

VOLUME 1
DEPARTMENT OF HEALTH AND HUMAN SERVICES
U.S. PUBLIC HEALTH SERVICE
ADVISORY COMMITTEE ON BLOOD SAFETY AND AVAILABILITY
THIRTY-FIFTH MEETING

The above-mentioned meeting was held on
Tuesday, December 16, 2008, commencing at 8:30 a.m.,
at the Hilton Hotel & Executive Meeting Center, 1750
Rockville Pike, Rockville, Maryland 20852-1699, before
Louisa B. McIntire Brooks, Notary Public and
transcribed by Paula J. Eliopoulos, a Notary Public.

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(The following is a transcription of the proceedings.)

P R O C E E D I N G S

THE CHAIRMAN: -- of the Blood
Availability and Safety Advisory Committee.

Once again, I'd like to emphasize my
sincere appreciation for the commitment of the
committee members and those members of the audience to
advance the health of our fellow citizens.

In this time of holidays for so many of
us, we must remember that many of our friends,
families and persons unknown are in need of health
services.

Giving is the central theme of the season.
It's therefore appropriate that we will focus much of
this meeting on those who give of themselves through
donation of blood, plasma and tissues to help others.

We will also discuss the role of
organizations handling these noble individuals in
promoting donor health and the potential impact of

their interventions on individual donor health and, in fact, the health of our nation.

But to begin, we'll first have a series of updates for the committee. Let me remind the committee members that our charge addresses developing policy effecting broad public policy issues regarding availability and safety of blood.

And, again, we're focused on the broad policy issues, not specifically issues related to regulation.

With that said, I think we'll go ahead and take the roll call.

PARTICIPANT: Thank you, Dr. Bracey. Again, welcome. I think that we're in store -- we're in store for a real change in weather. So they're telling us now that we might have an ice storm tonight. But if you're staying here, you're okay.

I also want to thank everyone for their tolerance as we work through some of the travel issues. I know that Dr. Kouides, we had a struggle last night.

And let me just explain a little bit for
some of you as far as the traveling under gov trip.

Gov trip is the system that the Federal Government uses and it's totally paperless.

One of the things that it does -- it does create some problems when people are traveling for other agencies.

For instance, if somebody at the table here is -- has spoken to the FDA, and the FDA has paid their trip or they are on an NHLBI conference or they're doing something for CDC, what happens is that you are detached from the Office of the Secretary and you then get attached to whatever agency is picking you up for travel.

And so it really creates some administrative nightmares as far as trying to get travelers back. And sometimes flights get cancelled because an administrator at another agency says, well, this person is not traveling for me and cancels the flight.

So, we had that problem with Dr. Kouides

last night. We -- fortunately he's here, and I'm very
pleased that he was very patient with the way we

operate.

I just have to say that I will be traveling in January for the CDC doing a blood assessment in Afghanistan. And I, since I will be traveling for CDC, I have no privileges now under Gov trip.

So, when I look into Gov trip, there's nothing there other than my local travel. So, I can't help you out, and that's one of my disadvantages this last time.

As we started off, I would like to take roll and also have to explain to you a little bit what -- explain to you what happened as far as calling back some of the individuals that were to rotate off of the committee.

The new nominations for those individuals that are to rotate has been -- they have been put forward. And with the new Administration, it was decided that the nominations of new candidates or new

individuals to take your place would be postponed
until the transition into the new Administration.

So, the privilege under the Charter says that we can extend committee members for 180 days, and so we invoke that privilege. And thank you for coming back and being with us.

Dr. Bracey.

THE CHAIRMAN: Present.

PARTICIPANT: Dr. Benjamin?

DR. BENJAMIN: Present.

PARTICIPANT: Anne Marie Benzinger.

MS. BENZINGER: Present.

PARTICIPANT: Julie Birkofer is absent.

Dr. Block is absent.

Dr. Duffell?

DR. DUFFELL: Present.

PARTICIPANT: Anne Marie Finley?

MS. FINLEY: Here.

PARTICIPANT: Dr. Haley?

DR. HALEY: Here.

PARTICIPANT: Dr. Ison?

DR. ISON: Here.

PARTICIPANT: Dr. Kouides?

DR. KOUIDES: Present.

PARTICIPANT: Dr. Lopez-Plaza.

DR. LOPEZ-PLAZA: Here.

PARTICIPANT: Mr. Matyas?

MR. MATYAS: Here.

PARTICIPANT: Mr. Nether?

MR. NETHER: Here.

PARTICIPANT: Dr. Pierce could not be with
us today.

Dr. Pomper?

DR. POMPER: Here.

PARTICIPANT: Dr. Ramsey?

DR. RAMSEY: Present.

PARTICIPANT: Ms. Wade?

MS. WADE: Here.

PARTICIPANT: And I have to say that Ms.

Wade has her husband with us today. So, thank you for
joining us. And it is his birthday today also.

So wish him a happy birthday.

Dr. Triulzi?

DR. TRIULZI: Here.

PARTICIPANT: The non-voting members. Dr. Keuhnert.

DR. KEUHNERT: Here.

PARTICIPANT: Dr. Epstein?

DR. EPSTEIN: Here.

PARTICIPANT: Dr. Klein?

DR. KLEIN: Here.

PARTICIPANT: Colonel Rentus could not be with us today. Colonel Rentus is replacing Commander Libby who retired from the Navy in October.

Dr. Bowman is not with us today.

Dr. St. Martin.

DR. ST. MARTIN: Here.

PARTICIPANT: And Mr. Rich Durbin.

MR. DURBIN: That's Durbin.

PARTICIPANT: Durbin, I'm sorry.

MR. DURBIN: Here. Present.

PARTICIPANT: I apologize for that.

PARTICIPANT: Okay, sir, we have a quorum.

THE CHAIRMAN: Okay, then.

Let's go ahead with the business of the

day. And our first presentation in terms of updates will be a summary of the report of the FDA's workshop on approaches to reduce the risk of transfusion transmitted babesiosis in the U.S. by Dr. Sanjai Kumar.

Dr. Kumar has an active research program at the FDA on blood safety from malaria and babesia infections and has presented extensively on malaria and the topic of babesia. And welcome.

DR. KUMAR: Thank you and good morning. Thank you, Dr. Holmberg for the invitation to present to this committee -- can you hear me? Hopefully it will be better now.

I'm going to summarize the workshop that the FDA had organized on transfusion transmitted babesiosis.

So, the workshop was held on September 12th and it's a rather recent event, it happened in September at the NIH campus. Both hands are busy

now.

So, it's a rather obscure disease, so I

think it would be fitting if I give some background and I'll explain the reasons why we thought it was the time to hold this workshop.

To me, the more I think about this disease, like malaria in the United States, and I think the reason will become clear as we go along why I said this.

It is rather malaria-like illness and it's caused by erythrocytes protozoans of genus Babesia. And they belong to phylum Apicomplexa. It's the same phylum where other more famous causes of Babesia belong, Plasmodium, Toxoplasma, and Cryptosporidium.

So at least Plasmodium is precedent Toxoplasma. They are the greater parasites of human public health and economic importance.

So, Babesia, I mean if you look at it phylogenically, falls very closely to these two other parasites.

It's naturally transmitted, several

species are transmitted in the United States. And the clinical symptoms range from asymptomatic infections

to mild disease to life-threatening. And from Babesia microtia, at least, the most prevalent species in the United States causes about deaths in five percent of infected individuals.

Clinical cases are reported in several states, but mostly disease is in (inaudible) northeastern states.

Clinical diagnosis and detection of Babesia are often difficult, and mostly also because people -- they are not so much awareness about this parasite still.

And what is intriguing is the highest number of clinical cases and transmitted cases occur in the United States. And I'm talking about all around the world.

So it is mostly our own problem. And it's not a nationally reportable disease in the U.S. In some states it is, but in most of the states it's not.

Just to give you a flavor for how the

parasite looks like. So this is the Babesia microtia
infection. There are (inaudible) red cells here, but

I just wanted to have a look. These are famous pyro-found parasites.

And even the expert hands and expert eyes, it's very difficult to distinguish from Malaria, if you're looking at the thick film, distinguish from plasmodium parasites, actually.

And those were experts in the field, for them.

So, again, just coming back to the same slide I showed you. So I involved the (inaudible) and inverted (inaudible) life cycle. So these are blood found parasites here, the one I just showed you before. This is a natural, these are (inaudible) they are white footed mouse, spiromiscus (phonetic) and this is the exoitis (phonetic).

So the infection is completed in these two hosts and then the humans get picked up by a tick bite here and the blood form infection proceeds.

Unlike malaria, there is no (inaudible)

cycle here. And there's a major role played by this
white area here. So, although they are reflected

infection themselves, but they are greater hosts for ticks to multiply.

So as ticks can feed on them, then they drop the ticks and go on. And the people who prefer outdoor activities, they become the prime target of infection.

And then from the infected host, especially from the asymptomatic carriers, disease is transmitted into donor blood recipients.

So what were the reasons we called this workshop? And I think there was people who were asking for it for a while, actually, and then transmission continued on several states.

Since 1979, approximately 70 incidents of transmitted and transferred Babesiosis have been reported. So these are reported cases. And we have no clue how many cases actually are. Actual numbers may be higher.

What drew our attention was there has been

a great surge in the reported cases of transmitted and transferred Babesiosis associated with death. No

approved laboratory test to detect Babesia infection, so the donor -- it's done based on the questionnaire, if somebody had clinical Babesiosis and they are deferred indefinitely.

So, there are large gaps, scientific gaps, exist regarding the transmission, number of clinical cases, asymptomatic carriers for the high risk of.

And I think this is the main reason that we called this workshop, so we can learn more about the disease and what needs to be done actually in terms of science, also.

And what, then to discuss the most important possible effort to help in minimize the incidents of transmitted and transferred Babesiosis. I think that's rather easier said than done.

And then there were two talks on the pattern and deduction technologies. I think that's something freely moving along now.

So we had -- so what is basic outline

here. We had four scientific sessions and one
discussion panel in the end. And then we had open

discussion panel in the end of each scientific session.

So we had discussion on the biology of human Babesiosis species. And we were fortunate enough to have the best minds in the field who are working in this area, actually. So it was rather very satisfying.

Epidemiology of Babesiosis and identification of babesiosis risk donors, clinical manifestations and pathogenesis of disease, incidence rates and mechanisms to improve prevalence of such incidents.

Because one of the problems is, it's not a reportable disease so we actually don't know the actual number of cases. So how to extend (inaudible) in that area.

And the laboratory tests that are currently available to detect Babesia infections and limitations for donor screening tests.

Because diagnostic tests do not
necessarily translate into a donor screening test.

There are very different requirements.

And there is priority to develop feasible donor screening tests.

So then what are the approaches that we could use to reduce -- then what are the approaches that we could use to reduce incidence of transfusion transmitted babesiosis includes urine testing and pathogen reduction and that algorithms for testing Babesia infections.

So how to test donors, if it's going to be geographically exposure based or universally screening. The same question sometimes which are posed to us for malaria also. So, some of the questions remain similar.

And then the most important probably is the donor re-entry. I mean, we can't just identify these donors and then leave them out forever, otherwise you create donor loss.

So I just want to give you a quick flavor

of these scientific sessions here, in case somebody
was interested in knowing about the workshop.

So, the first session was the biology, pathogenesis and epidemiology. There are three talks there, and then we had questions that we had posed at the end of each session to the discussion panel, to the moderators.

The next session was the risk of Babesia infection through transfusion. So basically, define who are the risk donors here. What are the current laboratory tests that are being used, and also how they are validated, actually.

And then it came to possible approaches to minimize the risk. So, Dr. Ritchard Cable gave a great talk on the universal versus regional exposure based testing, and some basically possible algorithms. And he did a very nice job, actually, presenting.

I hope I can do some justice to what he presented there.

And then we were fortunate to have two talks, both on the industry and pathogen reduction

directly showing the effort using pathogen reduction
technology and reduction in Babesia parasites in

blood.

In the end, we had panel discussion and I'm not going to go through the questions, but these are the questions that we presented.

So what I have done here is I picked a few of the slides which I thought I should share with you here today.

So the credit goes to the speakers, they are directly their slides, mostly unmodified.

So this is from Dr. Peter Krause from the University of Connecticut School of Medicine who has moved to Yale now.

So, this is looking at the number of babesia infections and Babesiosis in New York State. So, because I keep saying again and again, the actual cases are not known. So these are the known cases here.

