ADVISORY COMMITTEE
ON
BLOOD SAFETY AND AVAILABILITY

DEPARTMENT OF HEALTH AND HUMAN SERVICES

THIRTY-SECOND MEETING

AUGUST 22, 2007

Georgetown University Conference Hotel
3800 Reservoir Road, NW
Washington, D.C. 20057

WEDNESDAY, AUGUST 22, 2007

LIST OF PARTICIPANTS:

ARTHUR W. BRACEY, M.D. (Chairman)

JERRY A. HOLMBERG, PH.D.

ROBYN ASHTON, R.N., M.S.

WILLIAM RILEY, Ph.D.

JEFFREY MCCULLOUGH, M.D.

JAY S. EPSTEIN, M.D.

DR. PETER KOUIDES

ANN MARIE BENZINGER

JOHN McGUIRE

JULIE BIRKOFER

DR. CELSO BIANCO

M. GREGG BLOCHE, M.D., J.D.

ILEANA LOPEZ-PLAZA, M.D.

WILLIAM DUFFELL, Jr., Ph.D.

DAVID E. MATYAS, J.D.

ANNE MARIE FINLEY

DR. LOUIS JACQUES

THERESA WIEGMANN, J.D.

DR. SUSAN ROSEFF

LINDA THOMAS-WADE

DR. MARISA ST. MARTIN

MATTHEW J. KUEHNERT, M.D.

MARY MALARKEY

SCOTT BRUBAKER

BASIL GOLDING, M.D.

RUTH SYLVESTER

RICHARD BENJAMIN, M.D.

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P R O C E E D I N G S

THE CHAIR: We'll call the meeting to order. Executive Secretary Holmberg, would you like to do the roll call.

DR. HOLMBERG: Sure. Thank you. Dr. Bracey.

THE CHAIR: Present.

DR. HOLMBERG: Ms. Benzinger.

MS. BENZINGER: Present.

DR. HOLMBERG: Ms. Birkofer.

(No response)

DR. HOLMBERG: Dr. Bloche.

(No response)

DR. HOLMBERG: Dr. Duffell.

DR. DUFFELL: Present.

DR. HOLMBERG: Ms. Finley.

MS. FINLEY: Here.

DR. HOLMBERG: Dr. Kouides.

DR. KOUIDES: Here.

DR. HOLMBERG: Dr. Lopez

DR. LOPEZ-PLAZA: Present.

DR. HOLMBERG: Mr. Matyas.

MR. MATYAS: Here.

DR. HOLMBERG: Dr. Pierce (phonetic)

(No response)

DR. HOLMBERG: Dr. Ramsey. (phonetic)

DR. RAMSEY: Here.

DR. HOLMBERG: Good morning. Dr. Rosa.

DR. ROSA: Here.

MR. HOLMBERG: Dr. Sandler.

SPEAKER: He’s absent.

DR. HOLMBERG: Ms. Thomas Wade. (phonetic)

MS. THOMAS: Here.

(Laughter)

DR. HOLMBERG: And as you noticed I added another name to that.

(Laughter)

DR. HOLMBERG: And Dr. (inaudible)

SPEAKER: He’s absent.

DR. HOLMBERG: Dr. Kuehnert.

(No response)

DR. HOLMBERG: Dr. Epstein.

DR. EPSTEIN: Here.

DR. HOLMBERG: Dr. Klein.

(No response)

DR. HOLMBERG: Commander Libby. (phonetic)

CDR. LIBBY: Present.

DR. HOLMBERG: Dr. Burman. (phonetic)

(No response)

DR. HOLMBERG: Dr. St. Martin.

DR. St. MARTIN: Here.

DR. HOLMBERG: And Ms. Ashton.

MS. ASHTON: Here.

DR. HOLMBERG: Okay. We do have a quorum. And we will move on. The quorum really is only necessary as far as if we decide to vote on anything. However, we can continue on with discussions in the absence of a quorum. I would like to first read a conflict of interest, the Department of Health and Human Services is conveying today's meeting of the Secretary's Advisory Committee on Blood Safety and Availability under the authority of the Federal Advisory Committee Act of 1972 with the exception of the industry representatives, all participants of the committee, or special government employees, are regular federal employees from other agencies, and are subject to the federal conflicts of interest laws and regulations.

The Department has determined that participants

of this Advisory Committee are in compliance with the Federal ethics and conflict of interest laws. Congress has authorized waivers to special government employees who have financial conflicts when its determined that the Agency's need for particular individual services outweighs his/her potential financial conflict of interest, and where participation is necessary to afford the essential expertise.

Members of today's -- of the committee who are special government employees at today's meeting have been screened for potential financial conflicts of interest of their own, as well as those imputed on them including those of their employer, spouse or minor child.

I encourage all other participants especially during the open public forum, or if you are an invited speaker, from -- even from the floor, to advice the Committee of any financial relationship that you may have with any sponsors, products, direct competition or firms that could be affected by our discussions.

I would also like to recognize several individual that potential will be rotating off the committee. I say that because the charter does give us

permission to extend your service, and depending on the nominations, and the needs of the committee you may be asked to continue on.

But at the present time Dr. Sandler served from 2002 to 2005, and then a second term representing the American Hospital Association, and that term, his current term ends on September 30th of this year.

Dr. Rosa also served from January 2005 to the present. And Dr. Bracey served from October 2004 to the present. And he has served as the Chair for the last two years. So, we won’t definitely say, farewell, because we have a lot of work to do still over the next two days. But also their -- I leave that door opened that we may be calling you back to serve us, so we will address the finalities later.

And one thing, I do say is that many of the people that have sat on these committees very often come back as guest speakers because they do have expertise to share with the committee. We also have some changes in the Blood Safety and Availability and especially in the Office of Public Health and Science.

I know that several of you have received or most

of you should have received notification from the about Dr. Agwunobi, but I regret to announce that the resignation of Dr. John Agwunobi as the assistant secretary for Health, and the admiral in the U.S. Public Health Service Commission Corp is going to be effective September 4, 2007. Since joining HHS in 2005 Dr. Agwunobi has been a passionate voice for advancing healthcare of all Americans.

His leadership, council and expertise have contributed greatly to increasing America's awareness. And preparedness for pandemic influenza encouraging adoption of healthier lifestyles, and leading the renewal of the USPHS Commission Corp. Dr. Agwunobi has distinguished himself through the energy and commitment with which he has approached every task at HSS.

I personally will miss Dr. Agwunobi and his professionalism, and wish him well in his future endeavor. We also have changes in positions and a new person that I would like to introduce, Lieutenant Commander Rich Henry. Rich, if you could stand up. Rich has been advanced to the position of deputy director of Blood Policy and Programs, and is also the deputy executive secretary for

OS/OPHS Advisory Committee on Blood Safety and Availability.

We also have a new person in the office and she has been in the office since the 1st of August, so she is a real new-be. And that is Lieutenant J.G. Jennifer Lunney and she is the senior public health preparedness advisor. Jennifer joins the Commission Corp of the U.S. Public Health Service from her recent position with the John Hopkins University Bloomberg School of Public Health working on HIV/AIDS project in Zimbabwe.

She has spent several years onsite with the project in Zimbabwe providing research and programs support. And then of course I want to make sure that we do recognize Ms. Rene Wilson (phonetic). Rene can you stand up and show your smiling face please. and we all have known Rene over the years and I just don’t want us to forget the work and the endeavor that Rene does on a daily basis to make sure that the logistics of getting you all here is recognized.

I also would like to recognize at the present time that we have a call out for nominations to the committee. This was a federal registry notice that

appeared on July 30th, through the office of Public Health and science. And that the secretary seeking nomination have qualified individuals to be considered for appointment as members of the Advisory Committee on Blood Safety and Availability.

The Advisory Committee on Blood Safety and Availability is a federal Advisory Committee in the Department of Health and Human Services. Management support of the activities of the committee is a responsibility of OPHS. The qualified individuals will be nominated to the secretary of the Department of Health and Human Services for consideration of appointment as members of the Advisory Committee on Blood Safety and Availability.

Members of the committee including the Chair are appointed by the secretary. Members are invited to serve on the committee. All nominations must be received in my office no later than 4:00 p.m. on August 31st. I will not be there on August 31, but they must be received by that point in time.

I just want to also review a little bit before I turn it over to Dr. Bracey, just to re-emphasize the

1 charge of the Committee. And to emphasize that although
2 our name still says Blood Safety and Availability, our
3 scope, our charge has expanded, and I just want to read
4 the part of the charter to you to re-emphasize that.
5 The Advisory Committee on Blood Safety and
6 Availability shall provide advise to the secretary and to
7 the assistant secretary for heath, the committee will
8 advise on a range of policy issues to include definition
9 of public health parameters around safety and availability
10 of blood, and blood products, broad public health, ethical
11 and legal issues related to transfusion, and
12 transplantation safety. And the implication for safety
13 and availability are various economic factors affecting
14 product cost and supply.
15 Just as a reminder for today, I would encourage
16 everyone to at least turn their cell phones off, or to
17 turn it to a vibration or muted position, and also for
18 those committee members that have Blackberrys there is a
19 tendency that when the Blackberrys get too close to the
20 microphone, they do send off some interference, so if you
21 could maybe move your Blackberry to the floor or to your
22 briefcase that may interfere with our -- may eliminate

some of the problems with that.

We've been at meetings where when the phone, the cell phones have gone off, they have set up a little fund for different charitable organizations, I don't know if we have to do that in this meeting, but if it does create a problem we may do that later on. At any rate I would like to turn over the meeting to Dr. Bracey.

THE CHAIR: Thank you. Good morning and a warm welcome to the Thirty-Second Meeting of the Advisory Committee on Blood Safety and Availability. Once again I'd like to express my gratitude to those assembled here, for the purpose of advancing healthcare for your fellow countrymen. In our recent meetings we laid the ground work for the Department's recognition of blood, as -- and blood products as a critical component of the medical infrastructure.

We also made strong recommendations regarding that the department's role in developing a national system for biovigilance, addressing the safety of blood, organ transplants and tissue under our expanded charter.

In the first phase of today's meeting we will hear updates on some of these activities as well as other

1 evolving issues involving blood therapies. Over the next
2 two days a major focus, will be to hear from a variety of
3 experts on the important issue that the committee carries
4 as its namesake.
5 Namely, the availability of blood and blood
6 products. Specific areas to be considered will be the
7 elasticity of the supply, the ethics of distribution,
8 existing systems for monitoring supply, and strategies to
9 improve our readiness assessment in response. Given the
10 diverse perspective of this committee I look forward to a
11 rich debate, and input for the sake of the Department's
12 decisions regarding how best to manage the nation's blood
13 needs.
14 Before we move into the presentations this
15 morning though, I think its important I read the letter
16 from the assistant secretary Dr. Agwunobi from the
17 recommendations made from our last meeting. And the
18 letter dated 8/14/07 is as follows.
19 "Dear Dr. Bracey, it was a privilege to meet
20 with the Advisory Committee on Blood Safety and
21 Availability at the May 2007 meeting. I appreciate the
22 leadership that you provide the committee and the thought

1 for discussion of the proposed questions regarding the
2 need, opportunity and the scope of the master strategy for
3 transfusion, and transplantation safety.
4 "It is apparent from the response to the
5 questions that there is both an opportunity, and a need to
6 develop a process to enhance quality improvement,
7 transfusion medicine and transplantation. As the
8 Committee noted the benefit risk profile differs for
9 transfusion, tissue, and transplant recipients.
10 "However, all patients treated with these
11 modalities have the potential requiring life-threatening
12 infections. This risk increases if good laboratory
13 manufacturing tissue and transplantation practices are not
14 followed.
15 "The Committee also noted that there needs to be
16 a mechanism to detect and monitor emerging unknown
17 diseases which maybe transmitted by transfusions, or
18 transplantations. The scope of a master strategy is very
19 consistent with a previous recommendations made for
20 biovigilance to include all transfusion and
21 transplantation modalities.
22 "The department and its operating divisions are

working with the private sector concurrently with internal discussions to move forward on these recommendations. Some activities such as biovigilance partnerships have already been initiated with AABB, and the Untied Network of Organ Sharing, UNOS using HSS resources.

"Please express to the committee my appreciation for their service and valued recommendations. I look forward to the advancements in transfusion and transplantation safety which will be realized in the near future." Signed John O. Agwunobi.

So, with that I think that leads as a branch, and I'd like to personally express my gratitude for the involvement of Dr. Agwunobi. He has been very engaged in our discussions. And when I came on the committee we were in the period of having an interim and there was some question about the degree of engagement. But Agwunobi has been very responsive, and I think these are important messages that he is sending us, and the rest of the healthcare delivery system.

So, with that said we'll move into the first presentation for this morning, and that will be from Dr. Basil Golding, and the topic is an update on Measles

1 Antibody, Standard for Immunoglobulin Lot Release. Dr.
2 Golding is certified in Internal Medicine in Rheumatology.
3 He served in a number of positions at the FDA.
4 Relatively, recently as the chief of plasma derivatives
5 that particular lab, and he is currently the division
6 director of hematology for OBRR and CBER. Dr. Golding
7 DR. GOLDING: Thank you and good morning. I am
8 going to present to you the summary of what happened last
9 week, we had a presentation to Blood Product Advisory
10 Committee, and the subject relates to measles and antibody
11 levels in U.S. immunoglobulin products.
12 The issue as you see on the slide is that FDA
13 sought advice of the committee on a proposal to lower the
14 minimum recommended Lot release titer for measles
15 antibodies in Immune Globulin Intravenous and Immune
16 Globulin Subcutaneous.
17 The background is that measles antibody titers
18 serve as a potency test for Lot release of all immune
19 globulins licensed in the United States. Measles antibody
20 levels in products have been declining in recent years.
21 And failure of potency testing would result in rejection
22 of Lots with a negative impact on product availability for

1 primary Humeral Immune Deficiency Diseases. CBER proposed
2 at the Advisory Committee to lower the minimum measles
3 antibody titer of IGIV and IG sub cu to levels expected to
4 be effective in pre-exposure protection in patients with
5 Primary Immune Deficiency Diseases.
6 Immune Globulin Intramuscular is indicated for
7 post-exposure protection in normal individuals and will be
8 considered separately. In general a Lot Release Test,
9 what are the regulatory requirements. Laboratory controls
10 shall include the establishment of scientifically sound
11 and appropriate specifications, standards, sampling plans
12 and test procedures designed to assure that drug products
13 conform to appropriate standards of identity, strength,
14 quality, and purity. And this is from the Code of federal
15 regulations.
16 So potency testing for Immune Globulins. What
17 is the rationale, it is for to assure the strength and the
18 quality of these products and what do these specifications
19 provide? Well, they provide a measure of Lot-to-Lot
20 consistency, assurance of product integrity, especially
21 tests that measure antibody function rather than just
22 binding. And measure of activity that is relevant to the

1 indication for patients with Primary Immune Deficiency
2 Disorders.
3 So, the current U.S. Immune Globulin Product
4 Potency Tests manufactures are required to measure
5 antibodies to measles, diphtheria, and at least one type
6 of polio, and in addition we've been asking for Hepatitis
7 B surface antigen antibody testing. All of the above
8 tests except antibody to Hepatitis B surface antigen on
9 neutralization assays in other words functional tests and
10 the anti-hepatitis B surface antigen provides additional
11 assurance of viral safety.
12 In terms of Immune Globulin Intravenous and
13 Immune Globulin Subcutaneous and Measles antibody titers,
14 measles antibody levels are a standard measure of
15 potential for U.S. Immune Globulins. There were a
16 historically important specificity. Potency tests are
17 available and correlate with protection in normal
18 subjects. This is measured by bioassay and there are two
19 type of functional assay, one is a hemagglutination
20 inhibition test, and the other is a neutralization or
21 plaque reduction neutralization test. And the important
22 point here is that the declining antibody levels have been

1 observed in products over the past several years.
2 Why are anti-measles antibody levels declining
3 in donors? Natural infection results in high antibody
4 levels. And the proposition of vaccinated as opposed to
5 naturally infected donors is increasing. So the vaccine
6 was licensed in 1963, and implemented over the ensuing
7 years. The naturally infected population of donors is
8 aging, and as a result there are more deferrals of these
9 donors and fewer donors available with the high titer
10 antibody.
11 So this is a data from Markovitz and others to
12 compare the titers of the natural infection and of the
13 vaccination. So on the x-axis you have years of the
14 natural infection, and on the y-axis you have the actual
15 titer, and you can see that of the natural infection the
16 level are maintained at higher levels for a longer period
17 of time.
18 This is just a brief history of the development
19 of the potency tests for Immune Globulins. In 1944, we
20 had a demonstration of measles prophylaxis using Immune
21 Globulin Intra Muscular, in 1953 the NIH had a statement
22 that minimum requirements for Immune Serum Globulins

1 several lots should be effective in prophylaxis of
2 measles. And as measles potency tests became available
3 CBER developed standards for these tests so that
4 manufacturers could have a standard bioassay for measuring
5 titer in their products.
6 So, the history of the standard for the potency
7 assay in 1961, Lot 1 was a serum from actually Rhesus
8 Macaque that had natural infection and were immunized and
9 this was designated that Immune Serum Globulin should be
10 at least 0.25 times the standard Lot 1. The cutoff was
11 established based on a study of 60 Immune Serum Globulins
12 these are intra muscular preparation that we were
13 available at that time.
14 And the cutoff was based on looking at these and
15 considering the potency for measles prophylaxis. The
16 cutoff permitted future Lots to pass specification with a
17 probability of 95 percent. The standards are age over
18 time, in 1971 it was replaced with Lot 1 -- sorry Lot 1
19 was replaced with Lot 175, and in 1992, that Lot was
20 replaced with Lot 176, which is the current Lot.
21 And by testing the Lot side-by-side it was
22 established that the Lot 176 criterion would be 0.6 times

the potency compared -- that any Immune Globulin would have to be 0.6 times the potency of Lot 176 being compared at the same IgG concentration. And we are now planning for replacing of Lot 176 with a new Lot.

So, the Clinical issues related to measles prophylaxis in Primary Immune Deficiency Disorder Patients the measles incidence is rare in the U.S. only 66 confirmed cases in 2005, this is from the CDC. And the reports of measles infection in these patients are rare. There is lack of exposure to measles and/or protection due to treatment IgG.

The last major outbreak in the U.S. was in 1989-1991 with more than 55,000 cases reported. And the main reason probably for this was that the vaccination waned the titers waned off the vaccination, and now that they have introduces boost vaccination, there haven’t been outbreaks unless these are coming from imported cases.

So, the few outbreaks that have occurred they are probably not because herd immunity. Nevertheless, measles remains an important pathogen worldwide. 21 percent of disease-related deaths in children less than five years of age are due to measles. Antibodies are

needed to prevent infection while measles virus clearance depends mainly on CD8 positive T cells. Primary Immune Deficiency Disease Patients especially those with combined humeral and T cell deficiencies are susceptible to severe measles disease.

What is the protective titer against measles infections? So, these values were obtained by Chen and others, and it’s based on vaccine trails in relatively small numbers of patients. Nevertheless, this is the best data we have. So the serum titer of a 120 milli IU per ml was found to be protective against clinical disease in healthy vaccinated individuals.

But a much higher titer of over 1000 milli IU per ml is protective against infection in other words provides sterilizing immunity. So, this titer prevents against disease, and this titer prevents against infection.

There is a generally a lack of published pharmacokinetic data analyzing measles titer in IGIV products that are administered, and the consequent trough level measles neutralizing antibody in Primary Immune Deficiency Disease Patients.

Although at the Advisory Committee some of the companies did present data, and we are going to be looking at this data, and it will help us make decisions in deciding on the final number of the -- that we decide as the specification. The protective level in Primary Immune Deficiency Diseases are known more than 100 distinct syndromes exist, therefore protective measles antibody levels may vary from these -- in these different syndromes.

What is the CBER or FDA rationale for proposing an actual specification? The IGIV does for most patients is around 200-800 milligrams IgG per kilogram given every 3-4 weeks. Although when you speak to treaters very few treaters are out there are giving less than 400 milligrams per kilogram.

Trough level antibody titers for patients receiving 400 milligrams of IGIV every four weeks is estimated to range from 250-718 milli IU/ml based on CBER testing of Lots. So this is actual testing by CBER doing a bioassay, and then doing -- in calculated trough levels based on the large database of PK levels in these patients we have made that estimated range calculation.

The calculated theoretical minimum anti-measles antibody potency of IGIV, given at 200 milligrams per kilograms to achieve a trough level of 120 milli IU per ml, would be 1,200 milli IU per ml, or 0.48 times the CBER Standard Lot 176. Just to remind you the current standard is 0.6 times the CBER standard of Lot.176.

So what we are saying even at the very lowest dose, you would achieve a protective titer if you use the lowest dose of IGIV available. Just to remind you that the dose that’s usually used is at least 400 milligrams per kilograms. So, in most cases if we propose this as a specification, the patients would be achieving twice the protective level in the trough level.

Possible strategies to address declining measles antibody titers in Immune Globulin products, is to lower the recommended measles Lot release specification titer for Immune Globulin and Intravenous and Immune Globulin Subcutaneous, if there is assurance that minimally protective titers are present.

Another option would be to re-vaccinate plasma donors in an attempt to increase antibody levels. But the likelihood of achieving substantially higher and durable

level is estimated to be low in adults. In fact, when you look at adults that are boosted they do have a boost, but it is very short lived.

So, these were the question that we posed to the Blood Product Advisory Committee less than a week ago. The first question, do Committee members concur with the FDA proposal to lower the minimum measles antibody specification for Immune Globulin Intravenous and Immune Globulin Subcutaneous from 0.60 times the CBER standard, to 0.48 times the CBER standard? And this is the voting of the committee, 13 were in favor and 1 was against.

The second question we asked the Committee CBER is considering requesting additional studies to confirm that Primary Immune Deficiency Disorder Patients will achieve trough levels of measles antibodies above 120 milli international units per ml if treated with IGIV and IG sub cu products that meet the proposed revised potency standard of 0.48 times the CBER standard.

Do the committee members agree that this information is needed. And again the votes were 13 in favor, and 1 against. But this was actually a question, but posed to see if there were any ideas for alternative

strategies, so we are asking of the committee to please comment on the need for and feasibility of any alternative strategies that CBER should consider to reduce the likelihood of failed Lots of IGIV and IG Subcutaneous based on potency testing for measles antibodies in order to ensure availability of products for Primary Immune Deficiency Disorder Patients.

So, these were the action items that I summarized for follow-up based on the discussion at the Blood Product Advisory Committee to consider requiring testing for relevant antibodies in addition to measles such as entravirus, Hemaflex influenza, and streptococcus pneumonia, and consider requesting that manufacturers indicate actual titers on labels.

And this would allow physicians to make calculations as to what dose to be able to achieve adequate titers in their patients. For Primary Immune Deficiency Disorder Patients going through areas with endemic measles the question is should they be infused prior to travel, and preferably with high titer product.

So these two issues are related, if you know, the titer and you know, the dose that’s needed for

1 protection and patients with Immune Deficiency are going
2 to an endemic area, you would want them to be protected
3 and preferably have titers that provide sterilizing
4 immunity.
5 So they should probably be infused prior to
6 travel, and depending how long they travel, they have to
7 be re-infused. In addition the point was brought out that
8 there should be an attempt to educate physicians so that
9 they know about this issue of providing increased
10 protection for travelers with Primary Immune Deficiency or
11 in times of measles outbreak, there should be a
12 consideration of adjustment in therapy to assure that
13 protective levels are achieved.
14 This is the last slide. Just the other items
15 for follow-up from the discussions. This was actually a
16 side discussion with Dr. Epstein and some of the members
17 of the committee. If exposed to measles patients with
18 severe immune deficiencies such as severe combined immune
19 deficiency which is probably about less than one percent
20 of the total population of Primary Immune Deficiency.
21 The point is that these patients are usually
22 diagnosed very early and receive bone marrow therapy. But

in the interim they should get much higher doses. And others with profound T cell deficiencies, such as HIV infected individual with very low CD4 counts should be treated with higher doses to achieve titers that achieve sterilizing immunity that is doses that provide titers at trough, which would be greater than 1,000 milli international units per ml.

Just to mention that Immune Globulin and Intramuscular was not part of the presentation, but needs to be dealt with by the FDA because we have the same problem of falling titers and possibility of rejected Lots as a consequence, but that will be done sooner -- take care of that possibility.

Thank you for you attention.

THE CHAIR: Thank you Dr. Golding. Questions form the committee. Dr. Duffell.

DR. DUFFELL: You had one dissenting opinion obviously at the panel, I don't know if it is same individual in those cases, but what was the rationale?

DR. GOLDING: Well, there were two different individuals.

DR. DUFFELL: Okay.

DR. GOLDING: And the one individual as best as I can tell, maybe they'll get someone to comment, but as best as I can tell, wasn't absolutely sure, about the titers and the data, and you know, this is something we are going to look at these limited data, and we have to act I think quickly to avoid loss of product.

Because this product was used for a large number of individuals for life-threatening diseases, and we have to act with the data that we have. But, I think, she was a little bit concerned about the numbers, and we will be looking at that again, just to make sure that our numbers are correct. Some of the information from the meeting maybe helpful in that regard.

And I didn't bring it up during my talk and that is that there is, the CDC or one of the presenters had data about how the titers of donors is decreasing, so if we might get change in the specification we should take that into consideration. So we don't want to every year to change the titers and we should make a specification that is going to be at least for four - five years, so that it takes into consideration the decreasing titers.

The other dissent was for the second question, I

wasn’t clear that, a good reason was provided. But -- I am not sure that -- you know, that that was -- well, I shouldn’t say all that. I don’t think -- but I don’t think there was a good reason provided for the second dissent.

I mean, I think it was a -- the question was related to what titers or what studies will be required by manufacturers to provide data, and it was simply saying that we would like more studies, we think these products are somewhat different because they have different recipients, different manufacturing.

So we would like each manufacturer to look at titers in using their product to make sure that the trough levels are achievable using a lower specification. And that would be the basis for them getting approval to change the label. So, I think, that’s a reasonable proposal and from the data that was already presented to us by some manufacturers I can see this highly feasible thing to do. So we you know, I don’t think there’s a problem.

THE CHAIR: A couple of questions. One is presumably this new set point would change availability

for the better, is there any projection as to what the impact would be? And then the second question is noting the difference in terms of the disease rate across the globe, are there any international products, products available outside of the U.S. that have specificity for the (inaudible).

MR. GOLDING: Well, interestingly as you may have picked up from the slides that the measles that we see in this country is restricted almost entirely since 2001 on imported cases. And these are small outbreaks probably because there’s very good herd immunity, so the implication is that there is measles somewhere, and you know, children dying from it.

Say in Europe and in other parts of the world there are still measles outbreaks much higher level than you have the implication being that donors there would also have much higher titers. The problem that we have with that is that according to our own regulations we require that you only use for manufacturing of these products you only use U.S. licensed plasma.

And that goes and gets into the deferrals of the donors and the testing and so on, and you know, with the

possibility of CJD and that kind of deferrals it's very difficult logistically to use plasma from outside, or products that are made from non-U.S. licensed collection facilities for plasma.

THE CHAIR: And your projection on availability with the new set point, would they --

DR. GOLDING: Well, based on our calculations all the products that are out there now, would pause 100 percent of the time. With the one caveat that I have is that we have look now also some of the other information in terms of declining titers because the 20 percent of the donor population the aged population is decreasing and as a result the titers are decreasing by a small amount each year.

So, I think, we need to use that information to make a calculation. But my expectation is that the 0.48 times the standard would allow for a 100 percent of the products to pass and that that would -- it's enough leeway probably for several years, but we may have to make a small change to that.

THE CHAIR: Thank you. Any other questions from the Committee. Thank you, Secretary Holmberg.

DR. HOLMBERG: I don’t know if you have a answer for this but in your action item your follow-up several of those comments appear to be things that could appear in the package insert is there indication that that might be part of the labeling requirements in the future, or --

MR. GOLDING: No absolutely, I think that’s very important so I think, that should be part of the follow-up that we should not only you know, state that this has a less of a titer but give some information to the treating physician as what titer needs -- what doubts need to be given to achieve the protective titer and what adjustments should be made if your patient is traveling, or there is a measles outbreak, or if your patient has not only an antibody deficiency but has a severe T-cell deficiency, because we think in those cases you probably need much higher doses.

THE CHAIR: Thank you. We'll move on to our next presenter.

Our next topic will be Human Tissue Task Force report, which will be presented by Mary Malarkey. Mary Malarkey is the Director of the Office of Compliance and Biologics Quality at FDA center for Biologics Evaluation

1 and Research, thank you.
2 MS. MALARKEY: Good morning. I'm here to
3 provide an update to the Committee on the Human Tissue
4 Task Force and I'm not sure that you all are aware of the
5 Human Tissue Task Force, so the first thing, I think I
6 need to do is, is give you some background information.
7 My presentation will provide highlights of the
8 June 12, 2007, report, which was a final report from the
9 Human Tissue Task Force, which is available on our CBER
10 website. I'm also going to provide some additional
11 information that was gleaned from a number of inspections
12 that I'll go into more detail about on the overall
13 compliance status of the recovery industry, that is, those
14 establishments that recover human tissue for
15 transplantation and also industry practices affecting the
16 risk of communicable -- thank you -- disease transmission.
17 As a matter of background, the HTTF was formed
18 on August 2006, it was part of the Agency's effort to
19 evaluate and where-needed strengthen a risk based system
20 for regulating human cells, tissues, and cellular and
21 tissue based products or what I will refer to as HCTPs.
22 The primary goal of the Task Force was to assess

1 some of the challenges that we'd faced over -- since the
2 time that the final rules went into effect for a new
3 regulation, which was May 25, 2005. And I'm sure the
4 Committee is aware of the couple of cases that were
5 particularly in the media around human tissue and these
6 challenges kind of forced us and we really needed to look
7 at the implementation of the new system and to identify
8 any additional steps needed to further protect the public
9 health and also though to ensure the availability of the
10 these very important products.
11 This was an FDA Task Force; the members of the
12 Task Force came from our Office of Regulatory Affairs,
13 which is our FDA field force. These are the individuals,
14 the investigators that go out to the individual firms and
15 perform the inspections. The Center for Biologics
16 Evaluation and Research, of course, several offices there,
17 and our Office of the Commissioner was also involved,
18 Office of General Counsel, Office of Policy, as well as
19 the immediate Office of the Commissioner.
20 The Committee -- or the Task Force, I should
21 say, met for three months, we had a three month charge and
22 we considered the following areas; inspection and

compliance activities, and when I address those I will also talk about the additional information that was gleaned from the inspections.

We looked at partnering, leveraging, education and outreach; we looked at adverse reaction reporting and analysis. In the HCTP world adverse reaction is the terminology used legally in our regulations as opposed to adverse event or adverse experience; we looked at the need for possible additional regulations, guidance or policy development; and finally we looked at the science of tissue safety.

Beginning with inspections and compliance activities -- at the time we started this project there were 2,023 registered establishments, that is, establishments registered to perform some step in manufacturing of all HCTPs. Now this would be from both living and what we're calling here non-living donors. 856 of those establishments manufactured from non-living donors.

So from October 1, 2006, to March 31, 2007, 153 inspections were performed of domestic musculoskeletal recovery establishments and this was of course the

establishments that were implicated in the biomedical tissue services and donor referral services cases and there was a great concern that we would find similar practices in the industry.

So we felt it very important to get out there and to really look at what was going on. Now, the investigators were tasked with following our normal instructions, that is, we have a compliance program that directs the investigators what to look at during the course of a normal inspection but here we supplemented that program with an assignment that was designed to detect inaccuracies and deficiencies in records like those noted during those two -- inspections of those two facilities. We also asked them to collect information on industry practices affecting the risk of communicable disease transmission.

The summary of the findings is that there were deviations from the regulations noted during some of these inspections. However we did not detect any of the major inaccuracies or deficiencies in the records. None of the inspections resulted in the need for regulatory action and we did see that some of the firms -- of those 153, some of

them were out of business, they were still registered but they had not cancelled their registration.

Some were actually not performing recovery though they had indicated they were doing so, so some were actually processing or storing, for example. And some did not the donor records on site, and these were the important records that we wanted to look at for inaccuracies and deficiencies, so for example, the records would be stored at a central location and we had to look at them there.

So 134 actual establishment inspection reports were reviewed to assess the overall compliance status of the industry and 125 of them then were further reanalyzed because donor records could be reviewed to assess the industry practices affecting the risk of communicable disease transmission. And some of the results of these assessments are summarized here.

So, looking at the organization and operations of recovery firms what we did was divide them into three sectors; large firms, which have more than 50 employees, and this encompassed 22 percent of the establishments, most of these firms are also OPOs or they procure organs

as well, and some also are large processors of human tissue.

