: This is Justin (inaudible). It's great to sort of be hearing and seeing people I know (inaudible).

I kind of also want to talk a little bit about how we don't sort of sometimes know whether or not something is a bleed or not. And recently, I've had the experience of having some pretty intense elbow bleeding occur and went to a specialist to sort of have that be looked at. And this guy was telling me, "Oh, no, you're not bleeding there." And I'm trying to tell the physician, "This is a bleed. I can tell you right now. My arm would be moving to full extension if I wasn't having a bleed and I can tell the difference between what is an arthritic pain and what is a joint pain or what is a bleed." So I sort of think sometimes the opposition from physicians to sort of minimize our knowledge of this experience with what they're hoping to prescribe to you for a treatment plan.

MS. LIPSCOMB: Thank you. Thank you for that. Real quick, a couple of you have mentioned that sometimes you don't, you know, your bleeding is not obvious. Do you have any symptoms or do you kind of know when you have a bleed, even though there's nothing -- none of the normal or what's normally discussed that you want to mention or talk about to us, share?

MS. WILKES: A two-year-old gets real cranky before you see a bleed. Real, real cranky.

MS. LIPSCOMB: Amanda?

MS. HEISEY: Yeah, and I wanted to say that my son, he's four now, and a two-year-old gets real cranky. The four-year-old, when it's first starting, he kind of tries to hide it at first because he knows he's going to get his port accessed. He knows I'm probably going to leave it accessed, and he doesn't want it left accessed. So he'll usually start with a hint of a limp, and he'll try to hide that and he'll go find something to do and sit down somewhere to try to hide that, but for adults I'm sure that's different.

MS. LIPSCOMB: Wait a minute. We're going to talk to someone we've not heard from real quick.

SPEAKER: Oh, thanks. I was going to agree. I can notice the limp. My son is seven. I can notice when he's limping at the hip or the knee or the ankle before he even realizes he's doing it and tries to overcorrect so he doesn't have to stop.

But you did ask about symptoms that aren't common that have been spoken about, and I wanted to mention my son had a head bleed when he was 16 months old, and I missed the symptom that would have told me he was having it a week earlier and not led to such bad things had I known. There was some facial twitching. So there were different signs that I saw in him that I had not been aware of, and we were new to the community. No family history, so I think it's important maybe to collect some of that data and information so that others know there are less known symptoms of bleeds that are very serious.

MS. LIPSCOMB: Thank you. Thank you very much. Okay. We've got two people. We're going to go Christopher, and then we'll go to you, Dan.

MR. TEMPLIN: Chris Templin again. I'm sure everybody's sick of hearing me.

Mark was very good. Micro bleeds, I think that's an area that's underlooked. I have a lot of micro bleeds in my head. Not a place where you want to bleed. And when I think something is really going on and it's not being taken care of by clotting factor, it's sort of a pain to go to the hospital and say, "I need an MRI on my head," and they say, "You look fine. You walked in here. Everything is good. Your pupils aren't dilated." And it's like I know something's wrong. I've had blood clots, subdural hematomas. Spent months and months in the hospital, almost died, and I didn't. So micro bleeding is a big thing.

And the mild hemophiliacs, I have six percent. I prophy-treat. I catch heck because I prophy-treat. How can you prophy-treat? You have

mild hemophilia? Well, if I don't prophy-treat, I'm going to be laying on the couch rest 24 hours a day and not be productive to anybody. Not be productive to myself or my family. And nobody is carrying me to the bathroom except King Kong.

So many issues I think really need to be looked at, even to go to an HTC. I would really like to see HHS or FDA or NCHB or some alphabet designation really go to the treatment centers and go to the emergency rooms and say, "Look, if Johnny shows up with hemophilia, don't make him sit at the back of the queue. Take him in, get him his factor, get him what he wants, call his treating physician." You know, the doctor there that walks in and says, "How long have you had hemophilia?" I want to just like walk out but I'm already there. I've had it since birth. Or maybe that party last week, I might have picked it up there. I don't really remember. And I'm not trying to make jokes about it, but it is sort of comical because I went to my clinic appointment a few months ago, and I'm due for another one. And

the resident walks in and asks me how long I've had hemophilia. And I wanted to smack him with the closest thing to me because you're a resident in training to become a hematologist. I think you should know how long these people have had hemophilia. I didn't just acquire it. I was born with it.

MS. LIPSCOMB: Okay. Thank you. Dan?

MR. BOND: I just want to say my girlfriend can often recognize when I'm having a bleed before I'm at least willing to admit it. So, to the parents, it doesn't get any easier.

MS. WILKES: Great.

MS. LIPSCOMB: Thanks. We're going to take -- okay, we're going to take two more questions or statements.

MS. GATES: Statements. The kids, when they're younger, they get cranky and they stop using the joint. That's the first time I recognized my son had an ankle bleed. He would, instead of walking, he would crawl. He would know that. And also, my sons, as they got older, they

said they feel like a tingling in the joints right before the bleed starts and they recognize it that way.

One comment I wanted to make about pain is before my dad passed away, he got his three daughters and we, you know, we knew all about his experience but he said, "Whatever you do, make sure you take care of the pain. I don't want my grandchildren to suffer the way I did." He did not have access to the medicines that they do now, and that's the one thing we're very vigilant about is the pain. But they have developed such a high tolerance. You almost have to force them to take something because we know they're suffering.

So I just wanted to make that comment as well.

MS. LIPSCOMB: Thank you.

MS. CESTA: Hi. Jeanette with von Willebrand disease.

I just was thrilled to, you know, listen to your answers about what is a bleed. I was dying to know what your answer was because I think

that's a big confusion, and I think with my experience, with my family's experience with von Willebrand disease, so I looked at your thing and it says 12 bleeds. So if we are infusing factor every month to control our period, does that instantly put is in the 12 times, you know, just baseline? Because I'll tell you, it sure feels like a bleed to me. Now, whether it qualifies, I don't know. And again, I think this is one of the things we need to look at to help document and validate the bleeding that we're experiencing. And also, I think we need more education for mothers and for young adults growing up about what is a bleed, how to identify it. I mean, typically, von Willebrand's isn't supposed to have muscle bleeds, isn't supposed to have these different things, and you know, I miss it. I miss it when my child comes to me and is having a legitimate muscle bleed, but I go to the orthopedist looking for a broken bone. And, you know, we learn as we go along, but it would be much better to get this information up front so

we're aware of these things coming up. And so that concept of defining what is a bleed. That's not language typically von Willebrand's knows, but yet we experience.

MS. LIPSCOMB: Great. Thank you so much for that. I think we have a couple more Web comments, and then we're going to move on to the next question.

DR. PORTER: So one comment on the web talked about a women's daughter who was diagnosed at 15 years of age. She had a slow internal bleed, and just her concern around the difficulty of diagnosis. She has von Willebrand disease and that other physicians were really slow to pick up these symptoms. Another individual talks about the challenges related to labeling hemophiliacs with different levels of severity -- mild, moderate, and severe -- especially for those who have mild disease because they're often -- their symptoms are often overlooked. And a third, which talks about her eight-year-old son and how she knows that he is having a bleed because he talks

about this buzzing, I think, buzzing sensation.

MS. LIPSCOMB: Thank you. We've heard a lot about bleeds and joint damage.

Are there other symptoms or other issues not identified in the polling that anyone wants to talk about or share?

Okay.

MR. DRONEY: I have von Willebrand disease and my two main severe symptoms have been menorrhagia and GI bleeding. I had severe GI hemorrhaging for over two and a half years before they finally could figure out something to do to stop it. And I have found that most physicians discount me when I come in and say, "This is happening. I had a bleed." One, because I'm female. Two, because it's von Willebrand disease and many people think that you can only have mild symptoms with von Willebrand disease. And three, because they don't know anything about it. No one except for my hematologist and my GI doctor really knew about my bleeding disorder. So even though it's not talked about, the more common symptoms

for people with bleeding disorders, there can be others. It turns out I also have Crohn's Disease on top of the bleeding disorder, but to me, I mean, that doesn't matter. I was still dealing with this. And I found that, as many people have pointed out, most physicians aren't educated enough that they could know that a person with a bleeding disorder could have such severe GI symptoms.

MS. LIPSCOMB: Thank you. Right behind you.

MR. CURTIS: My name is Randy Curtis. I'm 60 years old with severe VIII.

One of the things that I've had trouble with is gout. And as we get older, we start having these other "old man" diseases that come along with hemophilia and they get kind of tricky. Because if you have gout and you have a bleed in the same joint, the bleed doesn't respond to factor because it's actually gout and the gout irritates, you know, it's a mess. And then, of course, your favorite treatment centers says,

"Well, you must have developed an inhibitor." "No, I don't have an inhibitor. There's something else going on in here." So then you have to get the rheumatologist involved in it. And as we age, we're going to be, you know, we're having more and more challenges with heart disease and diabetes and all those kind of things that come with age. And there really haven't been a lot of us around this long to kind of explore those extra areas.

MS. LIPSCOMB: Okay. Thank you. Anybody else? Well, I just had to look forward.

All right. We'll go in this order.

MR. SKINNER: So your earlier chart where you were asking sort of about major symptoms, I think the last column was anxiety and depression. And I think there's an issue that probably hasn't been raised, which is the whole psychosocial side of this. Our healthcare system is squeezing the ability for us as patients to access psychosocial support really out of our care system. And I would expect most of us -- and it's humbling to sit up here and hear all the stories

out here because probably our best therapy and support group is talking to each other, which is why we're such a close community. But we don't -- I would guess all of us worry at some level about our kids in school, about our careers and our jobs, and all of that is because of the underlying condition. And I don't think we should underestimate the importance of the psychosocial impacts of just the burden of living with disease, because that last number I recall was like 11 percent. I think it's something that we just assume we have to cope with and deal with, but if we really were able to treat and develop therapies that allowed a normal life, it would fix that number. So I didn't want that small number to underestimate the importance of that to all of us. And I'm happy for my colleagues and brothers and sisters in the community to disagree with me, but I expect it's a bigger problem than the data shows.

MS. LIPSCOMB: Thanks, Mike. I suspect, too, if we were able to pick more than one it

probably would have been higher.

Daniel?

MR. BOND: Another issue that's sort of masked by the bleeding disorders, I've had three bouts of septic arthritis in my knees and one in one of my replaced elbows, and they present very much like just an ordinary bleed. They swell up, a lot of pain, but it doesn't respond to factor. And after I had the three in my knees, I had my knees replaced. Years later I got my elbow replaced and I called my doctor and I said, "I think my elbow is infected." And he immediately called the orthopedist, called the emergency room. I was in surgery within four hours of telling him that. He didn't examine me. He said, "If Dan says it's infected, it's probably infected." And the orthopedist said that he's never saved a replaced joint from an infection. But because I was able to get in so quickly, he saved it.

MS. LIPSCOMB: Thank you. I can't imagine that. We'll go back here. Go ahead.

MS. WILKES: I was going to speak a

little bit about postpartum bleeding. I have three children. I have two daughters -- one older, one younger than my son Thomas. And so with my older daughter I was not diagnosed yet as mild hemophilia, and I bled for nine months postpartum and was told that that was normal. And, of course, was anemic and was taking iron. And with Thomas, I don't remember bleeding as much postpartum, but I was also dealing with a new diagnosis, so I probably did. But with my third child, we had already established my factor activity level at 26 percent and went in with a plan if I had bleeding, and did. I had significant bleeding with my third child. And again, had to fight. Even though I had the factor in my hand, my OB/GYN refused to sign off on me being able to infuse it. So I think there's still a real problem with postpartum bleeding for women that also have bleeding disorders.

MS. LIPSCOMB: Thank you.

MS. CHADD: I wanted to add to what Mark was saying. When you put up the slide and asked

what had impacted us the most, and I'm looking at that thinking joint bleeds and joint damage concern, but also I was really thinking I should lean towards the anxiety and depression. And in looking at that, we raised this next generation to know that their products are pure, they're safe, and you get to do whatever you want, and you get to go fulfill your dreams for those kids that are blessed to not be affected by inhibitors. But it puts so much pressure on them as well looking at, well, I'm going to have my children. I'm supposed to live this normal life. No one can see that I have hemophilia, but yet I do have limitations to the things that I can do. So I think the anxiety and depression is something that we're seeing in our next generation that looks so normal and so part of everyday "normal", being in quotation marks, because I agree. I think normal should always have these in the air. But I think that's going to be something that we see in this next generation that we may not expect because we think they should be so -- they should have everything

so much better than our generations past have.

MS. LIPSCOMB: Okay. Thank you. Does the Web have anything they'd like to share?

MR. THOMPSON: We do have a caller again, so Operator, if you can open up the line.

OPERATOR: Yes. Justin, your line is now open.

JUSTIN: This is Justin again. And, you know, a lot of times I think to some extent it's important just to sort of talk about the anxiety issues and how depression impacts people with bleeding disorders. Sometimes I think it's important to understand the disability is not just a medical condition or (inaudible) but it's sort of sets social and cultural barriers to the full participation in social life, whether that be the pressure of fully participating in a sort of (inaudible) masculine world, and especially coming from a predominantly male-affected community, the issues begin to be even more compounded. And especially even within the bleeding disorders community having to sort of look at that and not

include women or people with (inaudible) sort of in those parameters (inaudible).

MS. LIPSCOMB: Okay. We're going to go to -- thank you so much for that, Justin. And we'll go to the Web.

DR. FAULCON: We have one participant that wanted to share that even though her son has a diagnosis of severe hemophilia, he actually hasn't had many complications. And so really, it's just the stigma of having the diagnosis. But to date he's had a pretty disease- or complication-free experience. And so that might be something that we could explore.

MS. LIPSCOMB: Okay. Thanks. We're going to take one more comment and then we're going to get to my next question.

SPEAKER: I'd like to address what would have been my second choice, which is bleeding in the head, and is the reason why I'm here today.

Nine years ago, my older brother, a racquetball accident, head trauma, he's conscious in the ER with his wife and two daughters sitting

there with him. They come in and they say, "The CT scan says that your bleeding in your head has stopped." They had not infused him. A few minutes later his head blew up, he went into a coma, and subsequently died. It's very important that we get into -- I don't know if FDA can do this -- to get into the process in the ERs and the urgency of infusing stat. The mentality is -- it's the stroke mentality. We have a golden hour. We CT first. It's either a clot or a bleed. We treat accordingly. With hemophiliacs, that's not the issue. Infuse stat. We need to get that to ERs. I'm going to work on getting an app to do it or any other mechanism. But that's very important. I don't know if FDA can influence that, but if you can, please do.