But you see here, these are close to like more than 200 cases here, in New York State alone.

And the other thing is the clinical Babesiosis

manifests mostly in higher age group people, also. So

these are the -- helps us to identify the risk group, also, in terms of blood donations.

This is in Connecticut state here. And, again, I don't know whether these (inaudible) whether the people are not paying too much attention to, or whether for some reason the disease is increasing.

But in more recent years, the number of cases are increasing. This is in Connecticut, and these are the diagnosed cases of Babesiosis.

And also, as I said, the biggest challenge for us is how to identify the asymptomatic donors. So the infection in untreated individuals.

So, in most groups, if you look here, around 90 percent the infection is cleared around six months after infection. It stays longer in non-treated groups. But in some non-treated groups, it can go beyond two years, actually.

So after initial infection, and actually nobody knows for sure when the initial infection

happened. But the point here is that people can stay asymptomatic and infected. Those are the highest risk

donors.

Actually, this is a slide from David Leiby here. This is based on cyto prevalence data here. And if you look in Connecticut state, there are many states that are infection free. So that there are false ideas, there are hardest spots where the infection is.

And since in some states infection is much higher than (inaudible) per ten thousand, the infection rate is reaching in some states ten percent here, actually. Where the infection is milder, and other states are infection free here.

So, how to define these hot spots is very important for us, because that's where the donor deferral questions can be focused, actually.

In looking at the Babesia in the Connecticut blood donors here. So especially looking at blood donors. Again, Dr. David Leiby, they have put great effort into looking into these things.

So, it's not that people are not apprised
of these things, I mean, it's ten years of their

effort now.

So these are the numbers of donors tested here. These are random donors, rather. And so, this is by using (inaudible) test here.

So the range of positivity changes from year to year from .8 percent to 1.7. So these are the infected donors in a state where the disease is endemic.

And then again looking at the relationship, if any, what is the value of antibody tests. Is there any correlation between. So directly looking at the parasitemia by PCR and in cytologically positive donors here.

So, in endemic areas, by ELISA 6.6 percent cyto prevalence by IFA 1.4 percent. So probably true positive lies somewhere in between.

And this slide is important because it tells you the value of each test, could be more valued here.

So obviously the currently available
ELISAs may not be that useful, actually. So what

needs to be done to improve their specificity here.

IFA probably is more specific, but sensitivity may be a problem. And the great majority of those here, at least 50 percent of those are positive by antibodies are also carrying parasites at the current time given the sensitivity of the PCR test.

In non-endemic areas this ELISA is still giving high background here. Non-specificity. So that directly tells you that these tests which are being currently used by the Babesia (inaudible) are any sort of donor screening.

IFA looks more real here, .3 percent positivity. But some reason they are also showing two out of three Babesia positive.

So what could be truly non-endemic area may not be endemic areas also just simply because of trevors and so forth.

This is a slide done by Sharon O'Callaghan

from FDA. So, it's difficult to get a lot out of this
slide because the reason being, these are all reported

incidents, not these are unusual cases.

But one thing one could see is the number of reports to the FDA are increasing over the time here, actually.

Even in the more recent years. But what is more revealing is the next slide here. So these are the fatalities, those could be either directly or indirectly related to Babesia infections.

And this is what got our more attention and probably prompted us to hold this workshop. In 1998 we had one death where Babesiosis could be attributed as a primary or secondary cause of death.

But in more recent years -- so there was nothing in between these many years. But the last two to three years we are getting two to three reports of deaths those are being attributed to Babesiosis.

And that's something that drew our attention.

This is some of the highlights of the talk

that I gave here. So what are the detection methods
currently available?

So similar to malaria you can directly detect parasites by microscopy enough flushing sensitive and (inaudible) and by DNA detection.

So these two methods, with their sensitivity is questionable, and obviously they cannot be used in any of the donor screening setting.

DNA detection is basically PCR based. But also a lot of work is remaining to be done.

Because the biggest question is, we don't know what is the infectious dose actually for Babesiosis. How many parasites per unit of blood can cause infection.

And second, I think that's the main reason. So that's where the sensitivity would be questionable.

Antibody testing as a surrogate of exposure, IFA and ELISA are there. And I think a lot of work needs to be done there.

Currently there are no approved laboratory

tests for donor screening. And also there have been reports and many presentations showing antigenic

variations. There are at least four or five species of Babesia are present.

And by IFA, the whole parasite based IFA, one test cannot be used to detect the infections, antibodies against other species.

So that is rather challenging.

And there is some history that such as the presence of antibodies can be suggestive of acute or recent infection. But, again, a correlation is not absolute. IDD titers can last for months or even years. So how does someone who is detected for antibody positive, how long do you defer that donor.

So that becomes a question of donor loss.

And if you look at the ELISA test, the cyto positive that I showed you before, .3 percent in non-endemic areas even one before that go as high as 17.8 percent.

So, obviously that test is not ready for use.

So the biggest challenge to distinguish
against current infection and previous exposure, donor

loss of positive reactions, if the test is not well validated.

So this is a study that caught my attention. This is a recent paper from Dr. Phil Feldner. So what he had done, he had done a protein (inaudible). This is on Lyme disease here.

And then they use the antibodies against natural infection. And the reason I found this paper very interesting is that using protein (inaudible) for about 80 percent of genum, then can identify antigens that distinguish and recognize antibodies against acute infections, chronic infections and those who have either drug treated or self resolved their infection here.

So a strategy like this, if we can use in Babesia, we can recognize those antigens from genum (inaudible) antigens.

Those are distinguished and recognized by their convalescing sera, drug treated sera,

(inaudible) infections. So I think that will give us
great value in recognizing donors who are acutely

infected and also will have value in sero diagnosis.

The other strength of this technology is that it could be used as a multi-plex platform.

So the idea of, one idea behind the workshop was to bring these new ideas to the modern technologies together and how we can put together.

So if we can -- we can use -- we can (inaudible) against several pathogens. Those are only -- that are recognized by antibodies during acute infections only.

And then also we can multiplex them. So the question of how many we have to test to become (inaudible).

This is a talk by Marianna Wilson from CDC. She has many, many years of experience in testing both patients and blood donors who have fallen positive for Babesia.

So I just picked this slide from her talk. These are 19 patients with acute -- during acute

Babesiosis (inaudible) picked up all 100 percent, 19 patients. 95 percent with PCR positive, 84 percent

were blood film positive and then hamster inoculation was 74.

So all of these tests have their values.

But the question is the sensitivity and how they compare, and also mostly how do you distinguish current and previous exposure here.

She also has gone on to say that IFA titer of 1000 or more may reflect a more recent infection. But I think this will need to be validated in much large studies.

Value for IDM, and association, current infection, she has shown some.

I apologize, I didn't put the name of the presenter here. But this is a talk from Victor Berardi.

And, again, they have done a lot of work looking at the antibodies and the Babesia infections.

So this is a study -- so they tested a large number of Babesia samples, representatives of

this company here.

So antibody findings are in there. So

these are smear positive samples. So finding a correlation between an antibody and parasite positivity here.

So IFA picked up 100 percent of the samples which were positive by blood film also. IDM was a 97 percent here. IDD, 100 percent positivity. But ELISA was less than still here.

So, but again, one thing is appealing, that IFA is probably 100 percent sensitive and IDM may have some value in detecting a current infection here.

Now looking at the same data in a different, reverse way. So these are PCR positive instead of blood film positive.

And antibody positivity. And, again, the correlation is very tight, actually.

So, this is talk for, I think my time is running out now. So I'll just go through this quickly.

Dr. Ritchard Cable, he presented several

algorithms, how to apply a test for Babesia microti
and blood donors. During certain times of the year,

whether you test -- whether you test only red cell containing products only or whether you need to test plasma donors also.

And, again, he looked at the cyto positivity in Connecticut year around to see if there's certain time where the prevalence is higher.

So it does seem like there is during March and July and August. But I don't know what is happening in the intervening months here because the tick activity usually presents during this time, also.

But one thing is clear here, that the at least .4 percent to 1.5 percent cyto positivity in these donors here.

And again, then looking at cyto positivity in his data, based on different counties. And there are some counties where the prevalence at 10,000 rate is higher over the other counties. So there endemicity does vary from county to county.

This is a talk by Dr. Laurence Corash from

Cerus Corporation in pathogen reduction. So, this is the agent they used. So what is the important thing

to do here, to look at here?

They find that more than, greater than 4.5
lot for reduction in Babesia microti in blood by
treatment with their agent here.

So possibly is this something that could
-- of potential value? And also similar sort of data
they found in plasmodium falciparum. So about half of
their treatment is effective against specific
parasites.

This is another talk for Dr. Raymond
Goodrick. They are using Riboflavin, Riboflavin,
Vitamin B2, that's something very naturally used
vitamin.

And, again, they find more than five lot
fold reduction in Babesia microti parasites in blood,
in platelets and plasma.

So, I -- and they have tested it against
red blood cells, but for some reason I don't see that
here. But needless to say, there is an effect here,

how that could be implemented.

And there was a talk by Dr. Darlene Fullen

from the Rhode Island Blood Center. And I will just very quickly summarize what they are proposing to do.

They want to have a -- screen a pool of donors for Babesia and then they want to use it in a selected group of patients, the recipient (inaudible) immunocompromise or neonates. So that's the plan that they are working on.

So, I would just summarize it very quickly now. So, the disease is here in the United States. There has been noticeable surge in number of transfusion transmission cases, those reported to the FDA.

Currently empirical maps showing Babesia transmission and then donors are needed to identify at risk donors.

So these maps are current only then they will be of value, similar to something like we have malaria, but there's probably a lot of effort we need to put into that.

Asymptomatic carriers are the highest risk. Additionally, studies are needed to determine

the rate and duration of infection in asymptomatic carriers.

And I think that the basic science comes in the picture. Further evaluations are needed to determine the value of available laboratory tests.

And then I think most importantly, we need to bring in more modern tools in our technology. If you are doing this from ground up, I mean, the work needs to be done, so why not use the most modern technology.

And then also, the novel testing that's used to identify (inaudible) Babesia donor should be considered. These studies include testing of blood units for transfusion immunocompromised and neonates. And that's exactly what the Rhode Island Blood Center is proposing.

So what are the next steps? One thing we have already done, under AABB CDC task force, we have set up a new task for Babesia and we meet once a

month.

We already had our first meeting and the

mandate of this task force is to look into all issues including basic science and then make a recommendation of where to go from there.

And I think some of these efforts would include some sort of lobbying to bring new funds to this disease, because essentially it's not appearing that (inaudible) and INS or any of the major funding agencies.

So I want to thank the scientific program committee which helped us to do all of the scientific agenda speakers and so forth and different people from FDA who were involved and all of these speakers and parties.

Thank you.

(inaudible speaker)

DR. KUMAR: There was a discussion regarding the field, the Babesiosis field can do something about it.

And it's my understanding that there has

to be leadership from different agencies and blood centers to make it a nationally reportable disease.

But what I heard during those discussions that's not something very easy to accomplish, to make a disease -- a new disease nationally reportable.

So, I think those are some of the issues that perhaps this committee can pick up and help us.

But discussion was -- there was discussion about this.

THE CHAIRMAN: Mr. Holberg?

MR. HOLMBERG: Yes. I was just curious. Has there been any transmission to organ recipients since they are generally immunocompromised?

DR. KUMAR: There is no reported case. I mean, we looked and looked, but we could not find any direct organ induced transmission.

MR. HOLMBERG: And also a followup question on --

DR. KUMAR: I mean, it's very highly possible. I mean, it's highly likely, why it would not happen. Infected red cells are there everywhere.

MR. HOLMBERG: So it's something we need
to keep on the radar screen?

DR. KUMAR: Absolutely.

MR. HOLMBERG: The other question I have is, in regards to the task force. Is there a time line for any of their recommendations?

DR. KUMAR: It's a very good point. There is no time line, although probably we should consider a time line.

THE CHAIRMAN: Dr. Triulzi?

DR. TRIULZI: Yeah. Dr. Kumar, the current hydro-nucleic acid tests that are done for screening are plasma based. That looks like that's probably not appropriate for this.

So what sample preparation has been used for the greatest sensitivity for PCR? In other words, what would have to be done? It sounds like there would need to be a change in the sample type for this.

DR. KUMAR: So, so one thing that we are doing for malaria is -- some of the issues are very similar. Few infected red cells hiding in a unit of

blood, and how does one find one.