Medium firms we designated 10 to 50 employees and this represented 48 percent of the firms inspected, some of these did perform organ procurement and many of them also processed. And then finally the small firms which were less than 10 employees and this represented 30 percent of the inspected firms, and these focused mainly on recovery operations.

In terms of donor recovery volume and keeping in mind that this is just musculoskeletal recovery firms, this was not -- we have not looked at eye banks, for example or concentrate on skin or vascular tissue, for example -- the one calendar year we had the most solid data, there were 43,000 donors recovered.

Recovery volume by firm size, I think it's -- it really makes sense here the large firms recover the majority, 54 percent, medium firms 34 percent, and the small firms 12 percent. And what we saw when we looked at three years of records is that the rate of recovery generally was stable, that is there wasn't an increase or significant decrease in the numbers of donors recovered by

these firms.

In terms of recovery locations it's important to know that in general recovery firms don't just recover donors in one location, but in many different locations and the hospital or war was by and large the largest of the majority of recoveries that were performed, majority of recovery that establishments used hospital at war, at had 93 percent.

Funeral homes were used by 59 percent, medical examiners and coroner's offices, 59, morgues 26 percent, and then there are firms that were seeing more of these dedicated recovery suites, these are actually "Clean Rooms" that are designed specifically for recovery operations and this was at 18 percent.

Most establishments did have a contract agreement or arrangement with all the recovery locations and all of them had procedures related to control of aseptic conditions during recovery.

In terms of who determines whether the donor is eligible that is based on the medical history of the screening and the testing, none of the recovery establishments made that determination. They did of

course assemble information and provide it to the processors who all made the final DE determination. So it's important to know that the records that the processors are from these recovery establishments.

We found that the sending or dissemination of HCTPs as well as test samples and the information can be very complex. There are many parties involved all along the way and the inspections really greatly increased our understanding of these various relationships. In terms of the compliance of the industry, well, for all recovery establishments out of the 134 inspections, 35 of them resulted in what we call an FDA Form 483, which is a list of observations and this is a list of what the investigator feels are violations or deviations from our regulations.

It's not a surprise that establishments that had been inspected had prior inspections by FDA, that the numbers were around 24 percent while there were -- number 16 that had never been inspected by FDA and in those cases -- in that case 44 percent result in the issuance of a 483. And we found there was no significant difference based on the size of the establishment.

The most common observations and these are the regulations, this is our 21 -- 21 titled -- excuse me, titled 21 Code of Federal Regulations; these are sections 1271.200, which is equipment cleaning and maintenance and calibration and this is the equipments or utensils, surgical instruments that would be used in recovery operations.

We did see some issues with records but again not the major inaccuracies or deficiencies that were noted during the BTS and DRS inspections. There were issues relating to procedures and adequate procedures, lack of certain procedures both in our cord, current good tissue practice requirements and donor eligibility requirements.

Facility Cleaning and Sanitization: Perhaps not fully documented or procedures were not fully in place and finally the quality program.

So, in conclusion in terms of recommendations -- the HTTF did make recommendations for inspectional goals and priorities. It's important to note that there is no statutory requirement for biannual inspections for these particular facilities unlike our other biological products, so we did recommend biannual inspections for

1 what we would have considered to be high-risk
2 establishments and those would be establishments, which
3 change from year-to-year, based on our analysis of what
4 high risk would be in a given time; and then triennial
5 inspections for all the other facilities.
6 Clearly we would need resources to do this and
7 that was one of the charges of the Task Force, to
8 determine whether current resources could meet the needs.
9 We felt that more resources were needed, training time,
10 planning, human and financial resources.
11 Moving on to partnering, leveraging education
12 and outreach; we talked to many of our federal partners,
13 we've worked very closely with the CDC for many years, on
14 the tissue safety area and we continue to do so. We're
15 having monthly meetings with them, and feel very happy for
16 our collaboration. HRSA as well we've worked closely with
17 and we spoke to them about some of the regulations,
18 legislation governing organs as opposed to tissue, and the
19 FTC which actually has a role in the funeral home
20 industry.
21 We talked to many states, we actually had a 50-
22 State call that was arranged by our field force, and try

to understand what the States were doing in terms of regulation of tissue. We talked to the eye-banking industry as well as the tissue industry and we are very appreciative of their input and we feel that they have done a lot since those cases happened, to improve the conditions, if you will, and practices.

And finally we talked to the academic and professional organizations, the actual end-users to find what their thoughts were on the use of human tissue. We concluded that we would like to expand these activities and if we could expand them we feel that it would improve the communication network that we have with our State, federal regulatory partners, enable more sharing of information and greater knowledge of industry operations and clinical practices and finally we feel it would allow enhance communications with these academic and professional organizations.

In terms of adverse reaction reporting and analysis, we reviewed our current procedures for adverse reaction receipt analysis and follow-up. This is the charge of the tissue safety team, which was put in place in 2004 and we do have procedures that we follow when we

are made aware of a particular adverse reaction associated with a communicable disease.

We enlisted the consultative services of a -- an SGE, if you will, with extensive clinical experience to improve our procedures for this analysis, so the investigation, the classification -- it's often difficult to determine whether the adverse reaction was actually caused by the tissue transplant.

And finally, you know, analysis of these adverse reaction reports.

We concluded that with our current resources we can certainly refine the activities of the Tissue Safety Team, and we can continue our interaction with outside experts and we are continuing coordinating with the CDC regarding the proposed Transplantation Transmission Sentinel Network or TTSN, which I know Matt has spoken about here.

That project -- we're sure that it complements our existing surveillance systems and we're also very interested in active surveillance as a whole going forward and using whatever databases -- on health care databases that we can to glean information on transmission of

disease through tissue.

We're sponsoring a workshop with -- cosponsoring, I should say, with CDC and our Center for Devices and Radiological Health because they also regulate many of these products, and that will be held October 10 and 11, 2007. That has gone out in the federal register in terms of the agenda.

Healthcare providers and scientists as well as the industry have been invited to share knowledge and experiences regarding technologies and methods to enhance tissue safety. And other actions that we would love to undertake -- but again that would require additional planning and resources -- particularly in the area of the active surveillance. We are expanding our work with MedSon and we have work with AASPEE -- AASPEE on a particular project, but we welcome more of those.

In terms of divisional guidance and policy considerations, we did issue a guidance document clarifying responsibilities between establishments and their contract establishments, we are in the process of drafting a current good tissue practice guidance, and other issues are under consideration. We recognize that

1 our current regulations only require tracking of tissue to
2 the consignor or that would be the hospital, but not to
3 the recipient and that does cause severe issues during
4 recall or when notification of patients is important.
5 In terms of original records for certain DE
6 determinations, that is, in certain instances it may be
7 necessary to have certain original records, and finally we
8 thought additional guidance on how the industry could
9 audit contractors maybe useful.
10 Finally the science of tissue safety -- in terms
11 of testing a tissue it is very difficult. It is not an
12 easy matrix and it is something that we know many in the
13 industry are working on individually but we feel the need
14 to have some sort of a program in place around this, so we
15 are going to initiate a tissue microbiology program at
16 CBER, we look forward to partnering and -- with whomever
17 we can to get more information in scientific data and to
18 really look at the methods around testing and potentially
19 processing.
20 So, in future any issues that we feel require
21 cross agency or multi disciplinary perspective will come
22 back to the HTTF, it has not been disbanded but we are not

needing it as regularly as we were, we obviously have to track implementation of the recommendations and discuss any emerging issues and opportunities that may arise.

And that's -- my contact information if you happen to think of a question after today or would like additional information, so thank you very much.

THE CHAIR: Thank you.

I'll open up for questions from the Committee, if I could ask perhaps one question?

And that is, in terms of the universe of collectors out there, how many would you say are not inspected or accredited by any agency? In other words are there unregulated collectors?

MS. MALARKEY: Well, that -- there should not be, I guess that would be my best answer. Anyone who is collecting or recovering human tissue for purposes of -- or cells even, for purposes of implantation, transplantation are required to register with the FDA, and we have -- we did some research, you know, into that question.

We do not regulate "research use only" tissue, for example, so there maybe some medical hospitals or that

sort of thing that might recover particular tissue for research use purposes, and those would not be required to register with the FDA.

THE CHAIR: So, I guess a follow on to that would be one of the things that can help in the world of the end-user is if there is some specification that the source needs to be from a registered facility -- is that operative in most hospitals, as far as -- that requirement?

MS. MALARKEY: I don't believe so. I do believe that there are regulations in place that govern the individual who is making the donor eligibility determination and making the tissue available for distribution, that is prior to the hospital receiving it that requires that that individual know where the tissue came from and that goes back to the guidance on contracts and how you must assure, for example if you contract with somebody that they are registered.

But in terms of the end user I don't believe that there is anything in place to really go down to that level of detail. I think there is some dependence on the provider of the tissue.

THE CHAIR: Thank you, Ms. Birkofer.

MS. BIRKOFER: Thank you.

I have a few questions, I think on the same line as Dr. Bracey. Can you just give me an estimate on the number of processors in the U.S.?

MS. MALARKEY: I'm looking at my colleague from the ATB -- just kind of framing out, like -- what are we talking about?

There are less than a hundred, I would say processors, but I -- this is Scott Brubaker from the American Association of Tissue Banks that -- he'd able to --

MR. BRUBAKER: From our surveys and after I've taken a close look at the E-Hictor's (phonetic) database which is the establishment registration and listing database that FDA has, not all of the processors are accredited by AATB, most of them are, and that there's about 15 -- between 15 and 20, for musculoskeletal tissues -- major processors in the United States.

Most of them, there's only about three that are not, are accredited by AATB. For human heart valves, for instance, cardio vascular tissue, there is really only

five of those in the U.S. -- or four now.

MS. BIRKOFER: Does the AATB have any voluntary standards in place?

MR. BRUBAKER: Oh, absolutely.

MS. BIRKOFER: Okay.

MR. BRUBAKER: We've had them for years.

MS. BIRKOFER: And with regard to the donor eligibility requirements, it says here in your presentation, "All final DE determinations are made by processors."

MR. BRUBAKER: Yes.

MS. BIRKOFER: Can you give me a sense of the number of "fails" out of the total volume?

MS. MALARKEY: That -- that's a very difficult question and it is something that we looked at and I think that one has to understand that records are kept at different stages by different recovery organizations.

And by that I mean that there are those that -- as soon as there is a possible referral, they begin to keep a record. And it could be, for example, that the family does not consent or there is something else that prevents that individual from being a donor outside of the

1 donor eligibility determination.
2 So, we try to get a good handle on rates of
3 rejection, but it was very difficult. They are not really
4 very high in terms of testing, for example.
5 MR. BRUBAKER: I can offer a little bit of
6 information. I did a survey of our accredited banks that
7 processors last year -- for the first three quarters of
8 the year and it ranged between -- we call it suitability
9 or eligibility. But those are determined as unsuitable is
10 between 2 and 25 percent depending on the bank and how
11 they operate. I can tell you about 8 percent of those are
12 due to repeat reactive infections disease test results.
13 MS. BIRKOFER: Thank you sir.
14 MR. BRUBAKER: Thank you.
15 THE CHAIR: One question as a follow-on is, is
16 it possible although most of the processors are in fact
17 accredited by someone, but if as a -- would it -- is it
18 possible that a requirement for participation in CMS would
19 be that one would use a registered facility only, i.e., to
20 tie that into the Medicare eligibility?
21 MS. MALARKEY: I would have to defer to CMS --
22 THE CHAIR: Yeah. Again at the --

1 MS. MALARKEY: -- on that question as to whether
2 that would be a possibility.
3 THE CHAIR: Okay, because I would think that --
4 I would think that that along with, I guess the other
5 issues there seems to be a large issue that you mentioned
6 was that recipient traceability and in the blood world,
7 the regulations from the FDA have been very effective in
8 our being able to have that sort of traceability and it
9 would seem to me that the Task Force would consider some
10 ways to sort of put teeth into that -- into that need?
11 MS. MALARKEY: And we are looking at that very
12 seriously. I think it's important to note that the Joint
13 Commission put a new standard in place last summer, I
14 believe it was or maybe the year before about tracking to
15 the recipient, so that has proven helpful, it's certainly
16 not a regulation but it is a standard and so that has been
17 a positive move.
18 I think there are some differences between blood
19 and tissue in terms of the hospital setting where there is
20 a blood bank or transfusion center where there would be --
21 where the blood would be stored and would be instead of a
22 pharmacy. In case of human tissue we found that it kind

of goes to different places at different hospitals. It's more part of inventory and not necessarily controlled in a central location, like blood would be.

THE CHAIR: Dr. Kuehnert?

DR. KUEHNERT: Yes, and I know that this was something that was addressed with the Task Force, and I think it's very important because if you can't track a tissue and find out where it went -- and that does happen -- then it's very, very hard to see if there is an adverse reaction or something untoward that happens with the tissue. So I saw that -- in reviewing the Task Force findings that it said that there was going to be some review to see what legal constraints FDA had for -- for going from the tissue bank to the hospital as far as tracking, which FDA can't really have any effect on now, and I just wondered what conversations there has been about that, is there any -- I thought that, that there is some legal constraint that couldn't be overcome but what are those?

And then my other question was, if there is some hurdle to overcome, you know, how do you intend to work with Joint Commission and CMS, because of course they're

1 also as you mentioned, trying to develop standards in the
2 hospital for tissue.
3 MS. MALARKEY: Well, I'll address your last
4 question first, if I may. We are working very closely
5 with CMS and they have given us context with the Joint
6 Commission, and we're working with them. We're actually
7 going to provide some presentations to the Joint
8 Commission -- Dr. St. Martin who is here and was involved
9 in that particular project, so that we can impress upon
10 them the importance of this. So that is in the works.
11 I can't really discuss our internal
12 deliberations around the legal analysis, I will say that
13 we are looking at it very, very closely and doing what we
14 can, but as is often the case or I should say probably
15 always the case, developing new regulations or trying to,
16 is always daunting, I mean, this is a particularly
17 daunting task. So we are interested in all possibilities
18 and that is why we are interested in working with the CMS
19 and the Joint Commission as well.
20 DR. KUEHNERT: That's great to hear, and I know
21 we're going to -- CDC and FDA is going to continue to work
22 together particularly concerning TTSN, because any legal

1 changes that occur with tracking would also affect that
2 system as well.
3 And the final comment I just had is that you
4 mentioned that tissue in hospitals tend to be handled
5 differently in different places and just that that seems
6 to be changing and it seems that more and more blood banks
7 are actually being involved with handling tissue and that
8 may help to have a centralized location in hospitals,
9 concerning tracking.
10 MS. MALARKEY: it may very well, I think that's
11 a very good point and we are seeing that change. I think
12 it's also important to note however that the -- some of
13 these products are not distributed to hospitals but in
14 some cases to oral surgeons, dentists -- so outside of the
15 hospital community, if you will. So, that further
16 complicates this issue.
17 THE CHAIR: I believe we have one more question
18 -- another two questions.
19 Executive Secretary Holmberg.
20 DR. HOLMBERG: Mary, thank you so much for your
21 presentation and one of the things I do want to commend
22 you for is really reaching out to the other operating

divisions within HHS and I do want to let you know that if you need coordination from my office, through the Assistant Secretary, that we'll, you know, especially since our charter has been expanded to that, I do want to make sure that that's clear.

The other question I had for you or the comment -- question I had other than the comment was that, who actually are doing -- who does these inspections? And for instance you've mentioned a major problem that you may inspect the procurement organizations but the processors who may then do the donor eligibility may be somewhere else.

So, my question is, is this primarily a field activity or is this the headquarters activity and how do you coordinate to follow the trail all the way back?

And then as a question, if you could also comment on -- you mentioned about the breakdown in the compliance failures and you mentioned about the good -- or the good tissue practices and that currently you are working on a guideline for that -- how did that fall out as far as the frequency of events, and is that what's really pushing towards this guidance to be published?

MS. MALARKEY: Okay, yes the FDA field force does perform these inspections, but we work very closely with them. There is an Office of Regulatory Affairs Headquarters department at the Office of Regional Operations that we work closely in work planning activities, that is every year we put a work plan together of recommending what sites would be inspected and again this is based on our risk -- it's one of our risk based activities.

We are very conscious of the processors, we -- actually we've been inspecting these firms since 1993 and the processors probably have had the most coverage I would say -- than -- more coverage than any. It's important to know that with the new regulations that went into effect in May, 2005, the recovery organizations were now held to different standards, that is, there were standards around the current good tissue practices that had not been in place before.

And by that I mean around equipment cleaning and procedures and the facility itself, so we felt it was important anyway to get out and look at these facilities to ensure that their compliance with these current good

tissue practices. We have been working on the current good tissue practice guidance for some time, but I think these inspections help to inform us and to add some additions to the guidance that we hadn't really thought of before, often going out and really seeing what is going on and identifying the problems is very helpful in providing additional guidance to the industry, so this did help to inform us in terms of going forward with that guidance. But we do -- we do get all the inspection records back at headquarters.

We review them carefully because we -- with the new regulations in place we feel that, you know, we really need to be vigilant and see what's going on out there and I think these two particularly disturbing cases that occurred in the very first year, was certainly a wakeup call, that we really needed to go out and do this sweep, if you will, of inspections and thank you very much for your offer.

THE CHAIR: Dr. Epstein?

DR. EPSTEIN: Thank you very much Art and Mary.

I appreciate fully that the inspection program was carried out in a situation of significant resource

constraints. Nevertheless, it might be useful if we could have a quantitative handle.

What percent of donations do you think the -- is inspected establishments represent as fraction of the whole, or what percent of tissues processed do you think the number of inspected establishments represent based on volume of processing as a whole. In other words, do you think this is a one percent snapshot, a five percent snapshot, a ten percent snapshot?

MS. MALARKEY: No, this was all of the recovery establishments that were registered to recover musculoskeletal tissue in the domestic, so this was everyone that was registered with us. Clearly there were other recovery organizations or collectors that -- for reproductive tissue or stem cells or cord blood.

Again the eye banks -- we did not concentrate on the eye banks because that was not an issue, has not been an issue in the past, so this was very concentrated and meant to hit those establishments that recover musculoskeletal tissue, so this would be all the tissue that would be processed presumably in the United States.

DR. EPSTEIN: Art, if I could be permitted one

scientific question.

You know, I appreciate that microbiological monitoring of tissue is a daunting challenge because of the very diverse physical conditions of different tissues and the difficulty of sampling, you know, surface versus penetrating.

So my question is, is there utility for irradiation and has there been a finding that irradiation is utilized and could it be more widely utilized because we know that it's a penetrating, sterilizing method and most tissue is -- certainly musculoskeletal tissue is devitalized.

MS. MALARKEY: Yes, there is no question that irradiation is used in the industry, and for bone particularly it could be used with great success. One of the reasons we're having our tissue processing workshop is to get an idea from the surgeons around soft tissue because soft tissue is one of those tissues that we believe can withstand irradiation but there is some we -- there's -- at least we have anecdotal reports that surgeons may not want to use irradiated soft tissue in all cases.

1 So, that's one of the reasons for the tissue
2 processing workshop, to get information from them on their
3 thoughts and why this is and what body of data there maybe
4 out there and what additional data would be useful in, if
5 you will, allowing them to use this tissue, because we do
6 feel that really the processing is where it is because the
7 testing is so very difficult, so that's a very good
8 question and something we're looking into.
9 THE CHAIR: Thank you, there's been lots of
10 discussion and we certainly appreciate your presentations
11 and responses.
12 MS. MALARKEY: Thank you.
13 THE CHAIR: We will move on to our next speaker
14 and that is Robyn Ashton and Robyn is with the Division of
15 Transplantation, or HRSA and she will present an update on
16 the Advisory Council on Blood Stem Cell Transplantation.
17 MS. ASHTON: Thank you.
18 (Discussion off the record)
19 MS. ASHTON: I'm just going to be giving you an
20 update on this -- the Advisory Council on blood stem cell
21 transplantation as Dr. Bracey said and in order to do that
22 I have to first talk about quickly, the law that was

signed on December 20, 2005, which was the Stem Cell Therapeutic and Research Act of 2005.

It was Public Law 109-129 and its aims were to increase the number of unrelated donor transplants, to increase the public inventory of high quality cord blood unit from diverse populations, and to increase number of cord blood units available for research.

You might not be able to read that but I can. The key elements of the new law are for the National Cord Blood Inventory and sometimes it is called the NCBI, to collect high quality cord blood units, like I said just now, from diverse populations for use in unrelated donor transplants and there is a target of a 150,000 new units that would not include the existing inventory.

The C.W. Bill Young Cell Transplantation Program to facilitate transplant through cells from cord blood and bone marrow and to collect data on transplant outcomes and also -- and this is what I'm supposed to be updating you on, the establishment of the new HHS Advisory Council on blood stem cell transplantation for these programs. So this is an exciting opportunity to help more patients obtain transplants and other therapies.

1 So the purpose of the Advisory Council is to
2 consider and make recommendations to the Secretary of HHS
3 and to HRSA on matters related to the C.W. Bill Young Cell
4 Transplantation Program. Now the Advisory Council charter
5 was published in the Federal Register on January 23, 2007,
6 that's this year with nominations for memberships
7 solicited by February 22 of this year. And we've received
8 over a 100 nominations of very, very qualified candidates.
9 So the -- in total the Advisory Council will
10 consist of up to 25 voting members and the law requires
11 representatives from marrow donor and transplant centers,
12 cord blood banks, birthing hospitals or labor and delivery
13 elements to a hospital, blood stem cell recipients and
14 their family -- and/or their family members, people with
15 expertise in blood stem cell transplantation and that
16 would be both cord blood and bone marrow, people with
17 expertise in typing, matching and transplant outcome data
18 analysis, expertise in social scientists, that would
19 include or especially include ethicists, basic scientists
20 in the biology of adult stem cells and members of the
21 general public.
22 And then the ex-officio or nonvoting members who

1 would include someone -- a representative from the
2 Department of Defense, Marrow Donor Program, operated by
3 Navy, someone from the Division of Transplantation of
4 HRSA, the FDA, NIH, CDC, and CNS.
5 Some possible topics, and there could be many
6 more, this is just brainstorming -- this is what people
7 came up with. Targets for the national cord blood
8 inventory and for the adult registry sides and
9 compositions on optimal registry size; research
10 priorities. So, Hematopoietic Progenitor Cell
11 Transplantation Research, other therapy results from cord
12 blood and bone marrow, criteria for releasing units for
13 research, informed consent and accreditation.
14 Confidentiality issue is a very big topic --
15 they all are -- key cord blood characteristics that would
16 improve outcomes, criteria for recommending specific stem
17 cell sources for different diagnoses, demographics and
18 internal conditions, public and professional education
19 regarding donation, strategies and resources to expand
20 opportunities for eligible pregnant women to publicly bank
21 their infants cord blood units.
22 Also, regulatory policy including international

harmonization of regulation and importation issues, public and private insurers, or actions to increase donations and access to transplant, state and federal government actions and that's other than this payer -- payers to increase donation and access to transplant.

Now, as of this meeting the nominations are still under -- are under review in the department --

(Tape interruption)

MS. ASHTON: -- says with expertise in the biology of adult stem cells and members of the general public. And then ex-officio or non-voting members would include someone from the -- representative from the Department of Defense, Maradona Program operated by Navy, someone from the Division of Transplantation of HRSA, the FDA, NIH, CDC, and CMS.

Some possible topics and there could be many more, this is just brainstorming this what people came up with, targets for the National Cord Blood Inventory and for the adult registry size and compositions on optimal registry size.

Research priorities, so Hematopoietic Progenitor Cell Transplantation Research, other therapy with cells

1 from cord blood and bone marrow, criteria, for leasing
2 units for research, informed consent, and accreditation.
3 Confidentiality issue is very topic they all are.
4 Key cord blood characteristics that would
5 improve outcomes, criteria for recommending specific stem
6 cells sources for different diagnoses, demographics, and
7 cell conditions. Public and professional education
8 regarding donation, strategies and resources to expand
9 opportunities for eligible pregnant women to publicly bank
10 their infants cord blood units.
11 Also, regulatory policy including international
12 harmonization of regulation and impartation issues, public
13 and private insurers, so actions to increase donation and
14 access to transplant. State and federal government
15 actions, and that’s other than its payers to increase
16 donation and access to transplant.
17 So as of this meeting, the nominations are still
18 under review in the department, we are not certain when
19 the appointments will be made by the secretary and meeting
20 logistics contracts has been awarded to support the
21 council and we are prepared to hold the first meeting this
22 fall, late this fall.

These are some references. I apologize that this is not in your packet, but I believe it will be in the transcripts when the minutes are available. These are some of the reports that you can get some of this information I am talking to you about right now. And that's my information.

THE CHAIR: Thank you. Questions from the committee. One thing that's always a challenge particularly with organ transplant and stem cell transplant is the issue of availability, and their barriers for biologic reasons as well as non-biologic reasons. And is the committee with this particularly activity the Advisory Council be also addressing it?

MS. ASHTON: Absolutely, I don't think anything is out of bound or you know, not appropriate, that's an excellent topic, I am going to write it down when I sit down, because it's so important, and at times it's is a problem for cord blood, and adult donors.

THE CHAIR: Right. Thank you. Questions Executive Secretary Holmberg?

MR. HOLMBERG: Yeah, I just want to make comment. Thank you, Robyn, for your presentation. We

will have all of this information, the transcripts and all the presentations will be coming to each committee member on a CD, and so you'll have a summary of everything for the meeting for the -- in two days. And these will be published on the website along with the transcripts.

THE CHAIR: Thank you. In the interest of biology, we will take a break now, and then we'll come back with the Dr. Riley, and discus the status of Donors in the U.S. Thank you. Fifteen-minute break.

(Recess)

MR. RILEY: One is that we didn't learn anything that you don't know already. And especially the committee and the community of blood bank experts, the only thing we did was to attach the facts to what is already pretty well-known in the blood banking community. And we are able to enumerate the entire pool of eligible donors that was not been done before, so we simply added up all the factors that you already know of.

I'd like to cover five different sections in this presentation. But what prompted us to conduct this study is the realization that the current method for estimating the eligible blood donors only uses age as a

criteria factor for excluding the donors. And that -- we should say as far as the estimates and creating the denominators, but as all of you know that poorly reflects of the known factors that cause donor deferrals.

So, the model, the conceptual model has three parts to it. First of all we identified and prioritized the 31 main deferral factors. And then we prioritize them according to prevalence, and these factors all corresponded to the AABB standards.

And once we did that we selected databases to estimate the prevalence of each of deferral factors, and then thirdly we simply adjusted the prevalence data based on three different conditions, the age within prevalence, the duration of the exclusion, and then the presence of co-morbidities.

So, I don’t think this slide made the machine transfer, but I’ll try. This is basically the conceptual model and the result is the entire population of the nation is 294 million people. And based on the age exclusion formula that is typically used there are a about a 117 million of the entire population that’s excluded in the calculations, for calculating the eligible donor pool.

And this is about this leaves about 60 percent of the population according to their usual conventional methodology that's eligible to donate blood. That's reassuring. That's a large pool. However, we added up the known exclusions which are an additional 66 million persons who are excluded because of the exclusion criteria. And that's a little more concerning.

So, in other words based on the age exclusions, and then all the other 31 exclusions factors that we enumerated, that leaves this population eligible to donate blood. And what's even more concerning is that within this population there are well-known profiles of donors, and what is not known is the, you know, the -- excuse me -- the donor -- the profile of donors is white males, college educated and above average income.

Well, that profile of eligible donors interacting with this pool of non-exclusions leaves an unknown pool of donors, which is even more concerning in terms of what is the eligible pool of donors available to donate blood. And from that becomes the pool of current donors.

So, there are six steps to the methods, I won't

1 got through with the laborious methodology, but just to
2 say that in terms of the exclusion factors we identified a
3 total of 31 factors. They are on the table on the second
4 to the last page on your handout. And of the 31 factors,
5 18 are permanent factors, that is for a year or longer and
6 exclusion factor. Nine are long term factors, which are
7 any exclusion factors from 60 days to a year. And then
8 five are short-term factors which are 60 days and under.
9 So, I mentioned this slide on the second to the
10 last page in your handout, and then after we identified
11 the appropriate databases for each of the deferral factors
12 we adjusted them according to the criteria that I am going
13 to discuss next. The previous slide on the total
14 population of the country, and then how we subtracted the
15 exclusions is shown again. According to this calculus
16 that if we take the total population in the country and
17 subtract the age exclusions, and then from that we take
18 that pool, and subtract the known exclusions, and from
19 that adjust for comorbidities it leaves us with a 177
20 million persons who are eligible donors according to the
21 conventional criteria.
22 And then we adjust that 177 million by an

additional 37 percent of the population, which is excluded. And 177 million persons in the conventional methodology minus the 66 million persons that are excluded for all the criteria that you are already aware of leaves about a 111 million persons according to our methodology that are eligible to donate blood.

So, comparing the conventional methodology, 294 million persons, 117 million are excluded from the age exclusions, leaves a 177 million, who are eligible donors which is about 60 percent of the entire population. We started with the same population, we do the same age exclusions, however, the exclusions for the 31 criteria, results in additional 66 million persons that are excluded, and that leaves an eligible pool of about a $111 million -- a 111 million -- sorry, I am a finance expert, I always talk in dollars not people. That leaves 110 million eligible donors. So, it’s 37 percent of the population rather than 60 percent of the population.

The implications, first of all, that a more precise measure of the blood donor collection rates is needed based on an accurate estimate of the eligible blood donors in the catchment area. Again, the blood-collection

community is well aware of the donor exclusions, but has never added up the total impact of these exclusions.

The conventional model or the conventional formula that is used, the calculations are there about 81 units of blood donated per 100 eligible donors, but using the formula that we just presented to you really suggest that there are about a 129 units for a 1,000 eligible donors. And the question that rises and we go further into that is depending on how small this total pool of donors is we -- are we bleeding them dry?

So, the next implication is that there is an extensive amount is known about the donors, but much less is known about the total pool of potential donors, and that’s where we are focusing our interest. And likewise, it is not known that the extent of the changes in the eligible donors vary and contribute to the blood shortage.

And finally, that the strategies and the policies should be developed based on a more accurate understanding of the donor population. One thing we don’t know, for example, is that we know that based on this model that about 37 percent of the population is eligible to donate blood, but that’s on a national basis.

It’s very conceivable that in certain catchment areas or service areas, maybe only half of that 37 percent are eligible to donate blood depending on the criteria factor exclusions, which helps explain further why it’s so difficult for blood collection at times.

So, what are the questions that are asked? It raises a series of questions, one is that an empirical model, either this one or one that is developed further based on the limitations of this model, of eligible donors is certainly going to supplement what is already known and quite a bit is known about the socio-demographic factors and motivation triggers for donors.

And then based on that is the impact of donor exclusions increasing or decreasing overtime. You know, we think we know the answer while we don’t know for sure. And as I mentioned just a moment ago, what is the eligible donor pool size between regions? We know that nationally it’s 37 percent, but it is certainly higher in some communities, and probably lower in other communities.

And this model certainly can predict the impact of a major event that affects both the demand for the blood, and the supply of blood donors or even both. And

that’s important because the interaction between the known donor profiles and the eligible donor pools not known.

So, again what I mentioned earlier is to what extent could the interaction constitute a "tapped out" donor pool.

And three other questions is what is the relationship between the aging population. The age exclusions are an important aspect of both models, but there is a interaction between the aging population, and the exclusionary factors with the donor pool, and of course that’s going to have an impact on the demand for blood, so again there’s a multiplicity of interactions that are going to affect what could be a very small pool at the end of the day.

Secondly, what is the relationship between the exclusionary factors and new donor exclusions, either that are suspected or maybe occur especially in emerging infectious diseases and emergency response conditions. How will that affect the donor pool, and the demand for the blood? And so again it’s a receptacle interaction.

And then finally, to what extent would the increase demand for blood affect the diminishing pool of

1 those who can supply the blood? There are limitations to
2 the study. And I will conclude with that. Thank you very
3 much.
4 THE CHAIR: Thank you Dr. Riley. In the words
5 of Willie Sutton, "One robs banks because that’s where the
6 money is."
7 (Laughter)
8 THE CHAIR: Looking at your exclusions, the
9 biggest number that I could see, and it may have -- aside
10 from the acute illnesses, perhaps the second biggest
11 numbers those that fail the hemoglobin screen. It appears
12 to me that at least there is the opportunity here to have
13 some donor management that might hack away at this huge
14 number, which would A, be in the interest public health,
15 i.e. not having iron deficient individuals live their
16 daily life iron deficient, and B, bolstering our blood
17 supply. And that I’d be interested in your thoughts or
18 perhaps those of Dr. McCullough about that big number.
19 DR. RILEY: You are right and I think Dr.
20 McCullough can answer it very completely, but it is a
21 large number, it starts out at 58 million persons, and
22 then we refine it down to about 13 million that are

excluded. But the question you are asking is can either of those numbers be managed better?