MS. LIPSCOMB: Thank you. I see that we have over comments and questions, but I'd like to get to my next question which is really how have the effects of bleeding changed as you've aged? How have the symptoms changed?

Anybody?

MR. TEMPLIN: I don't think the symptoms have changed.

Chris Templin again for the record. I don't think the symptoms of bleeding have changed but I think what has changed is the stigma. You know, you're a big guy. Suck it up. Get over it. For me it's the fear of, you know, I'm a person with a good support system but my fear is the people without a good support system. You know, going back to anxiety and depression and pain. People may not go get the help they need because they're afraid of the stigma that comes along with it. And then they'll self-medicate or self-treat that pain or depression or anxiety. And that's what scares me because if I have a bleed, I take care of it and I act accordingly. But we're sort of taught to trust the doctors, trust the HTCs, trust that our treatment centers are on par. But I can tell you right now, I could walk in any one treatment center in one part of the country and probably walk into another one in another part and I'll get totally two different standards of care.

So what changes? I have to be more of an advocate now and take more of a heavy-duty advocate role than I do having to worry about a bleed. If I have a bleed, I just infuse. I just do what I need to do.

MS. LIPSCOMB: Okay. Thank you.

MR. SMOAK: My name is Shelby Smoak. I have severe B. And to address that question, I think I would concur with the ability or the necessity of being your own advocate.

But in terms of how it's changed from when I was younger, as I've aged, you know, now we're looking at severe joint damage. So recovery times are a lot longer, and a lot of times this doesn't necessarily get addressed in treatment protocols. So when I was a kid with elbow bleeds, you know, my recovery period might be 24-48 hours. Now, that recovery period can be weeks, and I think the treatment is necessarily much more intensive. And sometimes if you aren't aggressive, then those bleeds just linger and linger, and the consequence of that is, you know,

you're losing activity. And if you're trying to stay healthy and be active and keep your muscle tone well to reduce joint damage, you're losing that. So that's kind of a manifold system of decay that happens as you age, especially with the joint damage that you've accrued.

MS. LIPSCOMB: Okay. Thank you. Well, what continues to worry you about your health as you get older? I'm sorry. What continues to worry you about your health as you get older?

MR. BIAS: I'm Val Bias. I'm the CEO for the National Hemophilia Association.

Probably our ability to access product. You know, Chris said that, you know, he's mild and he's treating prophylactically. Well, there's no indication for that. So at some point he's going to have a problem with his insurer. And they're not going to believe him or he's not going to get the product, and then he will be on the couch. As the new products come out, our ability, especially in this healthcare transition to access products that work better for us, becomes sort of a roll of

the dice at the moment. Are they going to cover the new products that are going to come out? What difference does it make if you license them if we can't access them? It's sort of a catch-22. We've made a lot of progress in the last 25-30 years, but what difference does it make when we look down the line and we say, "Hey, there might be a cure for hemophilia but they're not going to pay for it"?

MS. LIPSCOMB: Thank you. Thank you.

MR. PEZZILLO: I would say that personally, the biggest fear about my condition is that the inhibitor is going to come back. My heart breaks when I hear stories like Sonji's and Debbie's son. For 10 years you go through this awful experience, and I almost feel that I'm lucky now that I can live at 31 years old and be active and run and infuse every other day. But in the back of my mind I always am fearful that this inhibitor is going to come back.

I think another thing that is concern that I mentioned earlier is neuropathy. The pain

of nerve damage by far was more severe than any joint bleed or muscle bleed that I ever had. When I did experience it, I didn't know what it was. And I can remember screaming in the middle of the night and having to be hospitalized for about two months, and still now I can't sit for long periods of time -- and this is seven years later -- because this area still gets inflamed, like a pins and needles type of thing. And I've gone to acupuncture. I've been on Lyrica. I've been on all different types of drugs. Heat, the TENS unit, everything. And these complications are less talked about but they're all -- it's not a side effect of hemophilia but it's a result of having bleeds. And especially when you're talking about muscle bleeds, it could really turn into other things. So those are the types of complications that because there is no cure for hemophilia, these are the things that as a patient, that you worry about when a bleed is uncontrollable.

MS. LIPSCOMB: Thank you. I'd like to

suggest you stand up then.

Oh, okay. Amanda.

MS. HEISEY: I was going to say, well, actually to, I guess, piggyback off of what Rich says, my biggest concern is that the inhibitor will never go away. We've been doing it for three years now, and I've gotten to know Sonji, and I love her but, you know, her story doesn't make me very hopeful. And as I said before, my brother has severe hemophilia A with an inhibitor, and kind of going off of what Val said, I also always have in the back of my mind that someday the insurance company is going to say, "Sorry, you can't infuse him every day." So, and, you know, that's just another worry that we have. And, you know, I don't know that that will happen, but it's always in the back of my head.

MS. LIPSCOMB: Thank you. Mark?

MR. SKINNER: Yeah, so, I mean, for people that were listening that didn't know our community, this could be awfully depressing.

I want to pick up on Randy's comment

about the aging issue. So, I mean, there are some problems that we never expected to have because we weren't supposed to live this long, but cardiovascular disease hasn't been mentioned yet. So, I mean, as we think about things that cause us to have a sedentary life, because of the joint damage, obesity we know is a bigger problem in our community than the general population. Many of us have been on heart therapies through the HIV drugs, and cardiovascular disease in patients aging with hemophilia is not well understood. And so interventions to manage cardiovascular disease, so many of the typical interventions are contraindicated with the hemophilia. So I worry about it because there's a long history of cardiovascular disease in my family. I've been on the HIV meds for a very long period of time, and I wonder how some of these sort of lifestyle aging issues, whether we're prepared to manage them as we go forward, so.

MS. LIPSCOMB: Okay. Thank you. Let me get over here real quick.

MR. ANTELL: Sure. Mark Antell. I'm 67 years old and I've noticed over the last decade, maybe even longer, that slowly I've needed additional factor. I don't know if that's because my joints have gotten worse, just an accumulation of joint damage over the years, or maybe muscle tension has reduced. But certainly in my experience, and I think it's not all that unusual that as we get older we find that we need more factor. We need to treat more frequently.

MS. LIPSCOMB: Thank you. Can we go to the Web? Any comments we have there?

DR. FAULCON: So we have comments about increased symptoms as Web participants age, including easy bruising, increased joint damage. There are concerns about insurance and insurance coverage. Issues with mechanisms for retirement. One participant comment that for hemophiliacs in particular there really isn't a mechanism for early retirement other than disability. And then there are complications from treatments that are still major concerns for some of our participants.

MS. LIPSCOMB: Thank you. Is there anything that's been said that gave our panel any questions that they want to ask? Stephanie?

DR. OMOKARO: I'm curious as to some ways that you cope or deal with some of your symptoms aside from treatment? What are some things that are helping? I was very interested to hear that it's not always just pain. You can sense tingling before you see a bleed. There are ways that you sense bleeds, but what are some ways that you're sort of coping or helping these symptoms that are not related to treatment?

MS. WILKES: I'll answer that. We keep a 20-pound bag of ice in our freezer at all times. Ice is a huge friend, and there is some controversy among our physical therapy friends in the hemophiliac community of whether or not that's best. But I'm kind of of the opinion, if it ain't broke, don't fix it. And it works for us. So ice is a huge help for us. And, in fact, it's oftentimes the first thing we turn to in times of pain more so than medication.

MS. LIPSCOMB: Thanks.

MR. CURTIS: Yeah. Ask how many hemophiliacs in here use Celebrex or something like Celebrex.

MS. LIPSCOMB: And there they go. Anybody else?

MR. LONG: Since Paul Brayshaw hasn't raised his hand -- he's more of a physical fitness fanatic than I am -- exercise, exercise, exercise to the extent you can. A lot of people have taken up swimming. I do the bicycle because my body won't let me run anymore. And bicycle is very, very common among hemophiliacs as a form of exercise. But exercise is extremely important. It helps you in general. It's just better for your overall physiology and helps with the bleeds, as soon as you can get away from the injury.

MR. BRAYSHAW: Thank you. And thanks, Steve, for mentioning that. I definitely find exercise to be a good alternative to the joint pain and trying to maintain the strength of the muscles that protect the joints has been a big

part of my life. Stretching has also been a huge piece, too, and I think just trying to maintain the range of motion helps keep the mobility and the joint functional. So it's very important.

MS. LIPSCOMB: Okay, thanks. Paul, did you have a question?

DR. MINTZ: Yes. The textbooks tell us that stress can be related to bleeding, and I'm wondering if the experience here in the room bears that out or not.

MS. WILKES: I'll chime in again first. There's going to be a bleed on a holiday. There's going to be bleeds at 5 o'clock on Friday night. There's going to be bleeds around back to school. I mean, there's almost some that you just know are coming. And I think it's in high part to stress.

MS. LIPSCOMB: Thanks.

MS. HAUGSTAD: Can I change topics now? Hello, everyone. My name is Kimberly Haugstad.

I'm with Hemophilia Federation of America. I also have a 12-year-old son with severe hemophilia.

And just to play on what Paul said, and maybe it's relevant, my son does actively engage in a sporting activity. He does taekwondo, and he has since kindergarten. We actually enrolled him because the discipline was important. He's a pretty dominant little guy. We were hoping that would help. He also was incredibly awkward and we were seeing an awful lot of issues with him and were worried about him being physically challenged by his awkwardness. I hope this isn't recorded and he reads it later.

MS. LIPSCOMB: Oops.

MS. HAUGSTAD: We have found -- yeah, I know. We have found that he has experienced several bleeds from doing the activity of taekwondo. He's gotten a thigh bleed. He's gotten a wrist bleed, several finger bleeds. However, over the years that he has been doing taekwondo, because his balance and his general health and just his physical fitness has been so ingrained, I'm absolutely, absolutely convinced that he has avoided many, many, many, many bleeds.

But it's a tough thing to really say. I mean, we know that we've gotten bleeds because of taekwondo, but I don't have evidence to suggest that that strength has prevented it, but I'm certain it has.

MS. LIPSCOMB: Thank you. I see a couple hands up so I want to take a little bit of time to answer, let you speak, but I will say we're getting very close to the wrapping up time before we go to lunch, and I know you all do not want to miss lunch. Or maybe that's me.

MS. PORTER: I just want to answer the question of what else, you know, besides just clotting factor for treating bleeds. Again, I'm coming from the inhibitor perspective, so it's a little bit different. But we have found that a surgical procedure is necessary most of the time. Once we develop a target joint, the bypassing therapies really aren't effective at that point to control bleeding, and we have had to resort to synovectomies.

MS. LIPSCOMB: Thank you. Go ahead.

MR. BRAYSHAW: I just want to make a comment on the stress-induced bleeding. I guess it piggybacks on something we talked about earlier, but it's definitely a common experience for me. And I also find just the arthritic pain creates stress. You know, not being able to walk and having that pain throughout the morning or until my ankles loosen up. But I think that that in and of itself creates some anxiety that I'm going to bleed worse and I usually end up doing just that. So I think that kind of all is part of that same cascade.

MS. LIPSCOMB: Okay. Thank you. Does anybody who has not spoken want to say something? All right. We're going to go to both of you.

Start with you.

MR. TEMPLIN: Yeah, I find if I get all stressed out I start to bleed a little bit more in the neck, because the neck muscles get all tight and tense.

Sort of complementary medicine other than a factor, TENS units, compounded pain creams

with ketamine. I live on a farm so I've got a lot of access to veterinary- type medications, so like horse liniments and stuff like that seem to work, and you can buy a lot of that stuff at the farm supply store. But aqua therapy, that's something the insurance wouldn't want to pay for but I did it. And how do you do aqua therapy on your head? I learned how to scuba dive so I can sit at the bottom of the pool and actually stretch my neck a lot better than the chiropractor could, which saved me a lot of having to additionally infuse by going to the chiropractor. So physical therapy worked as well, but aqua therapy was really the key. And I took the initiative to learn how to scuba dive so I could go under the water.

MS. LIPSCOMB: Thank you. Go ahead.

MR. SHULDINER: There was a comment earlier about receiving Factor VIII when you were Factor IX deficient. Do you have any ideas about ways that that could be addressed? Is there something that could be done with maybe product labeling that would help the physician understand

that better? Just a general question.

MS. LIPSCOMB: Thank you.

MR. SHULDINER: That's actually a comment I was going to make, which is I can't tell you how much I appreciate the fact that this event is occurring and that you are being respectful to the folks that deal with the issues every day.

What is problematic that you hear with so many of these stories is there's a lack of trust from the professionals to the folks that actually have the disease. And if there is any way -- and I don't know how this is even physically possible -- but when you hear about a gentleman dying because they didn't get their medicine when they know full well they should do their medicine, when you hear about mislabeling when they could have just said I know that I'm Factor VIII or Factor IX, or any of these other issues, if there's any way to say, look, in a community like this where you hear such articulate people, people that understand this disease so well and understand all the complications, if

there's a way that the professionals that are here to support us can trust the patient, trust the families, so many things would be better for all of us.

MS. LIPSCOMB: Thank you.

MR. SKINNER: I could respond to Jonathan's specific question.

MS. LIPSCOMB: Okay.

MR. SKINNER: There has been some work done to actually suggest moving away from Roman numerals to Cardinal numerals, that the VIII and the IX can be very confusing, and if people aren't accustomed to working in those numbers, to either look at treatment for hemophilia A, treatment for hemophilia B, or use the Cardinal numbers versus Roman numerals, that that might eliminate some of the medication errors when they're prescribing.

MS. LIPSCOMB: Thank you. Well, I think that is a good time for us to wrap up. We're going to go to lunch. We're giving you an hour. If you could come back at 12:45. There is a kiosk if you did not bring your lunch. I have heard

that sometimes it gets a little long so, but we will look forward to seeing you back here in an hour.

(Recess)

MS. LIPSCOMB: Good afternoon. If we can have people come back in and get settled down, please, so we can get started with our afternoon session?

As people are coming back in, I want to go over a couple of things. I think this morning we had a really good conversation and I think we really heard a lot of the situations that really mean a lot to you. And so we're so grateful. We do recognize that a lot of the issues faced in your community are with the healthcare industry, and people not being aware that they need that and we really understand that.

I'm not sure that there's a lot we can do at the FDA, but we certainly are going to have your comments in our report, so please take some comfort in that. I was also told to remind people that when they talk into the mic, get closer and

if we give you the microphone, if you could put it right up to your mouth, as if you're singing some Beyoncé, okay? Right up there. That's so people on the web can hear and also because this is being recorded and transcribed, it's real important for us that you state your name each and every time.