So, again, the same problem. We don't

know what the infectious dose would be. Are ten infected red cells enough? How do you find that in 415ml of blood?

So in plasmodium, there are some things we can do because of the presence of malaria pigment, those in (inaudible) we can do magnetic beads and stuff like that.

But Babesia is probably more involved than plasmodium. It utilizes malaria pigment very efficiently, so it leaves no pigment behind.

And that's why the pathogenesis is different, too, because there is no free pigment there.

So probably that technology will not work. I don't know what the answer is, how to go and fish for a few infected red cells in a large volume of blood.

What we could do best, I mean, one could go and waste 5ml, 10mls of blood, increase the

sensitivity. You can detect one infected red cell.

But if you can't find a parasite, you

can't detect it, no matter how sensitive your assay is. So that's where the challenge lies.

You have to do the rest (inaudible).

There's no method to go and attract the infected red cells and put it into the method for detection, yes.

(inaudible speaker)

DR. KUMAR: That will be, yeah. I think we're -- I think for now we have to rely on -- unless there's a breakthrough in technology, we have to rely on antibody based tests.

But the challenge is the last slide I showed from Dr. Phil Feldner was if you can -- a few of those antibodies, those are induced -- recognized by a few antigens during acute infection, I think that's what we need to do.

Unless we can find very novel ways, algorithms, how to screen those donors, that will work, too.

Or a combination of antibody positivity

and PCR positivity.

THE CHAIRMAN: Go ahead. Question.

MS. HOWSER: I'm Debbie Howser from the New York Blood Center. I just wanted to make a correction. In New York State Babesiosis is reportable and I am responsible for it, so I know.

And I believe that we did have a case of transmission through an organ transplant. I just wanted to add that.

THE CHAIRMAN: Thank you.

DR. KUMAR: Well, I think we would like to learn more about the transfusion.

The other thing I said is it's not a nationally reportable disease in all the states. We are aware in New York it is, in Rhode Island it is. In some states it is, but not in all states.

THE CHAIRMAN: The question in terms of the pathophysiology. Have there been deaths reported in non-transfusion cases?

DR. KUMAR: Could you repeat your question, please?

THE CHAIRMAN: Have there been fatalities reported in non-transfusion cases?

I guess what I'm wondering is, is the uptake related to an increase in perhaps the deer population that man and animals are living closer?

DR. KUMAR: Yeah. So generally microti -- Babesia microti that is prevalent in the U.S. is around five percent deaths. Mostly at risk are older immunocompromised as opposed to babesia divergencia that's prevalent in Europe that has 50 to 70 percent mortality.

So, yes, there is mortality. But in only in the high risk groups of patients. In young people with normal immune status, they may not even feel anything other than thinking they got a minor cold and become asymptomatic carriers.

THE CHAIRMAN: Okay. Well, thank you. I think we'd better move on to the next topic. Thank you very much, Dr. Kumar.

The next presentation will be a review of the National Blood Collection and Utilization Survey

Report. And executive summary will be presented by

Barbee Whitaker,

Barbee Whitaker is the Director of Data and Special Programs for the American Association of Blood Banks, which includes the National Blood Collection and Utilization Survey that's sponsored by the HHS or PHS.

MS. WHITAKER: Thank you. Can you hear me?

PARTICIPANT: I don't believe you have handouts. We will try to get those to you later in the meeting.

DR. WHITAKER: Is this on now? Can you hear me?

Good morning. Thank you. Today I'll be presenting the National Blood Collection Utilization Survey Report.

This is the report for the data that was -- the 2006 survey year. This is the most recent of five surveys and I'll be comparing it to the 2004 survey which is the one before it.

So, we have -- this is the cover of the
survey which is available. You can download it from

the HHS website and also from the AABB website.

First we'll talk a little bit about how the survey was conducted, some key findings, biovigilence which is one of the new things that we investigated in this survey and some information about donors, which was another area which was a new area of investigation in this survey.

So the purpose of this survey which HHS has supported and funded for the last two of these surveys is to collect critical data from the transfusion medicine community, particularly blood and transfusion information.

This survey year was 2006, and to get base line information, not just the information about what's going on, but also base line denominator information for the U.S. Biovigilence Network, which this Advisory Committee has supported in previous meetings.

New questions that were developed and

introduced for this 2006 survey year were -- included
questions on blood donation, infectious disease

markers, and also on bacterial testing, therapeutic apheresis.

There were questions on blood utilization, and also additional questions on tissue.

We've also included questions on cellular therapies which are -- we're not reporting on those today, but if you download the survey report you can see there is a chapter on cellular therapies.

So the survey instrument is sent to about 3000 hospitals and blood centers. In this particular survey year it was a 23 page questionnaire.

We've wrestled a lot with how long it is, but in general it is -- there's a lot of information that we're trying to collect. The community is very interested in the different, not only the base line information, but also a lot of questions about blood collection practice and hospital utilization practice.

So it continues to be a large questionnaire. We do it in two mailings, to try to

get as much participation as possible, with a reminder
post card in between.

This is the first year that we've introduced a web survey. We did this with just the critical items, so we had it go out about 30 days before the survey closed.

And it did increase our response rate about two percent. But we found that because it was so close to the end of the survey it wasn't really a very substantial increase response rate.

We're very interested in doing a web survey tool for the next survey and we think that we'll have better response.

The survey population includes blood centers, hospitals and core banks. We sent it out to about 100 -- well, all of the blood centers in the United States, which was 140, and had a 91 percent response rate.

We sent it to about 2800 hospitals for about a 60 percent response rate which was really pretty good considering what hospitals are doing on a

daily basis.

And we sent it to a larger universe of

core blood banks this time for about a 52 percent response rate.

So these -- the survey population is sampled. We don't send it to every hospital out there that transfuses blood.

So, we divide the hospitals by the numbers of surgeries that they perform a year. We did not send it to hospitals that perform less than 100 surgeries in a year, based on the AAJ database.

So in the hospitals that perform between 100 and 999 surveys -- or surgeries in a year, we sent -- we sample randomly at a third and we send it to a third of those hospitals.

In between 1000 and 1400 hospitals -- or surgeries per year, we send it to two thirds.

And then all of the other hospital strata we send to 100 percent of those hospitals, to all of the blood centers and to all of the core blood banks we send it to 100 percent of those hospitals.

And this is the response rate that we had
from those different strata. And you'll see that we

had a slightly higher response rate from the -- about 2400 to 4999 and the 5000 to 7999. That was our highest strata response rate.

And this is a little bit stronger response rate from this slightly mid-size hospital range than we had in the last survey, the 2004 survey.

In the 2004 survey we had the highest response rate from the 8000 and above surgeries per year.

We also looked at the response rate and the distribution across the U.S. PHS regions. And this gives you an idea of how it's distributed. So each of the ten public health regions is represented on this map.

You'll see that the blood centers are -- you have the Roman numeral for each public health region and then beneath that is the number of blood centers that are represented in each region.

And then underneath that with the

underline is the hospitals, number of hospitals.

So you can see that it's pretty evenly

distributed across the country, although there are different numbers of states.

Now, the data is also -- once the data is collected and received into our data center, we weight the data based on the number of hospitals and blood centers in the volume strata, the surgical volume strata and the number of hospitals sampled.

Then we make a weighting class adjustment which is the inverse of the response rate, which is those that were eligible that did respond which will correct the imbalance due to the differences in the surgical volume.

The differences in surgical volume between those responding and those that didn't respond. So then you get a final sampling weight which is base weight times this weighting class adjustment.

So the blood center data in 2006 -- I don't think I have a slide here that shows the different weights for the different hospitals.

But each one of the hospital surgical
strata, if you go back to this slide, you'll see the

different surgical strata. Each one of those is weighted based on the numbers of hospitals that respond.

And so that gives us -- it weights it up so that it's as if 100 percent responded.

And in the full report you can see our weighting tables.

In the 2006 report we weighted the blood center data. And in the 2004 report, we did not weight the data. We weighted it as a one, which is as if we did not weight it.

And now when we've taken a look back at the -- at the data, we think that the 2004 data should have been weighted because -- in order to make it comparable to the 2006.

So, we have re-weighted the data in the presentation that I'm going to show you today. So, if you look on the -- if you look at the report that is on the web page, you'll see that the 2004 data is

different than what I'm going to be presenting today.

So if you have any questions about that,

I'll be happy to talk about it afterwards.

So, some of the key findings from the 2006 report are that total collections of whole blood and red blood cells are 16,174,000 units. This is about six percent -- and this is allogeneic -- about six percent less than 2004.

And I'll show you in some detail on another slide how that's broken out.

The numbers of units discarded are 151,000, which is a 48.5 percent decrease from 2004, and this is statistically significant.

And this is one of the really, very large finding, and we'll talk about that in a minute.

And a 401,000 decrease in the number of units out dated, for an available supply of 16,230,000 units, which is also a decrease from 2004.

And if you look at this slide, you can see in our -- look at the collections, you will see that for total collections, which is the top line, you see

the decrease from 2004 to 2006.

The allogeneic collections are in pink,

and down at the bottom are the autologous collections.

The trends and estimated rates of blood collection and transfusion in the U.S. This is the rate of collection per population. And this hasn't changed very much between 2004 and 2006. So this is the rate of collection per donor or -- yes, collection per donor population and transfusion per population overall. These differences are not significant.

Okay. This sort of breaks out the collection table in a little bit more detail. The number that I mentioned at the beginning, the 6.1 decrease of allogeneic collections, you'll see that this is for allogeneic units. It's 141 -- 14,151,000, the autologous collections were significantly lower than they were in 2004, by 31 percent.

The directed collections were also significantly lower than 2004 by 43 percent. And the whole blood -- I'm sorry, the red cell apheresis collections were significant higher, by 80 percent.

So that's quite a big increase.

And then the total number of collections

were not statistically significant. There was no significant change, but they were down by two percent 2.4 percent.

So the total collections was 16,174,000.

And you see from this chart the change in the red cell apheresis numbers and the percent of the total collections. You can see that there was a slight decrease in the collections, but there was a large increase in the proportion that was represented by the red blood cell apheresis.

So, we have an available supply of 16,023,00 units. The total number of units transfused was 14,650,000. And so we have a margin between supply and transfused. So this would be your -- what's available, you know, your cushion of if you're counting both allogeneic and autologous, you've got 1,300,000, almost 400,000. But if you only count allogeneic, you've got 1,228,000 units.

Okay. And then coming back to what --

just to re-enforce that previous slide. The total
number, if you don't take out the testing, the

16,174,000 that was the number I showed you before --
and if you take out the number rejected on testing,
and this is a big difference from the previous year,
it's almost half as much as the previous survey.

And this is statistically significant,
this decrease of almost 50 percent.

And we believe that this difference is
difference in testing technologies. This is a big
difference.

So, this -- so the net difference between
the available supply or the collections in 2004 and
2006 is only 1.6 percent decrease between 2004 and
2006.

So the total is 16,023,000. So I know
that was a lot of numbers and it's a little bit round
about getting there.

So the total available supply for 2006 was
16,023,000.

And the transfusion numbers, the column to

look at is the column with the red -- the yellow
highlights here. The number of allogeneic

transfusions was 13,978,000. The autologous transfusions was 189,000, and that was a decrease of 30 percent, directed 126,000.

Pediatric, there was a large increase in the number of transfusions reported to us. And we believe that this had to do with the sampling that we did. We believe that we ended up sampling a lot more pediatric hospitals than we had in the past, in this particular sampling set, for a 14,650,000 total transfusions.

And that was a slight increase of 2.9 percent. That was not statistically significant.

As far as the number of components transfused, it's 30,000,000 components transfused, made up of 10,388,000 platelet concentrate equivalent, 4,000,000 units of plasma, and 993,000 units of cryo.

And all of these numbers are available from the report.

As far as recipients go, there are about

three units per recipient of red cells. That's based
on a calculation of 8,275,000 allogeneic units and

2,740,000 recipients.

And that is an extrapolation of the ratio of transfused to recipient with about 5,000,000 recipients. And this is the 6.6 decrease in the number of transfusion recipients from 2004.

We asked more detailed questions in this particular survey about -- to get some base line information about the biovigilance activities or hemovigilance activities that are happening out in the hospitals.

Primarily to get base line data for the program that we're rolling out with the CDC to see what's going on in the hospitals.

There were 72,000 transfusion related adverse events that were reported to the hospital transfusion services that they reported to us, which gives us a reaction rate of about 3.2 events per a thousand components transfused.