DR. McCULLOUGH: We did make the hemoglobin exclusion a short-term exclusion and factored that in out, so that, I forgotten the amount of time we ascribed to it. Two to three months presuming that possibly if a donor returned they -- the hemoglobin might be increased, but it’s an arbitrary decision.

The only other thing I’d say about it is, most of you know very well, that probably for the last at least 20 years there is good work that establishes that if you can use ferrous -- I forgotten which iron preparation to increase donor hemoglobin, but at some reason other this has really never been widely adopted by blood banks.

THE CHAIR: Yeah, that’s what kind of what I was getting at because I think the experience in the field among blood collectors, that there’s been a great deal of reticence about getting engaged, in terms of repletion. Other comments from the committee, questions? Dr. Epstein?

DR. EPSTEIN: In the international literature, there have been a lot of publications about sufficiency of

the blood supply in terms of units per number population. And I am just wondering if you could paint the picture, how well does this potential reservoir of donors correlate with the potential demand based on an optimal supply in terms of donations per se 10,000 population or it's -- what's the gap that we are talking about? How far from flat out are we?

THE CHAIR: You know, that's a very good question, and I have got two answers, for that I am not sure, and second Jeff might know more about it.

SPEAKER: I can't specifically answer your question (inaudible) but we think this approach as Bill has described gives the ability to look at the portion of the pie that remains after all of these exclusionary factors. Then you could overlay on that in a positive way, what is known demographically about existing donors, and that would indicate how much of the remaining pie fits what we -- the people who currently donate, it also tells you how much of that remaining pie is different from the kind of people who currently donate and what we hoped to put in place is the ability to work with blood collection organizations to develop strategies that could be used to

go after -- that’s remaining section of the pie that doesn’t demographically fit existing blood donors. And that how one might need to develop different kinds of donor equipment strategies based on the understanding of what the size of that remaining population is. So this approach gives us the ability to begin to think that way.

THE CHAIR: Any other questions? Yes, Ms. Finley?

MS. FINLEY: Thank you. Did your study take any -- get any specific conclusions regarding platelet donors? Did you address that?

SPEAKER: No.

MS. FINLEY: Okay. To your knowledge are there any studies ongoing regarding platelet donors?

SPEAKER: With respect to prevalence?

MS. FINLEY: Yeah, exclusion criteria and specifically in getting to availability of platelets?

SPEAKER: Well, for the most part these same exclusionary factors would apply to platelet donors.

MS. FINLEY: Okay.

SPEAKER: The only difference being they can come back much more frequently and so we did take into

account the fact that whole blood donors can only donate every 56 days where despite the donors could come back more often, but in terms of medical and other deferral criteria they would be essentially the same.

MS. FINLEY: Thank you.

SPEAKER: I read an editorial in our local newspaper yesterday about a set of disgruntled airline pilots, because they were concerned that the ceiling being set at 60 years of age being perhaps overly restrictive for their profession. The ceiling at 65 for blood donors -- I would be interested in your comments about that and perhaps also some discussion about what some blood centers have been advocating in certain parts of the country in terms of younger donors.

SPEAKER: Yeah, another very good question and I think that could also be listed as one of the limitation of this study, because we arbitrarily selected 65 and 18 and certainly an argument can be made that why not under 18, like why not 17 year olds, and likewise on the other side of the book end, which is why not 66 year olds? So that would certainly have an impact on what the ultimate finding is, the medical reasons.

1 SPEAKER: Well, we realize that 65 really isn't a
2 regulatory ceiling and that many blood banks accept donors
3 older than 65 if they meet the health criteria. To get
4 that data in these databases we had to select some
5 arbitrary age and so we just used 18 and 65, we also
6 realize that many states have laws that allow 17-year-olds
7 to donate without parental consent. So if we had the
8 ability to fine-tune this we could look at other age
9 brackets and refine that number better.
10 THE CHAIR: Okay, thank you. Any additional
11 questions, if not thank you very much.
12 SPEAKER: Thank you.
13 SPEAKER: All right.
14 THE CHAIR: Our next presentation will be on an
15 area that has actually been on the press quite a bit, and
16 that is the CMS update on Erythropoiesis Stimulating
17 Agents – for non-renal disease indications for -- and
18 importance of national coverage determination. This will
19 be presented by Louis Jacques. Dr. Jacques is newly on
20 the faculty at Georgetown my alma mater and he took the
21 opportunity to take this time to register and get
22 registered at Georgetown. He is a faculty member at

1 Georgetown and served as the associate dean for curriculum
2 from 1998 to 2003. He's got a number of research
3 interests including entry prevention, physician workforce
4 issues in medical education, and he's been actively
5 working CMS as well. Dr. Jacques?
6 DR. JACQUES: Thank you, and as I mentioned
7 before welcome home to Georgetown. This is probably the
8 quietest group that I have to have this discussion or to
9 spend some time, I don't want to break my jinx here, or
10 jinx my luck rather. This is the timeline of essentially
11 what happened what we're dealing with. As many of you
12 know starting in November of 2006 with the publication of
13 the CHOIR and CREATE trials in the New England Journal, we
14 started to see an increasing buzz about especially safety
15 issues related to ESAs.
16 During the wintertime, there was additional data
17 coming out form other trials some of which should have
18 been stopped early, dealing with particular outcomes in
19 cancer patients. These culminated on March 9th with FDA's
20 publication of black box warnings and labels of ESAs.
21 Shortly after that on March 14th, CMS then opened an NCA
22 which is a National Coverage Analysis.

1 I don't want to get too nuanced here, but the
2 NCD or National Coverage Determination is the language
3 that actually becomes manualized, and the NCA describes
4 the process and the decision memoranda that a company and
5 NCD. On May 10, 2007 FDA's ODAC met and a number of CMS
6 staff were in attendance at that particular meeting. On
7 May 14th we then posted a proposed decision memorandum and
8 then on July 30th posted a final decision. And my phone's
9 been ringing off the hook ever since July 30th.
10 (Laughter)
11 This is essentially the black box label, I
12 realize it's a little bit difficult to read, but I want to
13 fit it all on one slide. And of the things that really
14 hit home for us was in fact sort of the first imperative
15 at the top which is -- use the lowest dose of Epogen that
16 will gradually increase the hemoglobin concentration to
17 the lowest level sufficient to avoid the need to for red
18 blood cell transfusion etcetera.
19 And then in the cancer population specifically
20 the warning talked about shortened time to tumor
21 progression in patients with advanced head, neck cancers
22 receiving radiation therapy, shortened over -- or survival

1 increased death attributed to disease progression at four
2 months and patients with metastatic breast cancer on
3 chemotherapy, as well as increased risk of death in
4 patients who are not getting any particular therapy at
5 all.
6 The ODAC then made these recommendations, which
7 I won't go through in great detail because it appear that
8 half of FDA is actually in this meeting, so I suspect
9 you've already seen them. Dr. Otis Brawley was quoted
10 just saying you know, “Show me some evidence that ESA's
11 are essentially not miracle cure for cancer,” if I can
12 paraphrase just slightly but not the miracle cure part.
13 So in the context of this, one of the things we saw was of
14 that the discussion at the ODAC as well as the
15 conversations and the voting of the panel members that was
16 quite consistent with what our own independent analysis
17 had been of the existing literature about these things.
18 So the context of CMS's review, I think I can
19 summarize a little bit here. First of all ESAs are
20 labeled to reduce to transfusion risk, this is not sort of
21 a -- let's increase the hemoglobin as high as you can get
22 it, this is really a specific reason to use an ESA to

avoid a different sort of therapeutic intervention. We were sad to say disappointed as we look through the literature about ESAs, well over 500 published articles and what we've found in general was that there were very few randomized double-blind placebo controlled trials on this. There was a lot of retrospective post-doc analysis, there were lot of small trials that were not adequately powered to even discover safety events if there were any such signals.

There were concerns that trials may have had their involvements stopped prematurely, in fact possibly to avoid achieving statistical significance, we found that in trials that looked at transfusion that it was difficult to find anywhere in the protocol that the transfusion was based on some standardized set point within the trials that appeared to be -- to the physician well transfused whenever they had -- you want to transfuse and after the fact we'll just of figure out what you've actually did.

We found in general a lack of attention to other thing that contribute to anemia especially in an older chronically ill population including iron deficiency, B12 deficiency, folic deficiency, chronic inflammation et

cetera. And we also found that there was a -- how am I going to describe this? Healthy people tend to not be anemic simply because they're healthy people. And that if one simply looks at people with higher hemoglobin versus lower hemoglobin regardless of how they got there, what one tends to find and it's not a surprise that people of higher hemoglobin feel better and tend to be healthier. But as if you might appreciate there's a bit of circularity in that. What we found was that the methodologically better evidence supported a couple of things.

One, transfusion to high hemoglobin levels does not appear to be beneficial and in fact there's some evidence that in fact it is harmful. In the placebo controlled trials of ESAs, because many of -- many of the trials actually simply compared different doses of ESAs but when one actually look at the placebo controlled trials what we saw was that while the ESA treated group would increase their hemoglobin by approximately 1.5 to 2 grams per deciliter, that the placebo group essentially either stayed the same or had a very small uptick in their hemoglobin, but suddenly they were not clashing.

1 And this was in contrast to some of the things
2 that people had suggested to us that absent ESAs this
3 patient population would essentially keep falling and
4 falling and falling and eventually it have people of
5 hemoglobin of five or six. We also saw a lot of trials
6 where quality of life was reported as an outcome, but as
7 was discussed at the ODAC, quality of life is problematic
8 as an outcome at ESA trial.
9 We're also aware of evidence where people have
10 actually studied quality of life in cancer patients and
11 have suggested that quality of life increase that may be
12 associates with rising hemoglobin are actually due to
13 improvement in their underlying cancer and that the rise
14 in their hemoglobin simply reflects that they're not as
15 sick as they were before.
16 So in that context let me go ahead and go to the
17 next slide and then I'll come back to some other points.
18 So what we did in the final decision? For those of you
19 don't know the statutory requirements for Medicare
20 national coverage determinations, we are required to
21 publish a proposed decision no later than six months after
22 we open a national coverage analysis, we are required to

1 accept 30 days of public comment on that proposed decision
2 and we are required to publish a final decision no later
3 than 60 days after the close of the public comment.
4 So by practice although not by statute, we also
5 solicit public comment when we first opened the decision.
6 So there's a total of 60 days of public comment on this
7 particular decision. So what we did was we non covered
8 specific off label indications and in fact some of these
9 are actually contraindications in the label. For example,
10 patients with uncontrolled hypertension, patients with
11 iron deficiency, B12 deficiency, patients with
12 neutralizing antibodies etcetera.
13 We then restricted the coverage of ESAs beyond
14 the specified duration and intensity of ESA treatment in
15 essentially anemia's related to cancer. And I only
16 mention this because it got a lot of press. We had
17 initially proposed non-coverage of ESAs and
18 myelodysplastic syndrome as I'm sure you know its pre-
19 malignant syndrome that converts to leukemia and
20 approximately 30 percent of patients.
21 This was where we've actually heard the most
22 feedback from the public about the possible impact of this

1 NCD on the blood supply. And because MDS is actually a
2 pre-malignant syndrome, we actually removed it from the
3 scope of the NCD in response to public comments, so our
4 local Medicare contractors will continue to make local
5 converge determinations about ESAs and MDS as if the NCA
6 had essentially never happened. So this is the list of
7 things we non-covered, some of them I talked about before
8 and what was interesting with these is that the industry
9 by and large supported these, either because these
10 specifically sort of looked back to the black box warning
11 or looked back to other parts of the label where these
12 were not otherwise supportable.
13 This was our restricted coverage, and before
14 sort of walking you through part of this, let me sort of
15 go to the last point in my sort of underlying context of
16 this. One of the challenges that we face and we continue
17 to face is that we don't currently have adequate evidence
18 that the ESA coverage parameters is outlined in the NCD,
19 would materially affect transfusion demand at hemoglobin
20 thresholds for transfusions that are based on
21 methodologically rigorous evidence.
22 What we have heard a lot of is physicians tend

1 to transfuse at all kinds of places, sometimes at tens,
2 some times at elevens, sometimes for objective physiologic
3 changes in the patients, sometimes for quality of life
4 issues. And although people have said that based on this
5 particular utilization in light of the national coverage
6 determination transfusion demand would increase.
7 What we have not seen adequately addressed so
8 far is the issue of whether appropriate transfusions
9 supported by rigorous evidence would actually be
10 increased, so going through the restricted coverage we
11 apply these to solid tumors multiple myeloma, lymphoma,
12 and lymphocytic leukemia. We required that the hemoglobin
13 be below 10 grams per deciliter or the equivalent hermetic
14 rate I realize -- I'm sure there's a lot of experts in the
15 room who could talk more than I can about why those are
16 sometimes not a 3 to 1 correspondent. But be that as it
17 may for the purposes of most policy a 3 to 1 interaction
18 is generally used.
19 So what we required was that we would not cover
20 ESAs in this population unless the patient's hemoglobin
21 was below 10 grams per deciliter at initiation. And that
22 the starting dose, be no more than the recommended FDA

1 labeled starting dose and the numbers were there for both
2 epoetin alpha and for darbypoetin.
3 We also -- this equivalent doses may be given
4 over other proved time periods essentially speaks to the
5 weekly dosing of 40,000 units for EPO and the
6 corresponding numbers for Aranesp. And we basically then
7 said that we'll give you that first four weeks to go ahead
8 and titrate the dose, and as along as the patient is a
9 responder to ESAs of and their hemoglobin remains below
10 10, fine, go ahead and keep -- we will continue to cover
11 the ESAs.
12 For patients who have been defined as non-
13 responders i.e. their hemoglobin rise has been less than 1
14 gram per deciliter compared to the pretreatment baseline
15 after 4 weeks of treatment, and whose hemoglobin still
16 remains below 10 that we would go ahead and cover a dose
17 escalation of 25 percent. We then said for those patients
18 who are -- well might turn them hyper-responders, i.e.,
19 their hemoglobin has risen greater than 1 gram per
20 deciliter over the 2 weeks that we would not cover
21 continued administration in that particular patient
22 population unless their hemoglobin fell below 10 and there

1 was a 25 percent reduction from the previously
2 administered dose.
3 We have had some feedback from the community
4 that although those numbers may work a little bit better
5 for epoetin that the labeling for darbypoetin is a little
6 bit different in some of those increments, and we do
7 recognize that. We also specify that we would continue to
8 cover ESAs for the 8 weeks following the final dose of
9 myelosuppressive chemotherapy in the chemotherapy regimen.
10 We had initially proposed a 12-week ceiling on
11 ESA coverage, and in response to public comments from the
12 oncology community and from others, we basically extended
13 that so that the coverage of the ESA as long as the
14 patient's hemoglobin remains below 10, would extend from
15 that first ESA dose that they would get associated with
16 the initiation of the chemotherapy and extend until 8
17 weeks afterwards.
18 We thought that was consistent with the ODAC
19 recommendations that ESA should not be continued after the
20 cessation of chemotherapy. I don't know that anyone has
21 yet come up with a definition of the cessation of
22 chemotherapy. So based on the discussions that the we had

had our feeling is that if the patient remains anemic more than 8 weeks after the end of the chemotherapy, that it would be reasonable to search for other causes of the anemia ongoing as opposed to simply continuing to ascribe it to the chemotherapy.

So that is where we are now. We have had so far at least three requests to reconsider the NCD in the three weeks since it has been out. And we are having discussions with those particular requesters and I can't comment at this point on what the agencies, you know, action might be in follow-up of this. Well, I guess if anybody has any questions.

SPEAKER: Yeah. Thank you. One of the questions that I have relates to something that you mentioned I think early on, and that is the absence of, I believe the absence of data to assess the impact of any change in coverage. And that is do we have good information on utilization and specific categories of patients, so that one could then drill down and assess what the impact of regulatory change would be?

DR. JACQUES: That actually is one of our challenges, because ideally one would like to see what

1 transfusion utilization is in specific populations who
2 have specific pre-transfusion hemoglobin levels. What is
3 easier to find but is unfortunately or less than fully
4 informative is simply what the current utilization happens
5 to be absent.
6 The sort of detailed information and, you know,
7 any -- we're always open to suggestions where people who
8 want to provide us with useful information. We do
9 understand that it can be a little bit difficult looking
10 at Medicare claims data to get that, because the
11 transfusion is on the hospital side, and some of the other
12 parts of that information that one might like to have
13 frankly may reside in different parts of sort of the
14 universe of data.
15 THE CHAIR: If there's no questions doctors --
16 SPEAKER: Could you clarify, you know,
17 (inaudible) let me disclose I'm a (inaudible) oncologist I
18 prescribe this daily. You know the (inaudible) when you
19 start therapy with ESAs you don't check another CBC in 2
20 weeks. It's usually 4 weeks later. And in that sense if
21 your target -- if your hemoglobin is between 10 and 12,
22 guess I'm having trouble finding the fine print here. It

1 can't be administered?
2 DR. JACQUES: Yeah, we are not requiring you to
3 check a hemoglobin during the first 4 weeks. Now the
4 label for Procrit does recommend checking the hemoglobin
5 weekly until it stabilizes. But we did not in the
6 National Courage Determination, for example, require a
7 two-week post initiation hemoglobin. It is certainly
8 possible that there may be some patients who might have
9 been labeled hyper-responders if the physician had chosen
10 to check a hemoglobin, you know, at week 2 plus a couple
11 of days. We did not get into that level of detail in
12 terms of our courage.
13 SPEAKER: But at 4 weeks if your hemoglobin is
14 11.
15 DR. JACQUES: Yeah. If the hemoglobin is 11 and
16 it is known that the hemoglobin is 11, I mean, well we are
17 not holding people accountable for information that they
18 don't have. If a contractor were to review a medical
19 record and to find that the patient was continued to be
20 administered ESAs in spite of, you know, sort of the lab
21 is also right there in the chart that the hemoglobin is
22 11, I would expect that the contractor would then be

1 denying the claim for the ESA that was administered after
2 that hemoglobin was known.
3 Now, patients go to all kinds of places often
4 cancer patients, not only they have an oncologist, they
5 may also have a radiation oncologist a primary care
6 doctor, a gynecologist, and they may also go to the
7 emergency room. And, yes, it is possible that one of
8 those other people might at some point have gotten a
9 hematocrit. But you know to the extent that they did or
10 didn't if you legitimately had no reason to know that the
11 patient's hematocrit was higher than that I would not be
12 encouraging people to go chasing after you.
13 SPEAKER: But it still doesn't state here
14 clearly that after it says for over 2 weeks of its rapid
15 rise but it's not clear -- issues 4 weeks because most
16 local insurers use that as a requirement that someone on
17 ESA needs a, you know, 2-month CBC.
18 DR. JACQUES: Yeah.
19 SPEAKER: So is it -- somewhere in here that 4
20 weeks of it over 10 but under 12 it has this so be held?
21 DR. JACQUES: We are not covering continued ESA
22 administration after week 4 in a patient whose hemoglobin

is known to be 10 or greater.

SPEAKER: Okay. You agree that it's not clearly stated here. It doesn't --

DR. JACQUES: Well, I would agree that you're telling me it's not clearly stated and we can sort of continue to have the conversation afterwards if you want to. One of the things that does interact with this which is actually a somewhat different topic, but the Tax Relief and Healthcare Act of 2006 affectionately known as TRHCA instituted a requirement that all Medicare claims for ESAs related to cancer with dates of service of January 1, 2008, or later must include the most recent hemoglobin or hematocrit.

We have in the notice of proposed rulemaking for the fee schedule for next year for the physician fee schedule proposed regulatory language around that and we will as we would also do then developed contractor instructions about the implementation of that.

So a requirement for the inclusion of hemoglobin or hematocrit data while that may not be completely flushed out in a NCD is actually a statutory requirement as of January 1. So, there will be some interaction

presumably between that reporting requirement and some of the implementation issues of the NCD.

SPEAKER: Did you clarify again though from what data analysis you use the cut off of hemoglobin of 10 versus 12, the study that I'm aware of in terms of adverse events and tumor progression we're looking above 12. There is enough data between 10 and 12 to state that that should be -- or you're making a value judgment that 10, you know, kind of, you know, catch it earlier so to speak?

DR. JACQUES: What I'm saying is that ESAs are labeled to reduce transfusion. We don't have any evidence based reason to believe that patients between 10 and 12 require transfusions. So therefore it seems plausible that ESAs to prevent transfusions wouldn't be used to push people up well beyond where the evidence suggests they would require a transfusion. And I don't want to hijack this meeting and turn it into a NCD discussion. We can certainly talk offline later.

THE CHAIR: What are practical difficulties that exist in the blood world as being able to forecast the impact of a change in therapy or policy on blood requirements? And on this particular issue, if for

1 example, in a certain type of surgery one said that there
2 be an intervention which would reduce utilization by 50
3 percent.
4 Most of the transfusion services and blood
5 centers have a good feel for the need for blood and
6 certain surgical interventions. For me, on the medical
7 side, I think, it's a little fuzzier in terms of, you
8 know, what is the need to support a given patient from
9 myelodysplasia let's say per annum. Now that may be
10 because I'm coming largely from the surgical hospital, but
11 can you comment on what you would forecast the impact of
12 this change to be in terms of blood needs for the nation?
13 DR. JACQUES: Our understanding is that the
14 blood supply is flexible, and if there were some increased
15 legitimate need that the blood supply could respond to
16 that we did not on the NCD receive public comments from
17 the major suppliers of donated blood in the United States.
18 I don't want to read too much in to their silence.
19 But the feedback that we were getting that we
20 might some how jeopardize the blood supply was coming
21 largely from one segment of the physician population
22 rather than a more sort of broadly representative

healthcare segment. In that case when we do National Coverage Determination the issue is specifically around is it reasonable or necessary for you know Medicare to cover these particular agents or any agent or any device or whatever depending on the decision.

And to that extent the focus of the decision is specifically on that particular item or device and is not generally sort of an overarching sort of foray into you know, sort of other places.

THE CHAIR: Yeah, I understand that and I guess that's one of the things that I would see as a potential weakness and that there are elements within the department that can't assess the potential impact and try to gear up for that, but that's what my concern is.

DR. JACQUES: And the department is familiar we have a decision.

THE CHAIR: Yeah. Dr. Epstein?

DR. EPSTEIN: Well, I just want to elaborate on the same point in a different way. Will there be any prospective effort to monitor the blood need in patients who might have received ESAs but will not under the current coverage determination, because that's where the

1 answer lies.

2 DR. JACQUES: We have had ongoing discussions

3 with actually a large number of people in the stakeholder

4 community who have proposed ways of doing that. One of

5 the things that we do as part of all of our National

6 Courage Determinations is to do something called post

7 coverage analysis.

8 Now, depending on what that NCD is that

9 particular post coverage analysis may be more formal and

10 may be more involved or in some cases it frankly we might

11 conclude that a post coverage analysis in some formal way

12 is not needed on a particular topic.

13 Certainly we've heard a lot of interest in this

14 one about tracing sort of what happens down the road. We

15 are concerned though that that tracking should not simply

16 represent -- this is what we had before, this is what we

17 had after and throw it up in the air to try to figure out

18 what the impact and the causality were. Clearly, if

19 people wanted to simply start transfusing more people they

20 could.

21 That doesn't necessarily mean that that's the

22 appropriate care for that patient. Okay. So in something

1 that we would just simply look at before and after
2 snapshot, I think we would have concerns methodologically
3 about what conclusions could realistically be supported by
4 the analytic model.
5 THE CHAIR: Okay. Two questions, Ms. Finley and
6 then Ms. Thomas?
7 MS. FINLEY: It's really more of a statement. I
8 was wondering if we can reserve that topic that Dr.
9 Epstein raised for further discussion, and that would be
10 an appropriate recommendation from this committee. And
11 perhaps we can draft some verbiage for both later or
12 tomorrow that would respect CMS's position on this but
13 also recognize the potential impact on the blood supply
14 which is of course our responsibility.
15 THE CHAIR: Okay. Thank you. Right. Ms.
16 Thomas?
17 MS. THOMAS: Yes, thank you. Just a brief
18 question. In your presentation you talked about how the
19 higher hemoglobin a person does feel better which is true.
20 I'm very familiar with Procrit and Aranesp and have -- saw
21 results where the hemoglobin would get up to 10 or 12.
22 However, my concern is when a patient is removed from

1 those ESAs and the level drops back down, because I've
2 seen that as well, how is that reinstituted?
3 DR. JACQUES: If the patient's hemoglobin were
4 to drop below 10, Medicare would cover the resumption of
5 the ESA that they were on before. Now, if that patient
6 had gone higher than the physician intended, the physician
7 might certainly choose to administer a lower dose than
8 they had been administering beforehand.
9 We have also -- for some people who are unclear
10 about it, should the patient having finished one
11 particular chemotherapeutic regimen let's say lasted 12
12 weeks, just to pull a number out, and then 4 months later
13 were started on another chemotherapy regimen. The clock
14 essentially starts over at the point, so coverage would
15 resume with that next chemotherapeutic regimen subject to
16 the same coverage criteria that were operational for the
17 first one, assuming that there had been no change in the
18 policy anyhow.
19 THE CHAIR: Okay. I think in the interest of
20 time we'll move on to our next speaker, but I just -- one
21 last comment, I think a lot of the discussion that we've
22 heard in points you made in your discussion, the committee

has discussed before, and that is the need to have guidelines and recognizing that there are variations from guidelines but there is weakness in the nation right now in terms of the utilization of guidelines for transfusion therapies. It depends on which physician is treating, and where you are, what level of hemoglobin you're supported at? Thank you.

DR. JACQUES: Thank you.

THE CHAIR: Okay. I would like to move into the session for open public comments. We do have -- it's one individual listed and that is Matthew --

(Tape interruption)

THE CHAIR: The manager of provider economics and public policy for that entity.

DR. KOUIDES: Thank you very much. I want to thank the panel for allowing each of us here to come and speak with you today. And also we want to thank CMS for allowing us to work with them over the past few weeks and months around this issue of the NCD on ESAs. ACCC, the Association of Community Cancer Centers, is a membership organization whose members include hospitals and physician practices over 650 hospitals and around 550 practices.

1 And it includes physicians, oncology nurses,
2 social workers, pharmacists, (inaudible) administrators,
3 really everyone involved in the scope of cancer care.
4 Now, what we decided to do when this NCD came out both the
5 proposed -- you know, continuing to look at and now the
6 file is out is what we want to look at was what was going
7 to be the impact on hospitals, specifically what an
8 increase in blood transfusions might mean for hospitals.
9 You know, based on the idea that an increase in
10 transfusions would increase resources needed or to provide
11 the transfusions and also then a reduction in the blood
12 supply or a potential reduction in the blood supply at
13 those hospitals. Now, as was just mentioned in the last
14 discussion, there really is no scientific data or claims
15 that we can look at that’s going to positively identify
16 what kind of increase there might be in a transfusion --
17 in transfusion because of this ESA NCD.
18 But what we did was we asked our hospital
19 institutions, our members, “What is it going to mean for
20 you?” So yes it is anecdotal information, but in the lack
21 of more scientific data we feel this information is useful
22 and necessary at this point until we can go back and look

at, you know, what it did mean.

So just to give you a background, we tried to get a good variation of hospitals across our membership, and as you can see, we do have a nice variety between community-based facilities, nonprofit, teaching hospitals. Also in the location of these hospitals, again a nice mix -- and they're not all center in cities or in rural areas.

And then finally also the size -- we have a nice mixture as well from very large facilities all the way down to your very small facilities are represented as well. So looking at the basic information, the question that we asked our members -- and again we directed this survey at people with knowledge of blood usage in the hospital, of ESA usage in the hospital.

So, you know, we probably had a number of pharmacists answering these questions, potentially (inaudible) administrators answering these questions. You know, we asked, "If the ESA NCD is adopted as it was written in the proposal, it's most likely going to result in some kind of increase in transfusion. Now we don't know what that increase might be, so we're going to give you a variety of options of what the increases might be.

1 “Based on those increases if we see an increase
2 of 10 percent, 30 percent, et cetera, now what might -- at
3 what level would you become concerned that is going to
4 cause you to have reductions in your other services,
5 knowing that transfusions require, you know, extra
6 hospital beds, usage of the blood supply, more researches
7 from personnel, blood typing, administrative resources as
8 well?”
9 So as you can see, people have different ideas
10 of what, you know, increase there might be in
11 transfusions, but there are some lower numbers of
12 increases that are going to cause concern. The largest
13 number of respondents said that a 30 percent increase in
14 blood transfusions would potentially cause problems for
15 their hospital resources wise.
16 It also included about 22 percent saying any
17 increase will potentially cause a problem. And this is
18 more -- we think more problem in some of the smaller
19 institutions so the larger ones are most likely able to
20 take in those increases and not have a problem with that,
21 but some of your smaller ones is a problem. And then also
22 16.5 percent at just 10 percent increase was going to be a

1 problem.

2 So there are some low numbers there which

3 hospitals are definitely concerned about. Now, it was

4 mentioned in the last discussion we don't know what the

5 increase in transfusions might be based on this NCD, and

6 we're not arguing here what that is. But the general

7 consensus among our membership is that there is going to

8 be some kind of increase in the need for blood

9 transfusions based on this.

10 So the last question that we then asked was,

11 "Well, are you concerned then of this -- you know, based

12 on this NCD that's going to making up cuts or potential

13 resource allocation problems in your hospital?" And about

14 75 percent of the respondents said, "Yes, there is some

15 kind of concern." About 30 very concerned, and 44 percent

16 or so were slightly concerned.

17 But that is something worth taking note of. And

18 out of our 650 hospitals we had a 150 hospitals respond,

19 which, you know, in a short amount of time that we had

20 this available, there was a pretty good response where we

21 were very happy with that response rate, especially when

22 you consider this is some very detailed information,

1 difficult information that not everyone has access to, and
2 they will have to go and find the person in the hospital
3 who had this information for them.
4 So again, this is not -- we know this is not a
5 scientific survey. But in the lack of the scientific
6 information, we feel this is good information to use going
7 forward. And also going forward we'd like to say that,
8 you know, we have shared this information with CMS and
9 we're very much looking forward to working with them in
10 the future on trying to track this information.
11 And the question was brought up is, you know,
12 can we look at this in the future, and what the impact is
13 going to be. ACCC will be very interested in working with
14 CMS on measuring that impact going forward in the future.
15 So that's all I have. If there's any questions on the
16 survey, I'll be happy to answer them.
17 THE CHAIR: Thank you. Have a question for Dr.
18 Kouides?
19 SPEAKER: I was curious if you also surveyed
20 your membership, what is the typical transfusion trigger?
21 DR. KOUIDES: No, we didn't, because it's -- it
22 varies greatly from member to member and from patient to

patient. That’s where most of our membership would -- that’s the general information we had is that, you know, there is not one set number, one set level that we start transfusions at, but that it really kind of does depend, which is why it’s hard to get the information.

SPEAKER: I think it will be helpful if you have that information in terms of giving them scenarios. You can, you know, have a transfusion figure for those who have, you know, congestive heart failure, those who don’t, and the like. And they may give you a sense of any potential burden.

DR. KOUIDES: And I absolutely agree, and I think going forward trying to track this information and there will be a question that we would ask and try to get as much information as possible so we can have the best scientific data possible.

SPEAKER: This is possible the concern may be overblown then, right, if --

DR. KOUIDES: Right. I mean we don’t know exactly what that trigger is. I mean I agree, but the -- you know, when the proposed NCD came out, the general feeling from the membership that we were getting was that

this is going to increase blood transfusions across the board. And so, you know, using that information that's why we drafted this survey.

THE CHAIR: Question or comment from Dr. Epstein?

DR. EPSTEIN: Yeah, thank you. You were careful to show us that your survey was broadly representative of different types of hospital and different sizes of hospital. So I'm wondering whether the level of concern showed any correlations with type of hospital or size of hospital, because that may be revealing in general of the whole issue of how do care facilities face blood shortage above and beyond any issue specific to the ESA.

DR. KOUIDES: Within the survey we didn't see -- you know, we didn't look at that direct correlation. However, again anecdotally speaking with some of our larger facilities, I do know that a larger facility and with over 600 beds is more capable of taking in any kind of transfusion increase without having adverse effect on their other services.

So based on that information from some of our members, you know, anecdotally I would say that, you know,

it’s possible to look at the smaller facilities having more of promise. But I don’t want to really speculate without having looked at the individual data and, you know, kind of cross walking the questions.

THE CHAIR: Question from Ms. Benzinger.

MS. BENZINGER: Yes. Could you go back one slide? I have a clarification question. The survey response question at the -- statement at the bottom, you were saying that it may cause them to make cuts elsewhere. What type of cuts are you referring to?