So, if I go to you six times, I need you to say your name each time -- six times. And I'd like to remind the FDA panel that I need that from you, as well.

This is the best part. I have a nice little note to myself that they told me and I have no idea what the first word is, but it has something to do with the webcast. Graham?

MR. THOMPSON: I think it was just letting people in the room know that we had around 140 people or so on the website.

MS. LIPSCOMB: It is a number, you're right. I'm like, 140? So we have 140 people on the webcast and I think we have almost 75 in the room, so this is really excellent. I also know that the purpose of this meeting is to get the

patients' perspectives, and I understand that we have people here in the audience that are approaching our patients and taking some questions and research. And I just have to say, it's not part of the FDA program, it wasn't at our request and if you do not wish to answer those questions, please fell free to say you'd rather not. So no one is going to be upset by that, okay?

So I think that begins -- do I have any other things that I was supposed to say? We do have some new panelists here with us that weren't here this morning and we're going to go ahead and have them introduce themselves. Yeah, just hit the --

DR. HAUDENSCHILD: My name is Changting Haudenschild. I'm the medical officer in the Office of Cellular Tissue and Gene Therapies here in CBER.

MS. LIPSCOMB: Great, thank you.

DR. FAULCON: And Donna, if you'd like to remind our audience if they'd like to sign up for the open --

MS. LIPSCOMB: That's right, if anyone wants to sign up for the open public comment period, so far there are slots still available. Don't all rush out there at one time, but please, that is your opportunity this afternoon to get on the docket and at that point you can really talk about things really outside the scope, if you wish. Thank you, Lisa.

All right, this afternoon we're going to be talking about your perspective about on current approaches in treating inheritable bleeding disorders. And it really is a discussion on what you're currently doing to treat your condition, and the symptoms. Do these treatments work? What are the advantages or disadvantages? What's the complications that this treatment causes? How does that affect your daily life? How has treatment changed over time and why? And what aspects of your condition are not improved by your current treatment? So this morning it was symptoms, this afternoon it's treatments.

And then, also, what treatment has the

most positive impact on you. And then also in the discussion, we're going to start again like we did this morning with panelists. This afternoon we're going to have six panelists and we're also going to ask them to talk about if they could create their ideal treatment, what it would do for them? And then, if you have an opportunity to consider participating in a clinical trial and studying experimental treatments, what things would you consider when deciding? So that's kind of the framework, that's what we're going to do and -- I just had a blank. Are we going to the polling first? No.

Okay, what I would like to do -- and I did so sloppily and I apologize -- if I could ask the panel members to come on down. We have Mark, Donald, Ben, Josephine, Kimberly and Debbie. We've got nametags there, if you could sit in that order? And what we're going to ask you guys to do is try to keep your comments to about five minutes. We understand that that could be difficult. If you go too much over you might see

a little nudge from me, but that's only because we really want to hear everyone's perspectives in this.

So we're going to go ahead and get started and, Mark, if you could start for us?

MR. ZATYRKA: My name is Mark Zatyrka. I am 33 years old. I live in Connecticut with my wife and 18-month- old twin daughters. I have severe hemophilia A and, obviously, my daughters are obligate carriers of hemophilia. Currently I'm on an anti-hemophilic recombinant factor that's plasma and albumin-free. I currently infuse intravenously on a prophylactic schedule, so for me it's every other day.

My treatment's changed over a time. When I grew up I was on on-demand therapy, instead of prophy, so I would go sometimes weeks at a time without infusing. I would either ignore bleeds or try to hide the bleeds from my parents, which I think was pretty common. And by the time I was in high school, both of my elbow joints began to lock, so I could barely straighten it past 90

degrees. This is as far as I can straighten either of my elbows.

And then by the time I was in college, my shoulders, also, began to lock. It was at that time when I switched to prophy from on-demand and by doing so, I think it prevented further damage to my joints. It also allowed me to start using my shoulders more often, but because of all the bleeding I stopped using them and my muscle strength pretty much disappeared around then.

And so, when I was worried that it was more of a joint deterioration, it was actually more of a muscle issue and so by switching to prophy I started using my shoulders more and got more strength back and got a little bit more of a range of motion back, but my elbows were far too destroyed to get any range of motion back.

The other medications associated with hemophilia that I used, besides my HIV medicine and Hep C medicine, is really just pain medicine. I've been on OxyContin, oxycodone, Celebrex, methadone, morphine sulfate, and I found that I

really got very little relief from using any of those. By having a bad bleed, most of those medicines wouldn't really touch the pain that I was having, anyways. And for the past few years I've been trying to get off of the and it's been a long process there.

The most significant disadvantages of my current treatment is the fact that I still do need to infuse every other day. The aspects of my condition that has not improved is that my current treatment doesn't do anything to reverse the damage that's already happened in my joints, so my number one goal right now in life is to be a great father to my daughters, but -- especially with twins, sometimes I have both of them at the same time -- now I'm getting more and more elbow bleeds and shoulder bleeds just by carrying my daughters. So it does sadden me to think that I might be restricted in being the best father I can be and not being able to play catch or whatever other activities I wish I could do with them.

The treatments that had the most

positive impact on my life is probably when I was able to switch to a recombinant product. Being on an recombinant product I've great confidence in the safety of the medication and to protect me against any viral transmissions. However, other risks such as inhibitor development is still a major issue that worries me. I had an inhibitor when I was younger and I feel like we still need to learn a lot more about inhibitors and how to treat them.

If I could create my ideal treatment, it would have zero risk of inhibitors, and after that I guess it depends on how ideal we're talking? If I could have a longer acting Factor VIII product where I can infuse maybe even once a month, that would great. If we're talking more ideal, a subcu would be great; a pill, an oral medication, would be great; or some type of implant that releases or creates factor into my bloodstream would be great.

However, I do also want to make a point that -- and I don't think it's crazy right now to

say this -- my ideal treatment would be to find a cure for hemophilia. I know the federal government has done a lot to help provide grants to organizations that help people with bleeding disorders, whether it's living healthier lifestyles or psychosocial issue or the treatment centers, but I do feel like we're at a point right now where we can start to invest in our community a little more. Relying on industry to cure this disease or disorder, I don't think is appropriate enough right now with little motivation knowing they'll have life-long patients on high-cost therapies. There's little motivation to actually cure this disorder.

So I think if the federal government and other resources that we have, if we could put some more investment in curing this disorder it would be great. Recently we had a pretty major breakthrough with hemophilia B, and possibly coming close to curing that. So I think we're close and I don't think it's unrealistic right now to really make that leap to finding a cure.

And then, lastly, if I had the opportunity of participating in a clinical trial, I would certainly consider doing so. The things that I would look at would be the science behind it, the potential of what the product would be offering our community, and then how my current treatment is working and whether or not this would affect that.

And so, back in the '80s and '90s, I was on several HIV clinical trials and so I'm always happy to do so in the hemophiliac community, as well, and so thanks for having me.

MS. LIPSCOMB: Thank you. Don?

MR. GOLDMAN: I'm Donald Goldman. How are you, everybody? I'll be 70 on October 10th. Over seven decades I have seen major improvements in the safety and efficacy of treatments, as well as matters of storage, volume, ease of administration, length of effectiveness. I have every confidence that my great-grandchildren will benefit for miraculous treatment advances, and perhaps even a cure.

My recommendation to the FDA is that we continue to seek improvements in all of these areas. Patients and their hemophilia treatment center, HTCs, should have access to new advances with a full understanding of their risks and benefits. Phase IV studies should be mandated on all novel treatments.

On December 21, 1991, I made a presentation to the FDA's Blood Products Advisory Committee, which was then considering the first recombinant Factor VIII product. I was told that some physicians had urged that the FDA deny approval because of potential inhibitor developments. I decided to respond.

Almost 25 years later my advice to the FDA then still applies. I explained how the first time I received a pint of whole blood was before the Korean War. Next I received plasma and then fresh frozen plasma, and each transfusion carried the risk of strange sensations, stinging, unpleasant tastes, severe hives, and the risk of hepatitis.

When I wanted to try out for Little League I had to choose between the risk of injury and the risk of feeling different from my peers. When I started using cryo, 10 bags or more at a time, sometimes the units were tinged green, almost fluorescent; a result, I was told, of the donor taking birth control pills.

When we drove to Montreal on a vacation, we had to map out an itinerary that included places to buy dry ice, so we could keep the cryo frozen on the way. We used to call some of the initial attempts to lyophilized cryo bubblegum, which related to the consistency of the product that resulted. Efforts to further purify factor were ridiculed, comparing such efforts to the Pepsodent toothpaste commercial as trying to "get the yellow out."

After an NHLBI conference entitled, "Unsolved Problems in Hemophilia," my doctor reported that there were risks of long-term usage of factor causing liver damage, kidney damage, or infectious diseases from source-paid plasma.

Those risks did not deter me because before my life had been driven by painful bleeding episodes, being bedridden, spending time in emergency rooms. Prospects for school, career, and a normal lifespan were dim.

Factor and homecare liberated me from pain, severe disability, and made life fulfilling. When AIDS first reared its ugly head, some physicians said that AIDS was not even transmitted by blood products. Others said that AIDS was no more of a problem than hepatitis B had been. And still others were fearful. Questions of factor versus cryo were ever present because the voluntary sector, which made cryo refuse to ask blood donors about high-risk behaviors.

When heat treated product first appeared some thought that it might alter the molecule and cause inhibitors. Some argue the increased cost did not justify their use. Then there were many types of heat treatment, different temperatures, different stabilizers, different time periods. Once there was a shortage of factor and I only had

two doses left at home. It was a Wednesday night of a Thanksgiving weekend and I felt the beginning of a bleed in the knee. I had to decide whether or not I should use one of my two doses that were left, when I still had four or five days of a weekend still ahead of me.

When solvent detergents and monoclonal antibody products appeared on the scene, they seemed to be better choices, but I also remember learning of seroconversions in Germany and being reminded of the risk of manufacturing errors and Red Cross snafus. I explained to the Blood Products Advisory Committee that while I did not know what choice I would make if a recombinant product were available, what I wanted was for me and my HTC to have all of the options open, so that we could choose with knowledge of all of the potential benefits and all of the risks.

That presentation was almost a quarter of a century ago. When I learned about this FDA program, I reread my 1991 statement and thought how relevant it still was. Let me bring you a

little bit up to date: Between 1992 and 2009, I continued to use factor and had two knee replacements, which enabled me to serve as a superior court judge. I enjoyed that career in presiding over a substantial criminal and civil trials. I now mediate part- time and spend time with my wife and four grandchildren and travel when possible. I'm still on homecare and use recombinant factor. My doctors recommend prophylaxis, but I'm not fully adherent and have some breakthrough bleeds, so I use about 20,000 IU a month, which costs about $250,000 a year, all paid by Medicare and supplemental coverage.

The FDA has asked me to discuss considerations that go into trying new products. Let me use Biogen's new product, Eloctate, as an example. One consideration is cost. Using over $250,000 per year, even a small co-pay is far beyond my means. Currently the product I use has no co- pay. Using factor every four days, instead of three times a week, means less wear and tear on my old faithful vein that I won't even let any of

the nurses touch. On the other hand, if I develop Parkinson's disease, finding a vein might be more difficult. In addition, longer lasting product is important when traveling on many fronts, maintaining factor levels, storage, emergencies, to name a few.

Next February I'm traveling for 16 days and every other day I need to bring 8 doses, plus 4 more for emergencies, or a total of 12. I only need to bring eight doses of longer lasting product, a quantity much more convenient for traveling. Fitting lots of factor and other medications into little carry-on bags is a challenge and a dosing schedule of once every four days would also help overcome the problem of adherents.

On the other hand, I usually follow the adage that if current treatment is doing fine, don't change. Assuming the availability of insurance coverage and my age, I'll probably switch soon, but I'm not sure I would urge the same to a young child facing a lifetime of

treatment. And other companies will soon have new, longer-lasting products which use PEGylation, rather than fusion technology. These products will be controversial. Advocates of fusion may claim that PEGylation may lead to the accumulation of large molecular weight compounds in the liver and other organs, albeit with no known consequences. Advocates of PEGylation may point to the novelty of fusion and its unknown consequences over the long-term.

While I was able to escape infection with HIV, I did not escape hepatitis-C. In 2010, a course of interferon and ribavirin left me with no benefit at all. My viral load actually increased during treatment. I developed cirrhosis, had no energy or stamina, and entered a transplant list. Then, early this year, new drugs became available. My hematologist suggested an off-label combination therapy which insurers rarely cover, particularly for expensive drug combination costing $2,000 a day, but the agreed to cover it and within 10 days my viral load was

undetectable, no other side effects appeared, and it's remained undetectable.

When relapses were reported in persons with cirrhosis, who had been "no" responders previously, my doctor wanted to continue treatment for another 12 weeks. I'm not sure what I would have done if the insurers had denied the additional $150,000 in cost, but they approved it. So no hard choice was presented. Thus, as you can see, cost is an important aspect of the balance between choices and risks. Having an effective treatment is of no importance if it's not affordable.

In my travels to Latin America, I met a young man who could hardly walk and desperately needed a knee replacement, but couldn't afford the factor needed to cover surgery.

What is important is very individual. For the child with difficult veins and a history of infections in ports, a better way of administration is key. For someone with an inhibitor, a new treatment for inhibitors is key.

For those with already damaged joints, new arthroplasty components are needed. For those who cannot afford factor, particularly in less developed countries, bio-similars offer the hope of competitive pressure to make it more affordable.

For me, with grandchildren who are carriers, an absolute cure is required. And so I conclude with the message that there will always be choices and risks in treating a complex chronic medical condition. The decision as to which choices to make and which risks to take are highly individualized and require careful consideration by collaborative discussions between patients, their families, and HTCs. While long-lasting factor has the potential to make adherents an effective prophylaxis attainable from birth, treatments advances do not stop with fresh-frozen plasma, cryoprecipitate, lyophilization, heat treatment, solvent detergents, recombinant product, fusion, or PEGylation. And it must not stop now because even incremental improvements

offer important options for persons with hemophilia today, and for generations to come.

There is no single answer. There is no one choice. There is no uniform risk. The job of the FDA, I submit, is to maximize those choices and make sure that patients at HTCs are well informed, so they can choose their risks. Thank you very much.

MS. LIPSCOMB: Thank you. Ben?

MR. SHULDINER: I have to follow that? (Laughter) And what makes it worse is that I'm a professor, so I'm just going to talk forever, so you definitely just have to throw something at me.

