

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

1 PARTICIPANTS:

2 Welcome:

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

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6 Opening Remarks:

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

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

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

13 Background on Heritable Bleeding Disorders:

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

16
17 Overview of Discussion Format:

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

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

21
22 Topic 2: Patients' Perspectives on Current
Approaches to Treatments

1 PARTICIPANTS (CONT'D):

2 Closing Remarks:

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

7 Other FDA Panelists:

8 JONATHAN GOLDSMITH, M.D.

9 CHANGTING HAUDENSCHILD, M.D.

10 MENFO IMOISILI, M.D., MPH

11 DIANE MALONEY, J.D.

12 PAUL MINTZ, M.D.

13 NICOLE VERDUN, M.D.

14 Patient Panelists (AM):

15 DANIEL BOND

16 AMANDA HEISEY

17 MARK SKINNER

18 SONJI WILKES

19 Patient Panelists (PM):

20 JOSEPHINE DRONEY

21 DONALD GOLDMAN

22 KIMBERLY HAUGSTAD

DEBBIE PORTER

1 PARTICIPANTS (CONT'D):

2 BENJAMIN SHULDINER

3 MARK ZATYRKA

4 Other Participants:

5 LISA FAULCON, M.D.

6 SIMONE PORTER, M.D., MPH

7 KETAKI SINGH

8 GRAHAM THOMPSON

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1 P R O C E E D I N G S

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

1 So hopefully that's okay.

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

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

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

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

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

7 We had a public meeting and a process in
8 September of 2012 on through October of 2012 to
9 see what diseases we should consider. We put out
10 some criteria. We received about 4,500 comments
11 from the public about what diseases. We narrowed
12 that down to a set in the first three years of
13 diseases that I'll show you an overview of in a
14 second. And we are now going through the process
15 of identifying diseases for the last two years,
16 2016 and 2017 of this five- year reauthorization.

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

1 try to be accomplishing within the next year
2 basically.

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

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

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

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

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

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

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

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

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

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

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

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

1 group that range from mild to life-threatening
2 conditions and may be present lifelong. The
3 underlying reasons that prevent normal clotting
4 include problems with the platelet plug, such as
5 in von Willebrand disease; defects in the fibrin
6 clot because of low levels of clotting factors,
7 such as in low factor VXIII or IX in hemophilia,
8 as well as other factor deficiencies; excessive
9 breakdown of a clot or fibrinolysis can also be an
10 underlying reason, and this is seen in Alpha-

11 Antiplasmin deficiency. Finally,
12 fragile blood vessels can also lead to bleeding,
13 as seen in hereditary hemorrhagic telangiectasia.

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

1 severity, there are some patients with very severe
2 disease.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

22 In the afternoon, we'll tackle the

1 question of what about current approaches to the
2 treatment.

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

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

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

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

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

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

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

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

22 Again, now let's talk about the ground

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

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

22 The views today are personal opinions,

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

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

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

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

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

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

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

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

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

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

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

12 MR. THOMPSON: About 85 percent outside
13 the area.

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

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

1 things are.

2 And about 42 of you -- percent of you
3 actually have a heritable bleeding disorder, with
4 30 percent of your family members. So welcome.
5 We're so glad that you're here.

6 What was the percentage on the Web?

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

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

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

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

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

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

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

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

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

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

16 MR. THOMPSON: And on the Web it's very
17 similar, although there are slightly more in the
18 50 to 65 category.

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

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

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

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

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

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

20 How is it on the Web?

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

1 and 16, six to 10.

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

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

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

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

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

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

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

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

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

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

6 Like most boys, Thomas has a competitive
7 spirit, but because of his physical limitations,
8 most sports are off limits. He started swim
9 lessons at an early age, and in the summer of
10 2011, swam with a neighborhood swim team. He
11 excelled, and even qualified for the All-Stars
12 meet, and we continued with a year-round team, but
13 he spent much of 2011- 2013 sidelined as he
14 battled port infections and significant bleeds in
15 his iliopsoas and quad muscles. Last summer, he
16 returned to the pool but found he didn't have the
17 stamina or speed that he once had. Despite
18 sadness about not being able to do what he loves
19 on the level that he'd like to participate at, he
20 continued to have fun with his peers.