We asked for particular numbers of events

like TRALI, severe adverse reactions, Taxo and so on,
because these are the types of events that we're going

to be collecting data on in the biovigilence program.

And some of the high points are here.

There were 1,522 TRALI events reported, which gives us a ratio of about 1 to 15,000 components transfused.

And this is about three times the -- three times lower or a third of the -- a third of what you would expect to see if you were to compare it with other countries.

So, we think that there's probably more TRALI going on than is being reported.

The most commonly reported category of adverse events was severe adverse reactions, or severe allergic reactions. And there were almost 5000 events reported, which is about one in 4500 components transfused.

And we also asked about donor adverse reactions and there were 11,000 of those reported, which is about one in -- I actually didn't calculate that -- in .07 percent collection.

So, .07 percent of collection. So they

are exceedingly rare.

But these are severe adverse events. So

this would be loss of consciousness of greater than a minute, loss of consciousness with an injury, arterial puncture or a severe allergic reaction.

So this is not a power or feeling things, it's a severe donor reaction.

One of the interesting things that we saw with the hemovigilance questions was that the smaller a hospital is, the more likely it was to have adverse events.

So we thought that this was a pretty interesting curve here, that the large hospitals had fewer reactions -- or rates of reactions than the larger ones -- than the smaller one.

I think I already showed you this table. But just to mention again that this is the -- that the 2004 and 2006 rates of transfusion and collection are pretty similar.

And also, the key findings with the donors. We had not collected this information from a

national point of view before, so this was new for
2006.

We had 12,142,000 donors presented to donate. 9,000,000 of these were -- nine and a half million of these were allogeneic donors, and 2,725,000 of these were first time donors. So that's about 28 and a half percent. And 6,800,000 were repeat donors.

And these repeat donors provided 11,697,000 donations, which is about 1.7 donations per donor.

And as I said before, this was 11 million -- or 11,000 severe adverse donor reactions.

So in the 2009 survey which we hope to conduct on 2008's data, we have a few new questions that we'll be asking in particular about donors and donations.

We're looking to see how pervasive is the directed donor program, how many donors are involved in donating directed products. Why are donors being deferred and how many -- not why, but how many donors are being deferred for different reasons like low

hemoglobin, other medical reasons, certain risk
behaviors and travel.

How many donations are being given. We already know about the repeat donors, but what about 16 to 24 year olds. How many donors are donating, and how many of the donations are being contributed by this part of the population.

And how many donations are being contributed by minorities. We're also going to be asking about TRALI mitigation strategies on HLA and HNA testing,

And then adverse events in donors, we're looking at whole blood versus automated collection.

The 2007 report is available, as I said before. It's downloadable from the HHS website and also from the AABB website. There's a hard copy available from the AABB book store on line.

And this is the cover.

Thank you.

THE CHAIRMAN: Any questions from the committee?

I've got one question. Are there any questions or plans to have questions regarding

shortages of blood at particular hospitals?

We see that it looks like on par that there is an excess of blood. We know there is elasticity in the supply, though.

DR. WHITAKER: We do have questions about shortages, and what we saw in this last survey was that there were -- there were always a few hospitals that do report shortages.

But in general that it's not wide-spread. At least it wasn't in 2006, it was slightly smaller than in 2004.

We will continue to ask that question and to monitor it as a trend over the years.

THE CHAIRMAN: Thank you. Dr. Benjamin?

DR. BENJAMIN: Dr. Whitaker, it was a great presentation, great data, very useful.

One statistic that I have quoted to me that's, I think it's misrepresented, that you might want to clarify.

On slide 19, the key findings when you
talk about 30 million components transfused, it may be

useful to actually split that up, that it's 30 million component equivalents transfused in 22,000,000 transfusion events because of the apheresis platelet breakdown.

Because really there are only 22, 23,000,000 events of transfusion.

DR. WHITAKER: That's a good point. It does get confusing, so I will.

THE CHAIRMAN: Dr. Ison?

DR. ISON: I have a question going back to the issue with the under reporting for TRALI. Do you think that's under recognition or under reporting? And if so, why?

DR. WHITAKER: I think it could be either one depending on the hospital.

It's -- I think that it could be -- as we have developed the TRALI standards, that the recognition of it has become more common.

So I would expect that it is more likely

to be that as -- let's see, this was 2006 data. So

this is the time when -- that period was the time when

it was becoming more common to be recognized.

And I would expect that in 2008 we would see a completely different snapshot than we did in 2006. So the 2006 I would see as a transition year, and 2008. So I would say that would be both under recognition and under reporting.

2008 I would expect to see an improvement.

THE CHAIRMAN: Additional questions?

Comment from the floor?

PARTICIPANT: (inaudible). Did you all cross reference those 71,000 adverse transfusion events with the adverse events reporting system, AERS, to see if they lined up?

DR. WHITAKER: No, because it's all confidentially reported, so we can't -- the data is not visible to the government.

PARTICIPANT: So it doesn't give us a picture how AERS is functioning compared to what you have?

DR. WHITAKER: No, that's correct.

PARTICIPANT: We would hope that happens

at some point.

DR. WHITAKER: Well, the hospitals when they report are given a confidentiality assurance that their identities are protected when they report that.

So, at this time we are prevented from doing that.

PARTICIPANT: Thank you.

THE CHAIRMAN: Comment from the floor.

Dr. Davey.

DR. DAVEY: Barbee, thanks for the nice presentation. One question.

You noted that the available red cell units were 15,688,000, I believe, and transfused units were 14,400,000. That's a pretty big cushion. And it seems to me that that's a lot more than we can attribute to inventory or out dating. It seems that number is kind of large, in my estimation.

Do you have an explanation for that?

DR. WHITAKER: Not at this moment, but can

I talk to you about it afterwards?

DR. DAVEY: Sure. Okay.

DR. WHITAKER: We just recast those numbers, so we're looking at exactly where that might be.

DR. DAVEY: You appreciate the difference there, though?

DR. WHITAKER: Yes, I do.

DR. DAVEY: Thank you.

THE CHAIRMAN: Dr. Sayers, question, comment?

DR. SAYERS: No, just a comment.

This has to do with that apparent cushion difference between collections and transfusions. And I think we could run the risk of lulling ourselves into a false sense of security if we assume that one and a half million is an inventory that we could usefully distribute and utilize.

If our own experience is anything to go by, a significant percentage of that excess cushion inventory happens to be group A, which is not exactly

a product hospitals are enthusiastic about.

DR. WHITAKER: Thank you.

THE CHAIRMAN: Dr. Holmberg?

DR. HOLMBERG: Yes. I just want to make the comment concerning the survey. As Dr. Whitaker mentioned, this is the second survey sponsored by Health and Human Services.

And we have all intentions to go forward with the third one. We looked at this very seriously. We hope that it is giving the blood community the data that they need, and hopefully that it is useful for benchmarking and will also help with the various biovigilance activities.

Saying that, I just would encourage the committee to take a look at the survey and it is both on the portal -- I should say it's in numerous places. It's on the web portal for the committee, and it is also on our web page, as well as being at the AABB.

Once again, this data does belong to the American people.

THE CHAIRMAN: Question. One benchmark

that is an important benchmark is that against other nations. We know that if one looks at plasma, RBC

use, et cetera, the per capital usage, it varies.

Is there any plan to have a direct comparison?

DR. HOLMBERG: Very good question, Dr. Bracey. One of the goals of this survey is so that we can also report back to WHO. And in reporting back to WHO, we can do some of that comparison.

The problem that we have at the present time is the timing cycle and also I have to say that we have not had the numbers, nor the mechanism to report to WHO.

And it seems to have gone -- the request for the data comes through a different avenue.

So, we are trying to improve that, and hopefully within the next couple of cycles we will be on the same cycle with WHO so that we can do some comparison.

THE CHAIRMAN: Dr. Triulzi?

DR. TRIULZI: Just one quick question,

Barbee.

With the web based survey, will you be

able to survey then 100 percent? Or what is the limitation that requires that you do sampling?

Because one of the things I notice is the difference in pediatrics is a significant one because of the allocots per unit are far greater. You may have eight allocots or ten and so it's going to skew your transfusions and red cell ratios and the number of units per patient.

And one way to deal with that is if you're doing 100 percent sampling each time, then you're not going to get the wide variations in the pediatrics.

So with web based then, can you do 100 percent sampling?

DR. WHITAKER: Yeah. I don't -- I actually don't -- I mean, we've historically sampled rather than to hit 100 percent. And I'm sure that it was a limitation due to costs of mailing and production.

So, if we have the ability to do it on a

web based system, we ought to be able to do 100 percent.

THE CHAIRMAN: Dr. Holmberg?

DR. HOLMBERG: I just want to followup on several comments that people have made.

And that is that Dr. Whitaker mentioned that it was -- there is a certain amount of confidentiality with this. We did have to go through OMB, Office of Management to get approval.

And part of that is the confidentiality and also making sure that we didn't put identifiers with the data.

So, we do have the OMB clearance now for three more cycles. I make that mention because since we already have the OMB clearance, we hope that we will be able to turn the data around faster so that there can be greater comparison.

THE CHAIRMAN: We'll move on to the next speaker and then continuing the reports. We'll have an update on donor biovigilence. And this will be by Dr. Michael Strong. He's the Chair of the

Biovigilance Task Force and Steering Committee.

And he's well known to many in blood

banking, having had a leading role in many activities, serving as the COO of the (inaudible) Blood Center, and past President of AABB.

Dr. Strong.

DR. STRONG: Thank you very much.

Well, it's a pleasure to hear the term biovigilence showing up so frequently now. It was probably a term that was unknown in years past.

The -- this committee, in fact, adopted within their strategic plan in 2006 the need for a biovigilence network and coincidentally the AABB also put into its strategic plan in 2006 the development of biovigilence.

Now, we termed it biovigilence -- obviously AABB is more interested in the hemo part of biovigilence, and focused on that.

But in partnership with HHS, we have incorporated the term biovigilence into the activities.

In 2006, we also established actually
several components to the biovigilence efforts,

including a recipient hemovigilance portion, donor hemovigilance portion and concurrently the CDC in cooperation with UNOS, established a task force for development of an organ and tissue biovigilance effort.

I'm going to talk to you today about donor hemovigilance. But I did want to point out that there are working groups in all of these areas that are in -- essentially in parallel tasks.

And include working groups with content expertise in the development of these database programs.

The AABB has a working group in the recipient hemovigilance portion that is now well on its way. The training for pilot sites occurred, in fact, this month. And pilot testing will begin beginning in January.

On the tissue and organ side, the pilot testing has been completed actually in August and

reporting is currently underway.

So today we'll focus more on the donor

side since that was the task at hand.

And that also includes a working group made up of content experts from various organizations, the American Red Cross, ABC, hospital representatives, et cetera, working on development of donor hemovigilence.

Now, actually in comparison with these other components, the U.S. efforts in hemovigilence are at least comparable if not ahead of the rest of the world, unlike the recipient hemovigilence program which the U.S. is probably ten years behind in.

The current efforts really include individual publications which occur in publications such as Transfusion by various authors often from programs such as the ARC hemovigilence program, which has been active for some time, and a more recent development by ABC in the establishment of a data warehouse for collection of donor events through the independent blood centers in the U.S.

Now, one question that comes up, of course, is why do we even want to do this? In fact,

when we first discussed this, there was clear reason to establish a recipient hemovigilance task force.

But many organizations, because they were already collecting this data, there was some question about whether there was a need to do this.

But, in fact, after several discussions, it was quite clear that if we do have an aggregated data collection system in the U.S. for national statistics, it gives us the opportunity to use and make comparisons with a number of procedures, technologies and provides us with the ability to do robust analysis and hypothesis generation.

Because there are multiple approaches to donor safety, interventions that can reduce reactions and improve donor satisfaction would certainly be nice if we could have the ability to collect the data and actually make direct comparisons between different procedures.

The other component of this, of course, is

that with a large database it increases our power. So
for rare event pickups, the larger the database the

better.

We also, of course, want to encourage both in terms of standard setting and regulation, evidence based methodologies. And that has been a bit of a problem in the past. In fact, AABB itself has been criticized for putting in place things like moving to mail plasma collection, because we really didn't have any evidence in this country that that would make an improvement.

And it was based on the fact that the U.K. had demonstrated that moving towards reducing HLA antibodies in plasma might reduce the incidence of TRALI. Perhaps in the next survey we'll see whether or not that intervention actually has taken place, has had a positive outcome.