I'm Ben Shuldiner, hemophilia B. Again, as I said earlier, really, really happy to be here and really honored that my tax dollars are actually doing something that seems relatively important. So thank you for this and putting together this panel.

You know, there's not much more to say in terms of the history. I think everybody in this room -- many people know everything from the

fresh-frozen plasma and the whole blood to cryo, to all these things. So just to parse out what I think are probably the three biggest ones in my lifetime.

The first one, as was said before by a great man previously, was home infusion. That idea of control, right? Instead of having to go to a hospital, you could actually do the medicine at home. The power that that gave to families -- the idea of controlling your own destiny was such an important thing. Look, I'm lucky, I lived in New York. The closest hospital, I could see it from my window. Imagine if you lived in Montana or South Dakota? The closest hospital might be 14, 15, 20 hours away, so the idea of that control, home infusion, was huge and I hope what we take from that is how can we empower families to be more in control?

The second, of course, was recombinant factor. We all know the devastation that the community felt through the '80s and '90s with what was first not even seen as an issue, to what they

called GRID, because it was Gay-Related Immunodeficiency, where the hemophilia population was seen as this kind of abhorrent that were getting this disease that nobody really even understands, and so many horrible things happened in the '80s that so many of us went through.

And I have to really commend the gay community who suffered greatly through the AIDS crisis, as well, and with the hemophilia community really became, I think, an exemplar of what you can do to fight back, not only biasness and bigotry, but to fight for a population that nobody seemed to care about at that time.

And so the idea now of having recombinant factor where the medicine is really, really clean. I can't say it's 100 percent all the time, but, my god, to know that I don't know of any cases of HIV or Hep C through any of this stuff. People should be just unbelievably commended for that.

But again what's the symbolism there? The symbolism there is safety, protection, always

making sure that we can be in control of our own lives. And I think the last thing that just was approved very quickly was the long- lasting factor. Again, it's about control. So instead of having to do infusions every day, once a day, twice a day, maybe every other day, as a person with hemophilia B, the new long-lasting factors -- in essence I can take it once every week, depending on the dosage, once every 10 days. That is tremendous.

The ability, again, to be in control of my own self. I'm a terrible patient -- some of you in this room know that. I rarely listen to my doctors, in terms of taking my medicine when I'm supposed to. I'm just bad like that. I can actually do once a week. I mean, my god, and to now not have to suffer the kind of slings and arrows of the problems in my joints as much as I used to, it's really been tremendous.

And so, those three things -- you can see the history of what that meant. The family's in control, the family's feeling safe, and now the

individual's saying, I can really control this disease.

And then, kind of skipping around a little bit in terms of the ideal moving forward, how is the ideal not a cure? It's as simple as that. And with hemophilia B we're really close. The St. Jude's study is looking really good. The new stuff out of the technology that came out of North Carolina looks really good.

To jump to number 3, I am going -- what would consider participating in a clinical trial? That they could cure me from hemophilia? I'll sign up for that. Like, I'm pretty good there and so I am looking forward to enrolling as quickly as I possibly can to the new gene therapy trials that are showing incredible results, creating 20 percent, 30 percent, 40 percent of factor. As I said, I can kind of go on and on.

So in terms of ideal treatment, look, subcu would be fantastic, a pill would be fantastic, inhaling would be fantastic, but let's keep the eyes on the prize. Let's cure this

thing. And if we can figure out a way to really support gene therapy, I think we've got something.

And then, lastly, the stuff that's kind of not hemophilia E related, but is part of our community, you can't go into a room of somebody who has hemophilia who's over 30 and not see somebody that had hepatitis C. Hepatitis C is a huge issue, of course, in the community. And the fact that the new regiments that are coming out now not only don't have the terrible side effects that they used to, but are now having -- and people in the room can tell you better than this -- 90 percent plus clearance rates.

That's incredible. And so if the FDA can do whatever it can to get that medicine in the hands of every single person who has Hep C -- because it's one of those weird diseases where it can lay dormant for so long and then just turn on a dime and so many people don't know they have it, and this is not just the hemophilia community. But that medicine has been a real, real support for this community and the more that we can do to

get the word out there to get that medicine, and then of course to have it covered, so I don't have to pay $1,000 a day. That would be nice, too.

And then I'm certainly looking forward to questions from the panel, so thank you.

MS. LIPSCOMB: Thank you very much. Josephine?

MS. DRONEY: Hello, my name is Josephine Droney. I have von Willebrand's disease, Type 2A. I was fortunate enough to be diagnosed at birth because my father also has von Willebrand's disease. I did not have many symptoms until I was 15. I had a severe menstrual hemorrhage. I passed out, my hemoglobin was 4, and factor was not enough to control the bleeding. It was recommended to me that I undergo a hysterectomy. My parents quickly got a gynecologist on board and that recommendation was thankfully taken off the table. I was then moved to the adult hemophilia program because my bleeding had gotten so hard to handle.

As of now, I'm on hormone replacement

therapy. I've been on that since I was 15 and it's been a constant phase of adjusting and readjusting hormones to get my bleeding under control. A big symptom has been breakthrough bleeding and not being able to stop the bleeding when it needs to be stopped. Although many times when I've had a GI bleed, I've also had a severe menstrual bleeding, so I've had to have factor, but also have needed even more hormones to stop that bleeding.

So many of the therapies that I use have to be used in combination. I can't just use one therapy or else it won't work. I can't just use Hum AP, I can't just use the Amicar, I can't just use hormone therapy, they have to be used together, or else my bleeding won't be under control.

I'm very fortunate to be treated at a hemophilia treatment center with the team of my hematologist, gynecologist, and GI doctor, who are all very knowledgeable of my bleeding disorder and my history, which I think is so important.

I do wish that there was more targeted therapy toward women with bleeding disorders. I don't think that women respond quite the same as many other people who may be using the same type of therapies and I think that there needs to be more both research and trials, in terms of only women who are having issues with bleeding disorders, not just with von Willebrand's disease, but with any type of bleeding issue.

The menorrhagia has improved, but the side effects of the hormone therapy is less than desirable. Every time I go to the doctor I ask, can I please be taken off this? Every time the answer is no. And I understand why, but I would really love if there was some thing or some way I could find a therapy that did not have the side effects of the high doses of estrogen and progesterone that I experience. It does concern me for the future, in terms of fertility issues, in terms of menopause early. That has been a concern for me and my doctors, but at this point we find that the benefits of hormone therapy is

greater than any of the risks.

Another risk of me has been blood clots. When I am infusing with doctor and I have all these estrogen pills that I'm taking, it's been a great concern that I may develop a blood clot. But again, you have to weigh the risk and benefits and it's always been said that the benefits for me are more than the risks. I do also find that there needs to be longer-acting infusion agents. As I said, factor doesn't work well for me by itself. If it does work, it only works for a short period of time.

I had to get a PICC line and a port because I was infusing Q8 or Q12 with Hum AP and my veins were no longer accessible, so I was very relieved to be able to have that option of getting the implanted catheter, but it would be nice to have therapy that was a bit longer lasting than what I've found the factor to be.

I would of course consider any opportunity to participate in a clinical trial, but I would have to consider my current health

status, the benefits of the trial, and what you're trying to get out of the trial. Again, I would really love to see more therapies and more research into women with bleeding disorders and how not every woman and not every person with a bleeding disorder responds the same way and sometimes they need treatments that you may not know of yet, but hopefully you will.

MS. LIPSCOMB: Thank you so much. And now let's move to Kimberly.

MS. HAUGSTAD: Good afternoon, everyone. My name is Kimberly Haugstad and I am a person with a Factor V deficiency -- I know, a little weird -- and the mother of a son, Benny, who has severe hemophilia B and a mild Factor V deficiency. And I thank you for the opportunity to speak today.

We have no known family history of bleeding disorders in our family. I actually was undiagnosed until after my son was born in 2002, when I experienced some significant bleeding during and after his birth -- very similar to the

other stories that you've heard today, Sonji, et cetera.

The treatment for me was multiple transfusions of fresh-frozen plasma. And for me FFP is really only used as a treatment in case of trauma or surgery, and it's administered via an IV in a hospital setting, so I'm limited. There is no day to day treatment available for Factor V, however having a diagnosis has provided a huge explanation for years of prolonged, excessive menstrual bleeding, for all of the bruises and the hematomas of unknown origin. I, luckily, do not experience joint bleeding.

It is a different story for my son, however. His hemophilia is severe and his treatment is much more invasive and regular -- very similar to so many others throughout the country with severe hemophilia. As an infant, he had teeny, tiny baby veins and after several bleeding episodes as an infant, we had a PORT-A-CATH port implanted in my son at 18 months. The port remained until age eight. Prior to the

port he spent hours and days in the emergency room receiving treatment. Vein puncture in the arms, hands, feet, his heel, his head, you name it. His veins were so hard to access we would often find it required six to eight attempts before a needle successfully accessed a vein. He would scream until he passed out with fear and exhaustion.

A port enabled us to access him so much more easily and to access him at home instead of the emergency room. It truly was a change for us. We transitioned him then to regular prophylaxis treatment of recombinant factor concentrate several times a week. He does have hemophilia B, so we fluctuate between two and three times a week, depending on the schedule.

Those traumatic infusions in his first 18 months to stop bleeds did have a significant impact on my child. Evaluations by two neuropsychologists have confirmed diagnosis of both anxiety and ADHD, and the physicians feel very strongly that the trauma of those early, difficult infusions with those six to eight pokes

a time really did contribute to the development of those mental health conditions.

There have been no significant changes or advancements in treatment for my son since his birth. He has taken the same product since birth, and several new products have become available, but while they may enable him to receive a few less infusions per month, as a family we really have not viewed them as significantly different when weighed against the potential risk of making a change -- possibly developing an adverse reaction, like an allergy, or even an inhibitor -- when his current treatment basically delivers the same expected outcomes.

My son does experience breakthrough bleeding despite his prophylaxis schedule. In particular, we notice breakthrough bleeding during his growth spurts. When treated, factor concentrate does work to slow down a bleed, but almost always a week or more of daily -- or every other day -- infusions, a factor is required to resolve a bleed in a joint or a muscle. For his

more significant bleeding episodes, such as an iliopsoas muscle, he has been hospitalized and needed complete bed rest, followed by six weeks of extremely restricted movement, which is an interesting challenge in a young child.

During these incidents, factor is administered multiple times a day and then once a day for several weeks, along with oral pain medication. My son has nose bleeds daily, or multiple times per day, particularly in the spring and fall. These bleeds are not debilitating, but they are certainly disruptive. Cauterizing his nose has been discussed numerous times, but it was determined not likely to be successful for him, so we have not done so. We only use factor to control a nose bleed when it lasts more than an hour.

We incorporate infusions into our home life. And while a needle stick in a vein is not likely to be on anyone's preferred list of things to do, preparation and delivery of his factor concentrate treatment is fairly simple and takes

us 10 or 15 minutes to administer each time. Like so many families, we absolutely find the length of time factor concentrate lasts in his body has a significant impact in how we manage our daily life. Our factor schedule guides family and school activities. We schedule physical activities during the mild zone, when his factor levels are higher, or at their highest, and we schedule less rigorous activities when he is in his low zone, which we deem less risky for bleeds.

Looking ahead to what we specifically see as an ideal treatment is crystal clear and it marries what everyone else has said, the ideal is a cure. Barring that, or perhaps in the path to this cure, we look for a demonstrated safe product that would consistently maintain his factor levels in the normal or mild range for a month or more, maybe, between treatments would be nice.

Much of the current conversation and treatment revolves around achieving this factor level of 1 to 5 percent. We talk about that as if it's this ideal. It is not ideal for us. He

still bleeds at that level.

Eliminating the need for vein puncture with a subcu injection or an oral medication route, we've heard that before. Carletha mentioned it earlier, her son was interested. My son would be interested; very appealing. But regardless of the treatment method, ensuring it's safe in both the short and the long-term is paramount.

As an active person in the bleeding disorders community, a patient, and a mom, I thank you for having this meeting today and I just request that you keep asking us about our lives, our treatments, and about a better treatment for the future. Thank you for listening and thanks in advance for acting on what you hear today.

MS. LIPSCOMB: Thank you so much. Debbie?

MS. PORTER: Okay. My name is Debbie Porter. I live in Southern California and I have been part of the bleeding disorder community for over 50 years. My father had severe hemophilia A

and he passed away from complications from HIV/AIDS in 1986. I have a 20-year-old son who also has hemophilia. My son Matthew wanted to be here today, but he's just beginning his third year of college. He wanted to share with you what his life has been like with hemophilia.

He has had hundreds of bleeds and has spent a lot of time in the hospital. He has missed months from school and has received thousands of infusions of clotting factor and other medication, which are costing millions of dollars a year. He has endured numerous surgeries and years of physical therapy. He wants you to know that his biggest worry is that some day he may have a bleed that he wouldn't recover from. If Matt were here, you would see that he doesn't walk, and you might notice that he can't straighten his legs or use his arms that well. You would see the scars on his feet and knees, and a new scar on his elbow. There are scars that you wouldn't see, he has suffered a lot of pain.

My son is not your typical 20-year-old

with hemophilia. At six months of age he developed an inhibitor, an inhibitor is an immune reaction to clotting factor, antibodies inactivate the factor before it can work. We knew Matt would have hemophilia even before he was born and we consulted many hematologists about the safety of clotting factor treatment. We were not warned about inhibitors, it was a big surprise and it has affected his life and our family more than anything.

I'm grateful to have this opportunity to come here today to share my perspectives on the current treatments. There were two treatment decisions that we needed to address after the inhibitor developed. How do we treat or get rid of the inhibitor? And how could we treat bleeds?

The answer to the first question was immune tolerance therapy, or ITT. This is an attempt to overcome the antibodies to induce tolerance to clotting factor. ITT involved infusing large amounts of clotting factor daily. Matthew underwent four different attempts at

immune tolerance over 13-year period. None were successful. We have also tried various immune suppression agents. He has received prednisone, cytoxan, rituximab, and Cellasate. None of these have been very successful, either.

The second treatment challenge we had was treating bleeds. At first he received FEIBA, which sometimes worked and sometimes didn't. There were some serious bleeds that were treated with massive amounts of Factor VIII. One bleed used over a million units over a few days. He had a life threatening bleed that was treated with a porcine factor called, High 8C, which worked until he developed an inhibitor to that, as well.

In 1998, he began to receive NovoSeven, this is a recombinant Factor VII-A. We placed a lot of hope on NovoSeven, but have had inconsistent results. By the time Matt was only four years old, all the bleeding began to take a toll on his joints. He developed synovitis. He had four radio synovectomies, but continued to bleed almost constantly. By eight years old, both

of his legs were in braces and then in casts. When he was 10 years old he had open synovectomies, these were surgical procedures that removed the synovian completely.