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

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

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

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

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

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

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

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

10 Thank you for the opportunity to share
11 our experiences today.

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

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

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

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

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

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

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

1 Atlantic. It seemed like a good idea to a
2 19-year-old. As my ankles degraded with joint
3 disease, it became clear that I couldn't walk on a
4 pitching deck. I haven't sailed in over 40 years.

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

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

22 Sixty years is a long time with this

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

1 limited because of my disease.

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

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

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

7 MS. LIPSCOMB: Thank you. Amanda?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

8 (Applause)

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

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

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

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

1 1997 from HIV that he contracted from a blood
2 product.

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

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

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

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

1 you take an ibuprofen or aspirin or whatever.

2 Well, he doesn't take aspirin, but something
3 simple. That would make it even better for their
4 quality of life.

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

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

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

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

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

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

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

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

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

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

17 MS. LIPSCOMB: Thank you. Thank you.

18 Do we have any comments from the Web?

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

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

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

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

15 MS. LIPSCOMB: Okay. Thank you. Yes?

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

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

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

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

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

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

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

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

22 MR. LONG: I'd like to point something

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

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

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

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

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

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

9 MR. THOMPSON: On the Web, 54 percent,
10 joint damage; 18 percent, heavy menstrual
11 bleeding; 9 percent, bleeding in the muscles; and
12 27 percent for anxiety or depression.

13 MS. LIPSCOMB: Okay. How many times in
14 the past year did you or your last one experience
15 a bleed? Zero to four times, 5 to 11 times, 12 to
16 23 times, 24 times or more? This is within the
17 last year.

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

21 MR. THOMPSON: Twenty percent for 0 to
22 4, 40 percent for 5 to 11, 27 percent for 12 to

1 23, and 9 percent for more than 24.

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

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

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

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

17 Thank you.

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

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

13 MS. LIPSCOMB: Okay.

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

18 MS. LIPSCOMB: Okay, thank you. Mark?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

22 And I guess we can maybe potentially ask

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

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

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

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

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

8 MS. LIPSCOMB: Okay.

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

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

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

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

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

20 I'm showing no comments at this time.

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

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

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

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

12 DR. JAIN: Thirty percent.

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

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

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

22 MS. LIPSCOMB: Okay.

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

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

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

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

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

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

9 I saw some other hands up.

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

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

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

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

18 MS. LIPSCOMB: Thank you. Okay.

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

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

15 MS. LIPSCOMB: Okay. Mark?

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

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

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

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

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

9 MS. LIPSCOMB: Okay. Thank you. Thank
10 you.

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

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

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

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

22 MR. GOLDMAN: Hi. My name is Don

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

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

22 I have a question I want to ask

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

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

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

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

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

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

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

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

22 MS. LIPSCOMB: Okay. Do we have any

1 comments from the Web?

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

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

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

21 Operator?

22 OPERATOR: Yes, we do have a question or

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

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

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

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

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

11 MS. LIPSCOMB: Amanda?

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

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

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

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

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

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

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

20 And the mild hemophiliacs, I have six
21 percent. I prophylax. I catch heck because I
22 prophylax. How can you prophylax? You have

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

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

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

8 MS. LIPSCOMB: Okay. Thank you. Dan?

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

13 MS. WILKES: Great.

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

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

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

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

15 So I just wanted to make that comment as
16 well.

17 MS. LIPSCOMB: Thank you.

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

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

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

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

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

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

1 about this buzzing, I think, buzzing sensation.

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

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

7 Okay.

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

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

10 MS. LIPSCOMB: Thank you. Right behind
11 you.

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

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

1 "Well, you must have developed an inhibitor."

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

10 MS. LIPSCOMB: Okay. Thank you.

11 Anybody else? Well, I just had to look forward.

12 All right. We'll go in this order.

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

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

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

1 probably would have been higher.

2 Daniel?

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

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

22 MS. WILKES: I was going to speak a

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

20 MS. LIPSCOMB: Thank you.

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

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

1 so much better than our generations past have.

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

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

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

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

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

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

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

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

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

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

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

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

22 Anybody?

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

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

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

6 MS. LIPSCOMB: Okay. Thank you.

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

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

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

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

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

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

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

10 MS. LIPSCOMB: Thank you. Thank you.

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

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

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

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

1 suggest you stand up then.