But without a hemovigilance program we really have no way to test that.

Now, currently, as I've already mentioned, the donor hemovigilance piece is make up of a variety

of approaches, including the independent
organizations, the American Red Cross, hospital based

programs, of course we have the plasma collection through PPTA.

And these all provide valuable information, have generated multiple publications and contribute.

But we don't have the national approach. So currently, if we use the Rubik's -- if we use this little cube event as a demonstration. The big challenge was, can we come to an agreement on common definitions in order that aggregate data in fact will be comparable and that we can provide, therefore, a standardized logic to arrive at an ideal state and thus be able to prepare intervention testing and data collection that will have some value.

So the biggest challenge, I think, for the working group has been can we agree on definitions. Now, one would think that that might not be such a big task. But, in fact, if anybody who's ever tried to sit down and get people to agree on definitions have

tried that, they know that that actually is probably
the biggest challenge. Can we ever agree on anything.

And for that reason, we've also tried to harmonize these definitions globally, because that is an effort that's ongoing as well.

This is the working group, the team that's been working on this now for about a year. It's chaired by Peter Tomisulo from BSI, but you can see from the makeup of this working group it includes the independent blood centers, the American Red Cross representation, we have hospital based people on the working group. For example, Jim Stubbs from Mayo. The DOD is involved, PPTA actually, this is perhaps one of the first times that we've gotten the blood community and the plasma community to work together.

And we've incorporated as well representation from the European hemovigilance network to try to learn from their experience, incorporated under the funding of HHS and AABB.

So, we have tried to, as I mentioned, incorporate the information and the baseline

definitions that have been developed in the European
hemovigilance network, and to learn from how -- and

the mistakes that they've made what we can learn from them in incorporating basic definitions in order that the data can come together.

And, of course, there is a great deal of experience. As I mentioned in the U.S. we probably are at least equivalent or if not ahead of the rest of the world with existing hemovigilance programs such as the Red Cross.

So this was the -- essentially a road map that was established early on. We want to use internal reaction codes and data elements that have already been developed through existing programs, either through local blood center definitions or our national programs like the Red Cross.

We want to have the ability to map between organization and across organizations to achieve national reaction codes. And perhaps the biggest challenge has been to collect denominator data.

This would put us actually ahead of the

rest of the world because denominator data, of course,
will allow us to actually calculate rates, which has

not been possible with the data that's been generated elsewhere.

This also, of course, would allow us then to give the ability to analyze, to generate trend charts, bar charts, et cetera and advise intervention strategies.

The mid-term road map includes adopting standard elements in reaction definitions, and that's been the challenge of last year.

Collecting demographic data on all donations and denominator data, of course, gives us greater access to statistical approaches and eventually to design and analyze interventions across systems to improve donor safety.

Now, I'm giving essentially a 30,000 foot level breakout of the kinds of things that are incorporated in what's been developed thusfar.

You've already heard from Barbee some of the reactions that are being reported through the

National Blood Utilization Survey.

So these are general categories such as

allergic reaction, including anaphylaxis, local and systemic reaction, local injuries related to venipuncture, including arterial puncture, hematomas, nerve irritations, vasovagal reactions including injury, loss of consciousness of both complicated and uncomplicated, and even pre-faint data.

And, of course, a separate category which includes apheresis which would include air embolus, citrate and hemolysis events.

So these are all being incorporated in the working groups analysis.

At the same time we've been working with a contractor funded through HHS to develop the database system. I'm going to show you now a few screen shots of the kind of information that's being collected.

This is through KBSI, the contractor that's working on this program. And you'll see from this a little bit more detail of the kinds of things that we're capturing.

For example, here is race, ethnicity,
birth dates, donor I.D.s, et cetera.

The donation information is to be entered including height, weight calculations, collection sites, et cetera.

One of the concerns, of course, in all of this is maintenance of confidentiality, a point that has already been brought up. And we have a little bit to say about that as well.

Here are some additional screens that include here -- I don't know whether you can see these or not -- but include things like convulsions, hypotension, light headedness, loss of consciousness of less than or greater than 60 seconds, et cetera.

So these are all definitions that have been incorporated in the discussions.

Report options are also available through this reporting system, including -- we've divided the country up into U.S. PHS regions, including organization distribution and, of course, sites, demographics.

And there will be drop down menus that
allow choice of the various reaction types, including

the age break outs in much more detail.

This, of course, then allows us the capability to do various kinds of reports and analysis. These are hypothetical reports just to give you an example of the kind of things that will be available.

So, this one shows vasovagal reactions at different locations to see whether or not we can differentiate reaction rates from one place to another.

The associated characteristics with these and the interventions that may in fact come out of this such as race, youth, weight, body mass index, which is one that has been recently published as being important, blood volumes and first time status in terms of reaction rates are also going to be included.

It's actually quite interesting, just from a personal perspective, the differences between centers and how they approach interventions and

dealing with donors.

In Seattle we have been, for example,

collecting blood from 16 year old donors for probably 30, 35 years.

And only recently have other states picked up on this. And they did this on the basis of evidence that had been provided from Seattle to states to justify the use of 16 year old blood donors.

Last year at the annual meeting, there were a number of presentations about the discovery that there is an increase in reaction rates amongst 16 and 17 year old donors. This was of no surprise.

But quite obviously, a lot of interventions and protection of these donors had not been made, so these rates were actually quite high and surprised everybody.

For those of us that had been doing this for a long time, it was not a surprise. But the question is, what interventions could be put in place to reduce those reaction rates.

And these interventions are kind of

included here, such as, you know, increased hydration,
more monitoring at the canteen level, putting the

donors after they have donated on mats in the recovery room, things of that nature to reduce reaction rates.

These are all data that have not been comparable because we haven't had the ability to collect the data from place to place.

So this system should allow us to do that. And, of course, ultimately we hope to improve outcomes. But, of course, we're still in the development category.

So it's way too soon to say that this is in fact going to happen.

Now, just to give you the most recent update. One of the things that has been high on the list of priorities for AABB has been a mechanism to protect centers who provide data from disclosure.

And that has been possible through this patient safety organization public law that was passed a couple of years ago, but has only been put in practice recently.

So this is in response to patient safety
problems that have been identified. And this law

allows organizations to collect and analyze patient safety data to provide the ability to improve quality and encourage the culture of safety, including confidentiality and security of the data.

So, this is the most recent update as of last Friday. AABB has received the Patient Safety Organization status, which gives us that protection.

I think we were going to have a lot of difficulty with people participating in a program like this if they couldn't be assured that they had some confidentiality.

And so that, in fact, has taken place. And we look forward in great anticipation to getting this system off the ground.

So, that's it.

THE CHAIRMAN: Thank you, Dr. Strong.

Question regarding the great success that you've had in bringing in multiple parties to participate in this endeavor.

So, at the end of the day -- currently I
should ask you, what percent of the blood supply in

perhaps plasma donor engagement, what percent is currently represented in this collaborative effort?

DR. STRONG: Well, in terms of the working group, it's -- working groups, I guess you could say it's 100 percent, because we have representation from each of these areas.

That doesn't, of course, guarantee that 100 percent of blood collectors are going to participate when the system is open for participation.

In fact, that's one of the challenges that AABB is undertaking, is to try to recruit programs to participate ultimately.

The current effort would be to have these definitions put together, published for responses, and to pilot the activity, of course, to shake out the bugs, make sure that they work before it goes national.

THE CHAIRMAN: Dr. Benjamin?

DR. BENJAMIN: Dr. Strong, as you've

mentioned, the American Red Cross has a donor

hemovigilance program that has reported its data in

our 35 blood centers using a uniform set of procedures and training of staff.

And a major -- I think a lot of blood centers would like to use this sort of data to benchmark their own experience. But we have found something like a five fold difference in reported adverse events between our own blood centers with uniform protocols and are working at trying to understand this.

Does this -- does the donor hemovigilance group or the biovigilance group have any approach to try and standardize reporting such that the data can be used to benchmark between blood centers?

DR. STRONG: That certainly has been one of the issues is, one, getting to common definitions and then getting to common reporting.

Because if we have different definitions, the reports aren't going to be really much value.

DR. BENJAMIN: The point being that even

with common definitions in a single system like the
Red Cross, we have yet to be able to adequately

address the issue which we believe is mostly reporting and not significant or major differences in actual adverse events.

DR. STRONG: I think this is going to be an evolution. It's going to take us time, and it remains to be seen to what extent we get harmony and global acceptance of these definitions and interpretation.

THE CHAIRMAN: Question from Dr. Epstein or comment?

DR. EPSTEIN: Thank you. I want to both share a comment and ask a question.

This comes back to the question that Corey Dubin asked of Barbee Whitaker about comparing the reporting that occurred through the AABB survey to reporting to FDA through the AERS Medlock system.

I think there's a very important point to understand, which is that the FDA reporting is identified reporting as opposed to the reporting that

we're hearing about in the recipients which is through
the CDC and the NHSN program, and what we just heard

about the donor reporting system which is
De-identified.

And the current state of affairs is that
FDA only requires reporting for deaths. There's also
required reporting by manufacturers for device
failures, defects, you know, non-labeled drug
toxicities.

And then there's also required reporting
of biological deviation reports, in other words, that
there was something wrong with the product, it didn't
meet the quality standards.

But that leaves out a very, very large
domain of medical adverse events which are currently
not required reporting.

FDA did publish a proposed rule on safety
reporting which, when finalized, is likely to have the
effect of expanding required reporting to include
serious adverse events. In other words, that's under
discussion through the proposal.

So what I want to focus on is building the link between the reporting systems that are being

developed through de-identified mechanism, which of course, precludes specific followup.

You know, one of the most powerful effects of identified reporting is you can drill down, you can get more information, you can go back, you can talk to people, you can look at records.

So what this reflects is the difference between a surveillance system, which is what's being built -- in other words, you have certain things that you're looking for and you track their rates, and a sentinel system which is better able to pick up the unexpected and enable you to investigate it.

So what FDA is doing in cooperation with the developers of the biovigilance network is putting forward a concept that we try to embed, a mechanism to enable the user of the system to send information either because it's voluntary or mandatory to the FDA without needing to go to a separate system.

And this is being engineered in the NHSN.

It's not at the present time in the pilot, but it is
on the drawing board for the ultimate system.

So, again, just to clarify the point. The end user that participates in the NHSN would identify an adverse event, would be able to report it, de-identified through the NHSN, but would have the option to send that same report identified to the FDA.

And then that could either be a voluntary report to AERS or it could be a mandatorily required report, as I said, perhaps ultimately under a new regulation.

So now my question, which is whether a similar thing is being contemplated in the donor biovigilence report.

DR. STRONG: Actually in all of these systems there's been lots of discussion about how do we facilitate reporting because obviously everybody has got a big enough work load as it is. They don't want to have to go through three different systems to report the same thing.

So, there have been discussions about to

develop common language in order that a single report
could be generated from one report to multiple

systems.

So, for example, the Red Cross system, they have a reporting system, they would like to be able to simply push a button and have the report go to the national system.

That's part of the challenge will be interpretation and mapability of different types of reactions to a single reporting system.

So I think that's all in the works. And, of course, with any of these the challenge is to develop cross platform compatibility. So we're also working with various software vendors who provide the software to the centers, for example, for collection of adverse event reporting that they can build interfaces into these national systems as well.

So, these are all parallel activities that are going on. It's actually quite an immense endeavor to accomplish all of that.

And as you point out, we've certainly kept

in mind the mandatory reporting requirements. We'd
like the ability in any of these systems, whether it

be recipient donor or organism tissue, the ability to have those reports generated at the same time.

THE CHAIRMAN: So at the end of the day, I guess, if I get this right, there may be really two approaches, and one would be that the biovigilance network would have a -- sort of a global intervention in the sense of looking at the data, recommending to folks in the field various new interventions.

Whereas, it would also likely be that the FDA would have an individual facility approach drilling down and digging in.

So there would be an aggregate approach as well as an individual center approach at the end of the day.

DR. STRONG: We will have the ability to drill down. It's simply a matter of protecting the confidentiality.

So these working groups will also incorporate -- it's not particularly a working group

now, but at some point content experts will have the ability to drill down into these -- into this data and

actually single out differences.

We just can't make that public kind of report, because of confidentiality issues.

THE CHAIRMAN: Thank you. Additional questions or comments?

Oh, Ms. Whitaker. Dr. Whitaker, I'm sorry.