Except for the severe pain he experienced, this was somewhat of a success. The bleeding in his knees was finally stopped, however the damage was so great by this point that he has been confined to a wheelchair ever since. For the past several years, Matt has been using the bypassing therapies FEIBA and NovoSeven in various combinations. And he uses them both prophylactically and to treat bleeds. He receives an infusion of at least one of these every single day. He has gone from having three to five bleeds per month to having only one or two, however he is still experiencing joint damage. He had another surgery on his elbow this past year.

I was also asked to speak about some of the disadvantages of these treatments. Immune tolerance is an intensive and expensive therapy. It usually requires the placement of an internal

venous access device. These catheters come with risk and complication and require additional care. We had as many problems from the catheters as we were having from the bleeds. ITT was very demanding. We basically scheduled our life around giving him fusions. This went on for years and was really expensive.

In the first four years of Matt's life, he used over $5 million of clotting factor. We lost our insurance several times and struggled to find a way to get him covered. His inhibitor would fluctuate, but never went away. ITT is not successful in approximately 30 percent of inhibitor patients.

Next I will talk a little bit about the bypassing agents, FEIBA and NovoSeven. We are very grateful to have these products, but they cannot be considered a substitute for clotting factor. They do not work the same way. They have very short half-lives and need to be given often, sometimes as frequently as every two hours. It usually takes multiple doses to stop a bleed and

rebleeds are common. There are no laboratory tests to titrate dosing or to determine if treatment is effective. The have serious thrombosis risk if used too frequently or in too high a dosage, or in combination with other types of medications.

My son almost died from a blood clot. This is the last thing you really would expect from someone with severe hemophilia. The cost of these medications is also very high. My son's FEIBA is currently costing $1 million per year, and his NovoSeven is costing $5 million per year. His lifetime cost to date for medications alone is $65 million. These costs seem almost unbelievable and may be unsustainable. We anticipate Matt's cost to continue in the $6 million per year range unless something can be done to overcome his inhibitor or treat his bleeds more effectively.

I wanted to come here today and tell you about inhibitors because they are a serious problem. They are affecting many people and the cost associated with treatment are enormous. The

World Federation of Hemophilia has identified inhibitor development as the number one safety issue associated with hemophilia treatment, even over pathogen transmission.

Studies of people with hemophilia have revealed that the morbidity and mortality of those with inhibitors are greater and the quality of life is less. When we are contemplating new treatments, I hope we address inhibitors. You have heard several stories here today from parents with children with an inhibitor. These are difficult stories to tell and, hopefully, for you to hear. We need better products, and not just different versions of the same treatments. We need more effective ways to induce tolerance.

ITT in the current form is not the answer. We need stronger warnings and more detailed product labeling to make informed treatment decisions. We also need much better surveillance. Currently, we don't really know how many people get inhibitors, or if some products might have higher risks. A recent study in Europe

revealed the inhibitor rate in previously untreated severe hemophilia A patients is 32 percent. Think about it. One out of every three patients. Is this acceptable?

The risk in some patients seems to be even higher, but we are doing very little to try to modify treatments to prevent inhibitors. The FDA held a workshop on inhibitors in 2003, the EMA held a similar meeting in 2006. Many additional studies have been called for that will take years to complete. I think maybe we need some new approaches.

What if we set a goal to eliminate inhibitors within the next 10 years? If we work together and look for solutions, I believe they can be found. Only then will we all be able to participate in the dream of a better future.

MS. LIPSCOMB: Thank you. Well, let's give a round of applause, these are -- thank you guys for your stories. (Applause) We do have someone on the phone. Operator, is Linda on the phone?

OPERATOR: Yes, her line is open.

MS. LIPSCOMB: Linda?

MS. WRIGHT: Hi, I'm Linda Wright and I was born in 1949, which makes me 65 years old, with (inaudible) anemia. I was diagnosed at the age of two and part because, being a woman, no one considered that I might have a bleeding disorder and in part because, as I heard today, there are only 200 of us. And so, back in 1950, it was very rare. Not many of these cases had been actually diagnosed.

I began using fibrinogen concentrate almost immediately after I was diagnosed. It was readily available in maternity wards at that time and I used that product very cautiously. My hematologist at the time, who was Dr. William Danocheck, advised very early on that blood products were not safe and were only to be used in life-threatening experiences. And so, following that advice, of course, I had a number of joint bleeds and things that led to later arthropathy and certainly was, in some ways, easier for my

parents to marriage because it's also time when sex role stereotypes were playing to my advantage and I wasn't eager to play baseball or sports. I was quite happy to do things like read and sew and do projects that were considered more for little girls.

Somewhere in my young adulthood, and I'm unclear about when this happened. It was a long time ago, but fibrinogen concentrate was no longer available and I began using cryo. Also, at that point in time, I was 12 years old when I had my first menstrual period, which lasted 8 days and was extremely heavy and the doctor who was helping me through that said that that was normal.

It might have been normal, but two weeks later I had a stabbing pain which took three days for anyone to recognize as a bleed and it turned out to be an ovarian cyst that had ruptured. That became much more of an issue for me until I reach about the age of 20, when in fact I was able to take birth control medication. Again, that was when those medications were somewhat restricted

and very new.

At that point, as a young adult, I went to college, I was active for quite some time after college with the Hemophilia Association in New England. I was president of the New England Hemophilia Association. Again, because there were only 200 people internationally with (inaudible) I couldn't easily start my own group, so I became involved with the National Hemophilia Foundation. I learned a great deal and today I've had a real refresher on that. I thought I wasn't going to stay on the call for very long, but I've been intrigued to hear the discussion and it makes me feel like a part of the community again.

The 1980s were a very difficult time and at that point I was the Region 1 representative on the board for the National Hemophilia Foundation and as people began to die and the mystery developed, so many of us were absolutely devastated by watching our friends one at a time be struck with HIV.

I, on the other hand, was particularly

lucky. I had not had a doctor who followed the then very much en vogue motto, which was "in doubt, infuse" and after getting my master's degree I had taken a job and I remember quite clearly tripping on a stair and landing very hard on one of my knees and calling my hematologist and saying, I need to get infused and he said, not until I find out what's happening, honey.

And he said, go back to ice, go back to bed rest, I don't want to hear it. So I certainly have knee damage and that, but I did not encounter HIV and I think I owe that physician that debt. After that, when the HIV became identified, it was possible for it to be tested in blood donations. I used FFP for a while, but again the volume of both the cryo and FFP included a lot of things that I did not need, I only needed the fibrinogen.

So I was overjoyed when RiaSTAP became available and have been using that pretty much successfully ever since and so would like to give a shout out to Behring at this point. It seems to be very effective. Certainly the known

carcinogens have been taken care of, but there's always the issue of the unknown and that probably is one of my biggest fears; so that a non-blood-based product would be a much safer product and I would look forward to that.

Also, I would say that the dosage appears to be somewhat in debate and my hematologist has been in contact with people who have been doing research and discovered that despite what I'd come to believe, thrombosis is an issue for people with a fibrinogen whether or not they have been recently infused, so prior to that I believed that it had to do with the amount of dosage or the use of fibrinogen product, and it apparently is not.

Of the 200 people that were mentioned, I must know at least 20 of them now, thanks to the Internet. And we have an international online community that shares information and has been useful to so many of us. And I would say that, in terms of the ideal product, I would have to rate safety number one, although certainly

effectiveness is now a given with RiaSTAP, but I don't want to certainly take a step back from that. And the time for administration, at this point I do have a PORT-A-CATH, which I only got this year and I was doing it as long as I possibly could and so when I go into the infusion sector, which is in the cancer center at my local hospital, I get -- really, it's a three-hour afternoon for me to get infused because it's an hour to mix the product, an hour to administer the product, and a half an hour either side to access port and do whatever other things need to be done.

MS. LIPSCOMB: Linda, can you summarize your comments? We're running a little behind.

LINDA: Sure, I think I pretty much have, except that the only thing I have not addressed is my interest in participating with a trial. And at this point, I would like to say, "never say never," but I think that given the experience that I had with both PEGylated interferon and ribavirin, and then more recently Sovaldi and Olysio have taught me a very hard

lesson and have not only not been effective, but have put me backward, in terms of my HVB.

So I would have to be strongly convinced to participate in a drug trial. And that's the sum of my remarks. Thank you very much for inviting me.

MS. LIPSCOMB: Thank you so much for calling, Linda, we appreciate it.

Not surprising, we got a little behind because we were on time this morning, so what we're going to do is we're going to go straight to the polling questions because if you had too much for lunch, I want to make sure that I keep you awake. So normally I'd have you stand up, sit down, and do the Hokey Pokey, but I think we'll just do some polling questions. So, if we could go to the first polling question, please?

Great. Name one therapy used to manage you or your loved one's bleeding disorder in the past year: A, factor replacement therapies; B, platelet transfusion; C, DDAVP; D, clot stabilizing medications; E, hormone replacement

therapy?

MS. PORTER: Can I just say it would have been nice if you'd had bypassing therapy on there, because I can't vote for any of those.

MS. LIPSCOMB: We understand that. Full disclosure, I'm with the training group and the system we have only allows five, so it was originally in there, so they were eliminating it. So my next question will be, let's talk about others. So we reckon in that. If we could see the results of that, please?

Oh, well, 96 percent in factor replacement and 4 percent hormone. How does that shape up on the web? Very similar?

MR. SINGH: Very similar. Factor replacement is percent.

MS. LIPSCOMB: Okay. Can we get to the next one? If you or your loved one were being treated with factor replacement therapy, what is the current regimen?

Okay, let's get those. Okay, 55 percent routine prophylaxis. What do we have on the web?

MR. SINGH: We have on-demand therapy at 22, routine prophylaxis at 23, and both at 55.

MS. LIPSCOMB: Okay. What's our next one? If you or your loved one were treated with routine prophylaxis, how often do you receive replacement therapy: A, 2 to 3 times per week; B, once weekly; C, once every 2 weeks; or D, more than 3 times per week?

That's two to three times per week and more than three times per week? What about the web?

MR. SINGH: On the web very similar, 2 to 3 times a week is at 69 percent and more than 3 times is 23 percent.

MS. LIPSCOMB: Thank you. So which one of the following best describes how you or your loved one feel about your current treatment regimen: A, I'm satisfied with my current treatment regimen and do not want to change it; B, I'm satisfied with my current treatment regimen, but I am willing to consider new options; C, I am not satisfied?

Okay, it's kind of split between satisfied, but willing to consider and not satisfied. What about the web?

MR. SINGH: On the web the highest is the not satisfied at 50 percent, satisfied but willing to consider new options are at 34 percent.

MS. LIPSCOMB: Okay. Thank you. Let's follow up with those questions a little bit and find out more about your experience with that. For those of you who have recently changed you regimen, can you describe why you did this? Don't forget to state your name.

MR. CHADD: I'm Braiden Chadd. I'm hemophilia A moderate to severe. I recently changed my regimen because I shifted to one of the longer lasting products and it has actually been a really positive thing for me because I went from factoring three to four times a week to, now, two.

And -- I believe that answers your question, actually. (Laughter)

MS. LIPSCOMB: Very well, too. Thank you. Anybody -- okay?

MR. CURTIS: So once again, I'm Randy Curtis, and I have severe A. And I've gone to more of a modified Dutch protocol and I do a low-dose prophylaxis every four days. I'm only 1,000 units, and that's worked for me for the last 10 years and I don't bleed.

MS. LIPSCOMB: Okay, thank you. Is there anybody on the web? Any comments?

DR. FAULCON: We have one participant that commented that he was previously satisfied with his on- demand therapy, but as more information became available and he did some research, he realized he was actually bleeding more often than those that were on routine prophylaxis and so he switched his therapy to prophylaxis for that reason.

MS. LIPSCOMB: Great, thank you.

MR. TEMPLIN: Hi, Chris Templin here. What scares me is I'm on a product that I like because it works well and it has a long history -- 20-some-year history -- through the clinical trial and out on the market. What scares me is the fact

that there is this longer lasting product that somehow somebody's going to make a decision that it's cheaper for me to be on the longer lasting product then on the current therapy that I'm on, and I'm going to be switched over and something could happen.

I believe that if it's not broke, don't fix it. So I think the more these longer lasting products are out there, we'll learn from them, but the products that have been out on the market for so long have that history of safety and efficacy and I think maybe a Phase IV study would be really nice, such as Donald had alluded to earlier, to really keep an eye on these products so that if there is a problem it sends up red flags and fireworks and somebody catches it and stops it before it becomes a bigger problem.

MS. LIPSCOMB: Thank you.

MS. CESTA: Hi, I'm Jeanette, von Willebrand's, my three children are von Willebrand's. On this question, have we recently changed treatments? That is a life-long ongoing

project, it seems, especially with von Willebrand's and especially with the bleeding events surrounding the reproductive cycle.

It took me years to find something that worked for myself and it ended up in infusing every month, with my cycle. And now I have two teenage daughters and due to the risks of taking plasma-based products, the cost, all the things we all know about factor, they're now beginning that cycle of trying birth control pills, trying Lysteda, trying Stymate, you know, trying all the different options and weighing out all of the side effects, as Josephine was saying earlier. And it's a very long process to go through, so we're constantly changing and finding even that as more information becomes available, as more is known about VWD and our experiences, we're not even responsive in a couple of cases to Stymate, which two of the people in my family have been using, thinking it works and wondering why it didn't seem to be working.

So there's a lot of juggling

medications, trying to find something. We had a life-threatening side effect to Stymate that took one of them off of that, which I wish we'd had more education about. So there's a lot of medication changes, hoping.

MS. LIPSCOMB: Okay, great. Thank you.

MS. ORAM: I'm Diana and I am the parent of a seven-year-old with severe hemophilia A and we haven't started the longer-acting factor, but we are next week. And so I thought that I would comment to you guys -- and it's related to what you just said about having choices -- that we have the opposite opinion of you, that we're very interested in doing things that might help our son, as he gets older, comply. Some of the things you mentioned about how much easier it is as a young man to deal with longer- acting factors.

But I can completely understand that if you're an adult and you're happy with your current regimen, that the idea of having the choice as a patient to decided what's best and what risks you're willing to take on is very important.

MS. LIPSCOMB: Okay, can we go to the web?

DR. FAULCON: So we had two participants who talked about needing to switch to bypassing agents. There was another participant who talked about her son, who developed an inhibitor, and still has breakthrough bleeding. And another participant talks about being afraid of trying new treatments because of previous inhibitors.