DR. KOUIDES: Let me -- I will read you the question. As it was stated the question said, “Are you concerned that you may have to cut back on other services such as elective surgeries due to a shortage of blood supply in order to accommodate the increase in blood transfusion patients, e.g., due to possible workload or space reallocations or blood supply limitations?”

So we basically said, you know, if there is an increase in blood transfusions it may cause you to have workload, space reallocation, administrative, or blood supply issues. Knowing that, would you be concerned? That’s the kind of the basis of the question.

MS. BENZINGER: Okay. I just -- trying to clarify that in my mind against the balance of an elective surgery needing extra blood versus the patient -- the cancer patient needing a blood transfusion. Yeah, I'm wondering where that balances it or does the hospital have a guideline on -- well, this unit alone, you know, gets 100 units allocated to them.

You know, I've got a little bit of an issue there with, you know, saying what type of cuts you're making.

DR. KOUIDES: Right. And you know, again, these questions were based on membership responses just in general to the impact of the NCD. You know, some of our members said, "Listen, you know, when there are times when we are on emergency blood usage only, you know, when sometimes during emergencies or during the summer months and sometimes there is less blood supply, this is going to be a major -- have a major impact on our other surgeries as well, because we're going to have to -- you know, if this person has priority you're going to have to use that before we go ahead with other elective surgeries."

So based on that type of response that's why we

1 put that information -- this -- in the question.
2 THE CHAIR: I think that issue would be
3 addressed later on when we do talk about the focal
4 shortages and how hospitals address that. A comment from
5 Dr. John.
6 DR. JOHN: Yes, just one clarification if I
7 could and I would certainly agree we've had a lot of
8 positive interactions with ACCC. The proposed decision
9 actually had a hemoglobin threshold below 9. And it was
10 below 10 for patients with significant cardiovascular
11 disease. So just to put it in context that the hemoglobin
12 level they were considering with this was the proposed 9
13 as opposed to the final 10.
14 THE CHAIR: Thank you.
15 DR. KOUIDES: And I agree that there -- you
16 know, we wrote this after proposal, and obviously we got
17 the information then after the fact the final decision
18 came out.
19 THE CHAIR: A question or comment from Ms.
20 Birkofer.
21 MS. BIRKOFER: Oh, thank you. Clearly, NCD has
22 broad national coverage implications. It could also have

1 implications on patient access, on transfusions, blood
2 supply, et cetera. Were there issues with the local
3 carriers, the LCDs, were there issues that in your
4 organization's opinion may have prompted CMS to move in
5 this rather sweeping direction of an NCD?
6 DR. KOUIDES: That wasn't a question that we
7 asked as part of this survey. So I don't necessarily want
8 to potentially get into that now. You know, the impetus
9 behind this survey and trying to gauge the field from
10 their membership all came from -- you know, I guess it
11 started with the black box warning and then it, you know,
12 moved on to the NCA and then the NCD. So that's really
13 where we started, really kind of started to look at these
14 impacts -- sorry before then with the -- any potential --
15 MS. BIRKOFER: I guess my concern would be that
16 CMS not issue this NCD approach as a driver of
17 reimbursement or cost controls that could impact patient
18 safety. You know, I think -- I'm just curious as to the
19 balance in that decision.
20 THE CHAIR: Okay. We have a comment from the
21 industry. Dr. Bianco.
22 DR. BIANCO: Hi. This is Celso Bianco,

America's Blood Center. No, it's not really a comment; I will leave it for discussion. It's a question for you. Where is the hemoglobin trigger in your hospital?

THE CHAIR: Oh, in my hospital?

(Laughter)

THE CHAIR: It's variable. No, generally what happens within hospitals is that guidelines are promulgated. And then in some hospitals there is a transfusion committee that reviews whether or not those guidelines are adhered to. When these groups find deviations, they are noted on the physician profile. But the reality is that that has very little teeth.

So the issue in a hospital is enforcement of existing guidelines and having guidelines that are indeed well researched and put together. Most notable is that within the last couple of months or so the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists have put out a very nice joint guideline on the use of blood in that particular arena of cardiovascular surgery, recognizing that there needs to be improvement.

And I think the onus would be on other specialty

1 societies to promulgate similar sorts of guidelines. But
2 again, there is a tremendous weakness within hospitals.
3 Dr. Jacques.
4 DR. JACQUES: Yeah, if I could just respond to
5 the question about cost. Medicare, the coverage group,
6 does not consider cost in making a reasonableness
7 determination in an NCD. Some people find that
8 reassuring, some people who would propose to say there's a
9 lot of money find that somewhat frustrating that really
10 don't consider the cost.
11 So we have, for example, extended coverage to a
12 whole lot of very expensive things, including implantable
13 cardio-defibrillators, bariatric surgery, and all sorts of
14 stuff.
15 THE CHAIR: There's no comments or questions?
16 If not, thank you.
17 DR. KOUIDES: Thank you very much.
18 THE CHAIR: And what we would like to do at this
19 point is to move into some of the points for discussion
20 recognizing that as we've heard in the earlier discussion
21 some of the data points are limited. But I'll just for
22 the sake of discussion, start off by reading some of the

1 specific questions that the assistant secretary or the
2 department would like to know.
3 Number one is, we're restricting recombinant
4 erythropoietin impact in transfusion demand in general.
5 A, will restricting recombinant erythropoietin until the
6 hemoglobin is less than 10 increase transfusion demand in
7 general? B, will restricting recombinant erythropoietin
8 until the hemoglobin is less than 10 increase transfusion
9 demands specifically in the chemotherapy induced anemia
10 cancer? And C, we're restricting human recombinant
11 erythropoietin until the hemoglobin is less than 10
12 increase transfusion demand in ESRD, end-stage renal
13 disease patients?
14 As number 3, what is the current demand for
15 transfusion in general and the sub item A, what is the
16 current demand for cancer patients and sub item B, what's
17 the current demand for transfusion and chemotherapy
18 induced anemia for cancer patients? And number three is -
19 - is there's a blood shortage and you know, A is if so and
20 is there a particular patient population?
21 So I would just like to open that up for a
22 discussion, I think that -- I think what we've talked

about is we've recognized that there's a lack of data that's reliable.

SPEAKER: No, I didn't see any.

Ms. BENZINGER: Thank you Dr. Bracey. May I ask if we could get those questions up on the board and also to have a copy of them in front of us? I don't have one in my packet and those are important issues and I wasn't able to take them down as you read them all?

THE CHAIR Can we do that, Dr. Holmberg?

Ms. BENZINGER: Thank you.

DR. EPSTEIN: But again I think the first -- first point here revolves around the issue of the hemoglobin of 10, and whether the hemoglobin of 10 as a target point would impact the demand for blood transfusions. It appears that if one follows the rigorous trials, randomized trials, that it would not, that's been the analysis of HHS and quite honestly from my perspective I think that it's true there are sub segments, patients with congestive heart failure or and other perhaps segments that would require a higher -- that may require a higher level of hemoglobin, but my bias is that I don't think that it would have a tremendous impact, but

recognizing that there's no data. But comments from others on this question.

DR. HOLMBERG: I think fundamentally it goes back to you know, guidelines in terms of the transfusion trigger and if indeed they were a hereto a -- probably shouldn't have any major impact. But on the other hand there hasn't been, not to my knowledge as much data specifically and the cancer patient population in terms of the ideal transfusion trigger and this is a really difficult subject to study because quality of life issues in terms of also how multifactorial fatigue is in this patient population.

And I think what Dr. Jacques mentioned earlier as well taken that often when there hemoglobin is rising above 10, it's because there you know, successfully being treated for their underlying malignancy and that may be the main reason in part also why they're feeling better.

And often you know, chemotherapy, platinum drugs which cause -- which obviously cause you know, a significant degree of anemia, as those drugs themselves, even if the hemoglobin is 10 or 12 can really cause profound fatigue. So it probably you know, I think if the

1 guidelines are hereto, but this is a highly charged
2 emotional issue with patients who have potentially fatal
3 illnesses and they're coming to see -- they're trying the
4 doctor you know, they're really you know, tired and they
5 needed -- they wanted to -- you know, if only you could
6 (inaudible) if I'm accurate, I think I feel well and
7 there's no much data for that but that's what we are
8 dealing with I think.
9 DR. EPSTEIN: I think one other thing that we've
10 seen in our surveys is that and it's a practical issue
11 that sometimes in treatment there's a knowledge that a
12 dosing of a certain regiment of chemotherapy will lead to
13 anemia and there is a notion of sort of getting ahead of
14 the curve in terms of going over that number 10, because
15 we can't test these people on a daily basis, so there may
16 be some sort of practical limitations as well in terms of
17 the threshold. Dr. (inaudible)?
18 SPEAKER: I think -- I hope that people aren't
19 transfusing to some trigger -- some high trigger and that
20 the decreased use of ESAs wouldn't emotionally make people
21 feel like I have to do something, because I use to do this
22 and my patient sit well, so I need to do something in

1 response. I thin that we hear that in our transfusion
2 committee where we do go to the doctors and say, you're
3 transfusing it appropriately and they come back to us and
4 ask (inaudible) data. The trials that are available are
5 not encompassing, there's a lot of criticism of the way
6 some of these trials had been done, and also it still
7 relies on consensus guidelines.
8 So as a result of that to say we have data that
9 we can use to say this should or shouldn't be done is
10 still problematic. And therefore I guess we still have to
11 trade lightly and say what is going to be the impact, and
12 until we know what the impact is, we need to analyze the
13 impact, because I think its unknown what's going to
14 happen, especially using current data.
15 DR. HOLMBERG: Dr. Epstein?
16 DR. EPSTEIN: Yes. I think my comments go along
17 the same lines as to -- of our committee members have
18 already stated, we lack the actual data, so in attempting
19 to answer the questing you first could look at current
20 practice and that leads you to uncertainty because of the
21 variability and trigger and the lack of detailed knowledge
22 about how patients could transfuse in a variety of

conditions. You could then attempt an estimate based on guidelines, but it backs the question of whether guidelines are being followed let alone whether we have enough guidelines. And I think that leads me to end up saying that it's important to try to answer this question by a prospective study. And I appreciate what Dr. Jacques said about the methodological difficulties because you want to look at cause and not just practice. But I think practice is important, then you could stratify it based on current practice versus guideline that herein practice and -- so where I end up is just that this question is an important one and should be examined through a government's board of study.

THE CHAIR: Thank you, Ms. Finley?

MS. FINLEY: I would concur with Dr. Epstein's excellent comments. I just wanted to make an observation that the issue of transfusion guidelines has been kicking around longer than probably most of us had been alive. It was taken and discussed in sworn in testimony before the government reform committee in 1995, Dr. Pinard conducted the study, he probably was not the only person doing it, but he was one of the co-authors, and I believe Dr.

McCarty paid for it in his capacity at NIH. And they came essentially with the same conclusions that you have all reached that there are guidelines, but not everybody follows them. So it's obviously a longstanding problem. In responding to these questions, I think we have -- I agree -- we have to try it lightly, I think we should address the fact that we don't have the data and really encourage the department to try and address that -- that issue. And to acknowledge the fact that this -- that this issue is very long standing and NIH has had a commitment in this area in the past.

I don't know what their current activity level is in this area, but it would be useful, you know, to have that information if it's available and particularly if it is a current priority for NHLBI. But then I really do think you know, I'm trying to look and find a way to make a positive contribution here. And in the absence have been, you know, of actual information I think we should -- should be very careful about strong recommendations. But if there is information missing then I think -- certainly pointing that out in a constructive manner would help.

THE CHAIR: Okay, thank you.

SPEAKER: Dr. Benzinger bit concerned, the ESRDs in the discussion here to, renal disease, (inaudible)?

SPEAKER: Well, I think actually we couldn't --

SPEAKER: I don't think -- it's actually in the purview --

THE CHAIR: (inaudible) they're striking. It shouldn't -

SPEAKER: It shouldn't be within the discussion, it's not. I mean I understand it's undergoing review and there will be -- I would say a much larger, you know, the extrapolation issue.

THE CHAIR: You're right, right.

SPEAKER: But I'm not sure it's within our charge to say put that on the table right now.

THE CHAIR: That'd be going before the -- the cart before the horse.

SPEAKER: Great.

THE CHAIR Yeah, okay, good point. Dr. Holmberg?

SPEAKER: (inaudible)

THE CHAIR: Oh yeah. In terms of the -- actually the structure of that -- there was some input

1 from Dr. Jacques did you -- want to comment on that?
2 DR. JACQUES: We don't need the ESRD question
3 answered at this point. It is, you know, a lot clearly
4 ESAs in general are using Medicare beneficiary population
5 for a whole lot of different things, we do have a long
6 term interest in the ESRD population but if the committee
7 would prefer, you know, not to deal with that particular
8 issue, now that's certainly fine with us, thank you.
9 THE CHAIR: Okay. So it appears that there is
10 consensus that A, we should tread lightly B, we need more
11 data, C, we need to assess the status of current
12 guidelines and the utilization of such. Are the other
13 highlights that need to be considered.
14 DR. BENZINGER: I believe that Dr. Epstein's
15 point about collecting prospective
16 THE CHAIR: Prospective data.
17 DR. BENZINGER: Data is very important.
18 THE CHAIR: Right, exactly. Okay, Dr. Bianca?
19 DR. BIANCA: Celso Bianca America's Blood
20 Center, I certainly support everyone of the statements and
21 proposals that had been made by members of the committee.
22 I want to make a couple of comments.

1 The first one -- I think that these are
2 fundamental fallacy about what we're doing, I don't think
3 that the decisions about ESA's has to be based or should
4 be based on the impact that it may or may not have in
5 transfusion. I think that we should look at in absolute
6 value. Is it good for the patient or bad for the patient?
7 And it increases risk, decreases risk and those are the
8 questions.
9 The fallacy is that the effect that it has in
10 the blood supply is not the critical side of the question.
11 The second side is the question of elasticity of the blood
12 supply. In 2002, we followed FDA guidance and we've got -
13 - according to FDA estimates at that time the blood supply
14 by 10 percent, with the deferrals for variant CJD.
15 (Tape interruption)
16 SPEAKER: Oh, yeah. There are -- in terms of
17 the -- actually the structure of that, there was some
18 input from Dr. (inaudible) did you want to comment on
19 that?
20 SPEAKER: We don’t need the (inaudible) question
21 answered at this point. This -- you know, on what --
22 clearly ESA (inaudible) a lot of different things. We do

have a long-term interest in the (inaudible) certain populations (inaudible) prefer, you know, not to deal with that particular (inaudible).

THE CHAIR: So it appears that there is consensus that, a, we should tread lightly, b, we need more data, c, we need to assess the status of current guidelines and the utilization of (inaudible). Are there other highlights that (inaudible)?

SPEAKER: I believe that Dr. (inaudible) point about collecting --

THE CHAIR: Perspective data.

SPEAKER: -- is very important.

THE CHAIR: Right. Then -- okay, Dr. (inaudible).

SPEAKER: I’m (inaudible) because I certainly support (inaudible) point of view, statements, and proposals that had been made by members of the community. I want to make a couple of comments.

The first one. I think the days of fundamental (inaudible) about what we (inaudible), I don’t think that the decisions about (inaudible) has to be based or should be based on (inaudible) that they may or may not have

(inaudible). I think that we should look at it in absolute value. Is it good for the patient or bad for the patients and that it increases risk, decreases risk? And those are the questions that (inaudible) the fallacies that -- the effect that it has in the blood supply is not the critical side of the question.

The second side is the question of elasticity of the (inaudible). In 2002, we followed FDA guidance. And we cut, according to FDA estimates at that point, the blood supply by 10 percent with due deferrals for (inaudible). Yes, it took a while. It took a year or two or maybe three for the blood supply to restablize at a different level. But the decision was made that it was important for the safety of the blood supply and not necessarily because of extremist reasons. I -- it upsets me a little bit to see that the transfusion is being used to justify a drug -- the use of a drug that has totally (inaudible).

THE CHAIR: No, I think that’s a very excellent point because one thing that I was thinking of (inaudible) perhaps I didn’t bring that out is that if indeed there is a change and there is more utilization of blood, the real

question is are we adversely affecting those individuals who require more blood and do we have a way to assess that. Good point. Thank you. Comments, additional comments?

Okay. So what I think then we will attempt to do on the first question through the first three, a through c, is to draft a recommendation that will include those elements. And we won't finalize that now, but we'll work on doing that before the end of the meeting. Do we need to address -- oh, right. And we've said that number c, we'll defer on it.

Under number 2, what is the current demand for cancer patients, the current demand for cancer patients (inaudible)? Again, if you were to ask me, in my facility, it's largely a surgical facility so I wouldn't have a good answer. But I don't know if others have a good answer as well. Dr. (inaudible), what's your (inaudible) question to our understanding of the demand for population.

SPEAKER (off mic): Well, I don't have the numbers on that, I guess (inaudible). It's -- I think it's certainly a (inaudible) probably not as much data as

anyone would like in terms of what's (inaudible). But it's -- I think it's a (inaudible).

SPEAKER: I'm wondering if that question is broad enough. We're looking specifically at cancer patients. But, you know, (inaudible) we really address the necessity and demand for transfusion in general in all subtypes of patients?

THE CHAIR: Well, I think that's an important question. But right now in terms of (inaudible) down on the piece for ESAs and the impact of the ESAs (inaudible) that we're largely concerned about, it would focus largely on this group of patients. Recognizing limited resources and capabilities as well, it may be better to focus at this point. Dr. (inaudible).

SPEAKER: I remember too (inaudible) the demand for a sense of the (inaudible) attempts of transplants. And as you know, about 10 years ago there was an uptake because it was being used more and more for (inaudible) breast cancer and then obviously it's, you know, gone down. But there is obviously a constant demand (inaudible). But -- and it would be fair to say -- I don't even have the (inaudible) financial numbers. But I

do believe that it has plateaus in terms of the, you know, number of, you know, stem cell transplants. So I don't think that's an increase in demand. But it's a, you know, steady demand.

THE CHAIR: Actually the -- well, you're right. In terms of the (inaudible).

SPEAKER: But (inaudible) is probably --

THE CHAIR: It's probably (inaudible).

SPEAKER: (Off mic).

THE CHAIR: Robyn, did you want to comment on that?

SPEAKER: (Off mic).

SPEAKER: (inaudible) push to increase the number of (inaudible) that was what he was talking about.

SPEAKER: What I'm saying if you have any of the (inaudible) in terms of is there -- what is the number, you know, actually being done at the (inaudible).

SPEAKER: Well, (inaudible) pushes to go forward about 10,000, you know, (inaudible) a year and we're not there yet. (inaudible). Obviously the people don't (inaudible).

SPEAKER: (Off mic).

THE CHAIR: Right. I think what I'm hearing is that the push for increase in the (inaudible) comes under the (inaudible) contract which is within HHS. And so again it's this notion of being able to forecast what the demands are. But getting back to the base issue is that we don't actually understand the current. And so I'm -- what we need is good data to support current demand and then looking within the department to see what (inaudible).

SPEAKER: Yeah, I was just kind of (inaudible) what really could be the (inaudible). And my concern is that (inaudible). And what I wonder could happen is that these people are going to go out of Medicare or any other (inaudible). So again, I go back to the government's (inaudible).

THE CHAIR: That's a, you know, a good point. I think while I really -- but again the (inaudible) what you said is they would --

SPEAKER: Well, the anemia is more -- I mean a patient himself or herself cannot prescribe a transfusion nor a (inaudible). So I think again -- I thinking we're focusing on maybe, you know, using less (inaudible) and

1 using more blood products. But in the meantime, you have
2 that resistance to use blood products, that might have a
3 very negative impact on the patient itself.
4 THE CHAIR: Dr. (inaudible).
5 SPEAKER: I just wanted to echo what Celso
6 Bianco said that -- and it really needs to be kept in mind
7 that the risk-benefit of using erythro is not a benign
8 drug is that needs to be kept in mind --
9 THE CHAIR: But --
10 SPEAKER: -- in all of this decision.
11 THE CHAIR: Okay. So then is it the concurrence
12 of the committee that we don’t have enough information on
13 Item number 2 and more information needs to be garnered
14 for the general -- for both sub-elements a and b? Dr.
15 Epstein.
16 DR. EPSTEIN: I agree with that. And I just
17 wonder if a representative from CMS could comment whether
18 the CMS databases would permit us to get the answers or
19 its -- can the diagnostic codes and transfusion be
20 retrieved from, you know, hospital blood utilization
21 databases because I’m just struck that we don’t have the
22 information and that the efforts to study blood

utilization through the NBDRC have not given us, you know, enough stratification to answer the question. But the data certainly exist in hospital records and how accessible are they in general and through CMS.

THE CHAIR: Dr. Boleman.

DR. BOLEMAN: Yeah. Dr. Epstein, that’s an excellent point. As most of you know, the CMS Medicare so-called database, which is a claims database, traditionally has been an administrative database. And there has been a very paucity of clinical data in that database up until very, very recent times for some specific payment reasons for collecting certain clinical parameters. And Dr. Jacques pointed out a couple of impending -- I’m not sure if the mic is worse or my -- sorry, I’ll try this one.

Dr. Jacques pointed out a couple of impending parameters that will be collected beginning January 1st in response to statute. So in general, the Medicare database is accessible to researchers in the research community and anybody who can show that they can have the wherewithal to respect the privacy and confidentiality and decryption and encryption and all of that type of stuff and also all the

1 financial resources that entails managing those sorts of
2 research projects.
3 But it’s not going to be very useful. Again,
4 many of the transfusions are done in the inpatient
5 setting. And because the Medicare program pays inpatient
6 hospital stays on DRGs and does not collect transfusion --
7 clinical transfusion utilization data for inpatient
8 settings, it will be very difficult to obtain that kind of
9 information. So, yes, the data, to the extent that it’s
10 available, is accessible. But there’s very little actual
11 transfusion data available in there. There’s oodles of
12 diagnostic -- ICD-9 diagnostic codes for the diagnoses and
13 the procedures that are done in those inpatient hospitals.
14 And of course the DRGs are there.
15 And similar information is available in the
16 outpatient hospital setting. But the actual clinical
17 parameters, the hemoglobin levels, the number of units
18 transfused, the type of components that are transfused is
19 just not there. On the other hand, there are a number of
20 very well-known large cancer hospitals in this country
21 that probably do have, within their databases, transfusion
22 utilization data. They have laboratory data, trigger

1 points where the hemoglobin is -- at which point in time
2 transfusions are made. They do have the diagnoses codes
3 in ICD-9 format, procedure codes and all of that. It may
4 be an undertaking to assemble and correlate all that data.
5 So that would be a huge research project in and of itself.
6 But to the extent that fairly well-known and well-
7 respected cancer hospitals are considered so-called best
8 practices in this country, that might be a source of
9 representative data from which you could use as a starting
10 point.
11 THE CHAIR: Thank you for your comments.
12 Actually that reminds me of the (inaudible) papers that, I
13 guess, were largely focused on the cardiovascular
14 population that did use those codes to at least begin the
15 analysis for that particular set of patients.
16 So the issue then is that there is currently
17 need for information because we don’t fully understand the
18 demand. It’s an issue, but it’s an issue for which there
19 is incomplete information.
20 Under number 3, is there a blood shortage? It
21 depends on the time of year that one asks, I would
22 imagine. No, we know that there are focal shortages. And

1 specifically when you talk about blood shortages, you
2 really are primarily talking about shortage of all red
3 cells and/or platelets. And the platelets depend on the
4 time of the year, whether lots of people are on holiday.
5 So -- I mean I think that we know that there are periodic
6 shortages. I don't think it's really patient population
7 specific, though the platelet shortages would impact the
8 oncology patients more than the general population. But
9 that's a very -- it's almost like the deferrals; it's got
10 a short window.
11 Comments or -- from the committee? I mean we
12 all have experienced some shortages. It's -- we've never
13 had a overly abundant blood supply, I would say, on an
14 ongoing basis. It's been marginal. So I think that
15 question would be fairly straightforward to answer. Dr.
16 Holmberg.
17 DR. HOLMBERG: I think that we probably can just
18 address 1 and 2. And we'll be coming back to the issue of
19 the elasticity in the blood supply this afternoon.
20 THE CHAIR: Okay.
21 DR. HOLMBERG: I think that for CMS's benefit, I
22 think that if we focus just on the first two questions, I

think that that would be beneficial.

THE CHAIR: So what I would like to do then is we will work on preparing a draft in terms of the response to numbers 1 and 2 and have that really available for tomorrow or we can do it later this afternoon. But the idea is that we will address 1, a and b, and then 2, a and b with the -- to reflect the discussion we’ve had thus far.

At this point then, let’s take a break for lunch and that would be a one-hour break. So we would reconvene at 10 after the hour. Thank you.

(Whereupon, a luncheon recess was taken.)

A F T E R N O O N S E S S I O N

THE CHAIR: Begin to focus on the ethical considerations and the risk benefits for ensuring transfusion and transplantation -- transplantation safety during focal areas of shortages, blood shortages. In addition, the committee will review and discuss what has been referred to earlier as the elasticity of blood supply to support transfusion and transplantation safety. As well as strategies to reduce the barriers to receiving those therapies. The first speaker for this afternoon is Theresa Wiegmann. Theresa is well known to many of us. She's the director of public policy and special counsel for the AABB formally known as the American Association of Blood Banks. And -- thank you.

MS. WIEGMANN: Good afternoon. Today, I am testifying -- or speaking I should say.

(Laughter)

MS. WIEGMANN: I'm regularly in the congressional world where there is testimony. But here we are just presenting today on behalf of AABB's inner organizational task force on domestic disasters and acts

of terrorism. And most of you are aware of the task force since we have spoken to this group on several occasions. The task force is made up of the National blood organizations AABB, Red Cross, America's Blood Centers and Blood Centers of America and in addition, we have liaisons from government agencies including HHS, FDA, CDC and others.

And then other interested parties participate with the task force in helping us to prepare for -- in response to disasters. So the task force is here today to address the overall issue that we are talking about today in terms of whether the supply is adequate to deal with potential shortages including those that might come up about because of disasters. And also, to talk about a little bit about the blood supply in general and the elasticity of the supply.

I must start by talking a little bit about what data we have, about the national blood supply and the most recent data we have is from the national blood collection and utilization survey. The last one was done collected data from 2004. And I apologize that this slide is a little difficult to read. But what it is looking at is

1 allogeneic cord blood and red cell collections and
2 transfusions between the dates of 1989 and 2004. So on
3 your horizontal axis the first date is '89 and the date,
4 all the way to the left, is 2004. And the top line that
5 goes -- stretches that entire time span is collections.
6 But what is interesting to look at -- we found
7 is not just to look at collections but to look at
8 allogeneic screened collections so that you are looking at
9 really what amount of the blood supply is available for
10 transfusions. And that is that second line. And then on
11 the bottom is the line demonstrating what -- how many
12 transfusions were done. And what you see there is that in
13 2004, there was an adequate blood supply. However, the
14 margin of availability, the margin between the number of
15 transfusions and the number of units that are available
16 for transfusions continues to decrease. It decreased from
17 6.3 percent in 2001, to 4.5 percent in 2004.
18 So that in general we are okay with the supply
19 but there is some area for concerned there. It is
20 positive that there is some leveling off of the steep
21 increase in demand for red blood cells that had previously
22 been observed. But as you can see here collections remain

1 relatively constant. And again, the margin between the
2 available supply and transfusions was the smallest since
3 the time that we have been collecting this type of
4 national data. Now, some other findings from that same
5 report from -- using the 2004 data -- were promising in
6 that they showed that the blood system seems to be
7 becoming a little bit more efficient; that is the blood
8 centers and the hospitals.
9 And that was indicated by some evidence of
10 reduced out dating of blood units, as well as fewer
11 hospitals reporting unmet need.
12 Some additional data from the 2004 data, talking
13 about shortages that are faced by different areas of the
14 country. These are just some general findings. We found
15 that a 42 percent decrease in the total number of surgical
16 procedures that were postponed so that is good news.
17 However, the good news that shortages were less frequent
18 needs to be balanced against the notion that when they did
19 occur there were more acute. That is that among hospitals
20 reporting unmet blood needs the mean number of days of
21 unmet non-surgical blood need increased from 2.1 days in
22 2001 to 19.27 days in 2004. So -- but these are all

1 findings that we will have to look at again as we are just
2 getting out the new survey and are grateful for HHS'
3 support in that endeavor and so we will be looking at 2007
4 data in the coming year. And again tracking many of these
5 and other trends in the blood supply. So that is what we
6 have sort of on a national basis right now. And I'm going
7 to turn to more of the day-to-day picture of what we have
8 seen within the blood community.
9 The trend continues that we're not experiencing
10 any national shortages what we do see are more periodic
11 regional shortages. That is they are typically local and
12 seasonal with peaks in the summer and around the holidays;
13 January. And they are generally corrected within a few
14 days, both through increased collections at local blood
15 centers and imports from one center to another or from one
16 region of the country to another. Now, these are the
17 strategies that the task force has taken to meet blood
18 needs, including both the, sort of, regional spot
19 shortages that I just spoke to, as well as needs when
20 disasters have occurred that might need blood, or in
21 exercises where we have dealt with potential increased
22 blood needs due to disasters. Again, the task force was

pulled together post September 11th, to try to have the blood community and the government have a unified approach to responding to and to preparing for disasters.

And generally, this system has been quite effective, and the groups have been working together well. Of course, there have been some limited hitches mainly, due to logistics in terms of trying to get the state's assistance in giving us communications, transportation or fuel during certain disasters. But in general, we believe, the system is working well.

And then as a background I would like to just say that -- and I think that Ruth will go -- Ruth Sylvester will go into this in a little more detail in her presentation in a minute. But in general, our experience has proven that most disasters do not result in a notable increase in the demand for blood. However, of course, we want to be prepared and what we do is we focus on two things. First we focus on the need to monitor the supplies so the community does that together with the blood organizations. And then, we work together to move the blood from one region to another when needed.

Turning to the first of those items, in terms of

1 monitoring supply data, today, already there are systems
2 in places whereby America's blood centers, the American
3 Red Cross and the Blood Centers of America collect daily
4 supply data. And then through the -- where -- what we're
5 trying to do right now is to take each of those group's
6 data and to make them into a more uniform data set that we
7 can share through the task force with HHS. And so, I'm
8 going to talk in little bit about the sort of parameters
9 of what kind of data, we think, would be best to share
10 with HHS and what we need to know on a, sort of, more
11 routine basis about what is happening in the blood supply.
12 The critical elements, the task force thinks are
13 that we should be monitoring total red blood cell numbers,
14 plus focusing, in particular, on O positive and O negative
15 units. And we think, the task force believes that its
16 best to express these numbers in terms of days of supply
17 on our retail blood center shelves, as opposed to talking
18 about numbers of units that the days of supply gives us
19 some more useful number to work with in terms of tracking
20 supply over time. That we should collect this data at
21 least on a weekly basis. And that we should report this
22 data to the agencies to HHS on a national basis. Now, I

1 say national as opposed to local for a couple of reasons.
2 First, as we talked about in the past, again, we
3 are operating under the assumption that if there were a
4 disaster we would be able to move, we would operate our
5 system as we have in the past, where we would move blood
6 from one area of the country to another. So it is
7 important to know that overall national number.
8 And it's also just not very realistic to give
9 the local blood numbers in that blood centers -- some
10 blood centers would have, understandably, proprietary
11 interests in not making, as public, information about
12 their own particular supply, and number of units that they
13 have. So, we think it's best to start with the national
14 numbers. And so, that is what we are hoping to get this
15 system going that we could come up with again a uniform
16 numbers that we could supply to HHS on a routine basis.
17 And we look forward to try to work with Jerry's office on
18 that endeavor. So that is a little bit about the supply.
19 Then secondly, so the task force believes its
20 role is critical in trying to move blood from -- to where
21 it is needed. On a daily basis, it is routine that ABC,
22 Red Cross, BCA and AABB's National Blood Exchange move

1 blood from region to region depending on when we hear of
2 particular blood centers or particular regions
3 experiencing these more spot shortages. So that is
4 already done and we think those systems, in general, are
5 working. Then, during disasters, again, the task force
6 convenes and works on coordinating the movement of blood
7 into affected areas. And we have done that in a number of
8 instances of real disasters and then worked on it in terms
9 of the top TOPOFF exercises and other exercise drills.
10 And then on my last bullet there is, just to
11 clarify the task force's current position on a national
12 blood reserve. For those of you who have been on the
13 committee for a while you will know that, in 2004, the
14 task force recommended that we work towards creation of a
15 national blood reserve. And at that point we had
16 recommended that there be a real reserve of approximately
17 10,000 units of red blood cells at a cost -- that ran in
18 the area of about $2.6 million in start-up costs and $6.75
19 million annually. Now, over time, we've reconsidered this
20 position, in part, because we found that in advocating for
21 it, it wasn't realistic to try to get a program of that
22 dimension running given the significant fiscal restraints

that the country is facing and the department in particular.