2 Oh, okay. Amanda.

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

18 MS. LIPSCOMB: Thank you. Mark?

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

22 I want to pick up on Randy's comment

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

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

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

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

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

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

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

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

1 MS. LIPSCOMB: Thanks.

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

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

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

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

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

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

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

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

17 MS. LIPSCOMB: Thanks.

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

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

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

12 MS. LIPSCOMB: Oops.

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

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

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

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

22 MS. LIPSCOMB: Thank you. Go ahead.

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

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

16 Start with you.

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

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

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

16 MS. LIPSCOMB: Thank you. Go ahead.

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

1 that better? Just a general question.

2 MS. LIPSCOMB: Thank you.

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

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

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

5 MS. LIPSCOMB: Thank you.

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

8 MS. LIPSCOMB: Okay.

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

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

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

4 (Recess)

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

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

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

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

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

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

15 MR. THOMPSON: I think it was just
16 letting people in the room know that we had around
17 140 people or so on the website.

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

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

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

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

19 MS. LIPSCOMB: Great, thank you.

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

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

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

22 And then, also, what treatment has the

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

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

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

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

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

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

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

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

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

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

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

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

22 The treatments that had the most

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

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

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

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

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

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

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

13 MS. LIPSCOMB: Thank you. Don?

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

1 My recommendation to the FDA is that we
2 continue to seek improvements in all of these
3 areas. Patients and their hemophilia treatment
4 center, HTC's, should have access to new advances
5 with a full understanding of their risks and
6 benefits. Phase IV studies should be mandated on
7 all novel treatments.

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

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

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

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

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

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

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

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

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

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

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

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

14 The FDA has asked me to discuss
15 considerations that go into trying new products.
16 Let me use Biogen's new product, Eloctate, as an
17 example. One consideration is cost. Using over
18 \$250,000 per year, even a small co-pay is far
19 beyond my means. Currently the product I use has
20 no co- pay. Using factor every four days, instead
21 of three times a week, means less wear and tear on
22 my old faithful vein that I won't even let any of

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

7 Next February I'm traveling for 16 days
8 and every other day I need to bring 8 doses, plus
9 4 more for emergencies, or a total of 12. I only
10 need to bring eight doses of longer lasting
11 product, a quantity much more convenient for
12 traveling. Fitting lots of factor and other
13 medications into little carry-on bags is a
14 challenge and a dosing schedule of once every four
15 days would also help overcome the problem of
16 adherents.

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

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

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

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

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

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

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

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

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

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

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

9 MS. LIPSCOMB: Thank you. Ben?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

3 And then, lastly, the stuff that's kind
4 of not hemophilia E related, but is part of our
5 community, you can't go into a room of somebody
6 who has hemophilia who's over 30 and not see
7 somebody that had hepatitis C. Hepatitis C is a
8 huge issue, of course, in the community. And the
9 fact that the new regimens that are coming out
10 now not only don't have the terrible side effects
11 that they used to, but are now having -- and
12 people in the room can tell you better than this
13 -- 90 percent plus clearance rates.

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

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

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

6 MS. LIPSCOMB: Thank you very much.
7 Josephine?

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

22 As of now, I'm on hormone replacement

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

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

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

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

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

1 greater than any of the risks.

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

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

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

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

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

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

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

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

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

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

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

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

16 Those traumatic infusions in his first
17 18 months to stop bleeds did have a significant
18 impact on my child. Evaluations by two
19 neuropsychologists have confirmed diagnosis of
20 both anxiety and ADHD, and the physicians feel
21 very strongly that the trauma of those early,
22 difficult infusions with those six to eight pokes

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

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

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

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

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

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

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

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

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

1 still bleeds at that level.

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

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

17 MS. LIPSCOMB: Thank you so much.
18 Debbie?

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

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

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

22 My son is not your typical 20-year-old

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

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

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

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

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

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

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

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

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

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

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

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

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

7 My son almost died from a blood clot.
8 This is the last thing you really would expect
9 from someone with severe hemophilia. The cost of
10 these medications is also very high. My son's
11 FEIBA is currently costing \$1 million per year,
12 and his NovoSeven is costing \$5 million per year.
13 His lifetime cost to date for medications alone is
14 \$65 million. These costs seem almost unbelievable
15 and may be unsustainable. We anticipate Matt's
16 cost to continue in the \$6 million per year range
17 unless something can be done to overcome his
18 inhibitor or treat his bleeds more effectively.

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

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

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

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

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

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

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

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

1 OPERATOR: Yes, her line is open.

2 MS. LIPSCOMB: Linda?

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

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

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

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

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

1 and very new.