MS. LIPSCOMB: Okay. Do we have any patients with rare bleeding disorders like Factor VIII, Factor X?

DR. JAIN: Factor XIII.

MS. LIPSCOMB: A Factor XIII? I think we've just figured out the problem with marketing. Anyone who wants to speak? Okay. Anyone on the web?

All right. Well, that kind of leads us into the question about improvement in therapy. How could your medications be improved and what would you look for in your ideal medication?

MR. BOND: Dan Bond. I have something

that's not really a medication improvement, but a labeling improvement that you guys can do. The package inserts talk about dosing and a lot of physicians take that as gospel. If you could make it a little more vague -- (Laughter) -- so that they understand that these are just recommendations and not cast in stone rules?

MR. WILKES: Sonji Wilkes. I would say from the inhibitor prospective, with only having two products to really choose from, you're kind of damned if you do, damned if you don't because one is small dose, but very frequent infusions. The other is very high volume and, for us, over very long period of time because we have found that a slower infusion rate means less side effects. So it's either lots of infusions a day or one really long infusion each day, or twice a day.

MR. THOMPSON: We have a couple of people on the phone waiting to speak, so, Operator, can you open up Alana's line?

OPERATOR: Yes. Alana, your line is now open.

ALANA: Thank you very much, thank you for giving me the opportunity to speak. I just want to give a quick background, I am a mother to a young child. My son is 3 years old and he was diagnosed at birth, but didn't have his first bleed until he was 26 months old. After just nine infusions of recombinant product, he developed an inhibitor. I wasn't warned. We weren't told that this was a possibility.

It was an overnight change. He went from having one or two bleeds to having, over a four month period, five bleeds into the same joint in one month. We were told by his hematologist to try the (inaudible) products, NovoSeven. It didn't work. He just kept bleeding into that joint.

We were fortunate to have a home health nurse come and infuse him, even though the product wasn't working. We switched and FEIBA did work for him, but the nurse started losing his veins and was traumatized and a port was placed rather quickly. Everything just spiraled out of control.

I couldn't work any longer, it was a huge financial strain for our family.

I still don't know why this occurred. Nobody does. Nobody knows why this happened. We were just told, here's your diagnosis. He has the inhibitor, let's try a immune tolerance when his levels get to the point where he's able to -- under 10 Bethesda units.

I'm told that immune tolerance is about 70 percent effective. In my opinion, that's not successful enough. Why don't we know what causes inhibitors? Why are there no warnings for newer parents? After just nine infusions, you can hardly process the fact that your child has hemophilia and all of a sudden you have something more serious to deal with.

While we were waiting to start immune tolerance, my son started using FEIBA, which thankfully and luckily did work for him. It mostly worked. He's had one breakthrough bleed, FEIBA didn't work in that case and NovoSeven did, thank god.

We started immune tolerance one month ago and my son is responding to a plasma product, not a recombinant product. And there's a theory that perhaps my son, he didn't respond well to the recombinant product and that my have caused his inhibitor. It's a theory at this point. Perhaps the product was a mismatch for him.

I think personally there needs to be more research into whether products themselves can be matched more ideally to specific patients. I think we need to know why these inhibitors are developing at such an alarming rate, one- third of patients. This is a huge burden for us to bear and I really do thank you for taking the time to listen to us.

MS. LIPSCOMB: Well, thank you. Do we have another call on the line?

OPERATOR: Yes, Justin, your line is now open.

JUSTIN: Thanks, this is sort of, I guess, going off of what Alana just said. I think that when we begin to look at one-third of the

community being infected by an inhibitor, through understanding why that occurs -- and kind of going off what Debbie said too, I think we can also look at how maybe those numbers are little skewed, based on the population. I think we can look at non-Caucasian communities being highly more impacted by these inhibitors and I think when you look at new technologies and new treatments, we might start thinking about individualized medicine and how potentially the cell lines that are being used to create these products sort of perpetuate a kind of institutionalized racism when we're talking about inhibitor development in our community.

MS. LIPSCOMB: Well, I'm not sure he was done, but I think he got cut off, but thank you for your comment. We have someone who's been waiting very patiently.

MR. WICK: Hi, I'm Colin Wick. I'm 19 years old and severe hemophilia A. And on the topic of longer acting and wanting that, I'm a college student and I was one of the first groups

of hemophiliacs to exclusively use recombinant products to -- that's my treatment for hemophilia.

Luckily, I've never had an inhibitor, but I've never switched drugs, I've been using the same one since I was an infant. And we've been discussing, with my mom and my stepdad, we've been discussing switching drugs, but at the same time the risk of maybe not being able to get to class because I have to deal with an inhibitor and I can't walk or something like that. That risk outweighs the benefits.

I'm a little bit irresponsible in that I do forget to infuse; not often, but regularly. And that's probably a thing that's going to be starting to come up for younger hemophiliacs because we don't know what it's like to long- term not infuse and feel that pain in the joints, and the swelling, and things. We just know that I infuse and it's fine, so if I'm not hurting the what is the problem?

So today's one of the first days I've been able to walk confidently without knowing my

knee would be in pain because two weeks ago, I played soccer and had knee-to-knee contact and I've been trying to judiciously work at it, but I feel like a longer-acting thing would just take the edge off a little bit because if I forget to do it one day, then maybe it's not a big issue.

MS. LIPSCOMB: Thank you for that. I can barely remember to take my thyroid medicine, I can't imagine. All right?

MR. TEMPLIN: That's a real big question. Chris Templin here. That's a real big question, what my idea of treatment would be. A cure would be nice, but what are the ramifications two, three, four generations down the road to that cure if I was to get a cure and procreate.

I guess my biggest thing is just leave the treatment for me. I currently would just take the product that I'm taking now and infuse two to three times a week, as needed. Between them prophy treatments. But if these new longer lasting products come out, will that product that I take now that's been on the market for 20 years

still be around?

And that's what scares me. Will the manufacturer make another product, a longer lasting product, and then this product that you now take every other day or every three days is gone. And will the other manufacturers stop making the current products that they make because I have my opinion, you have your opinion, I value your opinion, you value my opinion, and that's the way it should be and I'm glad that your child would be able to infuse once every 10 days or maybe once every 2 weeks.

Hemophilia's become such a part of my life. I don't complain about having to infuse, I just wake up in the morning, take a shower, get dressed, infuse and go about my day. Well, on the days that I infuse, and when I travel I take it with me and hope that if there's an accident, somebody grabs the bag when they take me off to the hospital or they have to go find the car in the impound lot to get it.

It just worries me that these

manufacturers, and I'll talk to the manufacturers that are in the room -- I know the manufacturer of the product that I'm on are in the room. I just hope that you don't take that product off the market, if you create something new and long lasting because I'm not really -- I don't like change. Other than having children and getting married, I don't really like change, so same old, same old, but leave those products on the market.

MS. LIPSCOMB: Thank you, Christopher. We appreciate that. So we're still looking a little bit for what you would see in an ideal medication? Does anyone else have something that they'd like to add?

MS. CHADD: This is Wendie Chadd. I think we all have established that the ideal medication is going to be pertain to -- someone with an inhibitor's going to have a different opinion about that because that's going to be what's ideal for them.

Ideal in our situation, having a 45-year-old brother and myself, as well as my

18-year-old son, really looking for the longer acting medications to be extended even longer. Of course, a cure is going to be amazing, but having a college student son that runs for his college, that's an athlete, that does everything he can to keep his body in line, sometimes his body does not cooperate.

So having something that would be extending even longer would definitely not only give him a better quality of life, but give his mom a lot more peace of mind. Thank you.

MS. LIPSCOMB: Thank you.

MR. PEZZILLO: Yeah, just to echo that, I know that we're talking about a cure, but one thing that we haven't seen is, how can a patient living with an active bleeding disorder have more of a maintained lifestyle? And we see these different treatments that are coming out on different products, but, for example, my half-life fluctuates from 6 hours to 3 hours to 10 hours and there's no way of knowing, besides going to the hemophilia treatment center, which is time there,

time spent for pre, a post, 12 hours, 24 hours, and coming back.

It would be ideal, like a diabetic, to be able to take a sample of blood at home and to see where factor levels are because I know, in my case, if my factor levels are below 10 percent, I'm probably going to infuse more before I decide to do anything else because I could think that maybe the higher than 10 percent, because of the average.

But the reality is, most patients of hemophilia probably having these trough studies once or twice a year, if not less than that. So I think if a patient could be empowered to be able to do this test at home, I think that that would be in the best interest for patients, besides coming out with more products that are pretty much the same thing.

MS. LIPSCOMB: Thank you for that.

MR. LONG: Going slightly forward from this to the successful treatment that we're now seeing for Hep C, thanks to Paul and Mark, in

particular, who are phenomenal advocates to get hemophiliacs into our own clinical trial.

HIV is showing hints of having a cure, probably years down the line, but they're beginning to show the first signs they'll be able to cure it. I think our success, which we will have with the Hep C trials, with hemophiliacs is very knowledgeable and compliant patients. We are an excellent population to test your drugs. So please, when HIV comes along and it comes to clinical trials, get us in early, please.

MS. LIPSCOMB: Thank you. Okay, we have a couple more hands?

MR. SMOAK: I just wanted to address -- I think this might be a revisiting of some of them, but I do think that talking about treatment, we've been pretty product- specific, but I think in terms of education I think sometimes better transparency or access to trial and study results, especially we could throw in the inhibitors there. But I think sometimes this information is difficult to get and I think other times it's

published in journals and magazines that are either cost prohibitive or not really being disseminated to an audience for understanding.

And in line with that, I think, too, with the treatment centers and the hematologists that we use, sometimes the disseminate information on the products they favor, or we don't get all of the information that we need. And there isn't a thorough discussion of the pros and cons of these different kinds of therapies, so I think having more informed product discussions in our treatment centers, "treatment" being the operative word there.

MS. LIPSCOMB: Okay, great. Thank you. We have time for one more comment before we go to our next -- who wanted to say?

MR. SKINNER: I was going to build on Rich's comment about -- oh, sorry, Mark Skinner. I was going to build on Rich's comment and I know you're from CBER, but the medical devices -- and I think part of what Rich was referring to -- I think could be a huge potential to empower

patients. Mobile technology that allows me, as a patient, to just look at my iPhone or look at my Google watch and it tells me what my factor level is at any given time of day.

We've been accustomed, because there's only been one type of therapy out there for hemophilia, to what the factor level is? Now that there's multiple levels, we really need the FDA to advance quickly to move those mobile technologies and not just limit them to the clinician's hands, where I think they're starting, but to actually let them get into the patient's hands so they can monitor and learn to adjust their therapy on their own.

And my theory is that there's going to be a buffer in between when they get us -- and I don't think we're any less sophisticated than the diabetic population -- that we can learn to adjust on a real time basis our own disease.

MS. LIPSCOMB: Okay, thank you. Let me just have him go one more time and then I promise you I'll go to the next topic.

MR. CHADD: Braiden Chadd. I think in an ideal treatment for me, being someone with Factor VIII, I've a lot of options open, short and long-lasting. I think something big for me would be able to see advancements in treatment of people with inhibitors or Factor V or Factor X and XIII because with Factor VIII and having it be one of the most common, it's a lot easier to treat and these people have bigger issues than someone like me. I can factor twice a week and live at pretty close to what would be called a normal lifestyle, being able to be a college student and do sports, and all of that.

But you see these kids and these people with inhibitors and the other factor deficiencies that don't have options and they're still stuck on what I guess you could call "old school" treatment.

MS. LIPSCOMB: Thank you. I get a chuckle out of "old school." I feel like you're talking to me directly. But that kind of leads us to another question. We're talking a lot about

what ideal treatments are, but what treatments or alternative therapies are you using, or lifestyle modifications, maybe acupuncture, diet, massage. What are you doing to help, aside from -- I think we heard a little bit earlier about things we could do for the symptoms, but was there anything not mentioned before that someone wants to talk about? Ben?

MR. SHULDINER: The one I've certainly used on and off, and I'm surprised I haven't heard more of it is just physical therapy. Physical therapy is a huge, huge help for my lack of range of motion and things like that. And certainly the more that we can do to get physical therapy as something that is used more. It really is amazing, that great study of fake knee surgery that just came out last year that said that, in essence, most of the times physical therapy is just as good as surgery in these specific cases that they used.

It's cheap, it's effective, and it really will also deal with some of the pain issues

that we do. It certainly has worked for me.

MS. LIPSCOMB: Great, thank you. Anybody else before we move on to clinical trials?

Okay, can we have the next slide. I always like to start -- back to the clickers because I think you thought you were getting away with no more, but we're going to have at least two more.

Have you or your loved one ever participated in any type of clinical trials, studying experimental treatments: A, yes; B, no; C, I'm not sure?

Okay, let's see? Okay, 57 percent have not, but percent have. What about on the web, how does that?

MR. SINGH: Very similar, 60 percent no and 27 percent yes.

MS. LIPSCOMB: Okay, let's go to our next question then, if you or your loved one had the opportunity to participate in a clinical trial to study an experimental treatment, which of the following best explains your thoughts: A, yes, it

would depend on many factors, but I'm generally willing to consider it, sign me up; B, no, I probably would not consider participating; C, maybe I'm not sure whether I would be generally willing to consider participating or not, I just don't have enough information?

Okay, can we see? Ah, so almost 70 percent of you say yes, even though it would depend, but you're generally willing, with 14 percent not thinking about it. What about on the web?

MR. SINGH: 74 percent say yes and 21 percent say maybe.

MS. LIPSCOMB: Okay. That kind of is a great segue into our next scenario. So I want you to imagine that you or your child has the opportunity to consider participating in a clinical trial for an experimental oral replacement therapy? The study is going to enroll 50 participants, the clinical study last 1 year and it's going to involve 6 clinic visits, occurring every 2 months. More common side

effects may include nausea, diarrhea, fatigue, headache, rash. Rare but more serious side effects may include bleeding, blood clots, or life threatening allergic reactions.

So think about this, what would be your thinking in this kind of trial?

MR. MONES: I just wanted to say that I don't think there's -- oh, Glenn Mones, director, New York Hemophilia Chapter. I don't think there's anything on that list that isn't already in the PI of all the existing products.

MS. LIPSCOMB: Well, thank you for that.

MR. CURTIS: So, there in the hemophilia community there's a group of us that the treaters usually referred to as the "Study Boys," that were the more compliant patients of the group and that would always sign up for every trial they had. I was one of those.