And then going back, just realizing that a real reserve wasn't realistic, we think that we don't need an additional virtual reserve in that right now the blood centers, through the task force, are sort of operating what in essence is that type of reserve, and that we have the blood on the shelves of the blood centers across the country that we just need to be able to have a system in place to move around to where it is needed. So this is just to clarify a little bit about what the task force's position in terms of a reserve is. And what is needed in moving blood in terms of -- in times of a disaster.

So turning to the question of what are the barriers that we see in terms of having to -- being able to meet blood needs both in, I guess, focusing primarily, on situations where there may be shortages due to a disastrous scenario. The first, as we've said to the committee before, relates to logistics. We do need to continue to make our case to the states that there be transportation, fuel and communications resources made available to the blood community, and that the blood

1 community be given a priority in terms of -- an
2 appropriate priority in terms of getting these resources
3 during hurricanes or whatever other type of disaster we
4 are facing.
5 The second barrier that we see relates to
6 regulatory restrictions. And I highlight there that we
7 are looking at this issue, in particular, in light of a
8 pandemic scenario. And we have been in quite constructive
9 conversations with the FDA about this. For instance,
10 would the agency consider releasing guidance that in a
11 pandemic scenario they might alter certain restrictions
12 dealing with blood counts, or training of staff? And
13 again, I think you'll hear, in much larger detail,
14 tomorrow, from Alan Williams about those conversations.
15 And we look forward to continuing to work with FDA on that
16 notion of trying to get some more information from FDA
17 about what they are considering they might reduce some of
18 the regulatory requirements on a temporary basis if we are
19 faced with a pandemic, which could result in significant
20 reductions in the blood supply.
21 Thirdly, we need to control usage. And this too
22 has been looked up by the pandemic organizational --

1 pandemic task force headed by Dr. Louis Katz who you've
2 heard from in the past. And that relates somewhat to the
3 issue that you have been talking about this morning, in
4 terms of blood and transfusion guidelines. I should say
5 that AABB has been looking at the idea of transfusion
6 guidelines and the need for them. On the national basis
7 we are just starting to look at trying to create some
8 guidelines related to plasma. I would like to just
9 highlight though that these -- the creation of practice
10 guidelines are extremely time and resource intensive. And
11 it's also complicated. So you can't just say you setup
12 one set of transfusion guidelines.
13 They have to be very geared to particular
14 issues. We are looking at a model that is set up by the
15 thoracic surgeons, which I think you spoke to earlier this
16 morning, Dr. Bracey. And which is a widely admired set of
17 guidelines. And what we need to do is those guidelines
18 are focused on particular questions and often looking at
19 areas -- where you have to look at areas where there is
20 enough sound research and published data. And sometimes
21 we are finding within the transfusion medicine community
22 that there is not always as much clear data indicating

which way you should go. That is probably one reason why we don't have transfusion guidelines in some areas because some of the research needs to be bolstered. So, we're looking at that in the -- and I think that other -- we know of other organizations at a national level are also considering implementing transfusion guidelines.

And we are hopeful that we will be moving in the right direction there. In terms of pandemic, when we have issued guidance materials to our members, including hospitals and blood centers. We have urged them to prepare for a pandemic in one way by looking within their facilities at their own transfusion guidelines. So going to their transfusion service committees and making sure that they have their own facilities guidance on when they are going to make difficult decisions about who gets blood if there is a limited supply.

And of course, any such guidelines needed to be dictated to some degree by the particular patient population the facility is serving.

And then lastly, in terms of barriers that we consider in getting blood to individuals needing transfusions during a disaster. We are also limited by --

1 like any other portion of the healthcare sector, by
2 overall mass casualty constraints. So we have to be
3 realistic in thinking that even if we can get the blood
4 into a locality, is there going to be that -- the
5 wherewithal, and the people, and the other factors are
6 available that are needed to actually transfuse to a
7 patient.
8 So we're part of an overall larger picture that
9 we need to look at. Not just the unit of blood itself.
10 So in conclusion, I just wanted to say that the blood
11 community, the task force looks forward to continuing to
12 work with HHS on monitoring supply and sharing it with the
13 agency. And then with the logistical support, in terms of
14 again communications transportation etc. Moving blood to
15 effected areas when needed. And overall, what we think we
16 need to do is to continue our push as we say year after
17 year that what is needed to be done is to increase the
18 overall blood supply as much as possible, to closer to the
19 seven days that we consider ideal. And if we are going to
20 do that, that is going to consider -- that is going to
21 require that we make additional investments that we need
22 to pay for increased donor awareness campaigns.

1 And that we need to probably, educate the
2 American public that if we do that that the country needs
3 to be willing to accept the notion of increased out dates
4 of certain products because that will necessarily,
5 probably be a result if you got a larger overall supply
6 down the road. And that is it and if you have any
7 questions I'd be happy to try to answer them.
8 SPEAKER: Thank you. A question in terms of the
9 number of observations from the very first slides that
10 represents about 85 percent of the blood in the states or
11 is that the figures for '94 through 2004 the absolute, you
12 know, total numbers of collections, blood utilization; is
13 that 85 percent or 100 percent of facilities reporting.
14 MS. WIEGMANN: You know, I should know that
15 number -- do you remember Jerry --
16 SPEAKER: I can't give --
17 MS. WIEGMANN: It was the vast majority of the
18 blood centers.
19 SPEAKER: I can't give you the in on that but
20 it's a sampling and because it is a sampling it is
21 weighted so that we have an overall picture of the total
22 population. For instance, there is 15 million collected

1 and one of the things to that was recognized in 2001
2 versus 2004 was that there was an increase in collections,
3 and an increase in expiration of blood in 2001 because of
4 the ripple effect of 9/11. So, you know, where they --
5 shows the large gap there and that we had an increased out
6 date rate in 2001 was also a factor of increased
7 collections. But it's something like 3,000 facilities
8 were surveyed and it is weighted then to try to get a
9 determination.
10 THE CHAIR: Dr. Epstein.
11 SPEAKER: Yes, thank you Theresa for this very
12 helpful summary. I have two questions. When you speak
13 about blood inventory it is my understanding that it's
14 principally a report of inventory of collection centers
15 not encompassing inventories in hospitals. And yet, blood
16 available on an urgent basis really depends, principally,
17 on what is in the hospital. So I'm wondering how the AABB
18 is looking at the whole question of sort of a real-world
19 picture looking at all inventories. That is my first
20 question. The second question is, when you talk about the
21 ability to deliver blood where needed, especially, under
22 urgent circumstances, how is the system looking at the

time element? So, for example, there may be enough blood in the system somewhere but can it get to where it is needed in say two hours, four hours, eight hours because I think that that bears directly on the decision-making relevant to upping the reserve everywhere versus having a strategic reserve that is mobilized. Also just as a parenthetical comment, it's news to me that AABB has moved away from the concept of a reserve because I thought that there was a general consensus on that point at least in previous discussions with the advisory committee. So, again, my questions are can you get a handle on the hospital inventories as part of the available inventory? And how do you see the issue of speed of response in terms of being able to deliver blood urgently.

MS. WIEGMANN: Speaking first to the hospital point and I recognize that I should have covered that in the presentation. That is the notable hole in this approach, in terms of, through the task force we can get to the supply data on the shelves of the blood centers. There is no system in place, right now, to get any -- those numbers from the hospitals. And I think we need to work towards figuring those -- how to get that data. That

1 being said, the hospitals have limited time and resources
2 themselves.
3 So I would think there needs to be -- we need to
4 make sure if -- figure out if there is any way to get the
5 hospitals some sort of incentive to reporting such data
6 because I think it's proven somewhat difficult to get that
7 information. But we do believe that that is an important
8 area to work on because clearly there is blood stored on
9 the shelves of the hospitals and not just the blood
10 Centers. Now, I'm losing my mind, your third question was
11 the reserve, the second one was --.
12 SPEAKER: The second was the speed of response.
13 MS. WIEGMANN: Speed of response, yes.
14 SPEAKER: In other words, how utilizable are
15 these supplies nationally, if you need to get some large
16 quantity of blood to a specific location rapidly. And how
17 has that figured into the thinking about, you know, sort
18 of the best strategy for --
19 MS. WIEGMANN: Right.
20 SPEAKER: -- addressing shortages and urgent
21 needs?
22 MS. WIEGMANN: The -- and I think the other

1 groups will -- ABC and Red Cross will speak to this too.
2 Our experience has been that the blood centers have the
3 mentality that they will do whatever they can if a
4 disaster hits and there needs to be blood moved from one
5 region to another. I know for instance, just as an
6 example, blood -- since they are not here Blood Centers of
7 America have a system in place -- where Blood Centers of
8 America have a system in place where they will immediately
9 channel as much blood as they can into moving it so that -
10 - from one region to another. And I think that ABC and
11 Red Cross' centers will do that as well.
12 And that the time restriction is going to be the
13 transportation again and the communications and all. And
14 we think that the existing system is going to be at least
15 as viable as a so-called virtual reserve. And since --
16 and that it is not as realistic to do a national reserve
17 at this time. If that is addressing your question at all,
18 hopefully. And then lastly, again, we -- that is why I
19 wanted to make this point in this presentation that the
20 groups in the task force have reconsidered the National
21 blood reserve issue. And just do not think it is
22 realistic and necessarily needed at this point in time to

be in our disaster preparedness efforts.

THE CHAIR: Dr. Williams you had a comment or a question?

MR. WILLIAMS: Yeah, thanks. Alan Williams, CBER, FDA. Theresa, numerous times and this is again looking at slide one. We've seen the collection and utilization lines get closer together and as always kind of, you know, get interpreted as a warning signal that, you know, they could cross and we could have an inadequate supply. But I guess an alternate explanation is that -- is that this reflects better management practices fewer out dates and maybe more than anything, a greatly increased proportion of double red cell collections, which are targeted. And maybe just reflects better utilization of the available supply. Could you comment on that?

MS. WIEGMANN: Yeah, I mean that, there was a general sense within the report that there has been an increased efficiency in the usage of blood, and that's why we're not facing as dire a circumstance as we predicted a couple of years ago. If you'd looked at the numbers, a couple of years ago, we were fearing that eventually the lines would be crossing, and they are not, at least right

now, crossing -- or moving towards crossing as quickly as we had feared a couple of years ago. And I think that is partially through more efficient use of the products, reduced out dating et cetera.

THE CHAIR: Ms. Finley and then Ms. Birkofer.

MS. FINLEY: Thanks, Theresa. It was an excellent presentation. I had two questions for you. The first is, how would you characterize the extent of response in the blood system to a large-scale situation, such as an acute radiation syndrome attack, where there might be a heavy demand for platelets and over an extended period of time. Up till now our emergency response in -- both Oklahoma City and in -- on 9/11 was relatively constrained. This would be a longer term kind of response, considering the closeness of those two lines as you have showed us. How has the task force addressed that issue?

MS. WIEGMANN: I think that we are optimistic about the -- drawing from the goodwill of the American public that we have seen following other disasters, as you have mentioned; Oklahoma City, September 11, Katrina, that the American public would want to do what they could to

1 help. And I think that we -- if we were faced with a huge
2 national emergency like that, that we could meet that need
3 through the goodwill of the people and the hard work of
4 the blood centers.
5 You know, in the past, after September 11th, we
6 had the huge increase but then we had -- and it didn't
7 last at that rate for months afterwards. But that is in
8 part because we immediately or shortly thereafter sent out
9 a message, you know, we do not need your blood for this
10 particular emergency, but we do need the blood on the
11 shelves down the road. I think that we would have a
12 message that there was a need for platelets that lasted
13 longer and I think that the public -- or, you know, at
14 least we are hopeful that the public would be sympathetic
15 to that concern.
16 MS. FINLEY: Thank you. We -- I also have a
17 follow-up question on the reserve issue. There is a
18 difference between, we should have it and we don't think
19 we can do it. And I'm not entirely clear on your response
20 whether it's the former or the latter, or a combination of
21 the two.
22 MS. WIEGMANN: Right, the community -- the blood

groups within the task force, right now, did not think we need it.

MS. FINLEY: Okay. Thank you.

THE CHAIR: Ms. Birkofer.

MS. BIRKOFER: Thanks, Mr. Chairman. I appreciate your presentation, it was very clear. I do have a question and may be a follow-up. You said there was no national shortage and the task force would like to see up to seven days. What is the current blood level -- blood supply?

MS. WIEGMANN: Generally, one to three, I mean three -- it depends on regions. She will get into it in her --.

SPEAKER: Three days -- three to four days in the blood centers and another two to three days in the hospital, so I believe we are actually approaching seven days only in --

MS. BIRKOFER: And do you have a definition of a shortage? How is that defined?

MS. WIEGMANN: (inaudible)

SPEAKER: The center defines that there (inaudible)

THE CHAIR: Could you -- I am sorry could you introduce yourself for the record please.

SPEAKER: I am sorry I am (inaudible) America's Blood Centers.

THE CHAIR: Okay. Thank you. Dr. Lopez-Plaza.

DR. LOPEZ-PLAZA: I have two questions. Actually, how do you really describe or met blood needs. Is that that the center cannot supply the amount that they are supposedly supplying to that hospital or that the hospital have had to cancel surgeries or do something else because they don't have the blood they need?

MS. WIEGMANN: I would need to look at the survey itself. In one incidence, at least, it was that unmet surgical blood need.

DR. LOPEZ-PLAZA: Okay, so that would mean probably

MS. WIEGMANN: I mean, seriously unmet non-surgical blood needs. Excuse me.

DR. LOPEZ-PLAZA: I mean, the only way I can think about that is that they are not supplying the hospital with the blood. You know that the standard order. The other question I have for you is, are you

1 looking at out date rates as part of your national blood
2 supply, you know?
3 MS. WIEGMANN: Yeah, we do have data within it.
4 I don't have it here with me right now. But -- or I would
5 have to look through my little table since I haven't it
6 memorized every data point in the survey. But yes, there
7 were -- again, there were -- there was evidence through
8 this data that a number of out dating -- out dates was
9 being reduced -- had been reduced.
10 THE CHAIR: One of the concerns that I have --
11 MS. WIEGMANN: I'm sorry. There was a 40 -- for
12 instance there was a -- in 2004, there was -- compared to
13 the previous data from a couple of years before there was
14 a 42.9 percent decrease in the number of outdated whole
15 blood and red blood cell units.
16 THE CHAIR: One of the concerns that I have is
17 that lacking robust data from the hospitals I think we
18 probably are underestimating the incidence of delays in
19 surgical care. The experience in the real world is that
20 these often happen and are reported but not really well
21 captured by the supplying blood centers.
22 So I think that having a system that would give

1 detailed reporting from the hospitals would be most
2 important in terms of really anchoring down the real
3 shortfalls. The other point is that somewhat
4 disconcerting, I understand the general concept of having
5 the data looked at in terms of a day's supply. But often
6 that becomes difficult when you are looking between
7 different regions because a day in Houston is not a day in
8 Tulsa. And we really don't have a transparent blood
9 supply. No one wants to share the numbers. And to me that
10 suggests that there is a root problem. And I'd just be
11 interested in wondering why we can't have absolute data
12 rather than relative data.
13 MS. WIEGMANN: In terms of each blood center --
14 in terms of --
15 THE CHAIR: Well, in terms of the real number of
16 units that are available.
17 MS. WIEGMANN: We think if we come up with --
18 then actually Ruth, may be able to speak this a little bit
19 better, but that it makes a more understandable term
20 actually, in terms of if you there have been -- there are
21 ways for you to come up with a methodology of coming up
22 with days of supply and that that actually ends up in a

more usable term than number of units.

THE CHAIR: Yes. Okay, while you -- I guess my perspective has being that in times of a blood shortage it becomes real hard to get the real numbers. But a comment from the Executive Secretary.

MS. WIEGMANN: But then if we are talking about times of disaster certainly, I think the task force has been able to work with the local affected blood centers to figure out what the supply is in their community and then, you know, we have it -- a whole little algorithm, or what have you, to figure out what the demand we foresee as a result of the event. And so, we look at the supply of what is on the blood center's shelf and the centers have to contact their hospitals immediately to figure out what is on their shelves. So in disaster response we have tried to address that issue.

THE CHAIR: Dr. Holmberg?

DR. HOLMBERG: I just want to make a point of clarification as far as -- first of all, what Theresa meant by the blood community working with HHS in providing information as far as blood that was available in the blood centers. And then secondly, I want to address the

issue of how do we understand the amount of blood that is on the shelf in the hospital. And I have to take the committee back to numerous recommendations that were made way back at 2000 and the early 2000 and what we discussed at that time also the blood reserve.

And then also in the blood action plan the talk of monitoring the blood supply. And through those recommendations the HHS did set out to create a monitoring system. And that system is called the blood availability, safety, information system basis. And so what the task force is talking about is how do they parse out information to be able to feed into HHS' basis system.

Saying that I think that one of the key players that we have forgotten in our discussions and it is emphasized to me, over and over again, when I go around to the regional health areas, the public health regions and that is the state. The local and the state government is who we serve. HHS' response -- it has to be responsive to the state, local and tribal governments. And so, I have to say that the state is very much interested in knowing what is happening on a local basis within the state and how things are being responded to.

A good example is just even more recently and again it is a good example that blood was not needed during a disaster and that is the bridge in Minneapolis. And yet at that point in time the state health officials did not have the information to know what was available either in the blood centers or within the hospitals. The other part -- and this, just a correction, is that the statement was made that there is no mechanism to collect hospital data. I want to emphasize that we have had BASIS up and running since October of last year.

We have over 100 hospitals participating in BASIS and this is reported on a daily basis. The reason why we are asking for reporting from the hospitals and the blood centers is so that we can get a supply and demand and get a total picture of what is happening. But once again I have to say that we have about 100 hospitals for us to have a national consensus. We need about 100, I think the number may be about 135 hospitals, if we want to be able to satisfy the needs of the state and medical officers, we need to have much more.

And that is because for it to be a statistical sampling, of course, we have to have larger numbers. But

1 we are working with communities such as Boston, in which,
2 they have a plan right now, to be able to go and through
3 BASIS to be able to determine where their peaks and
4 valleys are over a period of time. So I just wanted to
5 really emphasize that as a recommendation of this
6 committee there was established a BASIS program and we are
7 monitoring.
8 We have a very small cluster of reporting
9 facilities from the blood centers. But over 100 hospitals
10 are participating.
11 MS. WIEGMANN: And I apologize I should have --
12 if I misspoke or misrepresented that -- that it's not a
13 total void there but that that -- just that that we think
14 that that data needs, probably, just to be made a little
15 more robust to be -- give you a full national picture.
16 THE CHAIR: Mr. Matyas.
17 MR. MATYAS: Currently, participation in BASIS
18 is voluntary?
19 DR. HOLMBERG: Yes it is.
20 MR. MATYAS: So -- I'm just going out at some
21 point do we not want to then maybe make a recommendation
22 to CMS that a condition of participation in the programs

is to participate in BASIS.

DR. HOLMBERG: That -- I would leave that to the committee to make that. If they felt that that recommendation needed to be made. We at HHS have relied on voluntary reporting and again, as I said before, we are trying to do this on a daily basis for collecting the data. As we validate the system we may be able to back off to less frequent reporting so that there is not a burden -- a reporting burden.

MR. MATYAS: What are the requirements associated with burdening -- with reporting I mean. I would assume every hospital has somebody who is collecting that information. Anyway, and it's just a matter of inputting it into the BASIS database.

DR. HOLMBERG: At the hospital level the hospitals do have that data on a daily basis. The problem is that many of the hospitals are really manpower stretched.

MS. WIEGMANN: Right.

DR. HOLMBERG: They really do not have the resources for someone to sit down at the computer even for five minutes. Now, we believe hospital reporting, it is

less than five -- it is about five to 10 minutes of reporting through a Web-based program. One of the other mechanisms that HHS has looked at and it is not currently in the contracts, with the -- what we used to call the HRSA grants to the hospitals -- HHS is currently looking at is this something that we add to the HRSA grants.

You will hear tomorrow in the presentation from the Assistant Secretary for Operation and Response. You will hear a little bit about how ASPR has taken over that responsibility from HRSA in the hospital grants. That may be an option and so I would just challenge the committee to think about those things on how we may be able to get greater participation.

THE CHAIR: Yeah, I think your comments on the hospitals personnel situation is right on target. And even though the time committed is very minimal absent a requirement the participation will be low. So I think we need to seriously consider about some methodology to increase the participation. Patricia. You --

SPEAKER: Yeah, I was going to echo that we hear from all -- and many of our hospitals members, you know, that their resources are just stretched so thin, I mean we

1 hear time and again at this committee that the payments
2 for blood to the hospitals are limited. That the
3 transfusion services are stretched thin. And at the same
4 point we need to think about comprehensively what we are
5 asking from hospitals, for instance, right now, we are
6 trying to work towards getting the hospitals to supply us
7 with data related to bio-vigilance. So we need to look at
8 the overall picture of what we are asking from limited
9 number of people within a hospital transfusion service.
10 And how --
11 THE CHAIR: But again that is related to the
12 infrastructure and currently because our infrastructure is
13 inefficient it doesn't mean that we could ultimately move
14 to having a more efficient infrastructure as the demands
15 were set forth. And so I think yeah, there is there
16 snapshot but we need to look beyond that. Dr. Bianco, a
17 comment, a question?
18 DR. BIANCO: Celso Bianco, America's Blood
19 Centers. Dr. Bracey, I want to make two requests. One,
20 that we reserve this discussion to appear after there was
21 a presentation by America's Blood Centers and the American
22 Red Cross. There is much more information that I think

1 that is very pertinent. And a second, so that our
2 executive secretary is prepared. There have been -- there
3 is BASIS that has been working for about a year with a
4 limited number of hospitals. And there was a pilot
5 program that was instituted by HHS from 2001 to 2005.
6 It's actually a publication on transfusion with the
7 results. I'd like Dr. Holmberg that after the
8 presentations to review, how was that data used. Where it
9 was the data presented? How useful was it for the
10 management of the blood supply? But first, I really
11 suggest that we hear the two other speakers.
12 THE CHAIR: Good point. Are there any
13 particular questions for Dr. Wiegmann's presentation? Dr.
14 Duffell.
15 DR. DUFFELL: Yeah, in looking at your report,
16 did you all consider -- and you made the remark about how
17 the American public response to national emergencies, and
18 I agree with that. But the industry is oftentimes moving
19 -- and certainly at the manufacturers level, and I believe
20 we see at the customer level, to a just-in-time delivery
21 type scheme. So you may have loads of people willing to
22 donate but will you have the equipment and disposables

available to actually do those collections. Was that considered? Otherwise, you will have a big supply --

MS. WIEGMANN: It has been, and she's going to address that in her -- so we tried to look at each other's presentations to not do too much overlap. But obviously, that is an issue. Particularly, as we look at a pandemic. And we have been trying to talk to suppliers about that. And then it also relates to that overall issue of mass casualties of us being part of an overall -- an overall healthcare picture.

DR. DUFFELL: And then also did -- was there ever a time in which this task force was in favor of, or promoting the idea of a National blood reserve?

MS. WIEGMANN: Yes. As I said in 2004, we came before the committee, they asked us to present on this issue and at that point we did recommend a reserve of -- a real reserve of approximately 10,000 units of red blood cells.

THE CHAIR: Okay. Well, let's move on then to the next presentation by Ruth Sylvester. She is the director of regulatory services for America's blood centers. And she will also address the issue of blood

transfusion and transplantation -- safety during blood shortages.

MS. SYLVESTER: I want to thank the committee for inviting the America's Blood Centers and giving me the opportunity to come forward and to discuss with you today whether or not the blood supply is adequate, and some of our experiences from the civilian side. For those of you that don't know, America's Blood Centers was founded in 1962. And we represent the independent community-based, non-profit blood bank organizations. We represent about 45 percent of the blood supply here in the United States to 100 percent of the blood supply in Canada and we're looking at about 9 million blood donations at over 600 sites. The discussion items that Jerry Holmberg asked us to look at, I've listed here, and I tried to use those as I prepared my talk.

So I hope I answer the questions that he posed to us as we move forward. When I first started -- you got to look at what the challenges are in the blood supply. And if blood could last more than 42 days on a shelf we wouldn't be here because this wouldn't be a problem, we could stockpile it as long as we wanted on the supply

shelves and life would be good. But red cells are only good for 42 days and platelets are only good for five to seven days depending on which methodology you are using.

Some of the challenges that we get into is that there is low reimbursement rates. Blood centers are not being reimbursed at the amount of money it takes to put out a unit of blood. They have incurred and the safety costs keep going up and up. And unfortunately, they are not able to pass those costs on to their customers and that is the hospitals. And so, they have to eat those costs. And then we also have looked at some disasters lessons observed.

When I was in the military, you know, we always had these lessons learned conferences and I realized that after, you know, 22 years that I saw the same lessons learned every time. And so I have learnt to call them lessons observed until I don't see them any more. Then we will have learnt and fixed them. But until then and the blood bank community communications, transportation and fuel continue to be our lessons observed.

I found it interesting, in an article I read in the paper right after the Minneapolis Bridge collapse,

that some of the emergency response was excellent except they had communication challenges. And so we continue to see, even after 9/11, communication challenges among our emergency response. We face those same challenges in the blood industry. And then, not only in our industry but in many, many industries as we move towards a lean and many other types of whatever the current vernacular is. We're going to a just-in-time logistics. The reality is the more inventory you have sitting on your shelf that is more dollars you have sitting on a shelf, not being available for you to use.

And so, as we go to just-in-time, we limit the amount of blood on the -- the amount of inventory you have on the shelves. And that equates to limited stocks. And so that is another issue and a challenge that we deal with in the blood supply. And that will be a tremendous challenge when we get into pandemic flu, and I will cover that in a slide later. You have already seen this slide. This is from the 2005 report that the AABB has, and as Theresa mentioned, you know, we have -- I don't if my -- I don't think my pointer moves forward -- there we go.

When you get up here, we have one of two things.

1 Back here is in '97, we're coming back out of the HIV and
2 a bunch of other issues in testing and stuff. And then we
3 were doing great. And then up here we can look at this as
4 one of two things. Either the sky is falling and if we
5 continue along these lines we're going to run out of blood
6 and people are going to die, or we can say that we have
7 gotten better, and hospitals have gotten better, and we're
8 managing our inventory better. Because again, inventory
9 in a shelf, is dollars on a shelf. And thrown away blood
10 is wasted dollars.
11 So if we have reduced our out date rate 42
12 percent as according to this study, then we are managing
13 our inventories better. And so, I put to you that this is
14 a partially a combination and mostly due to better blood
15 inventory management. Not only on our blood suppliers'
16 shelves but on our hospital shelves as well. Now, we are
17 looking at monitoring the inventory. A lot of people
18 monitor the inventory. We look at the inventory in ABC
19 and we have it available on our public sites, those that
20 anybody can go on any given day and look at what the blood
21 inventory is. We have it as a red, yellow, and green
22 status. Our members go in there on a daily basis, Monday

through Friday, and they put whether or not their inventory is red, yellow or green. Red being one day or less, yellow being two to three days, and green being greater than three days.

It is a manual entry on a Web-based system on a daily basis. Blood Centers of America, which is another non-profit organization representing -- about 60 percent of our members are also members of BCA. They have developed an executive dashboard which is excellent, and we are partnering now with BCA and looking at inventory data rather than both of us requiring our members to enter data into two different systems.

We are going to share data and try to move it as much as possible electronically, because I agree with the comment that was made, there is no reason not to see data. But I don’t think there is a need that everybody has to monitor everybody’s data. I think that is duplicate -- you know, duplicity and a waste of time and effort for everybody to be looking at everybody’s data.

And the partner for the last year now, we have been working with BCA on disaster preparedness. BCA does inventory management and inventory review on a daily

basis. So let us let the experts in that do that. And so they do that part of the disaster preparedness and ABC handles the scientific portion, and that has been working very, very well for the last year. And again, that is what we are going to do in the future.

These are some strange shots out of BCA system, this is the last 30 days and you are looking at -- this is group O-positive and group O-negative, days of supply, you could see that there is -- runs anywhere from four to six days of supply of group O on their shelves and two to three days of supply of group O negative on their shelves in the last 30 days.

Here is another screen shot from -- like I said, they have very, very nice dashboards they have established. Up at the top, you see this is by blood type. It is the amount of blood that is available, the amount of blood that is used, and then at the bottom this has by region the same data.

So you a see that a lot of monitoring and trending is going in to looking at the inventory of our blood centers. Here is another look and this is strictly usage data over the past -- it goes all the way back to

2001, so the past five years -- six years rather by blood type. So we have a tremendous amount of data. We are all going towards the area of building data warehouses where we get this data -- historical data and then we can analyze the data with sophisticated mechanisms.

Again BCA, during the inventory, ABC is about to launch its own data warehouse. So we'll be looking more at the scientific side and the deferral scientific information. Now this is data that comes out of our ABC stockpile. What I want you to see on here, this is 2002 through 2006, and mainly what I want to show you here is that every winter we have a drop and that is because Christmas is a busy time and people don’t have time to donate.

And then you get into January where everybody has a cold or a virus or the flu and they can't donate. And then we get into the spring time. Everybody feels better, everybody is coming up and our blood supply goes up. Then we get into the summer when everybody is on vacation. They are feeling fine, they are just not there. And this is the same cycle you see every year.

Again, this is our green, people who have at

1 least three days of supply on a shelf, yellow one to two
2 days and then red, those reporting red. So yes, I can
3 tell you that these centers will have a blood shortage.
4 Those are what you hear advertised on the radio in the
5 different areas that say, "We have an urgent need of
6 blood." But I have these centers over here that have
7 plenty of stock that we can move around.
8 I have centers and I have hospitals that I know
9 of that are 60 miles apart. The hospital has its own
10 donor collection center and when they are running short
11 and they are running appeals, they could buy it from 60
12 miles away because the have excess to export. But then it
13 gets into becoming an economic and financial issue, "I
14 don’t want to buy the blood at that price," you know, "I
15 want to buy it at this price."
16 So some of the stuff you see in some of your
17 hospitals is economically driven. And a question that was
18 asked about that 2005 study as to what is termed a blood
19 shortage, if you look at that study, if a hospital order
20 25 units of group O and got 24, then they could say there
21 was a blood shortage. So you have to be careful how you
22 interpret that data and understand all of the things that

1 went into that was all self-defined by the hospitals. And
2 that is the piece that is missing.
3 You can see in these last four slides that I
4 have shown you and then the Red Cross will show you, Dr.
5 Benjamin is going to show you, they have just
6 sophisticated monitoring of their inventory. The missing
7 piece is the hospitals. No one is looking at the
8 hospitals and I think that is perhaps where HHS can best
9 use its resources and basis is to look at the hospital
10 inventories, because that is the missing piece as you have
11 discussed here today.
12 You know, in your hospital you may say, "I am
13 always, I am canceling surgeries," although there is a
14 blood shortage when a hospital in the next town doesn’t
15 have a blood shortage. So that is the piece of data that
16 is missing and I think that is where basis can probably be
17 more beneficial. And this is just the same thing
18 presented a little bit differently and this is the last
19 year's worth of data, and again you see the same seasonal
20 drops that you see on the other one.
21 Now, that 2005 study, a key statement in that
22 study is, through efficient blood product management

evidenced by reduced outdates and low numbers of hospitals reporting unmet needs, the community has maintained adequate supply to meet the blood product needs. And again, I agree with this. I think what you are seeing in that narrowing of the gap is efficient and effective management of the blood supply.

The other thing it says is the community must remain vigilant, however, because the margin is smaller that ever -- than it ever has been. I also agree with this statement, and I believe that the blood communities today, compared to the blood communities pre 9/11, are at much greater state of readiness since that's preparedness.

And 9/11 was one wakeup call to them and I can guarantee you that Katrina was another wakeup call because one of our member centers was flooded in downtown in New Orleans and he gave a very poignant talk at our annual meeting after the Katrina the next spring. And he sat there and looked every CEO in the face and said, "Anybody that doesn’t do emergency blood planning is negligent in their job and should be fired today."

And I tell you that those centers took heart in that and I coordinate the disaster preparedness planning

for our members and they are all doing it, some better than others, some at more advanced stages than others, but they are all planning. And I also think that the other thing that you see is part of the just-in-time logistics. We had it in the military, we have it in the civilian side, you have it in the industry, not just medical industry, but in other industries and -- as well. There is less money out there, so how do you shave your margins? You keep less stock on the shelves.

Now, I would like to turn my attention a little bit right now and focus. We have looked at the inventory. Now let's look at disasters and responses to disasters. This is the common perception of a disaster. The American public in every single disaster in the last 20 years wants to react. They want to be able to do something.