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

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

22 I, on the other hand, was particularly

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

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

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

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

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

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

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

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

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

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

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

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

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

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

1 therapy?

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

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

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

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

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

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

1 MR. SINGH: We have on-demand therapy at
2 22, routine prophylaxis at 23, and both at 55.

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

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

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

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

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

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

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

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

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

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

1 MR. CURTIS: So once again, I'm Randy
2 Curtis, and I have severe A. And I've gone to
3 more of a modified Dutch protocol and I do a
4 low-dose prophylaxis every four days. I'm only
5 1,000 units, and that's worked for me for the last
6 10 years and I don't bleed.

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

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

17 MS. LIPSCOMB: Great, thank you.

18 MR. TEMPLIN: Hi, Chris Templin here.
19 What scares me is I'm on a product that I like
20 because it works well and it has a long history --
21 20-some-year history -- through the clinical trial
22 and out on the market. What scares me is the fact

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

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

18 MS. LIPSCOMB: Thank you.

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

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

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

22 So there's a lot of juggling

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

6 MS. LIPSCOMB: Okay, great. Thank you.

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

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

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

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

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

13 DR. JAIN: Factor XIII.

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

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

22 MR. BOND: Dan Bond. I have something

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

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

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

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

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

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

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

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

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

9 I'm told that immune tolerance is about
10 70 percent effective. In my opinion, that's not
11 successful enough. Why don't we know what causes
12 inhibitors? Why are there no warnings for newer
13 parents? After just nine infusions, you can
14 hardly process the fact that your child has
15 hemophilia and all of a sudden you have something
16 more serious to deal with.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

1 still be around?

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

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

22 It just worries me that these

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

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

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

21 Ideal in our situation, having a
22 45-year-old brother and myself, as well as my

1 18-year-old son, really looking for the longer
2 acting medications to be extended even longer. Of
3 course, a cure is going to be amazing, but having
4 a college student son that runs for his college,
5 that's an athlete, that does everything he can to
6 keep his body in line, sometimes his body does not
7 cooperate.

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

12 MS. LIPSCOMB: Thank you.

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

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

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

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

19 MS. LIPSCOMB: Thank you for that.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

1 that we do. It certainly has worked for me.

2 MS. LIPSCOMB: Great, thank you.

3 Anybody else before we move on to clinical trials?

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

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

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

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

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

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

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

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

14 MS. LIPSCOMB: Okay. That kind of is a
15 great segue into our next scenario. So I want you
16 to imagine that you or your child has the
17 opportunity to consider participating in a
18 clinical trial for an experimental oral
19 replacement therapy? The study is going to enroll
20 50 participants, the clinical study last 1 year
21 and it's going to involve 6 clinic visits,
22 occurring every 2 months. More common side

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

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

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

12 MS. LIPSCOMB: Well, thank you for that.

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

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

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

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

8 MR. CURTIS: They come along with the
9 package.

10 MS. LIPSCOMB: Thank you.

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

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

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

5 MS. LIPSCOMB: Thank you.

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

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

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

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

18 MR. WICK: Yeah.

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

1 MR. SINGH: It's correct.

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

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

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

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

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

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

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

17 SPEAKER: There's one more plan.

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

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

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

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

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

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

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

10 MS. LIPSCOMB: Okay.

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

15 MS. LIPSCOMB: Okay. Anybody else?
16 Donald?

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

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

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

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

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

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

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

1 future generations, given that he was an older
2 hemophiliac.

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

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

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

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

3 MS. LIPSCOMB: Okay, thank you.

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

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

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

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

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

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

22 MS. LIPSCOMB: Thank you. Mark, did you

1 have something you wanted to add?

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

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

17 MS. LIPSCOMB: Ben?

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

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

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

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

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

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

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

13 MS. LIPSCOMB: Thank you. Debbie?

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

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

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

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

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

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

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

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

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

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

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

22 I know I spoke earlier on behalf of my

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

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

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

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

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

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

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

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

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

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

21 MS. SCHARPF: Thank you, Kimberly.
22 Paul?

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

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

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

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

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

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

6 MS. SCHARPF: Thank you, Paul. Shelby?

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

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

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

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

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

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

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

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

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

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

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

6 MS. SCHARPF: Thank you, Steve. Val?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

14 There is certainly a need for new
15 products. Several of you mentioned that we would
16 love to have a cure and we share that wish that
17 you have for curing these diseases. It's
18 imperative that any new therapies be safe.