And I just got finished with 48 weeks of interferon and all of those, and even my wife and my teenage son were amazed at the past package insert for all the drugs, of which the most common

-- you know, "may cause death" was the first item on the list and even my teenage son said, you've got to be kidding me? So we're used to this, in general.

MS. LIPSCOMB: So you're telling me that the side effects don't come into your play when you're thinking about this?

MR. CURTIS: They come along with the package.

MS. LIPSCOMB: Thank you.

MS. CHADD: As a parent, if I was looking at putting my child in this study, my biggest question would be, what would be my concern about bleed. If bleeds did happen, how would we be able to get that under control? What would be the impact of his actual hemophilic disease state and the damage that could be done to the joints if they went untreated? But we would absolutely entertain it.

The side effects would not be a deterrent for us because of the Study Boys being such amazing role models, and how important

they've been to getting us to the place that we are today. We would sign up to make sure that my nephews and grandbabies would have that same privilege. Thank you.

MS. LIPSCOMB: Thank you.

MR. WILKES: Sonji Wilkes. I'm looking at it from two perspectives. I'm looking at it as me, myself, as the patient and as for my child. And for myself, no question, I would sign up. But for Thomas, and given his inhibitor status, I'd be a lot more hesitant to sign up because that child has suffered enough and I would really be concerned about the side effects. And I would be worried what more could possibly happen? That said, we need more studies that are available to inhibitor patients. There was a question earlier that asked how many studies have we participated in -- I think it was in the last year -- and, honestly, it's zero because we have not been eligible to participate in any of those studies.

MR. WICK: Hi, Colin Wick. So I have a first cousin on my mother's side and we both have

hemophilia, and we're the same age. We both have been talking about and want to participate in these studies for the new drugs coming out, but it's been hard to track that down. I'm recently an adult -- (Laughter) -- so it's like I have to get up to pace with everybody else because until recently it was mostly my mom doing all of this for me. She's not enthusiastic about me trying out drugs that have side effects, but I could deal with nausea. I could deal with issues like that if I had a faster or a more efficient treatment, or a longer treatment. That's something that I value.

MS. LIPSCOMB: Okay, I'm just going to repeat what I think I heard you say. For you, it's not knowing how to find out about the trials, is that right?

MR. WICK: Yeah.

MS. LIPSCOMB: Okay. I actually think I jumped the gun and I think if we go to the next slide I think we actually have a polling question that says -- is that the same one?

MR. SINGH: It's correct.

MS. LIPSCOMB: Oh, so that's where I jumped the gun. For this one that we just talked about, with those things, for all of you who have not yet commented, could you vote on whether, yes, you would, vote on that?

Okay, can we see what we have? Okay, 71 percent. Still very high, excellent. I think there's another polling question after that? Oh, on the web?

MR. SHULDINER: I'm sorry, I think she's motioning to me. I was just saying if, in the future, it's ever possible to differentiate some of these questions, it would be really fascinating to see some more a granual data, in the sense of, is it folks who are over 45 that are saying yes? Is it parents that are saying yes? Because what you see in this community, specifically, is you've got many of us who have done studies ever since we were little kids, to families, the parents, and I note there's only five buttons in all, but it would be nice to see that kind of data.

MS. LIPSCOMB: Well, we got hands, so how may of you who are parents would enroll your child into this clinical trial?

Okay, how many of your parents would not? Okay. Now of the people who said yes, how many of you were over 45? Is that what you wanted?

MR. SHULDINER: No, but what you saw was that it was -- I mean, who knows how scientific this is -- but you saw 50 percent yes/no amongst the parents. Then, by definition, if those numbers are right, it would be 80 to 90 percent of those with, so it's just an interesting dynamic there.

MS. LIPSCOMB: Absolutely. Thank you. Okay, can we go to the next slide? So which --

SPEAKER: There's one more plan.

MS. LIPSCOMB: Which of the following factors would rank as your most important decision as to whether to participate? So I think, the common side effects, rare but serious side effects, such as bleeding or life threatening

allergenic reaction? How the treatment might improve your health, how the trial might affect my current treatment plans, or requirements of the trial or length of the trial?

Well that is a pretty split. Rare, but serious, how the treatment would affect my current regimen and have the trial -- I forget what they were. What about on the web?

MR. SINGH: On the web, 0 percent say common side effect, rare, but serious is 37 percent. How the treatment would improve my health is 37 percent.

MS. LIPSCOMB: Okay, thank you. So when we're talking about this hypothetical or any clinical trials, is there anything else that we haven't heard that you'd like to mention?

MR. SKINNER: So I'm one of those people that answered, no, I haven't participated in the drug trials but, yes, I would like to. Because although I -- in consideration of your patient, my factor level actually sits around 2-1/2 percent, so typically I am a severe patient and I bled like

it and be characterized by it, but I'm not eligible for any of the trials. And I'm not sure there's a good, rational reason why 1 percent is typically the cutoff for the trials. And there's a range in the population that perhaps you can go to a higher percentage because those are at the low end of the factor levels. There's a group that's just plain excluded and doesn't have the opportunity.

MS. LIPSCOMB: Okay.

MR. SKINNER: I don't why there's that exclusion criteria and from conversations with some of the companies, I'm not sure they agree why it is, other than for comparison.

MS. LIPSCOMB: Okay. Anybody else? Donald?

MR. GOLDMAN: I'd just like to add that I have two connections with hemophilia. One of them being that I'm a person with hemophilia, but the other being that my granddaughters are carriers and they may have children with hemophilia. So that probably, at the age of 70

and somebody said you might have a treatment that would actually cure hemophilia, but would have a good chance of causing you to die, I'd probably go ahead and do it because my great- grandchildren are more important than I am, at this point. So it really depends on your prospective as to where you are, which goes back to what I was trying to say before.

Everything is very individualized. You really have to have -- the critical thing is to have a good family and a good treatment center and have a good collaborative discussion on all of these issues, whether it be participating in trials, switching products, every decision that you make. Whether or not you wake up in the morning and you decide whether or not you're going to take clotting factor that morning or defer it for the next day. Take it before you take an activity or not. It's a choice and a risk either way.

And I say to you, particularly, it really bothered me to hear from some of the moms.

Your children will be fine one way or the other. Every decision you make is a choice, but you're not god. You're not responsible for whether or not their hemophilia is going to cause and inhibitor or not. That's far beyond your control. Don't think that your decision as to whether or not to treat or not to treat is what is going to make that kid's life good or bad. You make the best decision that you can with the assistance of your treatment center and life has a funny way of working itself out one way or the other, whether good or bad. It's just the way things are.

MS. LIPSCOMB: All right. Do we have a question? Okay, I think -- do we have comments from the web before we go on?

DR. PORTER: We have a few comments on the web. One parent talked about her willingness to participate, however, she did not feel comfortable allowing her child to participate. Another participant talked about their concern being the serious side effects. And another participant was more focused on the health of

future generations, given that he was an older hemophiliac.

MS. LIPSCOMB: Okay, is there any calls? I don't think we have any calls. Okay, can we advance the slides?

Is there anything under treatment that you feel like we haven't mentioned or spoken about that you want to take a two minute chance to say?

MR. BRAYSHAW: Hi, Paul Brayshaw. I guess one thing that would be worth considering and maybe as you look to how trials are set up, or the inclusion or exclusion criteria. I think it's important to consider the sample sizes among rare disorders and that a lot of the information we might glean from these trials isn't going to actually be what's reproduced in real life, so I think that although we're a rare disorder -- or hemophilia, at least -- if there's ways that you can look at some of that extrapolating data to get beyond the sample size. Or, hopefully, allow companies to maybe bring in more data from other countries, or something, that allows us to get a

better sense of how the product will appear in real life.

MS. LIPSCOMB: Okay, thank you.

MR. MONES: Glenn Mones, New York City Hemophilia Chapter. There's all this discussion around decision making, around treatment regimens, and so forth. And the one thing that's come out a little bit, but I think not enough, is that there's an informed decision making, there's partially informed decision making, and there's well- informed decision making and -- allow people to make empowered and informed decisions by having the maximum amounts of information and the at least it's based on something that's meaningful to them and meaningful in the bigger picture.

A big part of the problem with what happened in the '80s is that people were not being given all the information to make informed decisions. And, to a certain extent, I think that's the same thing that's happening today and you've heard it from several of the people who spoke about issues around inhibitor development

who were not told that this was a possibility. We've heard it several times.

And why should anyone not have all the information that is currently available? What's not available is not available. Research has to be done, great. Research should be done, but why isn't every treatment center, chapter, national organization -- and I'm not saying that they don't. There's a lot of information out there, but we can do more to make sure that people have information and knowledge and are therefore able to make informed, empowered decisions.

MS. LIPSCOMB: Okay, thank you. Thank you very much. Does anyone on the panel have any questions they'd like to ask out to the audience?

DR. JAIN: The information on clinical trials, I know you're interested. It can be found at clinicaltrials.gov. So if you put in your hemophilia, you'll see all the information. Plus, you can also ask your treaters to give you that information, too.

MS. LIPSCOMB: Thank you. Mark, did you

have something you wanted to add?

MR. ZATYRKA: Yeah, I don't want to beat a dead horse here, but to speak a little more towards what Glen was just talking about. I know when I see my HIV docs, if I have a side effect, they report that back to the drug maker.

I think, especially, when it comes to inhibitor development, it would be great -- and this is like what we said about Phase IV -- why can't we make a mandate that that inhibitor is reported back and tracked, even by product, so that when we are asking physicians or patients to make an informed decision on which product to pick, we can see exactly what the inhibitor development percentage is by product, so that we can make those informed decisions?

MS. LIPSCOMB: Ben?

MR. SHULDINER: Yeah, for me I think the two really huge issues in the hemophilia community today, other than the joint damage and the HCB and the HIV is this inhibitor stuff, as well as female populations. So the inhibitor thing, I think two

things are important. One is, we have to know more. There has to be much more information known about inhibitors.

You can see the devastating effects that you've heard about in this room. I'm 37 years old. I was a Division 1 athlete. I can run, I do not have an inhibitor. If I had an inhibitor, none of that stuff was going to happen. It's a huge deal and we need to know more information. Where I think that information needs to go is as close down to the genotyping as possible.

We are starting to really differentiate, to understand the differences on a molecule level for hemophilia. What the FDA can do is to try to lead the charge for things like that.

And the second, which is a little off topic, but is important because we heard about it is, we need to stop thinking of hemophilia as purely this kind of male disease and that even the concept of a asymptomatic carrier, a symptomatic carrier -- I know there's been politics behind this for lots of reasons, but if we start just

using the term hemophilia, it allows people to walk into an emergency room and it allows people to talk to a doctor and say, look, I have hemophilia. You're a woman? Yes, I have hemophilia.

And those kinds of things allow for a better access to medicine, a better support for the community. And if we can try to address those two things -- other than all the kind of chronic stuff and a cure which, of course, that's what I'd really like -- I think we could really move the community quite forward.

MS. LIPSCOMB: Thank you. Debbie?

MS. PORTER: Yeah, just a couple of things to follow up. Obviously, we need better information on the products and I really think there is a big, big question that has gone down in this community for a very long time is whether there is a difference between the products? Especially whether there's a difference between plasma derived and recombinant products when it comes to inhibitor development.

There are studies under way, those studies have been going on for years, we have no conclusive results. Every time we get the results of some kind of study, somebody brings it into question because they say, oh, it's not statistically significant, it's not this, or whatever. I really think the information just needs to be given to the community that's there and let us make our own decisions.

I mean, really, who are we going to rely on to interpret this information? Everybody has a different opinion. Just give it to us in the raw form and let us make up our own minds about these products and what is a risk we want to take for our particular child?

The cost with this, you heard the numbers. This is crazy. We can't sustain this, we're going to have one- third of our severe patients developing inhibitors and costing millions and millions of dollars. There has to be an alternative. We have to put more priority on what that alternative is.

My other problem is in the whole design of the clinical trials. You're leaving out the most at-risk patients out of these trials. Somebody made decisions along the way that PUPs shouldn't be included in these trials for inhibitor development. Well, to me that seems a little bit crazy. You're using patients that have already proven that they're tolerant to products to test a product. You're leaving out a whole lot of patients who are at the most risk. And I understand that there's a lot of controversy over whether it's product or person, and all of that. But if you continue to leave them out of the trials completely, we cannot get full information.

MS. LIPSCOMB: Thank you so much for that. Time is getting away from us, so it's right now time for our open public comment period. And I, actually, am going to hand the microphone off to the stand.

MS. SCHARPF: Yes, so good afternoon. My name is Jennifer Scharpf. I'm with the Office of Blood Research and Review in CBER, and I would

like to extend my thanks to the panelists and all of you for sharing your experiences and perspectives with us today.

So at this point we will move on to our open public hearing portion of the meeting and I'll invite each individual who registered to make comments. Make your comments from the microphone on the right-hand side of the room here, for a maximum of about three minutes, if possible.

And please state your name and your affiliation before your remarks. So at this time I'll invite Kimberly to make your remarks. That's fine. Please, from there that's not a problem.

MS. HAUGSTAD: Great, I can do that. Hello, everyone. I'm coming at you from a little different capacity now. My name is Kimberly Haugstad. I am the executive director of the Hemophilia Federation of America. HFA serves as a patient advocate for safe, affordable, and attainable blood products for bleeding disorders patients.

I know I spoke earlier on behalf of my

son and our family, but as a community based organization, at HFA we only represent patients. So we felt it was important to make an extra statement today, strictly from HFA.

Through our high touch national programs at HFA and our patient surveys, we do collect qualitative data from a broad range of community members, many of whom do not have a voice in an arena such as this. Consequently, we have a unique perspective on which to comment on the questions posed today. We find that patients living with bleeding disorders do use a range of treatment options, including a variety of recombinant monoclonal plasma drive, as well as other alternative coping and pain management strategies, which we discussed earlier.

We do appreciate that we have access to a range of options and we worry about the future access to these options, with insurance. The use of prophylaxis treatment and the ability for patients to infuse at home are significant for the bleeding disorders community. This allows for

greater flexibility in treatment schedules and the ability to lead a more active and productive life.

Individuals who have developed inhibitors have significant and vital additional needs, as do older adults as they experience the common aging issues in tandem with their bleeding disorders. Women clearly also still are undiagnosed and underserved.

Access to multiple treatments are critical for the hemophilia community and that personalization of treatment is needed. I think you heard it today. Hemophilia treatment is simply not a one-size-fits-all. Based on anecdotal evidence, one patient might develop allergies or an inhibitor while on one product, while another patient will not. It is often reported that different products have varying levels of haemostatic efficacy. Inhibitors impact approximately 30 percent of previously untreated patients, we've heard that again and again.