You see the exact same thing today. People want to help the troops in a field and one way that they feel they can directly do that is to give blood because it is a very active thing to do. And we end up being in the blood bank industry is like the -- almost a social worker for the America conscience in that they can come to us and they can give blood.

But the reality of it is that all the way back to 1981 in the Kansas City Hyatt disaster, going through the plane crash in Sioux City, the Oklahoma city bombing, the Columbine shooting, the World Trade Center and the Pentagon, and these numbers all come out of a study by Paul Schmidt in the New England Journal of Medicine in 2002 regardless of the number killed.

Here you had as few as 15 in Columbine to as much as over 3,000 in World Trade Center. Same thing with the number injured, as little as 32 as many as -- this number is obviously false at low probably, but even in Katrina as many as 2,000 injured. The reality is, no matter how many you get -- get killed and injured, you are going to use less than 300 units of blood.

The exact same data was provided to you by Dr. Shenar (phonetic) of the Israeli Blood Bank Agency back when I sat on this committee about three or four years ago, where she showed that for a patient you may use in that individual patient's need a tremendous amount of blood. But overall in a disaster, this is about what you are going to see. You are going to use probably 100 to 300 units of blood.

What I would also like to show to you is, this is the available inventory where we did have the data that was on the shelves on that given day in that local area where the disaster occurred. And then this is what the U.S. response was immediately after, okay. 1500 units, most of these are within one to three days of the event occurring.

And after the 9/11, our blood bank industry and this is really before we started doing true emergency planning, they were able to collect 475,000 units in the weeks following 9/11. That is a tremendous surge capability. And so what I am here to tell you is that even just the other day, earlier this month, they doubled their daily collections in Minneapolis, and that is not a large center.

And so the capacity is there, I believe the will of the American people is there and we keep enough supplies on hand and enough in the pipeline that we can respond to these types of natural and unnatural disasters that we faced. So, are there shortages in the blood supply? Yes. But those shortages are short, they are local and regional and they are seasonal. There is no

question about that.

On any given day in the United States, we have roughly 40,000 units that -- of blood that are collected on a daily basis, and we have about 200,000 units that are spread throughout the United States on any given day sitting on our hospital shelves. Disasters in reality don’t require a large amount of blood.

Blood centers are -- have shown their capacity to at least collect three times their normal collections for a limited period of time. I mean, eventually in a surge, you are going to wear your people out as New York blood centers, you know, found after 9/11. But even there it was heroic, the efforts they made to collect all those people.

And then the Inter-Organizational Task Force, which was formed after 9/11 to try to brunt the force of having the large donor outtake that we had in 9/11, it has been very, very effective. I worked with the task force, both from my time in the military and I work with it today. And the organizations have come together, they have put aside their differences, put aside their competitiveness, and during disasters they worked very

efficiently and they move blood where it needs to be and they do so quickly.

As long as -- one of the questions that was asked earlier is how quickly can you move blood and that is going to depend. We can move blood immediately from our centers in the local area which we do. We just did that for the hurricane that passed through a week -- I think it was a week ago. The closest centers we had were Dallas and we shifted down to Houston. That was a matter of driving distance.

And in Minneapolis, we are able to drive additional units in there. As long as our air industry is intact, we can move blood anywhere in the continent of United States within several hours. If we can't get it on a commercial flight, then we can launch -- we have our agreement set up Life Flight, I believe -- no, Angel flight is the name of it

And they agree that in a disaster they will fly our blood products wherever we need them within the continental United States. So I believe that the ability to move blood is there. If we get into another 9/11 where all air travel is shut down -- I was stationed off at air

force base on 9/11 and the Community Blood Center of Lincoln as well as the Red Cross in Omaha, both called our base asking if they could shift samples and ship blood on our military aircraft, because they collected it and they wanted to get it to New York, because they wanted -- the people wanted it to be used.

So I am not concerned about the capacity, the will or the desire of the blood bank industry and the U.S. population to meet the needs in a disaster. Instead of a national blood reserve, what I would like to tell you is that we already have a blood reserve. It is walking around everywhere in the United States. It has proven itself in every disaster in the last 20 years. It is the ideal storage location. It doesn’t cost any extra money. It doesn’t take any extra shelf space and I guarantee you I am not wasting it. Because the reality is that the best place to store blood is in the body, not in a plastic bag on a refrigerated shelf.

And I think that we have today a natural blood reserve that already exist and I think it has proven itself the ability to meet our needs in a disaster. Now let us look at pandemic flu because that is a little bit

1 different type of a disaster. It is not a bridge falling,
2 it is not building falling. And I said on two different
3 blood bank pandemic flu planning groups and this one is an
4 alliance of blood operators which includes representatives
5 from American Red Cross, ABC, the Australian Red Cross,
6 the Brits, the Canadians as well as the European Blood
7 Alliance.
8 And we have been working together for about two
9 years now, and it doesn’t matter in what group I sit in,
10 this seems to be the standard planning assumptions.
11 Platelets, we do not believe there is going to be a change
12 in the need for platelets, because we believe oncology
13 patients are going to need their platelets regardless if
14 there is a flu or not.
15 We believe that Red Cross -- red cell usage is
16 going to decrease anywhere from 10 to 25 percent. The 25
17 percent comes from the experience of Canada and Toronto
18 during the SARS. They saw that their blood needs were
19 reduced by 25 percent because their beds were filled with
20 SARS patients and they didn’t need blood.
21 We don’t anticipate a lot of blood need, red
22 cell needs from pandemic flu patients. It's just not what

1 their symptoms are going to be. And frozen components, we
2 also do not predict a change. The frozen components are
3 not an issue because they have at least a 12 months
4 expiration date and so we don't believe that that is going
5 to pose as big a challenge during a pandemic flu.
6 And managing a blood supply during a pandemic
7 flu, I believe the key to success is planning. My time in
8 the military -- I learned that it is not the plans that
9 are sitting on the shelf that are so important because I
10 guarantee you they will not be executed as they were
11 written. It is the experience of going through the
12 planning process that is absolutely critical to succeed in
13 any event.
14 I also -- the groups recommend annual flu
15 vaccination for donors. Two things they believe will be
16 accomplished by that, one, we are going to have a
17 healthier donor population so that may help reduce the
18 dips we see in the winter time, but also they believe
19 there will be some residual protection factor going into a
20 pandemic for people who routinely get their flu vaccine.
21 That, of course, is a scientific assumption I think, more
22 than fact.

We also agree across the -- around the world actually that as we see, pandemic flu is not going to be like a bridge falling. It is not going to happen tomorrow. I believe we will have notice as you start to see cases, just as we've seen with the avian flu, it gets reported and I think as we start to see a climb in the pandemic flu alert levels who has their own, U.S. has their, the Brits, the Canadians, everybody has pandemic flu alert levels now, then it is critical that the blood industry follow those levels and start increasing their stocks so that they fill their shelves to the maximum capability.

I believe they should be educating the public today that as we come to a pandemic and get into a pandemic, we need you to donate beforehand and will need you to continue to donate after the fact. Because the general assumption -- and everything is on assumption for the pandemics because all we have is 1918 to go by.

But the general assumption is we will have enough red cells on the shelf to carry us through the first wave. It is going to be at the tail of that first wave where we are going to start running into problems.

And we know for sure that they are going to postpone elective surgeries. And ethical consideration is triaging the blood use in the hospitals.

We can, from the blood center's perspective, triage in that I will just cut everybody's blood supply in half, but I don't think the surgeons in the hospital would really agree with that. So there will have to be some guidance and some triaging at the hospitals and that is an ethical consideration that needs to be done that we, the blood industry, can only do so much with. It really will need to come from the physicians and from the hospitals in their efforts. And so that is something that I believe that this committee could recommend very efficiently and effectively and that will be helpful.

The other thing is antivirals and pandemic vaccines for our committed donors. We are going to need those donors to be healthy and we are going to need them for platelets because again we don't believe the platelet requirements are going to go down. So if we can get antivirals and the vaccines as they come available for our committed platelet donors, that will help carry us through a pandemic wave so that our oncology patients don't

suffer.

And then we needed to address the supply issue. Louis Katz (phonetic) -- Dr. Katz and I met with vendors back in April, and specifically discussed very earnestly and frankly our concerns about the vendors because we believe that the weak link in our planning is the vendors because we can't control it. And they do not have a very large pipeline. It cost money to have a large pipeline and amount of stuff in it and so they have narrowed it down.

And they told us, "You tell us how much you want and then tell us who is going to pay for it, and we will increase to that level." And so that is where we are at. We have manufacturers that don’t have the resources to increase their own hand stocks, we have blood banks out there that don’t have additional funs to increase their stocks and so that is a challenge that, as we get ready and prepare for a pandemic, needs to be addressed. I can save patients' lives with a blood bank. I can collect a unit of blood, I may not be able to test it right away, but I can still save their lives and I can test it after the fact.

But I can’t even do that if I don’t have a blood bag. I would like to suggest that collection bags and materials be added to the national strategic stockpile. Because I believe that will do more in a pandemic to help insure we have the right blood on the shelf than anything else, because without a bag the whole process stops. And so that is the key piece of logistics and supply that we need to address.

And again I can go back and freeze the serum and go back and test it later. And then I can approve -- you know, provide appropriate follow-up and testing for the patients. Now let us move away from pandemic flu and let us look at another scenario that could potentially, at least thought wise, overcome our thing and dirty bombs, rads and nukes, okay.

And the risk, again, I go back to historical data, says we are going to need 200 to 300 units in the immediate area. The biggest risk is that a nuclear device, a radiation device could defer an entire metropolitan area. And so that would render that donor population unusable for a certain period of time. And that period of time still needs to be determined and that

is what the work that Dr. Williams and Dr. Epstein's (phonetic) groups are looking at, DoD is looking at as far as what will be the effect.

And a lot about it is like any plan, you know, you have a plan on the shelf and you can make all the assumptions in the world, but until it actually happens you are not going to know. And then the other question we have, will the radiation affect the safety of the blood products on the shelf? Because if it doesn’t, then I just showed you slides to show that I have enough blood on the shelves.

Now that is if we have it only in one area. And what I am going to, I am going to do what I always do, I am going to ship it in from outside sources and so I am going to need support and transportation fuel and communication because I can get it close, but I can't break those cordon lined to the frontline emergency responders. And so we will need to be able to get the blood into the contaminated area and that is where we will need a HS (phonetic) to support.

Now what happens if we have multiple locations and multiple detonations? I go back to history and I say,

they are going to need 200 to 300 units in every location and I showed you data to say that I have enough blood on the shelves to meet those. I still have to get it there and so I am still going to need transportation fuel and communication support.

And I have the capacity in my geographically diverse blood donor centers because I don't believe that they are going to nuke my entire country. If they do, then we can just wrap it all up and go home anyway. But if they don't, then I have blood centers in every state and probably in almost every county, at least servicing every county in the United States.

And so those donors will respond. We saw after 9/11 if we have this type of event, I guarantee you we will see it again. Now, in summary, I think I provided you data and hopefully that data shows that the supply is adequate. This is a view from the 30,000 foot level; this is not from the hospital view. So the supply is there, I would encourage you to go forward and to monitor at the hospital level.

And -- but as Dr. Bianco referred to earlier at the nightingale story that was published in 2003, when you

read this its excellent data, but then you get to the ending you say, "And what did you do with it." And that is the question. We can monitor that the cows come home. But if we are not going to anything with the data, then all we are doing is extending manpower resources and IT resources to build systems so that we can collect data and publish papers.

If we are not going to do something to impact the outcome, then I don't know that it is really worthwhile doing. Yes, there are shortages; you saw those, the red dots. They are local, they are regional, they are not national. Disasters do not require large amounts of blood. I did not include Dr. Shenar's slides. The same kid of data is shown after these Spain, the train bombings in Spain, the train bombings in Britain as well as the embassy bombings in Kenya in Africa, 200 to 300 units will supply.

They are sufficient inventory tested red cells at the blood center and on the hospital shelves to address any emergency I think this country faces. The comment we heard about platelets long term, I believe after you get past the first 48 hours of a disaster, our industry is

certainly ready to respond and can replenish those.

And I believe if we put out a public appeal that we will get -- the public will come out if needed. But that appeal has to be very specific and has to be very clear, and I think that was our mistake after 9/11. We weren't clear in the message we were sending out. And I also believe that a natural blood reserve already exists, it is walking around and will respond if we ask it to.

So what are our unmet needs? Past disasters and exercises such as top-off which we participate in as an industry as well as local blood centers in the affected areas of the exercises. We have shown that there is an overwhelming response of blood donors. That can be good and that can be bad. It is very, very taxing and if you don't control it, you will do nothing but waste money and throw away a lot of products.

But you don't want to also tick off your donors so that they don't come back the next time. And so that is a public relations and media issue that needs to be handled with each disaster. Transportation, fuel, and communications, again those are lessons observed because we haven't learned them yet. I hope some day during my

life time or at least my professional lifetime we learn them and do something to finally fix that.

And available critical collection supplies and reagents, that is the weak link in the whole chain. And so if we can do something to address that at least that we can collect blood, then we have done something we have been effective. So what are the potential solutions that you guys have -- the committee can consider? Management of the influx of blood donors; I believe we do that a little bit better now with the task force.

I would encourage vaccination of regular committed donors in preparation for pandemic flu and I believe that will also help us in that dip that occurs in the winter time. Additional blood collection bags and venipuncture supplies in the national strategic stockpile I believe would be a positive step forward in preparation for pandemic flu.

And the crux of all of this of course is dollars. We would encourage government dollars to increase either vendor on-hand supply and supply of blood bags so that we would have a 2- to 4-week -- from a 2- to 4-week which is what exist today, to at least a 3 month

which would carry us through a pandemic flu wave. I want to thank -- again, thank the Committee for inviting me to speak and I will answer any questions you have to the best of my ability.

THE CHAIR: Thank you for a clear, focused and a talk full of recommendations as well. In the -- let’s try this, let’s try to avoid general questions and we can have the general questions following --

MS. SYLVESTER: Or if you would like we can go ahead and have Dr. Benjamin speak and then I can certainly answer any questions afterwards.

THE CHAIR: Are there any burning specific questions right now, Dr. Holmberg?

DR. HOLMBERG: Yeah, Ruth, I just would like you to go back to slide number 10, and there is two questions I have concerning that slide. First of all, what is the second number after the year at the bottom?

MS. SYLVESTER: I think that is the week, yeah, that's the week. Week of the year.

DR. HOLMBERG: Okay. Then also when I look at the peaks and the valleys and I see the red area and the yellow area that has dipped, but I also see blood centers

that are in the green that are on the -- at the top of the mountain. So the peak and the valley there, I don’t understand why it's -- and in the same period --

MS. SYLVESTER: Well, if I have fewer centers that are reporting a less than 1-day supply, I have more reporting greater than 3-day supply. And as I have more reporting a less than a 1-day supply, I certainly have less reporting at least a 3-day supply, that’s why they tend to -- to be opposite. Yes, sir?

DR. HOLMBERG: It almost appears from this slide that there are some facilities that are much more efficient than others at pulling themselves out of the shortfall.

MS. SYLVESTER: You know, and I will be honest, some of those is just in time. When I moved from the civilian -- from the military sector over to the civilian sector, I realized that I have some centers that are always red. And so I went and asked, “Why are these guys always red? Maybe they ought to be out of business." And I was -- I was told that some centers choose to do that; they would rather have their inventory pushed forward to the hospital shelves than their shelves. And so they

intentionally keep themselves in the red at a 1-day supply, whereas -- and keeping their hospitals at a higher inventory. So we have to take some of that into consideration too. Staying in a red may be a business decision that that blood center chooses to do. Yes, sir?

THE CHAIR: Dr. Duffell.

DR. DUFFELL: How do I reconcile in my mind your summation with the fact that you said during those natural disasters, we had the donors and we obviously had the bags and needles to go with those donors.

MS. SYLVESTER: Right.

DR. DUFFELL: So how do I reconcile those --

MS. SYLVESTER: Our concern is in a pandemic flu, the blood industry will not be the only one affected. My transportation that will bring the supplies from my suppliers to me will be affected. They will have probably a 35-percent sick-out rate as well as we will. The bag manufacturers and the test kit manufacturers and the people working on the lines manufacturing those items will have a 35 -- they will be affected just like everybody else.

DR. DUFFELL: Got it.

MS. SYLVESTER: The suppliers to the suppliers, we have small industries that rely on small businesses located in Podunk nowhere to make one piece of a critical piece and so if they are not going make that, I can’t make that bag. And that is our concern in a pandemic flu. Not in a regular natural disaster, but in a pandemic flu, it's strictly in pandemic, because that’s the weak link in our pandemic flu planning.

THE CHAIR: Okay, well, let’s move on then to Dr. Benjamin’s presentation.

MS. SYLVESTER: Thank you.

THE CHAIR: Dr. Richard Benjamin is well known to the members of this group and has presented many times before. Dr. Benjamin is the Chief Medical Officer of the American Red Cross, he has been extensively involved in transfusion medicine for many years now, having trained at a number of fine institutions. And he will present to us on Blood Supply Challenges and Red Cross Strategies and Response.

DR. BENJAMIN: Well, thank you very much. The Red Cross appreciates the opportunity to present on the topic of Blood Supply Challenges and the Red Cross

Strategies and Response.

Just to remind the new members of the Committee, the Red Cross represents just one blood collection agency that has been in this business for about 65 years. We collect 9 million blood components distributed to about 3,000 hospitals nationwide. And every year, we interact with some 50,000 organizations to hold more than 135,000 blood drives. We collect about 6 million red cells from about 4 million volunteer donors; we also maintain the largest inventory of regular antigen negative and rare blood units. We also have extensive immunohematology reference labs and other specialized services and some direct patient care services.

Out topic today really is blood supply challenges in disasters and in the light of seasonal variability in supply. We’ve had two superb presentations on the disaster front already, so I’m really going to focus most of my talk on seasonality and the ongoing challenges of maintaining a regular blood supply. But I would be open to questions around disasters as well. So I will be talking a little bit about the donor-based challenges, the shrinking donor base, the aging donor

base, a little bit about optimal donor utilization and optimal utilization of the supply and a little bit about blood utilization by hospitals.

This is my one slide on disasters, just to reiterate that we concur completely with the ABC and the AABB around the issues of disasters that during single natural disasters the blood supply itself, the blood on the shelf is the blood that is the most useful. And within 18 to 24 hours we can transport additional blood if necessary to areas from the other regions of the country and transportation and communications become the key issues. And during those circumstances the blood supply is highly elastic in that our biggest problem is a donor search.

The other issues of pandemic influenza and multi-site terrorist attacks et cetera is a different issue and we are working as are other blood centers on plans for pandemic flu in particular. And Ruth Sylvester mentioned something about some of the assumptions we've made around pandemic influenza. We -- we're working on the assumption that we might see a 30 percent reduction in collections with about a 10 percent reduction in

distributions during pandemic flu. And I show here a graph pf what we expect over the first phase of a pandemic, how you might -- inventory might fall.

The standard Red Cross inventory is about 100,000 on a good day and over a 12-week period it would fall down to about 20,000.

So one of the key messages in pandemic flu for us is that if we have a warning in terms of, as the government warnings go up levels, to build that inventory certainly through the first wave and we believe there would be gaps between the waves to rebuild inventory and really the most desirable donors at that point would be recovered flu victims. But that’s all I’m going to say about disasters; I do want to talk about seasonality.

We see great seasonality variation in supply and clearly there is very little seasonality in demand. This graph shows by quarter our collections, and what we can see -- that in the fourth quarter, this sort of May, June, July, early summer areas are when we see our first collections here on every year. What’s also interesting here is the increase in collections around 9/11, also Katrina. Katrina we saw, you know, we did not go on

appeal in Katrina; in fact we sent our donor recruiters down to New Orleans to help out with the disaster effort and we were told -- we didn’t pay for any media and we told everybody there was no need for blood, but they came. The donors came, and we certainly saw a 5 or 10 percent bump in collections and would that collections were always that easy.

Okay. So with this variation in collections, we do see reports -- our hospitals do report shortages to us and on our latest survey, some 53 percent of our hospitals reported shortages at some point in the year. But we concur with the ABC and AABB that these tend to be local and regional. During this period, this summer, we have maintained a group O negative and group O positive inventory of at least 1.5 to 2.5 days, as they were dipped below one day, which is our cutoff for going on appeal, on a national appeal; so we haven’t had a national appeal. But there certainly have been local areas that have been very short of blood.

So again, there is blood available, we also concur we like to push blood into hospitals, we don’t like blood on our shelves. So that 1.5 to 2.5 days is a -- has

to be taken into perspective.

One of the factors around this seasonality may be the fact that we've been concentrating very heavily on recruiting from the youth. In the last 10 years we have had approximately a 50 percent increase in collections from youth from age 16 up to 20, the high school and the college students. And so you might say that the summer problem is the fact that, you know, we're exacerbating the problem by collecting from more youth. It is interesting though that while indeed we do collect no 17- to 24-year-olds in the fall and the spring, we were seeing the stepping collections in the fourth quarter, when it is actually the first quarter that -- where we have the fewest youth collections, so youth is an issue. But in fact all donors go on vacation in the summer, of all ages, so it's not just the youth issue.

While I am mentioning youth, I want to raise a -- part of the title of this presentation of the invitation was around the ethics of blood shortages. And we should just mention that we're collecting more youth, we're recruiting more youth and we -- I think we have presented in the past the youngest donors are more likely to have

adverse events related to donation. And there is an ethical question whether or not focusing on the very young donors especially high school donors is an appropriate thing for us to be doing. I will just put that in there for more general discussion.

So the ongoing blood supply challenges, we're -- we see shrinking aging donor base with increased deferrals and I'll talk to some of the initiatives that we have around those. We -- optimal donor utilization is something we need to focus on and I'll talk to some of that. Optimal utilization of the available supply and we will talk about the hospital blood utilization.

So we have seen a decrease over the last 5 years in the actual number of donors joining the Red Cross and that's a significant number. We've also seen an increase in the average age in the donor base in the Red Cross. This -- we have seen a decrease in donations by this key demographic, 30 to 45, who used to be our biggest demographic, and that demographic is decreasing. We are collecting more very young donors and more very old donors, so that is again I think impacting the seasonality, making it worse than it was before.

We're also seeing increased deferrals over time with things such as the CJD travel restrictions that cause self-deferrals mostly. But we introduced the UDHQ, and the UDHQ in fact caused for us an increase of about 1 percent of deferrals and with no increase in safety at all essentially, as far as we can measure in terms of our analysis of our data. So you know, we're putting things in place that are increasing deferrals without necessarily measuring an impact in safety.

One of our favorite topics of course is travel restrictions for malaria that the Red Cross at least believes are deferring many, many donors from donating, causing a lot of issues around post-donation information for marginal benefit in terms of safety for the blood supply.

You had a talk this morning from Dr. Riley around the decrease in available eligible donors; I believe that from Dr. Riley's and Dr. McCullough's paper about 8 percent of the eligible donors donate each year now from their calculations, which is about 3 percent of the overall population. So it's a very small group of donors that are out there that are actually donating. So

deferrals clearly are an issue for us.

There are other factors that are impacting the donor base; the donation frequency is pretty much static at 1.6 donations a year, where other countries have done a whole lot better. So any influence we can have on that could be highly beneficial.

We're also seeing the changing demographics of our donors; we are focusing on minority donors. Well, minority donors tend to give less frequently and that may have an impact. We're also dealing with the changing work patterns in America, the downsizing of corporate America, the growing virtual employee base, sitting in your home office, it's very difficult to go and collect those bloods, right? And now, we're also faced with additional safety measures that are coming down the pike including things like male-only (phonetic) plasma and TRALI mitigation, which may definitely affect the donor base.

Chagas' disease, future tests, bebeseosis tests and others will impact our donor base adversely. So we are challenged.

How are we responding to the challenge? Well, clearly we are focusing quite heavily on the youth, and we

have seen a dramatic increase in recruitment of high school and college donors. We have the Ad Council campaigns; the Red Cross is involved with the National Athletics Association and some of the Greek fraternities in terms of attracting youth, and as I say, we have been very effective. We are collecting more and more -- I think 7.5 percent of our donations now come from high school kids, which is a large proportion. We're investing in a client relationship management program, computer-based, that will help us to manage our sponsors and our donors better, to increase collections by attracting new donors, increase customer satisfaction by managing each interaction better and help build loyalty with existing donors and sponsors.

We are putting forward recognition and rewards programs and increasing the donor and sponsor pools by implementing formal referral programs. And also we work very hard with our hospitals to try and get an entrance into communities to do blood drives through the hospital facilities with their support.

We talk about blood shortages; don't need blood shortages, do we? We need O positive and O negative,

right? There is never a shortage of AB blood on the shelf, and A positive, just about never. So let's be specific about what we're talking about, and so days of blood supply means nothing, let's talk about platelets and A, O positive, O negatives. Well, what's that about? Well, our hospitals buy O negatives and O positives from us. Red Cross sales, 50 percent of the blood is group O while only 46 percent of the population is group O.

If we met all demands, what proportion of O would we be selling, right? Because that 50 percent it's constrained by what we can collect. So if in fact we talk about having a reserve supply it has got to group O and I can tell you now, if we create a 10,000 reserve supply the hospitals would take it tomorrow and the supply wouldn't exist, right?

That they -- it will be a virtual supply, because there is unmet demand around O's and my -- our experience has been that the more blood on the shelf that's available the more blood the hospitals will use, or abuse, as the case may be.

So what does the Red Cross do? Well, we definitely set collection goals by type and try to collect

a higher proportion of group O blood, we don't like outdating group AB blood, but we do. We leverage the group O donors for double red cells and we try and push A's and AB's into plasma and platelet collections as all blood centers do. And we work with our hospitals to try and incentivize them not to abuse group O's and a lot of those are financial incentives.

On the positive side, we've seen technologies come in that help us to selectively collect blood of the correct type, we've got the double red cell programs, we've got increases in platelets with doubles and triples that allow you to select ABO types preferentially and we're very active in doing that and I know that all blood centers are.

We are also working on optimum utilization of the supply. We've seen the reduction in the difference between collections and actual usage and the Red Cross has worked hard to do that. In fact, last year, we collected less blood than the year before, but we distributed more, which we think is a -- it has made us more efficient and more certainly more cost efficient. But that is the nature of the game, these are our collections, these are

our distributions; distributions went up, collections went down.

And this has been an active result of Six Sigma programs and lean manufacturing programs to reduce outdates, reduce wastage and get blood to the hospital shelves where it's really needed. We've also been working on the demand-driven planning with sales and operations planning techniques to try and better match supply to demand and we are getting better at doing demand forecasting and collection forecasting.

We believe that the biggest area still for improvement is basically in the hospitals, where there is tremendous variation in utilization of blood between countries. The U.S. uses more red cells per 1,000 population than most other countries. And between hospitals; if you actually look at the amount of red cells used per procedure across various hospitals, the variation is dramatic. So we believe that there is a great opportunity to improve utilization of the supply we have and I would -- you know, fully endorse any recommendation from this committee to back this.

We are working with certain companies that run

1 blood management programs and are basically endorsing
2 these companies and introducing them to some of the
3 hospital clients to help them manage their blood supply
4 better through auditing and implementation of best
5 practices and education and data tracking and analysis.
6 We believe that you can do -- hospitals can do better than
7 they're doing now.
8 So then in summary, we do see broader challenges
9 with the blood supply driven by changing donor
10 demographics, by changes in the society and the workplace.
11 Our enhanced safety initiatives are decreasing the
12 available blood supply and we see inconsistent and
13 suboptimal transfusion practices as being a big issue.
14 The Red Cross is responding through donor recruitment
15 initiatives, manufacturing and testing yield improvements
16 and working with our hospital customers to improve blood
17 utilization through education and collaboration. Thank
18 you.
19 THE CHAIR: Thank you, Dr. Benjamin, for also
20 presenting us with a clear talk with some important
21 recommendations. I might ask about one and that is on the
22 issue of utilization, which we have talked about before,

1 and actually discussed in this meeting -- I believe in the
2 main meeting. One concept would be that we would try in
3 some way to put some teeth into the utilization of blood
4 for specific procedures.
5 And one thought I had had was about the
6 possibility of trying some sort of a linkage to CMS
7 participation for hospitals falling within a particular
8 zone. I would be interested in your thoughts about that
9 or whether you think that these organizations which are
10 the blood conservation organizations might be sufficient
11 to drive this perhaps.
12 DR. BENJAMIN: I think it’s a great opportunity
13 and any influence we can bring to bear would be opportune.
14 I am not sure of CMS, but certainly JCHO through
15 accreditation could, and I believe they are interested in
16 looking at blood utilization as one measure for
17 accreditation. I think that would be a very positive
18 move.
19 THE CHAIR: And in terms of O shortage which is
20 in fact -- that is the issue with red cells. One question
21 that always comes to mind is the changing demographic.
22 And where I come from, folks from Latin America and Mexico

really are the predominant demographic group; however, they may not represent the predominant donor group. Is part of the disparity related to recruitment?

DR. BENJAMIN: Part of the utilization disparity?

THE CHAIR: Well, yeah -- the disparity between utilization and availability on group O.

DR. BENJAMIN: Well, I'll put it this way, I think we actively go for minority groups because some minority groups have higher group O proportions for sure, that’s one other good reason. But the utilization -- over-utilization of O's is widespread through the country in those areas where minorities aren't in the predominant groups either. So I think it just has more to do with day-to-day blood practices.

THE CHAIR: Just blood practices?

DR. BENJAMIN: Yeah.

THE CHAIR: Questions from the Committee for -- and we are going to also field questions for the previous -- Ms. Sylvester as well. Ms. Finley?

MS. FINLEY: Thank you. This question is to Sylvester. It was an excellent presentation with a lot of

very good information, thank you very much. I did want to ask you to elaborate on your recommendation that we store bags at the Strategic National Stockpile. I was curious as to whether you think -- why you're recommending that as opposed to storing them in four or five locations where you would have access to them.

MS. SYLVESTER: Well, that's what the Strategic National Stockpile is, it is prepositioned medical --

MS. FINLEY: Yes, I know.

MS. SYLVESTER: -- and they are strategically located around the country.

MS. FINLEY: I'm aware of that, but what I am concerned about is that in an emergency you would -- there is a lag time for them to --

MS. SYLVESTER: The locations -- and my knowledge of the locations of the Strategic National Stockpile are that -- I believe they are such that they are within an 8-hour driving distance of everywhere in the country. Most of the blood banks out there have usually a 2-week supply on their shelves and so that gives them that buffer to be able to bring additional supplies in even if you have to truck them in versus flying them in.

MS. FINLEY: The minimum amount of time for shipment is higher, as I understand it, than that number that you just cited.

MS. SYLVESTER: Okay.

MS. FINLEY: So I think that it's an interesting concept and maybe we should look at it a shipment perspective, what could in essence --

MS. SYLVESTER: And I used the SNS just because that is a concept that already exists and for the same purpose and that is to preposition -- anticipate the medical needs. The locations of them could be wherever they wanted, you could actually preposition them in large donor center hubs if you wanted, but then you get into a storage issue. The advantage of storing blood bags is they have a longer expiration date, but yes, I understand what you’re saying.

MS. FINLEY: I’m just wondering if it would be in your better interests to store them in four or five locations where you would have access to them immediately.

MS. SYLVESTER: Yeah, where you put them is really I think immaterial as much as the fact that we would have them and have them available. I certainly

wouldn't store them here in Washington, D.C.; you know, this is Ground Zero. But -- that’s why I live in Omaha. I am one of those that actually work from home, so -- but that -- yeah, the location is immaterial to me as the concept.

MS. FINLEY: Okay, thank you.

THE CHAIR: Dr. Epstein?

DR. EPSTEIN: I guess this is a general question for any of the previous speakers. I have been struck from interactions in the international blood community by the absence of donor organizations in the United States. And I wonder what the major blood collectors think about the concept of encouraging the emergence of donor organizations as a mechanism to, you know, recruit and retain donors, especially young donors.

DR. BENJAMIN: And I agree with you, you know. When we hear about the countries that are having blood clubs et cetera and very actively recruit -- doing the recruitment -- recruiting that way, I don’t think we’ve done a good job with that. I think we do try through fraternities and through clubs when we can, but I don’t think we -- the Red Cross certainly does not have a

national program in that area. And certainly it's an area of deficiency.

THE CHAIR: Dr. Bianco.

MS. SYLVESTER: I believe there is a very committed donor population that is out there and you could consider them a club of their own. You have a gallon, your 10 gallon, your platelet apheresis donors. Unfortunately we're all part of the bifocal club, and that's the point I think he was trying to get across. The key donor clubs that exist are ageing. And so it's how do you get the youth as they've been focusing on to replace those of us that are ageing as donors.

THE CHAIR: Dr. Bianco.