DR. WHITAKER: I just wanted to respond to Dr. Benjamin's question about the differences between reporting across different facilities.

We also anticipate that it's an evolution. The reporting -- the consistency of reporting will probably take years, three to five years, before there's consistency seen across the system.

And while there will probably always be differences seen amongst individual facilities, there will be a maturation process among the different facilities as they grow into the system and learn to adopt the definitions.

So we don't expect that even in the first
few years that we're going to see consistent reporting

across the system. So, it will be a while before rates really reflect the national rates of adverse reactions.

DR. STRONG: Yeah. Just to add to that. I think if you look at the experience of other national hemovigilance reporting systems, it takes about five years to get to a consistent reporting level.

There's always a growth curve. Part of that is recognition, part of that is the ability to understand what reactions should be reported.

I think in this country a good example would be Taxo, we get very few Taxo reports. In fact often we recognize Taxo through a reported TRALI. And part of that is just education.

So, a huge portion of these efforts are going to have to be educating the medical community, and that's not just the transfusion medicine medical community, it's also our partners, anesthesiology,

acute care, et cetera, to help us recognize these events and get involved in the reporting process.

THE CHAIRMAN: Thank you. We are a bit ahead of schedule, but that's a good thing.

Why don't we take a 15 minute break and reconvene at 10:30.

(Pause)

DR. HOLMBERG: --progress that we have made, especially in data monitoring for the blood centers and hospitals.

I hope that all of you appreciate the presentations that have been made so far. I think that it really shows, and what I was trying to do is to really impress upon you some of the influence that this committee has had in various outreaches to other organizations, agencies within HHS or even some of its stakeholders.

As I have done in the past, all the recommendations are posted on the web-site. I have gone back and looked at the recommendations from 2000 to 2008. And if someone would like to have these in

more detail, I can provide those to you.

But all of our recommendations are posted

on the web-site which is listed there and also the National Blood Collection and Utilization Survey is also at that web-site.

The Advisory Committee has been -- has been organized since the late 1990s, and we're probably on our 12th year. This is the 35th meeting of the Advisory Committee.

And in looking at the recommendations since 2000, year 2000, there has actually been 45 different recommendation topic groups. Now, these are areas where I've sort of clustered some of the recommendations because we have a lot more recommendations, if we were to tease each one out.

But I think what's very impressive is that out of those 45 recommendations, there have been over, well over 110 actions by the Department and the operating divisions.

And when I refer to operating divisions, I am referring to the Public Health Agencies, CDC, CMS,

FDA, CURSA, NIH and also NHLBI, which is one of the institutes within NIH.

In just going back to 2000, I thought that I would only take the last two years and look at some of the recommendations.

The committee accepted -- made some recommendations regarding 2000 -- I'm sorry, biovigilence. This was based on the recommendations of 2006, August of 2006 on biovigilence.

And at that time there were several questions that were asked in May of 2006 by the Assistant Secretary for Health, Dr. Agwanobi, concerning the master strategy of biovigilence.

And also how would we put this together for blood organs and tissues.

Just to give you some of the action that has taken place on that, I would like to let you know that we did have the Charter renewed. The Charter for this committee must be renewed every two years. It's under sunset laws, and that if it is not renewed, the committee goes away.

And the committee was renewed in 2008 by
Secretary Levitt. And in support of the biovigilance

activities, the scope will remain as far as transfusion and transplantation safety.

Moving towards the biovigilance with the private sector. We have, as you have heard already this morning, we have moved ahead with the blood and plasma donor adverse events.

And that has been ongoing since last year. We also, in that blood plasma donor biovigilance, we have leveraged the opportunity of the software developer with the DOD. So, as Dr. Strong mentioned earlier, this was being developed by a contractor within -- or for HHS.

The blood recipient aspect, which has already been also been mentioned, is built and is being piloted started in January through the NHSN system.

As Dr. Strong mentioned, the TTSN was piloted in August of 2008 and at the present time we are moving forward with our gap analysis within HHS.

In August of 2007, we also identified the
ESA, the erythrocyte stimulating agents and the claim

that if CMS changed their criteria for reimbursement that it would have a great impact on transfusion practices.

This is another reason why we do the bi-annual survey. And I just want to report here that we have had some discussions with CMS regarding some additional data collection and analysis of some of the data.

In August of 2007, we also -- we had recommendations from the committee to establish sufficient hospital and blood center participation and inventory reporting.

And also to develop the comprehensive model to address and respond to the needs of blood and related critical matters in various situations and to work with the blood community to define shortage scenarios that would require alternate strategies and also to support operational research to characterize and recruit donors who do not routinely donate.

At the end of my presentation, I will be
giving you an overview of the basis system, but just

to highlight. Basis is our blood availability safety information system.

We have 270 hospitals that have agreed to participate, and approximately 65 of these 270 hospitals report on a daily basis.

We also obtained the blood availability through an aggregated report of ABC and ARC facilities through the AABB.

And I will explain a little bit more about the basis system.

We also have been very active with the biomedical advanced research and development authority, which is part of the Assistant Secretary for Preparedness and Response.

And Dr. Nemo and myself are co-Chairs of that blood and tissue working group. We have done extensive modeling with the ten kiloton bomb, radiological situation.

And I presented a little bit of what I

could present to you, I believe it was in August of
2007. We have refined that model and hopefully in the

future I will be able to come back to you as far as some of the requirements from the model. But at the present time, we're still working through that.

We have also, as far as the scenarios, of critical situations, we continue to work with the AABB task force. We've done quite a bit with them on various events throughout this last year.

Primarily, Topo four, but also with the political conventions, we were very active this year and in anticipation for any blood needs that might take place.

Topo four included Guam, Portland and Phoenix. This was a radiological situation. And it was very interesting, also, that Portland and Phoenix had some of our regional testing locations.

So it was very interesting to follow how that would be impacted, and also some of the requirements there.

The disappointing factor as far as Topo

four was that I don't believe the numbers were
adequately represented, as far as the number of

patients that would be coming in.

So in the future I think we need to do a little bit better job with some of our scenario planning and exercises.

But I wanted to give you a highlight there of some of the followup on the recommendations on 2007.

In January, 2008, we dealt primarily with the pathogen reduction technology. The committee recommended that there was an urgent development for -- urgent development of safe and effective pathogen reduction technology and implement as available.

Provide resources to overcome current barriers, insure adequate safety monitoring of pathogen reduction technology products post marketing, and to insure other efforts to improve blood safety -- that blood safety efforts were not compromised by the PRT efforts.

In your package, there is a letter from

the Assistant Secretary for Health, Dr. Garcia, dated
July 14th, 2008.

In that letter it does say that the Department fully supports cooperative efforts with public health agencies and stakeholders.

That the Department is committed to providing regulatory, scientific and surveillance advice. And also NHLBI has met with its subject matter experts to review status related research, and also potential status forward.

The Assistant Secretary also made mention that funding was always a challenge, but he also recognized that there could be some cost neutralization or even cost reduction or avoidance with pathogen reduction technology.

I would like to say that we have made more progress on pathogen reduction, but I think that there's a lot more that we can do. I think this has laid the groundwork and working with NHLBI and some of the other stakeholders, I think we will make progress.

We are looking at different things as far

as within the Department, looking at a task force to actually move this forward within HHS.

In May of 2008, the recommendation was for additional measures, whether that be prevention, detection or pathogen inactivation. We adopted to reduce the differences in safety profiles between whole bloods, dry platelets, and apheresis products.

And also that the Department should monitor the progress, the current status of platelet availability and potential for meeting future needs.

Once again, I will refer back to the July 14th, 2008 from the ASH on pathogen reduction technologies. And I think once again we are moving in that direction.

Once again, basis, as I'll demonstrate in a few minutes, has the capability of monitoring the platelets -- the platelet availability. We are also working within the Assistant Secretary of Preparedness and Response and BARTA to identify different technologies that would help the country be better prepared.

Also, I want to emphasize that I believe
at the last ASH meeting, last week, that Dr.

Schlechter from Pujit Sound (phonetic) presented some data from the platelet dose to prevent bleeding in thrombocytopenic patients.

And I think there's more to come out on that, but definitely there's some progress made there and some preliminary data as far as the ideal dosing or potential dosing for patients.

In May of 2008, there was also a recommendation on clinical outcomes as a result of age of transfused red cells.

There was also a recommendation on the optimum blood transfusion practice, a call for research in clinical practice guidelines.

NHLBI has moved forward with their transfusion medicine and hemostasis network and the red cell storage age study, RCSAS, it will be working with taking a look at cardio -- patients from cardiac surgery, and also looking at the multiple organ dysfunction scores post seven days.

Also, and I might ask Dr. Triulizi to
comment on this since he's a little more familiar with

what RCSAS is doing. But there is collaboration with the cardiothoracic surgery network.

Dr. Triulzi, do you want to say anything?

DR. TRIULZI: At our last meeting, we heard a presentation by Marie Steiner on the design of that study.

And in order to facilitate getting as many patients as quickly as possible, we approached -- the transfusion medicine network approached the cardiothoracic clinical trials network, there's a separately funded network -- and their network agreed to participate.

So it adds eight or nine additional sites to the TMH site. It's a large study and it will take about 1500 patients. So this we felt was a good way to get the study done as soon as possible.

And interestingly, one of the sites is Cleveland Clinic, the ones the published the paper in New England Journal. And they were very interested

and willing to participate in the RCSAS study.

DR. HOLMBERG: The clinical practice

guidelines, the only thing I can say as far as that is that, you know, we have been working with the Joint Commission on blood measurements, parameters. And those have been posted. There were comments received by the Joint Commission and there are three representatives from the government that are on that panel for the blood measurements.

Let me turn a little bit to our way that we are monitoring the blood supply within the country. I think it's been a few years since we gave you an update on our blood availability and safety information system, basis.

This last couple of months, we have moved -- we have migrated the server to a third party hosting for protection of the critical infrastructure information and to give those reporting facilities protection under that PCII act.

We also have changed the site location. The site location is now referred to as

usbloodreport.net. If you are enrolled, you can go to
that.

If you are not enrolled and you want to report a shortage, you can also go to that and report it. And I'll show you in a few minutes how you can do that.

It has the capability to record shortages both for participating and non-participating hospitals. And that's what I'll show you in just a minute.

As I mentioned already, we have 65 facilities that are reporting on a daily basis. We do get an aggregated report from the Americas Blood Centers and also the American Red Cross through AABB. And we monitor the availability from the donor centers through that.

This is sort of -- I don't have a screen shot of the actual web page, this is sort of a reproduction of it.

But you can see on one side of the screen, on the lefthand side, there is a sign in to basis.

And with the sign in to basis is for anybody that is
assigned a password and -- user name and password.

And this is for a facility to report in.

On the righthand side you can see that there is a report, open issues. And that is for anyone to go and to report an open issue.

This could be a clinician, it could be a consumer, it could be someone working within a facility that could go in and say, we're having problems with availability of a test kit or reagents or blood supply, whatever it could be. And they could report a shortage there.

Let me move on to some of the reports that we are generating. This is from the aggregated report, from the American Red Cross and the ABC. It's aggregated by the AABB.

And you can see that we're in a very good condition right at the present time. But don't get your hopes too high that, you know, we've really conquered the recruiting efforts and everybody is doing great.

As Dr. Sayers mentioned, I think that we
might be lured into a false impression here. But over

the last couple of weeks, we have seen an increase.

This -- these are data from December 10th, just last week. And you can see the Group O positive blood, we're at almost an eight day supply.

The week of December 3rd -- and we get this report every Wednesday. And December 3rd, it was actually at eight days blood supply.

You can see that the O negatives are at 2.73. And as you go down the road, down the map here, you can also see that AB positives are at a 23 day supply.

So this is basically what is within the blood centers as far as days of supply.

Here's another representation of what we have as far as within the U.S. blood supply. And then breaking this down using some of the constant numbers established by the 2006 inventory survey, you can see the 7.74 days and the amount that that represents within the blood centers.

And then also an estimated amount based on
what the blood centers estimate that most hospitals

have an eight day blood supply.

So, these are all estimated numbers there and estimated U.S. blood inventory is down at the bottom in the righthand corner.

Now, this data come from the aggregated report that AABB provides to us.

If we take a look -- this may be a little bit more difficult for you to see -- but this is the aggregated report of the nation.

We have the blue blocks are the red blood cells, and the red is the moving average. And then the yellow block is -- are the platelets, availability of the platelets and the light blue box is the moving average.