19 Easier administration is something that
20 you would like to see, perhaps a therapy in pill
21 form or for subcutaneous administration, or other
22 modes of administration. And even longer-acting

1 therapies would be desirable. Therapies that
2 would not cause inhibitor formation would be
3 certainly a great plus and, in those patients who
4 do develop inhibitors, you would like to see
5 better therapies or a greater number of options,
6 both for treatment of bleeding episodes and for
7 immune tolerance induction.

8 And also better information should be
9 shared with the community on inhibitors themselves
10 and what options exist for management. We need
11 therapies, a greater number for the very rare
12 bleeding disorders, and this is something that was
13 highlighted by someone who made a comment, and I
14 think it's something that we're concerned about,
15 as well, and there needs to be advancement in that
16 area.

17 Certainly, I'll mention again that
18 there's need for products for pain management, or
19 better strategies for pain management, treatment
20 regimens for some of the complications, such as
21 hepatitis C infections and HIV infections, and
22 others.

1 You mentioned the need for improved
2 labeling, with respect to dosing regimens and,
3 perhaps, having labeling that give greater
4 latitude to clinicians when treating patients. It
5 was mentioned and I will mention it again,
6 therapies targeting women would be very desirable
7 and it appears that there's a lot of interest in
8 moving that area forward.

9 It was mentioned that assays for
10 monitoring factor levels at home could be very
11 helpful to patients as they manage their disease.
12 We heard about the desire for mobile technologies,
13 perhaps mobile apps so that you could have a
14 greater role in actively managing your treatment.
15 We were told that the choice of therapy has to be
16 very patient dependent, every patient is unique in
17 his or her needs. It's very good to have options
18 in terms of therapies, and it's very important
19 when it comes to therapies for this community to
20 have transparency, in terms of what the products
21 can deliver, what potential adverse reactions you
22 may suffer, what is the comparative effective of

1 these products, and so that's also something that
2 we heard.

3 Finally, I want to talk about
4 considerations that you have for enrolling in
5 clinical trials. You've talked about whether the
6 science is sound, the potential benefit that there
7 may be to you, the benefit to the community, as
8 well. I heard many comments that underscore the
9 altruism in this community and how you seek to not
10 only better your lives, but lives of others in you
11 community.

12 And I should just mention that there was
13 some consideration of whether enrollment of a
14 child would be done as readily as the enrollment
15 of an adult with this disease, and this is a very
16 challenging area.

17 Phase IV studies are desirable. We do
18 know that these new treatments are studied in a
19 very small number of patients and so we hear you
20 on that point. And we also were asked why we are
21 excluding PUPs from the study of new therapies,
22 and that's something that we will take back with

1 us for further consideration.

2 There's a need for this community to be
3 able to better access trial results and also to
4 have access to information on trials that are
5 getting underway, so that you can participate if
6 you so desire. So we did receive, evidently, a
7 lot of information at this meeting. We very much
8 appreciate the dialogue.

9 Now, if you have other comments you
10 would like to share with us, even if you were here
11 in attendance or on the webcast, you can submit
12 comments to the docket and the docket is open
13 until November 28th. After we receive all
14 comments, we will publish on our website a meeting
15 report that will summarize what we have heard. I
16 also did hear that you want our actions to go
17 beyond the publication of a report and we will
18 endeavor to do that.

19 And to close I want to acknowledge the
20 time, effort, and courage it took to voice the
21 daily challenges and uncertainties that faces
22 patients and families living with heritable

1 bleeding disorders. We thank you for
2 participating in this meeting and for sharing your
3 unique insights on living with bleeding disorders
4 and your use of lifesaving therapies.

5 I also thank the clinicians and the
6 representatives of the pharmaceutical industry for
7 your attendance, and for being available to hear
8 the experience of this patient community. And so,
9 on behalf of the Center for Biologics Evaluation
10 and Research, thank you for your time and for
11 making today a success. Thank you very much.

12 (Applause)

13 MS. LIPSCOMB: And with that I ask that
14 those lovely clickers you leave on the desk and
15 meeting's adjourned. Thank you so much for
16 coming.

17 (Whereupon, at 3:08 p.m., the
18 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;
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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
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(Signature and Seal on File)

Notary Public, in and for the State of Maryland
My Commission Expires: November 6, 2016