DR. BIANCO: I just wanted to add that the experience, Jay, is kind of mixed around the world. There is a very active organization that is based in Norway, and -- but in several other countries where they have the donor clubs, they work more as unions instead of as donor clubs. For instance, about a couple of years ago the donors in France, they are very organized, protested, then stopped donating because there was a new requirement that they had to sign their informed consent and donor

histories, and they had never to do that over the past 40 or 50 years. So it’s a balance, and I don’t think that they would necessarily resolve the issues of donors that we have.

THE CHAIR: Well, one of the questions that I have -- and actually this morning I was going back over some literature and Harvey Klein wrote a -- sort of a piercing editorial right after 9/11 -- earthquake in America. And the main -- a major flaw that he pointed out was the problem of communication, the voice. And when the ASH (phonetic) position was created this was the notion that the ASH would be the spokesperson, particularly in disastrous situations, but even what bothers me is when you are in the yellow, and you need blood, but it’s not disastrous, how does the public get that information? I mean, you know, there’s lots of information that we get pounded with everyday, you know, with the little banners running at the bottom of the news clips. But how do you communicate effectively?

MS. SYLVESTER: The task force actually will get involved at times when the supply starts to get low like that, and a decision will be made as to whether not to go

to -- have Jerry go to the ASH, and asking put out a public appeal on a national level. That is a decision that’s actually made. Again, you do not want to cry wolf on a national level very often, but it is a decision that’s made among all of our organizations uniformly.

And it in it is not as -- it is not something that is implemented lightly. And -- but it is considered -- and it usually -- it’s usually in January. I mean, there is a reason January is National Blood Donor Month, you know, because that's when we get the most appeals and stuff out. But it is through the same mechanism we would for disaster -- we actually -- the Disaster Task Force actually considers a low inventory in a non-disaster time to be a cause for convening the task force and discussing.

THE CHAIR: Now -- and I have heard, I believe in Puget Sound they have systems wherein they view some technologies like text messaging, et cetera. Are those of sys -- are newer communication systems being --

MS. SYLVESTER: When we look at from a disaster point of view we have identified those alternative mechanisms of contacting staffs. We have other groups that are working in the donor recruitment area that are

highlighting those and identifying those best practices in passing them all through educational forums as ways of contacting the donor. If you want to get a hold of a teenager today you do it via text message on their cell phone; that's the bottom line.

If you want to get hold of an adult you do it through a laptop because I can't see my cell phone to text message. You know, and so I think we are recognizing as an industry that we have to adopt our messages to our customers and our clients. We can't just rely on posters anymore; posters don't cut it. And so I think we're being more innovative in doing that.

It's just a little bit slow, and it costs money and it takes resources, and I think that's where we seal some shifting of the resources. It would be ideal if we could stop spending so much money on infectious disease testing and shift some of those resources over to recruiting new donor because eventually if we don't recruit new donors I can have the safest blood supply in the world, but if I have no blood on the shelf it doesn't make any difference.

You know, that's really as he said, a challenge

as to lower the age group of those donating, because we all eventually will -- I think some in the room might take exception that 60 is really old. But anyway --

(Laughter)

DR. BENJAMIN: I think getting the right message to the right donor multiple times -- I think we work on the adage that it takes about, you know, six asks before somebody actually comes through that door. I mentioned to you that we were developing this client relationship management program on a national basis within the Red Cross, to try and create a more uniform method of doing exactly what you're proposing of having layered asks to donors.

We certainly right now within our divisions and regions have many different ways of doing -- of collecting e-mails addresses -- of databasing them, and certainly through e-mails, through tele-recruitment, through postcards, through paid media, through free media. We use every trick we can to get to the donor because it does take six asks before they come through that door.

THE CHAIR: Thank you. Dr. Roseff.

DR. ROSEFF: I think an interesting point was

brought up earlier, what is the blood shortage in my hospital, you know, when do I consider myself short, and there are obviously different levels. The first level is we don't get the usual order, and if that happens on an isolated basis on a day when your blood needs are low, you don't even notice that that's happening, but if it happens over a few days, and it starts creeping and then suddenly the liver transplant comes, when the trauma comes then that becomes more significant.

The next level is triaging products, especially with platelets. You know, in our hospital we go through a process of first screening the orders, then decreasing the orders, and then the last level is are you canceling surgeries or are you not able to supply. So I think that's not a trivial question, what do we consider a shortage in our different hospitals. The other point I want to make though is the blood shortages in our hospital are fewer and further between. When they happen, and they are regional and they are local, I'm happy that the rest of the country is happy, but we are not.

And if you get to the point of talking to your chief of surgery and your CEO about canceling surgery,

that has a tremendous impact in the competitive environment on your hospital. So I think that those are things that have to be thought of when you talk about blood shortages, and when you talk about planning.

I think we that we all try to plan for the worst case, we have to. You know, if everyday we have the right number of cases and the right number of units coming in we are fine, but what we plan our inventory for is not that ideal; we plan for the liver transplant or for the emergency transfusion. And over days if you keep getting less than your optimal inventory, at some point, that hits.

THE CHAIR: You know, actually that’s a good question in terms of defining the shortage and then how do you capture it. What we did in our hospital and the problem is that there is -- just like utilization of blood there is no uniformity in what the hospitals do. What we are hearing from -- I think the message is clear that we need to sort of clean up the hospital site so we get a better picture.

I mean, there are opportunities now where the cancellation of surgery could be considered a variance,

and a variance that is measurable, and by the given accreditation bodies for example, it could be considered almost akin to wrong blood (inaudible) but, you know, something where we would be able to gain the number. Right now our system is very loose, so perhaps one of the things we could consider is trying to define exactly what you are talking about. But Dr. St. Martin, you had a comment, question? Dr. Epstein, Ms. Thomas -- Thomas-Wade (phonetic), I'm sorry.

MS. THOMAS-WADE: Thank you. I really enjoy the presentations, and as an O positive individual in minority, I am a proponent of minority donors. But my question to you, Dr. Benjamin, is regarding the Chagas' disease -- Chagas, thank you, Dr. Epstein. I just want to know are individuals being screened for that. And if so, are they being deferred? If not, I just want to know what impact does that have on the recipient.

DR. BENJAMIN: At this point in time, there is a license test for Chagas' disease and the American Red Cross on January 29th, I believe, of this year implemented universal screening of all blood for Chagas' disease. We have picked up many positives. Only about 20 percent of

the initial reactive test we get, turn out to be true positives on confirmation. So for those true positives we are deferring both the true positive donors, and we also referring for -- probably false positive donors at the same time.

So like any new test, it's not just the true positives that of course you want out of the, you know, out of the donor supply, but you end up deferring quite a large number of other donors that aren’t necessarily dangerous that are false positives. So it’s about four to one ratio at this point of false positives to true positives that we are deferring from that dimension. I of course can not speak for other blood centers other than the Red Cross.

THE CHAIR: Tough competition. Any additional questions? Otherwise, what we will do now is take a 15-minute break, and then we’ll come back and we’ll address questions from earlier and have some further discussions of questions related to these presentations. Oh, actually, I’m sorry, I forgot the open public comment will be the first item. Fifteen-minute break, so we’ll reconvene at 3:30.

(Recess)

THE CHAIR: –- public comment and the comment that we have is from Dave Cavenaugh representing the Committee of 10,000. Yeah, you can take the podium, Mr. Cavenaugh.

MR. CAVENAUGH: Thank you.

SPEAKER: They’re considering him for the scientist --

MR. CAVENAUGH: It’s not that I have slides; I just need a little room. Thanks very much. I’m Dave Cavenaugh, government relations staff for the Committee of 10,000, and my comment concerns a particular matter that has come to light recently. The topic today is shortages –- no one wants to see standards lowered in times of shortage; no one wants to see standards lowered to seek profit.

I’m not saying that this report that I’m going to give is either of those; I’m just saying that from the patient perspective we can’t not consider those things as possibilities.

COT has alerted FDA to a press article detailing the operation in Texas of a number of apheresis centers

close to the Mexican border, even providing buses from the border to the center and back. They typically pay border area Mexican citizens with tourist visas $25 for the first donation of a week, and $56 for a second; many clients make more money in this manner than through their jobs.

The Committee of 10,000 is troubled and concerned regarding the commercial collection of source plasma on the Texas-Mexican border. We continue to state our discomfort with what we can only define as the exploitation of the populations and peoples living in serious poverty.

The collection of source plasma from developing rural countries presented an ongoing safety risk for the users of plasma derivatives in the 1970s and early 1980s. Dengue and dengue hemorrhagic fever, according to last week’s MMWR, are increasingly prevalent in exactly the area those centers would operate.

We’re in the process of looking at viral marker data for 2005 and 2006 for one of the company's operating centers in the border region and it’s our understanding that the viral marker data will show zero incidence of HIV, HBV, and HCV for the donors at this company’s

facilities. That’s great. However, this is not just an issue of science and viral marker data. It must be viewed in the context of the exploitation of populations mired in poverty, and lacking access to good medical care.

This is not a population one would associate with stable donors who in their daily lives have access to ongoing medical services. Have we seriously looked at the question of donor screening by questionnaire when those being queried are present at the collection center?

In part -- in large part due to the probably they experience on the Mexican side of the border, this process may need tighter examination. How do we look at the value of the donor questionnaire when the context of the donation is poverty and need? For some donors the money that’s paid for the donation are critical parts of the economic survival of themselves and their families.

At a minimum the poverty context must clearly reduce the value and dependability of the donor screening process. For COT source plasma collection along the Texas-Mexico border is designed to circumvent the ban on plasma collection in the developing world. It is as if the donor’s possession of a tourist visa is an indicator

of the health and wellness of that donor. Obviously we reject this construction of reality and we point to the serious lack of health and wellness in border populations, especially those employed in the free trade zone along the Mexico side of the border.

For the hemophiliac community, this is representative of the collection practices that drove the HCV and AIDS blood epidemics of the 1970s and 1980s.

Science does not operate in a vacuum. It too is subjected to the economic and social conditions it operates within. Thank you very much.

THE CHAIR: Thank you. Questions or comments from the Committee? Ms. Birkofer?

MS. BIRKOFER: Thank you, Mr. Chairman. Thank you, Dave. I appreciate the concerns that you've expressed by the Committee of 10,000.

I have two comments, one specific to your remarks when you talked about dengue fever being increasingly prevalent in the border areas –- and myself -- I guess I'd first like to disclose that I'm a representative of the PPTA, the source industry; we represent the collectors of plasma as well as the

fractionators, so I'd like to state that for the record. And I'd also like to note that being that I'm not a scientist or a medical doctor, it is my understanding, and there might be people around the table, that dengue fever is a flavivirus similar to West Nile virus; it is a lipid envelope virus.

And plasma therapies, as you know, are validated for elimination of West Nile virus and BVDV, using solvent detergent and pasteurization techniques, and furthermore, current FDA guidance does state that the manufacturer's methods are validated to inactivate flaviviruses related to West Nile virus.

So just looking at dengue in terms of alignment of the model with West Nile virus, I just wanted to make that comment. Furthermore, the plasma –-

MR. CAVENAUGH: Can I just –- can I make a point on that?

MS. BIRKOFER: Please.

MR. CAVENAUGH: Do we know whether dengue is viremic during incubation? That's been a painful discovery about some others that we looked at and the percentage -- the small percentage of dengue fever

infections that turn into dengue hemorrhagic fever with this fatal outcome, it’s just –- our point is just to describe something that’s part of border health; so is tuberculosis, for example.

THE CHAIR: This topic is often overlapping jurisdiction in terms of –- we clearly are concerned with areas of safety, but the regulation of these collecting agencies is something that actually is under the purview of the FDA and they have been addressing these issues and –- so again, this committee, in terms of the direct line of control –- you know, we don’t really control the plasma centers as such. I just raise that as a point.

MR. CAVENAUGH: The creation of this committee was to acknowledge that there is a need for an expert panel that can review cost issues as well as quality issues.

THE CHAIR: Right.

MR. CAVENAUGH: That’s the reason –-

MS. BIRKOFER: And Dr. Bracey, PPTA has a statement for the record on this issue. Would you like me to read the statement or simply enter it for the record?

THE CHAIR: If you could give us a synopsis of

the statement, is that possible?

MS. BIRKOFER: Yeah. Basically the plasma protein therapeutics industry works to ensure that comprehensive safety measures are in place to collect plasma used to produce lifesaving therapies for consumers and rare diseases.

To the point you just made regarding the FDA, all collection centers meet stringent regulatory requirements by the FDA and in addition to those, the plasma collection centers voluntarily adhere to the plasma protein therapy very stringently.

THE CHAIR: Thank you. With that what I would like to do is to move into follow up discussion on questions that were presented earlier this morning. The first set of questions addressed the issue of ESAs, and we have a small group that worked on drafting a response to the questions. And it's not in the ideal typing format, but first let me make sure that all of you have the questions, and they're on page -- well, my page 8, it's 1150 committee discussion. Do you all have a copy of the questions?

SPEAKER: It wasn’t in our -- but we got a copy.

1 THE CHAIR: But it was distributed, yeah?
2 SPEAKER: Yeah.
3 THE CHAIR: Okay, so what's listed -- and
4 there's sort of a false dividing line, which is the double
5 line in the middle, the response to question one is in
6 essence listed at the top, and I'll just read through it.
7 The question again is, will restricting human recombinant
8 with erythropoietin impact transfusion demand in general,
9 will restricting human recombinant with erythropoietin
10 until the hemoglobin is less than 10 increase transfusion
11 demand in general, and then will restricting recombinant
12 with erythropoietin until the hemoglobin is less than 10
13 increase transfusion demand in chemotherapy and disk
14 cancer? We decided not to address C.
15 The committee feels that there's inadequate
16 information to accurately asses the impact of CMS's
17 national coverage determination for ESA on the management
18 of anemia in the general population and in cancer
19 patients, whereas the revised position on ESA coverage may
20 increase blood demand. ACBSA recommends that CMS perform
21 an analysis of the impact of ESA regulation on blood
22 demand in selected patient population.

1 This doesn't need to necessarily be separated.
2 The information needed should be derived from prospective
3 collection --
4 SPEAKER: Data collection?
5 THE CHAIR: Scratch the second prospective, and
6 that would be “from prospective data collection”.
7 Comments, edits, Mr. Matyas?
8 MR. MATYAS: I don't know, but I don't think CMS
9 is really the appropriate agency to perform an analysis of
10 that? Aren't there other segments of HHS that are better
11 suited to analyze that information? I'm not saying DHHS
12 shouldn’t.
13 THE CHAIR: Right. I understand what you said,
14 but some -- what is the appropriate agency within --
15 MR. MATYAS: Yeah.
16 MS. FINLEY: Oh, I --
17 THE CHAIR: Ms. Finley?
18 MS. FINLEY: I was going to respond to that as
19 well. It's not -- our job is to make recommendations to
20 the secretary. It's the secretary's responsibility to
21 find the correct mechanism to carry that out. I concur
22 with the comment and I would suggest that we just change

CMS to HHS, which you did. Thank you.

THE CHAIR: Okay. Dr. Holmberg?

DR. HOLMBERG: Yeah, that’s a very good point from, both, Mr. Matyas and Ms. Finley. One, for instance, when we were looking at the IGIV issue and the various reports that came out of that, there was, both, an office of the inspector general report. And then also the assistant secretary for planning and evaluation did a report. So I think that there are mechanisms within HHS. And I agree; I think it would be best to leave it to the decision makers to decide who should do the analysis.

THE CHAIR: Dr. Epstein?

DR. EPSTEIN: I agree with that point in general, but Dr. Jacques did inform us that CMS has a program of post directive evaluations and that there was some discussion about whether the need for it existed in this case. So, I think it's probably appropriate to say CMS and/or other federal agencies.

THE CHAIR: Dr. Jack has a comment?

DR. JACQUES: Yes, I -- we certainly would not object to any assistance that the entire department would want to provide us. So, you know, whether it's written as

-- and I can understand your charges to make recommendations to the secretary, and certainly, we could have discussions with the department about whether they want -- what role they wanted us to take versus other roles. There are some types of analysis that we can readily do in-house, there are others that, frankly, may require access to resources beyond the agency itself. So, I mean, whatever the committee recommends, I think we can work with it.

MR. MATYAS: That's -- I see --

THE CHAIR: Yes, Mr. Matyas?

MR. MATYAS: Forgive me, but “derived from prospective data collection,” I'm not sure I understand what that means.

THE CHAIR: Right. Basically, what we're looking at, initially the language was -- language that would suggest to controlled trial, it's unlikely that a controlled randomized trial would take place. So prospective data collection, as I see it, and others please comment, would mean that there would be a planned process for looking, going forward and collecting data rather than going backwards and trying to sort the impact

in a backwards direction.

MR. MATYAS: Understood.

THE CHAIR: Ms. Benzinger?

MS. BENZINGER: Yes. I had another question about regulation on blood demand in selected patient populations. If you're involving health and human services, which is basically going to be looking at the figures from CMS reimbursement, is that what you're considering?

THE CHAIR: Well, yeah, basically --

MS. BENZINGER: I think you wanted, on the whole, patient demand. You're looking at it because trauma patients are going to be affected if the blood is not available due to -- and I think you don't want to limit it on your patient populations.

THE CHAIR: Right. I see what your point is, but I guess what I was thinking of in terms of trying to see if we could get our hands around some hard data, it would make it easier if we focused on a relatively limited population that would be primarily impacted. In other words, if we see that there's more blood utilization within this particular group of individuals, then we would

1 know by virtue of that increase, that the others would be
2 affected.
3 So in other words, if we go -- if we have a 20
4 percent increase in the utilization of blood in patients
5 with chemotherapy or cancer, then we know that that’s
6 going to be draining from others. I mean, it would be --
7 it's -- there's not that much blood in the system.
8 MS. BENZINGER: I understand that in theory.
9 THE CHAIR: And again, it's -- the idea is that
10 our resources, you know, are limited, but this would give
11 us some real information about the target population. But
12 others please? Yeah, Dr. Bloche?
13 DR. BLOCHE: This is just an editorial on the
14 fifth line down. It says, "The impact of ESA regulation,"
15 I will defer to Dr. Jacques, but I think it's ESA payment
16 policy, and I don't think that includes a regulation at
17 this point.
18 SPEAKER: The technical term would be “National
19 coverage determination” because it's not a reg in the
20 sense of notice and comment we're making; it's NCDs. And
21 then strike “regulation”.
22 THE CHAIR: Okay.

1 SPEAKER: Thank you.
2 THE CHAIR: What -- Dr. Kouides?
3 DR. KOUIDES: We also insert a recommendation
4 about the need for further study of the transfusion
5 triggers, specifically in the cancer patient.
6 THE CHAIR: That's coming below.
7 SPEAKER: Okay.
8 THE CHAIR: That -- what I was -- well, I tell
9 you what, let's -- well, let's see if we can get a wrap on
10 the first piece. Any -- there was the issue about other
11 population. Does the committee feel comfortable with
12 drilling down on the cancer population? Okay, let's move
13 to the second piece. And so the second piece, and we can
14 get right into the double line, that was just my way of
15 segmenting.
16 “But whereas current demand for transfusion in
17 various patient groups is not well characterized in varies
18 with local practices including adherence or non-adherence
19 with available transfusion guidelines, the ACBSA
20 recommends that HHS support -- one, HHS support studies to
21 characterize transfusion in specific patient groups
22 including cancer patients, and two, HHS takes steps to

1 promote the utilization, needs to be some a typo,
2 utilization of clinical practice guidelines for
3 transfusion recognizing that current transfusion
4 guidelines and the utilization, need analysis and periodic
5 updating to reflect changes in clinical practice and
6 availability of new products." This is kind of a mouthful
7 but -- so --
8 SPEAKER: New products you're referring to?
9 THE CHAIR: Well, really more or less new
10 interventions perhaps. We could change that to "new
11 interventions" because it's likely that really there would
12 be more new interventions that would impact blood
13 utilization. So this, kind of, this gets at the guideline
14 piece, but think about it. And all the rest of that below
15 you can scratch. Comments?
16 SPEAKER: Could I ask just one question? The
17 new interventions are those interventions in the treatment
18 of anemia specifically or is interventions including, you
19 know, different anticancer therapeutic --
20 THE CHAIR: Oh, the broad context? I was --
21 SPEAKER: The broad, okay.
22 THE CHAIR: Yeah, the broad context.

1 SPEAKER: All right, thank you.
2 THE CHAIR: So ready for one more read through
3 or comments? Can we comment in here and we -- can we take
4 it to the top? So the -- so the entire recommendation
5 then would be, “The committee feels that there's
6 inadequate information to accurately access the impact of
7 CMS's national coverage determination for ESAs” -- is that
8 ESA or ESAs? I don't know.
9 SPEAKER: ESAs.
10 THE CHAIR: “ESAs, on the management of anemia
11 in the general population and in cancer patients, whereas
12 the revised position on ESA coverage may increase blood
13 demand. ACBSA recommends that HHS perform an analysis of
14 the impact of ESA NCD on blood demand in selected patient
15 populations. The information needed should be derived
16 from prospective data collection, whereas current demands
17 for transfusion in various patient groups is not well
18 characterized and varies with local practices including
19 adherence or non-adherence with available transfusion
20 guideline.
21 “The ACBSA recommends that, one, HHS supports
22 studies to characterize transfusion in specific patient

1 groups including cancer patients, and two, HHS takes steps
2 to promote utilization of clinical practice guidelines for
3 transfusion recognizing that current," you can make that
4 lower case, "transfusion guidelines and their utilization
5 need analysis for periodic updating to reflect changes in
6 clinical practices and availability of new interventions."
7 Yeah, Dr. Berlin (phonetic)?
8 SPEAKER: It's a minor point, but I'm -- the
9 number one paragraph, HHS supports those characterized
10 transfusion. I suspect that the focus of that is
11 transfusion practices rather than the scientific basic
12 research of transfusion. And that's the direction you
13 want the secretary --
14 THE CHAIR: Okay, that one.
15 SPEAKER: It might be worth putting that in.
16 THE CHAIR: Mr. Matyas?
17 MR. MATYAS: I don't mean to be difficult. I
18 just don't understand still what we're -- what that's
19 asking for. I mean, I'm --
20 THE CHAIR: The sub-element one or the entire
21 second piece?
22 MR. MATYAS: The entire second piece, because

1 from the discussion today I understood the relationship of
2 the question of what's the demand for transfusion for
3 cancer patients. I guess, I'm still not sure what need
4 there is and what specifically would be studied. And,
5 maybe, I'm just not understanding some of the clinical
6 transfusion practice issues --
7 THE CHAIR: Yeah, I think that --
8 MR. MATYAS: -- that there's a lack of
9 information.
10 THE CHAIR: Yeah, I think that what we're
11 getting at here is that the demand may not reflect best
12 practices. And so the idea would be to assess what really
13 is best practice in this particular patient population.
14 And one of the realization I think or one of the -- we
15 suspect that best practice and guidelines for this
16 particular group are underdeveloped.
17 MR. MATYAS: Yeah, I guess that’s my question,
18 which is, I haven’t heard enough to know that there is a
19 dearth of either an abundance or lack of studies that
20 already exist on this issue based upon what I’ve heard
21 thus far today. I've heard that so far in the morning's
22 discussion a few people not know how to characterize it.

1 But I don't know if I'm in a position to support and
2 suggest that HHS study it because I don't know whether or
3 not there are studies currently being undertaken by
4 various organizations or what transfusion practices are
5 being studied and the like.
6 I guess, I just don't -- I see that there is a
7 question that we have as to how to characterize it; I just
8 don't know if there is, in fact, a need, based upon what
9 I've heard, to suggest that a study be initiated. I'm not
10 saying there isn't a need.
11 THE CHAIR: No, there -- no --yeah.
12 MR. MATYAS: I just don't know --
13 THE CHAIR: Right.
14 SPEAKER: And there's a need just even based on
15 the premise that since, you know, these agents have been
16 available, clinicians have, you know, utilized them with a
17 presumption they could very well be false. It has been
18 well studied that the higher the hematocrit, the better
19 the outcome, the better for the patient, the better their
20 quality of life, the better they are going to feel. And,
21 again, it's not based on -- I think, it's fair to say,
22 there isn't, you know, adequate. I think that Jacques

alluded to the fact that there is inadequate quality of life data to say they're going above, you know, 10 as a positive impact.

THE CHAIR: Yeah, actually I think that there was a fairly detailed analysis of hemoglobin set points in CMS's review of the data. And what CMS, at least I think what I heard, and -- is that when CMS looked at the data between 10 and 12, which represents a lot of the variation in guidelines, that they really saw nothing, that they did find a dearth of information in that area, but you might want to comment on that Dr. Jack?

DR. JACQUES: Yes, I think you basically characterized it the same way I would that although there are a lot of individuals who may say that 10 to 12 is the place to be, when one looks at what kind of evidence would, sort of, be the foundation for that particular range, what we find is it appears to be cobbled together from methodologically problematic studies, and that in the face of, sort of, more methodologically robust studies that suggest that if you transfuse someone to keep their hemoglobin between 7 and 9, that’s better than transfusing them to 10 to 12, at least in some populations, what we're

1 left with is people claiming that 10 to 12 is good, but
2 lacking evidence for us to feel confident that that is
3 indeed the case. So, I mean, I just, in a long way, I
4 think, said what you just said.
5 THE CHAIR: Does --
6 SPEAKER: And I understand based upon the
7 national coverage determination for one, but you've gone
8 from a very specific to a very general request for
9 studies, which I don't know. I'm not saying it doesn't --
10 that the issue isn't there, but I understand what CMS is
11 saying and I won’t disagree based upon that, but you've
12 gone from a very specific into asking for a general study
13 to support characterized transfusion practices in specific
14 patient groups including cancer patients. But that’s not
15 the only --
16 THE CHAIR: You know, but one --
17 SPEAKER: I mean, if we're talking specifically
18 to deal with issues of number one, then I think we need
19 that specificity.
20 THE CHAIR: Yeah, one of the activities within
21 NHLBI, there is a clinical trials network, a transfusion
22 blocking the clinical trails network that’s looking at

transfusion thresholds and they're going component by component. And the premise of that particular group really is -- this is, sort of, the foundation of the premise, is that they there is a dearth of information regarding transfusion practices aside from a few large well conducted trials in critically ill patients. When you look outside of that group, there's not much data. There's very little data. Dr. Epstein.

DR. EPSTEIN: I agree with that, Art, but I find myself resonating with David’s point, which is, if this set of recommendations is intended to address the implications of the national coverage determination, then we really ought to narrow the recommendation in the second part to patient population affected by the NCD.

THE CHAIR: Right.

MR. MATYAS: Or if we need to address, Dr. Bracey, a more general issue, and forgive me for not remembering the acronym NHL --

THE CHAIR: B-i.

MR. MATYAS: Thank you. Then I'd like to -- I mean, then I would suggest that we hear from that organization saying that there's a dearth in various in

order to be able to support that second statement in a more general way.

THE CHAIR: Okay. Dr. Epstein, comment?

DR. EPSTEIN: Yeah, you see, I think what's going on here is that the set of questions to the committee went beyond that which we materially discussed because, you know, question three, is their blood shortage, is really a question about blood utilization in patient populations as a whole.

THE CHAIR: Right.

DR. EPSTEIN: And likewise, question two, what is the current demand for transfusion in general, gets the issue of patients as a whole. And I think what you're hearing, David, is that those of us who have dealt with that question are aware that there's limited data on why we transfuse certain patients and how much. And that's what's leading to the general form of the response.

MR. MATYAS: And I don't disagree then that it exists.

DR. EPSTEIN: Right.

MR. MATYAS: I'm just saying, as a member of the committee I'm objecting to supporting a recommendation,

which generally we have unanimity in terms of support. I just haven’t seen that.

DR. EPSTEIN: Yeah.

THE CHAIR: What about this then? Let's say that we -- but, don’t strike it right now, let's say we strike a bullet number, item number two, and we would say that HHS support studies to characterize transfusion practices in cancer, yeah, cancer patients.

MR. MATYAS: Patient groups affected by the NCD?

THE CHAIR: Yeah, patient groups affected by the NCD, yeah, and leave it at that, because you're right, because it's almost like the point of getting to how would it affect the whole mass, and we're saying, “Well, wait a minute, let's just focus on the cancer group”. So, yeah.

DR. EPSTEIN: Well --

THE CHAIR: Well, Dr. Epstein?

DR. EPSTEIN: You see, I think this problem arises because there is an issue with the larger patient population. It, sort of, goes like this. What's been asserted at least in the media by the manufacturers of the ESAs is that the effect of the NCD would be to create roughly a 5 percent increased demand for blood in general.

1 And therefore that will impact on transfusion demand in
2 general.
3 The problem is that you can’t really tell if
4 that’s true or not without understanding the rest of the
5 patient population and how appropriate transfusion is for
6 patients in general. So it's very hard to dissociate the
7 issues. And I think what we've been trying to suggest
8 with the nature of that response is, rather than trying to
9 analyze all patient groups and the effect on the system in
10 the large, let's see what happens in the patient groups
11 affected by the NCD because that’s what will inform us how
12 it might affect blood availability in general. But a
13 little bit it begs the question of whether we over-
14 transfuse or under-transfuse in general.
15 THE CHAIR: Did -- Ms. Finley, you had a
16 comment?
17 MS. FINLEY: I concur with Dr. Epstein's
18 statement.
19 THE CHAIR: Okay. Well, you know, actually,
20 we're talking about striking number two. Well, we could
21 paste that away for somewhere maybe related to the
22 discussions that we heard actually from our other

presenters on blood utilization in general, but not for this specific.

MR. MATYAS: We're just going to -- as someone who raised that as an issue, I'm not -- I don't think we are ready to dismiss that. I just didn’t see how it flowed necessarily from number -- from the whereas in number one to jump immediately to number two. And I think we need some more discussion to jump to that what you had as number two.

THE CHAIR: Dr. St. Martin (phonetic)?

DR. ST. MARTIN: I was just wondering if Dr. Jacques might be able to talk about what information CMS would've liked to have seen, what data CMS would've like to have seen, either to address gaps in information or to resolve conflicting study outcomes.

THE CHAIR: Dr. Jacques?

DR. JACQUES: Sure. One of the questions that we have been challenged with is essentially the claim in some of the stakeholder communities that the transfusion needs of cancer patients undergoing chemotherapy will be significantly increased as an effect of this NCD. And one of the reasons why that’s problematic for us is that we

1 are not sure that the current practice of transfusion in
2 that population reflects what that practice would be if it
3 were based on methodologically rigorous evidence.
4 So if something is being done in a less than
5 ideal way, one could then say, well, of course, the
6 effect, if you keep doing it in a less than ideal way, is
7 to simply do more of it in a less than ideal way. And
8 what we'd like to get as is, sort of, if there is, in
9 fact, an evidence-based right way to deal with
10 transfusion, what would be the effect of the NCD on the
11 right way of transfusing as opposed to assuming that the
12 current practice is, in fact, good practice?
13 THE CHAIR: Okay.
14 DR. JACQUES: Am I sounding too different?
15 THE CHAIR: Yeah, I understand.
16 DR. JACQUES: Not the least?
17 THE CHAIR: I understand what you're just
18 saying, yeah. So in essence, number one would serve to
19 characterize and/or capture the practices, but it doesn't
20 necessarily -- well, one could assume that if they were,
21 in fact, studies and the studies would make commentary on
22 whether the practices were appropriate or inappropriate

1 without having it stated directly. But there is nothing
2 that we have there that specifically speaks to your point.
3 SPEAKER: I mean, if, for example, if it turns
4 out that a third of cancer patients are getting
5 transfused, that hemoglobin thresholds that are much
6 higher than a reasonable guideline would support, then
7 even if there would be a somewhat smaller increase in
8 appropriate transfusion in some patients at the lower end,
9 one might find that the net is still a reduced demand on
10 the blood supply.
11 THE CHAIR: So what if we had HSS support
12 studies to characterize the appropriateness of transfusion
13 practice?
14 SPEAKER: Or in other way, I mean, if the
15 committee is bit a leery of support, one could also say
16 CMS -- oh, sorry, HSS access the need for studies to
17 characterize, et cetera et cetera, coma, and then, support
18 whatever studies are found to be needed. I mean, that
19 would be, and I don't want to read into your committee,
20 I'm just --
21 THE CHAIR: All right.
22 SPEAKER: I'm getting the sense that some people

are little reluctant to say let's support something if we're not even sure if it's really needed. So the directives were rather to access the need and then to follow up with the appropriate support of the needs that are identified. I don't know if that solves, you know, some of the debate.

MR. MATYAS: And I was going to raise another question, which is --

THE CHAIR: Yeah, Mr. Matyas, go ahead.