So you can see that the moving average is pretty stable here. What you see at the end is a trailing off of reporting at some facilities when I took the report on the 11th, they had not reported completely.

Some facilities may report only once a week or a couple times a week. So we see a trailing

off here.

But generally speaking you can see both the red cell inventory and the platelet inventory.

This is the group O blood cells for the nation. The moving average is the steady line, the yellow here is the O positive. The red is the O negatives and the light blue is the moving average.

So you can see that there's a little dip here. I think this was the weekend of the 3rd and 4th. Now, these are primarily hospitals that are reporting this.

And you can see that their inventory dropped off about, I believe that that is the December 4th, is the meter there.

And the same way with platelets.

We also did a representation of the blood supply in a red, yellow and this should be green. You can see that we're doing pretty good here. Again, this is the trailing off of the reporting.

And this chart is the platelet supply.

It's giving you a false impression here. We need to

go back in and change some of the parameters because the red is defined as less than two days supply of platelets.

And so we need to look at this because most of our hospitals will only have a two day supply of their platelets based on the bacterial testing.

So we need to look at that a little bit better. But you can see that we do run quite a bit in the two day supply range.

Now, this really shows you a little bit more of the actual shortages. This is a report of the inventories of blood product below the minimum established level for the hospitals. And you can see that these are the number of facilities -- at one point there were nine facilities on the 5th of December that reported that their inventory was below minimum.

We can go in and take a look at each one of those facilities to find out specifically what took

place there and try to analyze that a little bit
better.

But you can see that here we have very few reports of shortages of their hospital inventory.

Now, this is orders not filled. You can see again on December 4th there was the highest quantity of red cells not being filled, orders not being filled and also platelets.

And then this is the blood products purchased from an alternate supplier. This is a good indicator whether there's a problem with the local supply of products.

And you can see here, platelets once again going into multiple suppliers for the platelets.

And so that's just an overview of what we're doing within our basis system. And we are monitoring both the red cells, the whole blood red cell inventory and then also the group O positive and negative and also the platelet inventory.

Are there any questions? Yes.

PARTICIPANT: So there were three other

recommendations that were passed at the last advisory committee related to organ transplantation. One was

on testing, one was on infectious and malignant blood transmission and whatnot. Where do we stand on those?

DR. HOLMBERG: That's a good question, and I apologize, I thought that that slide had been in there.

What we have done is we have met internally with the Blood Safety Council, which is composed of the senior leadership, and we have discussed that with HERSA and FDA and how we can get better reporting on those.

So, you know, we don't have anything concrete at the present time, but it is on our radar screen.

THE CHAIRMAN: Dr. Epstein?

DR. EPSTEIN: Jerry, you know, all of us have wanted for years to have this kind of on-line rapid reporting of the situation of blood supply and shortage monitoring.

But the question remains open whether

anybody is utilizing the data. Do you have any
comments on how the data are being used?

DR. HOLMBERG: Well, the data are being sent to senior leadership within HHS and the operating divisions.

It is being used to monitor, for instance, at the present time just trying to analyze why we have a surplus of blood. At an eight day supply, I think that's what we all dream of.

And we have used that data to try to understand where we are.

I think that in conjunction with other reporting, you always have to take a look at what's the total picture. And I think that one of the things that we have seen most recently with the increased days of supply has also been the American Hospital Association's report on the decrease in elective surgeries.

And, so, we have a situation because of the economic times impacting the elected surgeries. So, we are seeing a drop there and consequently

there's a little bit more blood available.

We are looking at that as far as potential

recruiting, you know, how -- is there a need for a national recruiting. And also what the data is being used for are primarily -- I can say within the last couple of days, we've actually looked at it within the Assistant Secretary for Preparedness and Response and BARTA in determining what the gaps are between the capacity and the actual.

I have to mention that this report does -- I said it does go to the senior leadership. It does go to the Assistant Secretary for Preparedness and Response and it is posted within the Secretary's operation's center, so that at any one day and time it will be visualized what is our daily blood supply.

THE CHAIRMAN: Is there a plan to interface with the public? For example, if there's a severe blood shortage, rather than to have reports to the new media, et cetera, to use this as a basis of information to inform the nation about this blood supply?

DR. HOLMBERG: Yes. And what we have
built into the basis system is the capability to add

facilities on the spot. So that if we have a situation in a major metropolitan city we can add additional places that would give us immediate reporting that could report.

What we really tried to do with the basis program is to limit the number of data elements. In contrast to what New York State has with the multiple data elements, we only look at the total inventory and O positive, O negative and also the platelets, whole blood derived platelets and apheresis platelets.

To answer your question a little bit more, not only do we have the capability of enrolling a location, a geographic location in so we can get what is the actual situation in that area, but we also have built in within basis to give the State Health Department the capability of seeing what's happening within the State.

So, there's a state analyst privilege that the State Health Officer can either have personally or

can give it to someone else to monitor what's
happening within our state.

THE CHAIRMAN: Thank you. Dr. Sayers has a question or comment. Dr. Sayers?

DR. SAYERS: Thank you, Dr. Bracey.

Jerry, I was just interested -- the 65 hospitals, do they have a common definition of shortage? And what is that definition?

DR. HOLMBERG: Well, that's a good question. And as far as their shortages, they actually put that definition into their profile.

And so we ask them specific, what is their inventory level for a shortage. And we also ask them questions like who do they consider to be a platelet dose.

And so that we get an overall feeling for what is their profile for that individual hospital.

THE CHAIRMAN: Dr. Ramsey?

DR. RAMSEY: Thanks, Dr. Holmberg. This is always very interesting to hear and we appreciate the -- all of the effort that goes into this from all

of the participants and the coordination of the data.

I had a question about the -- one of the

data elements is the estimated hospital inventory at a constant eight day supply. Is that -- I realize that the hospital inventory is very difficult to get at currently.

Is that a sort of fixed assumption for working purposes or how does that work?

DR. HOLMBERG: That is a fixed assumption that is provided to me by the blood suppliers. And they have agreed upon that.

We need to verify and validate that number. I understand in the previous article that appeared, I think in 2003, on the predecessor to basis actually said that there may be a ten day supply of blood within the hospitals.

I have no way at the present time to validate that. But I'm in hopes that maybe through the basis system and also with our national blood collection utilization survey to be able to determine is this really an adequate number.

That's why you saw up there that this is
an estimate.

THE CHAIRMAN: Any other questions or comments?

If not, we'll then move on and begin to --
Dr. Donald Wright is here. He is the Principal Deputy Assistant to the Secretary of Health, and he will review the committee charge and have recognition of committee service.

Dr. Wright?

DR. WRIGHT: Thank you, Dr. Bracey. Let me say that it's a pleasure to return to this group. I've had the opportunity to attend several of your previous Advisory Committee meetings and it's always a pleasure to be here.

I want to start this particular Advisory Committee with remarks similar to ones I make at others.

We have 12 different advisory committees within the Office of Public Health and Science. And I can't stress to you enough the value of what you do.

As I sit back and read the resumes of the
individuals that have agreed to serve on our advisory

committees, I'm just overwhelmed with the quality, the expertise, of the individuals that have been willing to serve.

And I just want to take just a moment first of all to thank you for your service. I realize all of you have day jobs, very busy professional lives. And just want to acknowledge the commitment that you make.

It's invaluable to us at HHS. And I really extend my thanks from me personally but also on behalf of the Assistant Secretary for Health and Secretary Levitt as well.

As I understand, this is the 35th meeting of this particular advisory group, so it's been in existence over ten years now and it provides incredible input into the Department on issues around blood safety and availability.

Before I talk a little bit about the charge that we have for you for this particular

meeting, I just wanted to acknowledge the tremendous effort by five of you who will be actually exiting

this board and this will be your last meeting.

First of all, let me say that I want to express my appreciation for your willingness to attend one more meeting of this particular group. Your replacements have been recommended, although the appointments have not been made.

We will be waiting on the new Administration to look over the proposed slate of officer -- slate of nominees for service on this committee.

And as soon as we have a new Administration in place and they have looked at that, we will announce replacements.

There are five of you that are exiting. And I just want to express my appreciation and appreciation on behalf of the Secretary. Dr. Benjamin, I guess you're one of the newer members of the Advisory Committee, and although your tenure has been short, your expertise has been invaluable to the

group. We appreciate your service.

I just want to say that I hope in upcoming

months and years as this committee goes that you will have an opportunity to continue to share your expertise with the group here as well.

Greg Welsh -- Greg is a professor of law at Georgetown. Certainly his service ought to be recognized as well. He has had keen perspective in the area of legal issues that are also important around issues of blood transfusion and transplantation.

So we appreciate his service.

William Duffell. Well, let me express my appreciation for your service. You are another one of the members that has completed a full term, I believe, starting in December of 2005.

I know that you bring a great deal of expertise in the area of medical devices, and that's such an important issue as we look at blood safety and availability. And you contributed in a great way to this committee.

David Matyas, I want to acknowledge your
contribution as well and express appreciation for what

you've done. I know that you have a great background in the area of law as well as regulatory compliance and those sort of issues. And your expertise in those issues have been so important, especially as it relates to issues of Medicare, Medicaid and third party payers. So we appreciate your service, and certainly you will be missed.

And last of all, Dr. Ramsey, a special word of appreciation to you, coming from Northwestern.

I know that you're a leader in the field of transfusion medicine and laboratory medicine and bring a vast array of experience and scientific knowledge in that area and have been a valuable asset to this committee.

So, I just want to, on behalf of the Secretary, thank all five of you for your service. And I want to give you a quick round of applause.

And more than that, I actually have a letter for each of you from the Secretary as well as a

certificate of appreciation. So I'll come around and
distribute these.

Okay. At this time let's move on with more of the substantive matters that face this particular committee.

You know, this is a very informed audience and distinguished committee here. And all of you are well-acquainted with how important blood products are to quality health care delivery within this country.

Over the years, the safety of the blood and plasma supply has really increased, and that's really related to the vigilant review process that we have, and the adherence to a number of safe guards.

While I think all of us would acknowledge that safety and availability is of paramount importance to the recipients of blood and plasma products, it's the donor that we want to focus on today.

The pre and post donation care of the donor is clearly important and an issue that needs to be addressed. And a commitment to the donor, as well

as the patient recipient, is truly necessary to build
a strong health care system within this country.

As we look back over the last year, I understand that 37 percent of those that are medically eligible are capable of donating. And if you look at 2006 data, there were over, approximately 16 million units of blood that were donated.

Of those -- well, in reality that 16 million was 7.8 percent or almost 8 percent in excess of what the demand was. So we were clearly able to meet the demand in the year 2006.

Now, as I looked at the data around these donors in 2006, it was interesting to note that almost 30 percent of those donors were actually first time donors.

The other 70 percent were individuals that donate more regularly. In reality, they had donated -- those 70 percent had donated almost two units of blood over the previous year.

So, a routine part of their daily or yearly life. I think one of the issues that we

struggle with in Washington is the aging of the baby
boomer generation.

Clearly we're going to have more seniors in the future than we've seen in this country before. And as that occurs, we're going to have to rely on the young donors to really help meet the need that's going to be out there for blood and blood products.

Now, I understand that in some states donors 16 and older are now helping to meet the demand for blood and blood products.

Donor selection processes really have the potential and are paramount importance to detect health abnormalities or risks which could effect the donor and the public at large.

Any time you have a procedure such as blood donation, adverse events can occur. And adverse events to the donor, either a result of the process of donating blood, either through the loss of volume or the loss of iron or abnormal tests that may be discovered can impact donor health.

And the question is, what do we do with

that information?

I understand that from a whole unit of

blood, an individual can lose up to 300 milligrams of iron or for a plasmapheresis, 25 milligrams of iron.

Certainly in medicine one of the issues that is so important is that of informed consent. And that issue is also important to the blood donation process.

It's required prior to donations and it has to include the donation procedure, the risk of the procedure and the test to be performed on the blood sample for infectious diseases to the recipient.

It's during this particular meeting that we're going to focus on the issues that I just talked about, pre and post testing -- pre and post recipient followup, pre and post followup of the actual donors, informed consent, those very important issues to the overall safety and availability effort.

There's about five questions that we're going to put before this committee that we would like your opinion on, we would like some recommendations.

First of all involves informed consent.

As you look at the current status of informed consent,

what we require for the informed consent process for blood donation, is it adequate.

Does it need to be altered? Do we need to change that process in any way. What kind of mandate is ethically mandated.