So much is still unknown in our community about how or why our treatments do or do

not work. With these uncertainties, there is a need for patients to continue to have access to a variety of treatments and a need for transparent and open dialogue about any data collected on the impact of treatments.

The most critical treatment concern for members of our community is that treatments are safe. We do not forget the staggering impact of HIV and hepatitis from tainted products had on our community. This emotional impact was not only on the health of those affected, but also on the entire family unit.

Problems definitely still exist that need attention. Frankly, an inhibitor rate of 30 percent on previously untreated patients is simply not acceptable to us. Families and HFA believe in the importance of a stringent, constant, and demonstratable dedication to the safety of treatments to ensure the well-being of our community. Thank you for your time.

MS. SCHARPF: Thank you, Kimberly. Paul?

MR. BRAYSHAW: Hi, Paul Brayshaw, a consumer. I just wanted to thank you all for having the meeting today and the opportunity to share the comments. And I wanted to make some additional comments, specifically that it's hard to probably grasp all the information we've presented and come away with it thinking we can respond to each and every one of these things.

So I guess I challenge the FDA to maybe come back with things that you can do and hope that you can list some of the things that we might expect -- what we might expect from you in response to these issues. And keeping in mind that you have to recognize the patient in a holistic way and not just the fact that we depend on these therapies, but also that our lives and quality of life and day-to-day activities really get to how these products are going to be adhered to, as well as how they're going to be affordable. If we can't afford new products, then it's not going to really make a difference to have an advanced therapy that's going to improve our

quality of life, it's just going to be our of reach for us.

One point that we didn't delve into very deeply was the geographic areas of patients. The treatment centers are very limited, especially in rural settings where patients might not be able to get to a center and get access. So I guess in addition to that it's important to keep in mind that a lot depends on the state you live in as to what providers are going to be available, or paid for by your insurance company, as well as products. So that's something, too, that the quality of the benefits matter if you're in a state with a state marketplace versus a federally facilitated exchange. It's going to have an effect on what products patients might have access to.

So I guess I would encourage you to maintain some frequent communication with the patient population, specifically with the bleeding disorders because I think that all of these issues continue to evolve and it will be helpful to

maintain the dialogue going forward. And I also would really like to hear some of the things that you all think you can do to respond to the questions or issues that we've brought up today. Thank you.

MS. SCHARPF: Thank you, Paul. Shelby?

MR. SMOAK: Hey, I'm Shelby Smoak, consumer. And most of the topics that I was going to touch have been covered and I'm very glad of that and I want to thank you for your time and for listening. As Paul intimated, it's a lot to absorb, so my reiteration of what we covered today would be just the access to information.

We are a very intelligent population and we're able to easily disseminate this through our chapters and I think there is or has been a lack of getting the information and having access to it that is able for us to qualify on our own terms. I would also reiterate that the vulnerable population here are often those that aren't represented at meetings like this, and so being able to get the information to them via networks

that we've set up is a very vital thing.

So, transparency and access and the last thing that I hope that was achieved and that you started to understand is how hemophilia is the root of everything we endure. So when we're talking about all our healthcare needs, it always seems to trace itself back to hemophilia, which is why it's so critical to be on top of this and to have it treated.

So even when I go to the dentist, before the dentist can adequately treat me, we have to deal with the hemophilia. Even when I go to the orthopedist, all the problems born in the orthopedic arena for me are the nature of hemophilia. You know, even going through hepatitis C therapy and enduring treatments for liver related to the hemophilia. So I have procedures, we have to go back to the hematologist. So they are a key ingredient in all our healthcare needs. So I think that's something to recognize, how these things are very integrated and that holistic treatments -- so just treating

the bleeding disorder is one thing, but it's going to trickle over into everything else that we have and need. Thank you.

MS. SCHARPF: Thank you, Shelby. Mark, we welcome your comment? He's here.

MR. LONG: Okay, so I'm actually Steve Long. Mark had to leave early. He said that you've pretty much covered everything that he wanted to cover. And actually I've managed to get in and the others have the other things that I came here to speak about, except I want to reinforce what Don had to say about support for women.

Mother used to have these odd nosebleeds now and then, we never thought anything of it. My niece is 25 percent and has a son that's 3 percent. She is on the HFA board pushing for victory for women and those issues. I support that absolutely.

I have a cousin who we brought in because she was mentioning bleeding things, we had her get tested. It's very important that we deal

with it for women as well, with hemophilia in the classical sense, but also with von Willebrand's because that's a whole big population we have to work on. So pay attention to von Willebrands's, as well.

MS. SCHARPF: Thank you, Steve. Val?

MR. BIAS: I'm Val Bias, CEO for the National Hemophilia Foundation. I also happen to be a patient with severe Factor VIIII deficiency and all of the comorbidities, as we have spoken about today.

You've heard from many of our patients in the audience today and we have a new blood safety issue and it is what happens with inhibitors in our population. So I want to be very supportive of that. As the National Hemophilia Foundation, we're dedicated to finding cures, treatments for people with inheritable bleeding disorders. But having lived through many of these comorbidities all my life, I don't expect you to save us, but it really took for HIV, it took a conversation that all the federal agencies

had to have. And if you just write it in a report, people will just maybe not read it.

So I would encourage you when you're in a meeting with your other federal agencies, whether they'd be at NIH, who will likely hold the key to the research for inhibitors, or CDC, who will look at our demographics, or HHS, who will have some control whether we have access to new products and new treatments that you've voiced verbally.

We're all here together. I hope we're one of the largest patient groups you've gotten an opportunity to speak to. We just completed our annual meeting and our theme was, nothing about us with us. You have an army, we are here to support you. Please help us. Thank you very much for today.

MS. SCHARPF: Thank you, Val. And, Tom, would you also like to make a comment?

MR. HOWARD: I just wanted to -- this is a question. Well, I'm from Los Angeles and I'm a physician and a scientist and an entrepreneur, but

the question I was going to ask is directed toward I'll just make this quick Sonji and Deb and other parents of kids with inhibitors. If there were two products coming out that might make the lives of your kids better and easier to treat them, how would you go about deciding which one to be involved in the study with and/or use. Or, eventually, if one might be more easily to explain how it worked, but it might be a more risk of making your kids inhibitors worse and the other one might alleviate it somewhat, but not totally negate the fact that you still have to do FEIBA treatments.

And I guess, since I'm not with either of these companies -- one is this new bitypic -- biphenotypic, whatever they call it -- the antibody that can hold maybe Factor IX-A together with X in the substrate. It may bypass the need for Factor VIII inhibitors patients. And the other one being an anti-thrombin SIR that will decrease the level of an inhibitor of coagulation and therefore maybe make the extrinsic pathways

ability to generate thrombin more potent, let's say.

So how would you answer that? I was just interested in how you might decide those questions.

MR. THOMPSON: I think this is a good time to remind people that, since we're almost out of time, that we do have a public docket for questions like this, or anything you didn't get to address during the meetings, so please feel free to send your comments. They're just as important as stuff we heard here.

MS. SCHARPF: Thank you, Graham. And that concludes our open public comment period, thank you. Donna?

MS. LIPSCOMB: Well, it has been a long day and we have a heard a lot of information and I know from the perspective of the FDA, we are really grateful. And, Val, I've got to say, I wrote down your little motto and I'm going to find a way to use it, too. So thank you so much for that.

I do want to say that if you have picked up a evaluation and filled it out, please, at the end of today's meeting, drop it off. But besides saying thank you to those of you who are here and to those on the web. We just want you to know how important we find the information you give us and how much we appreciate that you've taken the time to call in, to sit with us today, to come in. And we would like to now conclude with some closing remarks from the deputy director from the Office of Blood Research Review. She talked to you earlier, Dr. Jenette Michaud.

DR. MICHAUD: Thank you. So as we close today's meeting I want to thank you all for you participation, and certainly for your valuable input. It's been a very productive conversation and we're very grateful to you for engaging in this process.

We've heard many recommendations, great insights, we've heard your experiences and you've been able to very clearly describe the burdens of your disease and the gaps in therapies and this

information will be used by FDA as we seek to facilitate advancements of new treatments when we work with manufacturers, researchers, clinicians, and others. And it will help in the design of clinical studies and help us ensure that the measures of benefit and effectiveness of new therapies actually reflect what matters most to patients.

The information we heard today will also be useful to manufacturers, I believe, and I know that a number of them were here in attendance today. And that will hopefully help to develop new products to meet a specific patient needs.

So now I'll attempt to very briefly summarize the salient points from today's discussion. You've made this particularly challenging for me because you've brought forward such great recommendations and information, but that's a good thing.

So our first discussion this morning focused on disease symptoms and daily impacts that matter most to patients. What we heard is that

there's a great desire to be able to lead a normal life. And for a patient to be able to have a family life, a career, pursue his or her dreams, and that is a very important goal to this community.

We've heard also that disease presentation can be quite variable among patients, even with the same disorder. And we also heard that there's under-recognition of disease symptoms and diagnosis in women with bleeding disorders, and in symptomatic female carriers. There is a need to better define and recognize bleeding episodes, and micro-bleeds were mentioned a few times in our discussions. Patients and their caregivers know their diseases very well and it's important that we be able to listen to patients.

This certainly ties into the FDA's interest in patient reported outcomes in clinical studies, and so we thank you also for bringing forward that comment. We also heard that factor levels and annual number of bleeding episodes may be insufficient in characterizing disease burdens

in patients with heritable disorders. We also heard that micro-bleeding can be a very significant component of hemophilia and there's a need for better recommendation and treatment of internal organ bleeding episodes.

We need to recognize the burden of pain in these diseases and the need for better pain management and we heard about unmet medical needs, those associated with inhibitors and the need to be able to treat inhibitors and the need for bypassing agents. The need to treat the complications of longstanding disease and for the management of aging patients and all the complexities that that brings about.

This afternoon we heard a number of perspectives on current therapies for the treatment of heritable bleeding disorders and among those comments were the following: The community has certainly benefited from prophylactic therapies, longer acting treatment, home infusions, and safer products. And this has collectively given more power to patients and

their families and given them a greater sense of safety in facing these diseases.

We also heard that there's a great inadequacy of treatment for women and for the bleeding disorders as they are manifested in women. Inadequacy of pain management, certainly the inadequacy of immune tolerance therapy and the few options that patients with inhibitors have, in terms of bypassing agents. And it was also mentioned that there are no therapies to reverse damage that has been caused by these longstanding illnesses, and it would be wonderful to be able to do that.

There is certainly a need for new products. Several of you mentioned that we would love to have a cure and we share that wish that you have for curing these diseases. It's imperative that any new therapies be safe.

Easier administration is something that you would like to see, perhaps a therapy in pill form or for subcutaneous administration, or other modes of administration. And even longer-acting

therapies would be desirable. Therapies that would not cause inhibitor formation would be certainly a great plus and, in those patients who do develop inhibitors, you would like to see better therapies or a greater number of options, both for treatment of bleeding episodes and for immune tolerance induction.

And also better information should be shared with the community on inhibitors themselves and what options exist for management. We need therapies, a greater number for the very rare bleeding disorders, and this is something that was highlighted by someone who made a comment, and I think it's something that we're concerned about, as well, and there needs to be advancement in that area.

Certainly, I'll mention again that there's need for products for pain management, or better strategies for pain management, treatment regimens for some of the complications, such as hepatitis C infections and HIV infections, and others.

You mentioned the need for improved labeling, with respect to dosing regimens and, perhaps, having labeling that give greater latitude to clinicians when treating patients. It was mentioned and I will mention it again, therapies targeting women would be very desirable and it appears that there's a lot of interest in moving that area forward.

It was mentioned that assays for monitoring factor levels at home could be very helpful to patients as they manage their disease. We heard about the desire for mobile technologies, perhaps mobile apps so that you could have a greater role in actively managing your treatment. We were told that the choice of therapy has to be very patient dependent, every patient is unique in his or her needs. It's very good to have options in terms of therapies, and it's very important when it comes to therapies for this community to have transparency, in terms of what the products can deliver, what potential adverse reactions you may suffer, what is the comparative effective of

these products, and so that's also something that we heard.

Finally, I want to talk about considerations that you have for enrolling in clinical trials. You've talked about whether the science is sound, the potential benefit that there may be to you, the benefit to the community, as well. I heard many comments that underscore the altruism in this community and how you seek to not only better your lives, but lives of others in you community.

And I should just mention that there was some consideration of whether enrollment of a child would be done as readily as the enrollment of an adult with this disease, and this is a very challenging area.

Phase IV studies are desirable. We do know that these new treatments are studied in a very small number of patients and so we hear you on that point. And we also were asked why we are excluding PUPs from the study of new therapies, and that's something that we will take back with

us for further consideration.

There's a need for this community to be able to better access trial results and also to have access to information on trials that are getting underway, so that you can participate if you so desire. So we did receive, evidently, a lot of information at this meeting. We very much appreciate the dialogue.

Now, if you have other comments you would like to share with us, even if you were here in attendance or on the webcast, you can submit comments to the docket and the docket is open until November 28th. After we receive all comments, we will publish on our website a meeting report that will summarize what we have heard. I also did hear that you want our actions to go beyond the publication of a report and we will endeavor to do that.

And to close I want to acknowledge the time, effort, and courage it took to voice the daily challenges and uncertainties that faces patients and families living with heritable

bleeding disorders. We thank you for participating in this meeting and for sharing your unique insights on living with bleeding disorders and your use of lifesaving therapies.

I also thank the clinicians and the representatives of the pharmaceutical industry for your attendance, and for being available to hear the experience of this patient community. And so, on behalf of the Center for Biologics Evaluation and Research, thank you for your time and for making today a success. Thank you very much.

(Applause)

MS. LIPSCOMB: And with that I ask that those lovely clickers you leave on the desk and meeting's adjourned. Thank you so much for coming.

(Whereupon, at 3:08 p.m., the PROCEEDINGS were adjourned.)

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CERTIFICATE OF NOTARY PUBLIC

STATE OF MARYLAND

I, Christine E. Allen, notary public in and for the State of Maryland, do hereby certify that the forgoing PROCEEDING was duly recorded and thereafter reduced to print under my direction; that the witnesses were sworn to tell the truth under penalty of perjury; that said transcript is a true record of the testimony given by witnesses; that I am neither counsel for, related to, nor employed by any of the parties to the action in which this proceeding was called; and, furthermore, that I am not a relative or employee of any attorney or counsel employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

(Signature and Seal on File)

Notary Public, in and for the State of Maryland

My Commission Expires: November 6, 2016