MR. MATYAS: -- always supporting studies to characterize because I don't think you do studies to characterize, do you? I think you support studies to analyze what the result being maybe characterizing and establishing practices. But I'm thinking through. I think some of my issues may be with the word "characterize" and what a study would do to accomplish.

THE CHAIR: That's a good point. How about -- another comment was identified because we actually don't know what the practices are. Although if you say analyze, you would expect that then there would be some assessment of, you know, rather than simply identifying, a commentary. Ms. Benzinger?

MS. BENZINGER: Identify and -- I had the thought and that’s gone. I'll come back to you.

THE CHAIR: About identify and analyze?

MS. BENZINGER: Well, it was to collect the data, to collect the -- it will come back to me, the wording that I had in my mind; give me a minute.

THE CHAIR: So how about in the interim we say, HSS assess the need for -- no, no, sorry, sorry, what was the original statement? Support studies to -- yeah.

MS. BENZINGER: Or identify and analyze.

THE CHAIR: To identify transfusion practices.

MS. BENZINGER: What about support data collection or something?

THE CHAIR: Well, we've got --

MS. BENZINGER: Because it is really gathering data that we're doing because they don't know yet.

THE CHAIR: Well, what the data we specifically want is data related to transfusion practice.

MS. BENZINGER: Right.

THE CHAIR: Because then -- because we're talking about data collection up in the front piece. Let's see. Dr. Epstein, you had a comment?

DR. EPSTEIN: Well, to me what part one is dealing with is impact on current practices and what part two is dealing with is whether current practices really conform to guidelines.

SPEAKER: You're right.

DR. EPSTEIN: I thought that is sensible. And it's really the same question that Dr. Jacques just stated, which is the -- what's concerning CMS is that although the NCD may affect current practices, perhaps its effect is not so great if those practices were established as more suitable. And I think that’s really what we're trying to get at in part two. So I think it really should somehow be focused on the issue of measuring current practices against guidelines. But that the fly in the ointment is how well established are the guidelines.

THE CHAIR: All right.

DR. EPSTEIN: So that’s why it's kind of saying, you know, look at suitable practices and determine to what extent current practices are conforming.

THE CHAIR: Okay.

DR. EPSTEIN: So I'm not suggesting wording at the moment, but trying to clarify why there's a part one

1 and a part two.
2 THE CHAIR: Right, right, yeah, I understand.
3 So if we had identifying characterized transfusion
4 practices, groups affected by the NCD --
5 DR. EPSTEIN: In relation to available
6 guidelines.
7 THE CHAIR: Yeah, that we'll get, in relation to
8 available guidelines.
9 SPEAKER: Which guideline?
10 THE CHAIR: Well, you would --
11 SPEAKER: (off mic)?
12 THE CHAIR: Well, the transfusion guidelines.
13 SPEAKER: Okay.
14 THE CHAIR: Yeah.
15 SPEAKER: We could argue there aren't specific -
16 - there aren't guidelines specific to the cancer patient.
17 I mean, you could argue that's an area worthy of study,
18 right?
19 THE CHAIR: Well, we could study available
20 guidelines -- I mean --
21 SPEAKER: General guidelines you're saying?
22 THE CHAIR: In relation to available guidelines,

if -- well, no, I can’t say -- to -- well, I mean, but there may not be available guidelines, and that would be what the study would say. I mean, in relation to available guidelines.

SPEAKER: I mean, now we're looking -- it's okay.

THE CHAIR: You want to know -- basically you want to know what are the practices, you know, the practices within the bounds of available -- of transfusion guidelines?

SPEAKER: Do we also want to encourage the -- I'm just asking, do we also want to use this opportunity to encourage the development of better guidelines in this area or do you want to leave it just at available guidelines, as we have them at the moment? Maybe that’s a bigger --

THE CHAIR: That's a --

SPEAKER: That's -- I sense, part of the issue about this is how do we know that some of these proposed indications are actually valid or not, and you're -- and the Medicare saying, no, there's not really -- data, they're valid, but we don't have data. So I don't know.

You know, if you want to go take the -- another step to, say, looking at developing -- you know, towards developing more guidelines --

THE CHAIR: Yeah, so the question would be if you, sort of, find new guidelines, then you can go to step two.

SPEAKER: Studies to --

SPEAKER: But we -- no, specifically, there aren't guidelines for the cancer patient. I mean, if you're saying, guidelines for the cardiac patient that has -- there had been studies, right, literature about the hematocrit in relation to cardiac function?

THE CHAIR: Right.

SPEAKER: But a cancer patient, I don't have knowledge in.

THE CHAIR: Right, I guess, the only part that’s -- that in our discussions and deliberations we haven’t reviewed all that data. We --

SPEAKER: I see.

THE CHAIR: Those of us who know these patients know it's not there, but for all on the committee it may not be clear that there is a -- there are guidelines.

1 SPEAKER: I am confused.
2 SPEAKER: I think one of the -- one of our
3 questions with guidelines is that guidelines can sometimes
4 be based simply on people's opinions. And part of our
5 issue is not so much that there are no guidelines. I
6 mean, I think people would argue that there are
7 guidelines, but rather that the robust evidence to support
8 the guidelines about appropriate transfusions in
9 particular groups are solely lacking, and what we are left
10 with is guidelines based on, frankly, opinion.
11 THE CHAIR: You're right. So really, you get to
12 the issue of whether or not there's evidence-based
13 medicine or practice?
14 SPEAKER: Right. Yeah, I think getting at the
15 evidence behind the practices and all the transfusion
16 practices supported by robust clinical evidence is
17 probably more helpful to us than are they supported by
18 guidelines because otherwise someone will just come up
19 with a set of guidelines and say, look, here they are,
20 those guidelines.
21 THE CHAIR: Dr. Epstein?
22 DR. EPSTEIN: So perhaps a way to capture this,

instead of saying in relation to available guidelines, say in relation to clinical outcome measures metrics, or just in relation to clinical outcomes.

SPEAKER: Yes, I think that would be very helpful.

THE CHAIR: Yeah.

SPEAKER: Thank you.

THE CHAIR: So the point, right, you know, guidelines, you get in a trap, because the guidelines are all opinion-based and what you're asking for is "Show me the evidence".

SPEAKER: Right.

THE CHAIR: And so what this says is HSS would support studies identifying characterized transfusion practices in patient groups affected by the NCD in relation to clinical outcomes. And if there are no outcomes available, that would be an important message.

SPEAKER: But do we mention some of those outcomes or -- I mean, are you --

THE CHAIR: No, I think we would leave it in -- yeah, I think we would leave it in general -- I don't know, should we mention specific outcomes?

SPEAKER: Well, survival wellness, quality of life. I mean, I think that the practitioners of the art know what that means.

SPEAKER: But the problem is that historically some of those outcomes have been lacking, and there is some value to perhaps highlight the need for that in terms of solid quality of life. Say, they're using validated instruments, for example.

THE CHAIR: Well, that’s a good point. So you would say, e.g., survival --

SPEAKER: Quality of life.

SPEAKER: Quality -- progression of free survival, quality of life per validated instruments.

SPEAKER: We'd also want to look at adverse events related to the treatment.

THE CHAIR: True. So survival, quality of life, what was the rider on that? The -- not just quality of life, but quality of life related to --

SPEAKER: Whatever, I think the data you probably reviewed is, you know, patient surveys or questionnaires, that’s not entirely valid. So it's validated using validated instruments.

THE CHAIR: Using validated instruments?

SPEAKER: Yeah, I mean, if we used critical care as a paradigm, we'd also have been looking at myocardial infarction, congestive heart failure and things like that.

SPEAKER: Cardiovascular end points.

SPEAKER: Yeah.

THE CHAIR: Well, I mean, if we just have some specific examples, that’s a lead and then --

SPEAKER: Sure.

THE CHAIR: I like the point about adverse events as well because that’s important.

SPEAKER: Adverse events, cardiovascular --

SPEAKER: Was quality of life using validated instruments?

THE CHAIR: Yeah, put "using validated instruments" back in; that’s important.

SPEAKER: I think it's a parenthetical, "After life".

THE CHAIR: And then how about after "adverse events", just et cetera, or --

SPEAKER: "After life" is beyond our realm, I think, but sorry.

SPEAKER: Adverse events, cardiovascular end points or --

THE CHAIR: You want to do a parenth on that?

SPEAKER: Let's see. Let's see this, yeah, e.g., yeah, maybe, e.g., cardiovascular ends?

SPEAKER: One type of experience I have had is that some people would not want, like, assuming that they don't have their medication available, the transfusion triggers for that particular setting are higher, and those peoples end up -- they're not able even to get blood, and they will refuse to get transfusion. So one of the adverse events would be that although the, you know, the reimbursement is limited based on what they're proposing, is that people will be asked to try to get a medication by self-pay.

And then one of the things that might happen is that those persons might not get transfused, but they might not have the agent and still have some sequela to it. I mean, one of the things that has happened in here was thinking that if -- with the reimbursement limitations people would then go to transfusions after automatically, but I think there is going to be a group of people on that

nonetheless will go to transfusion. So, I mean, there is different adverse events. There might be some clinic adverse events; there might be some other negative outcomes that we need to look into.

SPEAKER: And we can see why there is iron overload, as you had asked me about.

SPEAKER: Yeah. I mean, if they're going transfusing, there might be iron overload. So I think there is all those things beside maybe an increasing need for transfusion that needs to be looked into too.

THE CHAIR: Well, when we capture the outcomes that captures both under-transfusion and over-transfusion --

SPEAKER: Yeah, but transfusion is not the only outcome. I mean, there's going to be other outcomes that, you know, maybe --

THE CHAIR: Well, yeah -- no, but we're not looking at transfusion as the outcome; we're looking at what happens to the patient. And we're just giving specific examples because hundreds of things could happen. But we don't want to be too prescriptive of things.

SPEAKER: I still doubt that that factor -- you

1 know, a cyclic clinical setting what else can happen. I
2 mean, we have to look at, (inaudible) some medications,
3 the patients, if they don't get paid for the medication,
4 they have been taking. And that’s going to hurt the
5 patient. I think that’s one of the things that we'd have
6 to look at. You know, when you're looking at -- when you
7 have some clinical outcome point, you need to have some
8 things in addition --
9 (Tape interruption)
10 SPEAKER: -- that, I don’t know what kind of
11 group is really trying to use -- erythropoietin to
12 maintain higher crit levels, okay. I mean, usually where
13 I am familiar, we've seen the oncology population, usually
14 transfusion trigger is going to be like a hemoglobin of 8,
15 and they don’t want to achieve a hemoglobin of 12. They
16 just don’t want the patient to get too symptomatic, at
17 least, you know, from working with people, that’s the
18 overall impression I have.
19 So one of the concerns I have is why -- what
20 you’re trying to do is, like, limit the reimbursement.
21 You have some indications to qualify for reimbursement,
22 okay. But that doesn’t mean that in a way you’re going to

control the practice of using erythropoietin itself because there are other pathways to get erythropoietin that necessarily are related to reimbursement by Medicare. I mean that’s what I’m trying to understand in here.

SPEAKER: What other -- you mean --

SPEAKER: I mean, like, you know, stopped pay -- I mean I think there's all these things that can affect the patient. I’m concerned that what you’re doing, yes, from the clinical practice I understand it, but I think that what the premise is the way clinicians are practicing and somehow what you’re proposing can have an effect on the patient from that point of view because you might have people that are very scared of transfusions, and they will not want to be transfused, so -- and they might need a transfusion so what they’re going to do. And they might decide to go on self-pay, you know, for the erythropoietin. And that’s what I’m seeing from side and I think that’s, you know, that’s a concern.

THE CHAIR: Yeah, I think the problem that exists thus if we address that, the analysis will get diffused and we would lose a point of focus, but I --

SPEAKER: But you have a very valid point

1 because there is also this other issue I’ve seen out
2 within the preview of this committee, but there is direct
3 marketing to these patients by the pharmaceuticals to, you
4 know, that you will feel much better when you start
5 chemotherapy. Ask your doctor about, you know, this drug.
6 SPEAKER: But -- it’s true, but they are not the
7 one prescribing it, it's their physician prescribing it.
8 THE CHAIR: So let’s try and see if we can close
9 on this. Is this is a point that we want to include,
10 because we need to --
11 MS. FINLEY: I’m sorry.
12 THE CHAIR: Ms. Finley?
13 MS. FINLEY: I have one other thing to point
14 out. Are we really asking HHS to support studies or are
15 we asking HHS to identify and characterize transfusions
16 practices? I’m just suggesting that maybe we should take
17 that support studies out of there -- I know that
18 researchers don’t like that, and hold them responsible
19 essentially for the intent here which is really to do
20 something about complaint with transfusion practices where
21 they exist.
22 THE CHAIR: well, I thought we were actually

specifically asking them to support studies.

MS. FINLEY: They will support studies.

THE CHAIR: Yeah.

MS. FINLEY: But I'm saying that's not the end result. They have supported studies in the past.

THE CHAIR: Yeah.

MS. FINLEY: And we were not happy with the outcome. We want them to be responsible for identifying and characterizing transfusion practices.

THE CHAIR: What's the Committees favor on that? Leave it, take it?

SPEAKER: If there were studies, where are they?

THE CHAIR: What's that?

SPEAKER: If there were studies, where are they?

MS. FINLEY: Where are they?

SPEAKER: Yes.

MS. FINLEY: We know from the past that they have done them. Now, unfortunately nobody from NHLBI is here today to discuss that.

THE CHAIR: Right.

MS. FINLEY: So I don't know whether George is coming tomorrow and might have that information, Jerry,

but -- I mean, you could -- if you wanted, you know, put this on hold pending, you know, NHLBI coming in tomorrow, if they were coming, and asking them for some specific information. But I guess, you know, I mean, I know we've had this conversation, you know, 12 years ago. And I don't think the bar has moved considerably since then.

THE CHAIR: Okay, so --

MS. FINLEY: Based on what you're telling me.

THE CHAIR: Yeah, the question is -- I would like to go ahead and move on this if we can.

MS. FINLEY: I won't stand in your way. I'm just saying -- pointing out that we are not asking them to do studies for the point of doing studies, especially since they've done them in the past. The issue is really to get to the heart of it, of the practice in transfusion.

THE CHAIR: Yeah, but if they support studies that would identify these we would get to the heart of the issue, I think.

MS. FINLEY: Okay. I mean, all I'm saying is that they have supported studies in the past.

THE CHAIR: Comments from the Committee. Strike it, leave it?

1 SPEAKER: I prefer to leave it, because I think
2 there is a pressing need right now. I think this is a new
3 era of, you know, the management of these patients the
4 last 10 years has been, you know, with ESAs and so I think
5 --
6 THE CHAIR: Right, so the studies that were done
7 before were in a different era?
8 SPEAKER: Right.
9 THE CHAIR: Right.
10 MS. FINLEY: Okay. Well, I'm not going to lie
11 down on the tracks for it, but --
12 THE CHAIR: All right.
13 MS. FINLEY: -- you know.
14 THE CHAIR: So let's see, comments -- Dr.
15 Epstein?
16 DR. EPSTEIN: I want to suggest some minor
17 grammatical changes. We really have two recommendations
18 and so they ought to be number one and two. In the first
19 paragraph we have -- "whereas the revised position on ESA
20 coverage may increase, ACBSA recommends that" -- that's
21 number one, HHS performing an analysis as number one. So
22 in paragraph one "ACBSA recommends that," you know, indent

one, that’s one.

THE CHAIR: Okay.

DR. EPSTEIN: Right. And then just bring the next sentence up as part of one.

THE CHAIR: Right.

DR. EPSTEIN: It’s intimately linked. Right. And then just it’s minor grammatical, but where we have in the next paragraph "whereas" it shouldn’t be a second sentence. It’s "available transfusion guidelines, the ACBSA recommends that" and then it becomes recommendation two.

SPEAKER: And where your cursor is --

THE CHAIR: What's that now?

DR. EPSTEIN: Just go down one more line from -- where the cursor is. Right. And pull out the period and take the capital out of “the."

THE CHAIR: Oh, yeah.

SPEAKER: Guidelines, comma.

SPEAKER: Say that --

THE CHAIR: Just go to guidelines and back out of the --

DR. EPSTEIN: On that same line, just scroll

over three words. Right, take that period out, make it a comma, and put in “the” and then number the next one "two."

THE CHAIR: Yeah, that’s a good point. Okay. All right.

SPEAKER: Can we change in the first line, “feels to,” is that the opinion, or "believes"?

THE CHAIR: Believes, actually, yeah. We did that but we forgot to change that.

SPEAKER: Okay.

THE CHAIR: Yeah, believes. Yeah, right, good pick up, okay. Okay, so "The Committee believes that there is inadequate information to accurately assess the impact of CMS’ National Coverage Determination for Erythropoiesis Stimulating Agents, ESAs on the management of anemia in the general population and in cancer patients. Whereas the revised position on ESA coverage may increase blood demand, ACBSA recommends that 1) HHS perform an analysis of the impact of ESA, NCD on blood demand and selected patient populations; the information needed should be derived from prospective data collection." Pretty non-controversial.

1 And then, "Whereas current demand for
2 transfusion of various patients groups is not well
3 characterized, and varies with local practice, including
4 adherence or non-adherence with available transfusion
5 guidelines, the ACBSA recommends that HHS support studies
6 to identify and characterize transfusion practices in
7 patient groups affected by the NCD in relation to clinical
8 outcomes; e.g., survival, quality of life, using validated
9 instruments, adverse events; e.g." -- we have too many
10 e.g.'s there.
11 SPEAKER: Yeah.
12 THE CHAIR: Maybe we could just do a
13 (cardiovascular events).
14 DR. EPSTEIN: How about "including
15 cardiovascular" --
16 THE CHAIR: -- "including cardiovascular," yeah,
17 yeah. "Including cardiovascular events." Yeah. Okay.
18 Is that --
19 SPEAKER: We are talking about moving in
20 relation to -- moving their phrase in relation to clinical
21 outcomes. What would you think about moving that to after
22 transfusion practices?

1 THE CHAIR: In relation to clinical -- let's
2 see. Oh, I see what you're saying. I’m comfortable with
3 that.
4 SPEAKER: Something like that.
5 THE CHAIR: HHS support studies of patient
6 groups.
7 SPEAKER: -- transfusion practices --
8 THE CHAIR: Yeah.
9 SPEAKER: -- including --
10 DR. EPSTEIN: Transfusion practices in relation
11 to clinical outcome is what it should say.
12 THE CHAIR: So in relation to patient -- so then
13 you just go to the “outcomes” and the “in patients”.
14 DR. EPSTEIN: Add the word “in”.
15 SPEAKER: Yeah, inpatient groups affected by the
16 NCD.
17 DR. EPSTEIN: You have to add the word “in”.
18 THE CHAIR: “In”.
19 SPEAKER: I-n.
20 DR. EPSTEIN: Okay, in relation -- wait a
21 minute, if there is -- okay, "HHS supports studies to
22 identify and characterize transfusion practices in

relation to clinical outcome, in patient groups" -- we don't need the comma, right? Well, no, we actually --

SPEAKER: Well, take out the first comma.

THE CHAIR: First comma comes out.

DR. EPSTEIN: And take out the second "clinical outcomes" at the end of the second line. After NCD, now take out "clinical outcomes" there and then put -- okay, yeah, okay.

THE CHAIR: Okay, so "HHS supports studies to identify and characterize transfusion practices in relation to clinical outcomes in patient groups affected by the NCD; e.g., survival, quality of life, adverse events including cardiovascular events." Dr. Epstein.

DR. EPSTEIN: Okay, back up to the first, whereas it's HHS performing an analysis, the impact of ESA, NCD, on blood demand instead of saying "selected patient populations" how about "affected patient populations"?

THE CHAIR: Better; okay, further comments? Are we ready to vote? There is lots of discussion.

SPEAKER: Yes.

THE CHAIR: Ready for vote? Motion for -- a

motion?

SPEAKER: Let me second.

THE CHAIR: Second? All in favor?

SPEAKER: Aye.

THE CHAIR: Opposed, abstaining? Unanimous, thank you. Okay, well, that was easy. But actually it was an important -- I think it is an important recommendation, it is an important recommendation. The second thing that we want to do is just to have some general discussion on the major questions related to the presentations from the ARC, AABB, and ABC, and those have been put up so that we can just begin to talk about the questions themselves, the first question being how elastic is the blood supply --

SPEAKER: Yes.

THE CHAIR: -- that’s to meet unexpected needs. The general gist of this is -- I think we heard some important points in the discussion and the points in the discussion that I took out -- basically an important point is that the blood supply -- first of all, there is not a national shortage.

There’s not the -- we don’t have severe national

shortages, that’s what I hear. What I hear is that we have focal regional shortages but we don’t have national shortages. So to me that suggests that there is a sufficient degree of elasticity in the blood supply, ability to move it back and forth to support the needs. The issue would be about response time. Dr. Roseff.

DR. ROSEFF: I’m not sure we can say that based on the discussion that we don’t have the transfusion -- the transfusion services side of the discussion. We talk about inventory, we have very good data now from blood suppliers, but as we talked about, we don’t have that other side and --

SPEAKER: Right.

DR. ROSEFF: -- Dr. Benjamin brought up that 53 percent of their customers report shortages; is that elastic? You know, I don’t know if we can say that at this stage without having the other side of the --

THE CHAIR: Well, yeah, because actually most of the information that we have on the blood supply is from the blood collectors so we really don’t know the full extent of the blood supply; Dr. Kuehnert?

DR. KUEHNERT: I think this was mentioned before

1 and I thought it was a really good point, is it's
2 important to define what a shortage is. I heard the
3 answer was -- I thought I heard the answer was everyone
4 defines it differently, depends who the local group is
5 you're talking about, whether it's the blood center or the
6 hospital.
7 THE CHAIR: Right.
8 DR. KUEHNERT: And I'm just going to briefly,
9 just tell a little story, okay, to maybe energize people,
10 it's a 4:45, you know. Last week we had a pandemic flu
11 exercise at CDC, okay, so we all -- we're in the emergency
12 operations center and they simulated a pandemic. And I
13 was manning the desk and they said, well, there's a blood
14 issue. Major blood collection agency has asked that,
15 because this was an advanced stage of the pandemic -- they
16 said they've asked CDC to cancel all elective surgeries
17 because there's not enough blood. And I was asked to
18 respond to this, how -- what should we say to this, you
19 know. It said exercise all over the e-mail but it still
20 made me quite anxious and I was very happy to be able to
21 say that there are inter-organizational task force -- a
22 pandemic flu task force, both AABB, that have

contingencies for this sort of a situation to actually helped manage this.

t that the first question really should be why are you -- why are you asking this question, what are the data that there is actually a shortage and it may be realized that that data exists but it’s -- but how is it nationally coordinated and -- but I think the more basic question is how is a shortage defined because if you can’t -- if you don’t know the definition for that I don’t know how you can start to coordinate the data because you’ve got apples and oranges and grapefruits and all kinds of other things.

THE CHAIR: That’s a good point because actually in ABC’s data they had the less-than-1-day supply, less than 2 -- you know, 2 days. They had certain thresholds but then when you talk to the hospitals it’s a different story, so --

SPEAKER: It's going to be very -- I mean, it’s going be very variable. You might have a surgical team that is very cooperative and you work with them and although you’re tight, I mean, you’re going to be able to do certain things. I mean, in another place it might be

that you cannot even tell anyone that they can have one unit less because they're going to start screaming so that means that you really are short. I mean, I can be short with 10 units and I can be short with 5 units, it's going to depend who I'm dealing with. And even -- I mean, and from my point of view is -- who I'm dealing with, you know, that person would be even the blood bank or how they want to deal with the situation, so there's a lot of variables when you come to the hospital.

THE CHAIR: So again we have an issue about the definition of shortage and I think that's something we can try to grasp and then perhaps we can deal with the initial issue of elasticity. Let's go on then to number two, understanding that 50 percent of the blood that's used on a daily basis for elective surgery -- who determines transfusion priorities, we don't know, and that's the clear message, I think, from this -- what happens in the hospital is unknown and there is no standard.

SPEAKER: It's not always --

SPEAKER: You're talking about in a shortage you mean? In a shortage --

THE CHAIR: Well --

SPEAKER: -- that sentence would be?

THE CHAIR: Well, understanding that 50 percent of the blood that is used daily -- basically it’s who determines the -- who -- the triage process, and what we’ve heard is that’s something that needs to be considered but thus far it’s only been considered and there’s just -- there’s no data, there’s not much information.

SPEAKER: But I think what you’re asking is who determines priorities everyday or when there is a shortage. Is that what’s --

SPEAKER: Right, right, I assume you mean in a shortage.

THE CHAIR: Yeah, I would think -- yeah, I would --

SPEAKER: Not just in general because they all --

THE CHAIR: -- yeah, I would think this would be in a shortage.

SPEAKER: Yeah, right, right.

SPEAKER: Where is the number 50 percent from?

THE CHAIR: Well, it that depends on whether or

not it is one of those ready -- the lean transfusion -- a lean blood center or a not so lean center. Because the lean -- the not-so-lean centers tend to use 3 days' reserve, you know.

SPEAKER: But then you're talking from the --

THE CHAIR: I think there are a lot of -- there's a lot of uncertainty about both number one and number two. So the current system for -- in the U.S. for management of blood inventories, we have a clear picture of that from ABC, we have a clear picture of that from ARC, we have -- there is no system that I'm aware that drills down to the hospital level. So the collectors is clear, there are systems, in fact there's a subsystem of BCA within ABC, so there are three systems, but they are all blood collector systems and no hospital systems. Oh, there's been -- I'm sorry, I'm sorry.

SPEAKER: Yeah, I was going to say --

THE CHAIR: BASIS -- I'm sorry, there's BASIS.

SPEAKER: I know Dr. Holmberg would be able to comment about BASIS in terms of -- since the question keeps coming up how are the hospitals doing, could you comment on how -- what BASIS is showing us in 25 words or

less?

DR. HOLMBERG: Twenty-five words or less, okay. You know, really I think that this was a question that Dr. Bianco asked also, it is just how would we use or how do we use the data. First of all let me go back and comment about the previous monitoring system that was in place when I arrived. And that system, to be honest with you, I agree, it really did not give us the information that we needed. And at that time I think that it was primarily thought to be a system to help with policy decisions on how -- what is the effect of maybe like a donor deferral. If we went through CJD deferrals again, something similar to that, what would be the impact on the blood supply?

Also you’ve to understand that the first system that we had also consisted of only, I believe, 26 hospitals and 2 blood centers that also did transfusion service. So it was totally hospital-based and what we did see was that when there was a shortage at the hospital blood was immediately pushed in from the blood center.

What was really clear with (inaudible) was that we needed to have both supply and demand. We needed to be able to see what was available at the blood center and

1 what was available at the hospital collectively together
2 to be able to give us a determination of whether there was
3 really a problem.
4 Post 9/11, I would say that the most dramatic
5 impact of using BASIS is to determine whether there is a
6 local or regional or national shortage of blood. And then
7 as we plan for the different -- 15 different scenarios
8 that we've been tasked to look at will we be able to
9 supply the need if something happens. Now what have we
10 recently seen with a hundred hospitals reporting? We have
11 been able to see specific situations were there have been
12 local shortages and based on what we've seen in our
13 reports we've been able to contact the three major
14 facilities such as ARC, ABC, and the AABB to ask them, is
15 it time to go out on a national appeal, do we need a
16 statement from the Secretary saying the nation needs to
17 step up to the plate and support the local blood center.
18 Since then it has come back to us saying, no,
19 let's -- they would rather handle it on a local level.
20 Now, specific instances that we've been able to uncover
21 with BASIS has been situations like transplantation
22 centers that have had to close because they have had no

blood available. Shortages, because the BASIS system not only collects data but it also collects qualitative data such as did you have a supply that did not get filled, a request that did not get filled? Did you have to cancel surgery, how many days have you cancelled surgeries?

So we've been able to see that and that prompts our action to really start having communication not only with the blood centers, or I should say the blood organizations, but also to the task force. And in ESF-8, we are mandated to monitor the blood supply. The other thing that we have is, for the use of the data, is that we have to be able to determine what the cost would be in a disaster.

And for instance the recommendation came this morning or this afternoon about adding blood bags to the SNS, the Strategic National Stockpile. We have to have data to be able to support the addition of blood bags in a disaster if we have to be able to support after the fact. The government has to pay for the situation, we have to give a price tag for what it costs for that to respond to fact. So those are some of the things we use the data for and what the data has uncovered to date.

THE CHAIR: I think one of the things that we talked about when I was characterizing the other groups, all of them have more or less like a 85-80 percent snapshot whereas again this is an audit snapshot, BASIS. But one of the things we did discuss that I think we'd probably want to spend some time tomorrow on is thinking about ways to encourage participation in BASIS to expand the data availability.

DR. HOLMBERG: One more thing I forgot about -- what we use the data for is also to give us a denominator if we have an event that happens, for instance like back a few years ago with the white particulate matter down in the Atlantic area or let's say something pops up again, we don't have a good handle on what the denominator is throughout the country. As we move forward to the surveillance programs, the bio-vigilance programs that have been advocated by this committee we need to have a denominator. Now, yes, we do do the bi-annual surveys and that gives us a certain denominator but having a denominator that we can say this is a current denominator -- but primarily what I also want to say is that it gives us a denominator or the starting place if we have multiple

-- if we have even a disaster or multiple disasters we know what the starting place is for that disaster.

SPEAKER: Yeah, I just want to let Dr. Bianco speak -- but the -- there’s -- I think what I’m hearing over here is two different -- there’s like two crosscurrents going on here which to me maybe should be separated to -- in some cases. One is the day-to-day inventory, we’re short, we’re having cancellations, or we're -- you know, and then this the secondary -- and then the other arena for this is the disaster planning and I think those are two somewhat separate issues.

Some of our questions have been directed to one or the other and then the answer comes back to the other -- to the other one. So I think there’s -- these are two separate -- to me they are two separate issues, they are obviously very related but, you know, I guess we need to decide which context we’re addressing.

THE CHAIR: Good point, actually why don’t we have Dr. Bianco have the last comment of the day and then we’ll adjourn?

DR. BIANCO: I’d love it. The -- I just want to make a couple of comments, I don’t think that that’s a

1 final discussion. On the first day that the first effort
2 by HHS to collect data and the initial effort, I was very
3 much in favor of it and supported it tremendously. As I
4 saw it progress I realized that there aren't really
5 actionable items that are generated by the type of data
6 collection. The snapshot that you got with the HHS study
7 carried out by AABB and a repeat of the survey, yes, that
8 was a very, very productive effort and I refer to that
9 study, I'm sorry that it is a couple of years old already,
10 but almost everyday.
11 The actual detail of the daily inventory at
12 blood centers is for me a little bit like the Mondays that
13 we get the how many million dollars each one of the movies
14 made over the weekend. It tells me that one movie was
15 more popular than the other one, it's essentially an
16 assessment of what the movies are, but it didn't create
17 any actionable items, and that's my concern in terms of
18 the effort that is there. I think that if we focus on the
19 hospitals, you see, we -- the blood centers can generate
20 that data and deliver the data in different ways, in
21 aggregate, this way, that way. We're developing a big
22 database, the Red Cross has already the database,

ultimately this data is there and is available; the data about the hospitals is not.

The data about like Dr. Roseff raised is almost a satisfaction survey of what job we're doing as providers of blood, that is more important than actually knowing that number on the shelf. And for the disaster planning, I think that what we're trying to reassure you is that we have worked very hard in recent years, I mentioned before, we overcame the incredible impact of the deferrals for variant CJD, we got to a more or less stable blood supply. It's not perfect and it will not be perfect because we made the decision to rely entirely on volunteer donors and so we still have to beg and convince people to stretch their arm and donate blood, but people respond and respond beautifully, particularly in disasters.

So what I would suggest is a refocus of BASIS -- it's not to throw it out, but before ask really what are the questions that you want to answer, what are the actions that you want to take that will be based on the -- on the daily understanding of what the numeric inventories are, it's just my thought.

THE CHAIR: Okay, thank you, Dr. Bianco. And

let me just take the chairman’s prerogative for maybe the last word, so that you can sleep on the remainder of the questions -- and again I’ll just read them down. One of the issues is can the data be linked to collection efforts or how is it -- is the public aware of blood inventory status? What is the appropriate role of media and government informing -- in informing the public of blood status, how does the system prevent disparities in blood availability and what are the ethical issues related to donor recruitment of blood distribution; we’ve heard some of that discussed. We’ll have time for discussion tomorrow; sleep on that, thank you.

SPEAKER: Jerry, do we have those questions in writing anywhere?

SPEAKER: We'll get you a copy.

SPEAKER: If we’re going to sleep on them it would be nice to take them home, put them under our pillow.

THE CHAIR: Because that's -- that reflects on how you handle it, your efficiency, your operation. Right, right, because the science of inventory is --

(Tape ends abruptly)

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