(End of transcription, the following portion took place before Louisa McIntire-Brooks. No testimony omitted.)

MR. WRIGHT: What kind of follow up is ethical and mandated? And second of all, what kind of follow-up is required with an adverse event occurs as a result of the donation process as, I called it. Third of all, what we'd like to know is how well does the current medical management of the plasma, blood and plasma donors align with the Department's Healthy People goes. As you know, we're working currently and monitoring very closely the Healthy People 2020 -- ten bill. We actually have an advisory committee group looking at Healthy People 2020. This is a set of

objectives that HHS releases at the beginning of each decade that sets where we would like to be in a major

health objectives ten years down the road.

This is a three decade old process that started in 1990. We're now on our third decade, we'll soon be on our fourth, and in reality, the number of objectives that are actually monitored by this committee increases every year. In 1990, we can have right around 200 or a little over 200 objectives. Healthy People 2000 had over 300. Healthy People 2010 had 480 objectives and we expect 2020 to have a number of objectives we need to follow. And what we would like to look -- for you to look at is the medical management around donors as is it aligns with the Healthy People process.

Clearly, for those of us that are involved in public health, one of the issues that we are constantly trying to address is bringing additional stakeholders to the table to get our message out and to improve the overall health.

And the next question we'd like you to

answer centers around that, and that is, is there a
line or role for blood plasma centers as community

health providers as it relates to issues such as sickle cell screening, perhaps providing PSA testing or cholesterol testing, iron status, glucose testing, hemoglobin a1c, just a number of things. If, indeed, there is a role for donation centers to play in this community health effort, what are the obstacles to implementation of that? What are issues and barriers that need to be removed for us to move forward?

Obviously in light of these five questions that we're posing before the group today, and you have a hefty day ahead of you, and we're certainly looking forward to your recommendations moving forward.

Before I actually go back to HHS, I thought I would just take a moment to see if any of you have any questions that you'd like to ask of me as we move forward. It's no secret that we're in a very -- we're very much in a transition in Washington right now. The transition team arrived at HHS several weeks ago and has been busy obtaining information on the current

status of affairs at HHS so that they can be ready to
take over the leadership.

Specifically to the function of this group, have some people mentioned that we have already received calls from the transition team saying that I've either shown a direct interest in particular to the area of government or not? That's what I am kind of looking for. I know you can't read tea leaves, per se, but any positive indicators, I guess?

MR. WRIGHT: I will say that I'm the head of the transition team, perhaps secondarily at HHS, and they went through the various offices within the Office of Public Health and Science that specifically asked about the advisory committee on blood safety and availability, what was the current status, what were the current issues? They did not indicate what their agenda would be moving forward. I think that they understand. In fact, many of the members of the transition team actually served in HHS in the previous administration. So, we're aware of the activities of this particular committee from their previous tenure at

HHS. Clearly they realize that it's an important committee and I think will continue to be functioning

in that regard.

It's my understanding that the transition team and many in the Obama camp are currently reaching out to external stakeholders. So, I'm not surprised that some of you are being asked your opinions as it relates to blood safety and availability as an external advocate, and I think that will continue. As far as a definite agenda, I'm afraid I don't have an answer for that question. But, they do understand the importance.

DR. BRACEY: Given the challenges in terms of some of the goals that have been stated, vis-a-vis, a more broad access to health care and the economic challenges, would you project that the focus on appropriate utilization of health care resources would become an even more burning -- more of a burning issue?

MR. WRIGHT: Dr. Bracey, I think clearly that's one issue that will be addressed. Health care reform, I think, is going to be a topic for the new leadership at HHS. Many of you know that the designee

for -- to be our secretary will be -- secretary of HHS,
but will also be in the house -- live house office

looking at health care reform as well. So, clearly, health care reform is on the issue and they're on the agenda and we're looking at many issues that are so important to that issue.

I testified last week to the Senate on the issue of prevention. Many feel that that will be a view for us as we look at health care reform.

DR. BRACEY: Any other questions, comments?

Thank you very much.

MR. WRIGHT: Thank you. Again, thank you for your service.

DR. HOLMBERG: Dr. Wright, I have one last question. Since you're formally from Texas, we have a room full of Texans here. For some reason, we have a lot of people here. Do you have anything to say to the Texans?

MR. WRIGHT: Merry Christmas. I know we can have good things, this is a Texas dominated group.

DR. BRACEY: So then we move on with the

business of the day, and that is to address the role of
blood and plasma centers vis-a-vis donor health and the

overall public health. First topic would be the current status of regulatory professional standards on donor health and public health. And for that presentation, we have Gilliam Conley from the FDA who is currently the director of the division of inspections and surveillance from the office of compliance and biologics and he will present the FDA current issues. Thank you.

MR. CONLEY: Controversy. If someone could help me pull up my slide. Controversy. I'm delighted that we're running ahead of schedule because they gave me 15 minutes in which to cover what for our field investigators is roughly a three week training program. So, it calls on me to be concise and succinct, both of which are running against time for me. So, bear with me as we try to walk through a lot of information here on a very short basis.

What I have been asked to cover here today is the regulatory background. I think this is the

baseline. This is where we start from. What does FDA
require? I was asked to talk about FDA regulations.

Where -- and I am going to cover under each of the topic areas both our regulatory bases, where there is guidance or additional data and examples of data that's relevant to today's discussion, that is surrounding donor health and public health. And the topic areas we'll be talking about are donor selection. That will be the biggest chunk of the talk because there's a lot of information in our regulations and our guidance about donor selection.

We'll talk about adverse reactions. I was specifically asked to talk about fatality reporting, but those requirements are tied in with other adverse reaction requirements. So, we're going to talk about a broader topic. We're going to talk about biological product deviation requirements, BPDR, again requirement. We're going to talk a little bit about their system which comes under -- so, ready to take off.

The basis for donor selection for a long

time has been donor interview, donor physical exam,
some minor testing that's done on the day of donation,

such as hemoglobin, hematocrit of all donors, total protein and source plasma donors and testing of donor samples that are collected at the time of donation, but then evaluated later.

The next three slides will be an overview of the regulatory framework. They'll help you with those party games when you sit around and do CFR and see who has the first sign of requirements for the donor hematocrit and the regulations. I lead those kind of cue cards. I don't memorize those numbers well myself. I will bring your attention to a few that I thought were more key and more focused to the overall issue. Then we'll go back and we'll take a look at a more practical approach of what are the requirements and what do they cover?

First section I want to focus your attention on is in part 640, which are the so called additional standards for human blood and blood products. Additional because there are baseline

manufacturing requirements elsewhere in the regs.

640.3 in particular we'll take a closer look at in a

bit. It's key because so many of the later regs also refer back to 640.3 on suitability of the donor as a baseline and you'll also note that there is this whole section that talks primarily about whole blood and then there is a whole separate section on source plasma which, in some cases, is more specific.

Next section that I draw your attention to is the CPMG section, current with manufacturing practices for blood and blood components. That's in part 606. Some of these regs relate tangentially. For example, when you talk about personnel requirements, if I'm going to talk about donor safety, you have to have people that are appropriately trained to do those evaluations and do those donor interviews. And so it may not talk directly about donor health, but it certainly talks about how it ends up being assessed. Again, 606170 is the adverse reaction section, and we'll talk in more detail about that because that's where fatalities are required to be reported to us at

the agency.

A couple of other areas that I brought in

are the general biological products standards which also apply to manufacturers of blood and blood products. They include the test requirements and donor referral, and the test requirements we'll come back to a little bit later. And I also included the section that requires donor notification. Because to me, that's a very important part. If you're worried about -- concerned about donor health, it's very important that the people who collect blood from donors be required to make communications back about their health findings to the donor.

For each of the topic areas I'm covering today, I want to talk a little bit about guidance. And you will see when I do some of the later sections that I can be very specific about guidance. When it comes to donor eligibility, donor selection, there are a host of guidance documents that relate in one way or another. So, I'm giving you the web page. Given the short time that we have here today, if you want to read

about it in detail, you can find it there on our web
page.

Another way that we have influenced what's done with donors is the requirement for products that have to be reviewed and cleared before approved within the agency. Part of the labeling for the product are the instructions for use that relate to that product. And so that's another way that the agency can reach into the process by controlling that labeling. And so if there is a new apheresis device out there, that has to be cleared from the agency. Product labeling is cleared by us and that will include instructions about how that new device is to be used that could affect donor health or donor safety.

Another way, and I didn't make a slide for this, but all licensed manufacturers of blood and blood products do submit their procedures to us for review, their SOPs. So, that's another reach of the agency as long as we're being comprehensive about where the agency touches on these issues.

To me, 640.3 is -- this is kind of an

essence slide. This is the heart of a lot of what we
do with donor selections. There's a lot of open

language in here where we have enforceability. For example, there is -- the determination shall be made on the day of collection, is an important point. The fact that donors shall be in good health is right there, and that's a broad area that we can interpret in guidance about what constitutes good health in a donor.

For those of you who don't routinely deal with our regs, we have now gone through the first two weeks of the training program, to give you that background on the regs, CFR is on line or you can purchase it through a number of resources and can go back and look at the details of any of those regs. But, what does that mean, where the rubber meets the road? And so I try to extract from donor health current regs. I've also included some of the recommendations that are proposed regs. And I have to include a disclaimer. This was the rule that was -- a proposed rule published back in November of '07, gave you the document number, comments from the public and

from the industry are currently under consideration.

So, nothing on the right is final. It's all still

proposed. But, on the left, we'll show you exactly what's currently in all of those regs that I looked at a moment ago.

So, we have specific requirements for the hemoglobin, must be greater or equal to 12.5-grams per deciliter, or if you're measuring hematocrit, greater than 38.7. Blood pressure, current regs simply say normal both for whole blood donors and plasma donors. Temp, also says normal, whole blood donors includes plasma donors. I couldn't find a mention about pulse or weight for whole blood donors, but for source plasma donors, we're more specific. The pulse must be normal and that the weight must be greater than or equal to 110 pounds. Whole blood donors don't typically get their total protein measured on a routine basis with every donation the way source plasma donors do, and for source plasma, it must be greater than 6-grams per deciliter.

Again, time doesn't allow any specific

discussions on these issues, but I wanted you to be
aware just as I wanted you to be aware of what was

proposed in the rule about blood pressure, pulse, weight and total protein for source plasma. I'm not going to read that slide to you.

The regulatory requirements for testing talk about disease states that have to be tested for. So 61040, again which is referenced over and over again in later places in the regs, require testing for HIV, types one and two, for Hepatitis B virus, for Hepatitis C virus and for HDLD types one and two. You will find in our guidance more specifics about which testing methods should be used.

Later on in the regs, after 61040, there's a reference for whole blood, red cells, platelets, cryo plasma, that in addition to those minimum testing requirements in 61040, there will also be a serologic test in blood group in our age. And then in source plasma ratings, which again refer to our baseline 61040, in addition as for serologic test of syphilis and total serum plasma protein which is usually done on

the day of donation. And further then samples are sent out for serum protein electrophoresis. Obviously the

concern with plasma donors is with repeated plasma donations, you can donate up to twice a week, and we want to be sure that their protein levels don't drop below acceptable levels.

It doesn't look good to a donor to have these health measurements done if they're not notified. And so there is a requirement in our regs that donors be appropriately notified and that it be done in a timely basis and that all of that be done.

You have now had the whole three week training course for the regs surrounding source plasma and whole blood donations and donor control and I'll move on to some of the other topic areas I was asked to address here today.

Adverse reactions, this is to fulfill the requirement talk about fatality reports. And so I've listed here for you the reg requirements about adverse reactions. The first thing I want to draw your attention to is that there is a requirement for

everybody to keep records and perform investigations
for all adverse reactions. But, the only reporting

requirement is when a fatality occurs and when a complication is confirmed to be fatal.

We also have a requirement that that reporting be done as soon as possible. I'll talk a little bit more -- I'll talk about it here. People tend to follow that as soon as possible, and we get a fair number of reports that ultimately on further evaluation, turn out not to be related. To us, that's a good thing because it's a rather insensitive indicator if we -- if you wait too long to report and there are fewer things for us to evaluate.

This is a perfect example of what Dr. Epstein identified earlier as an opportunity to report now. When we get a fatality report, depending on what it's about, we do send investigators out to collect additional information. We have learned over the years, for example, Tolley's, we can get enough information just through an exchange of information directly with the center and we rarely send

investigators for a Tolley report any longer. But,
anything that may affect the safety of other products

or may show that a particular service, transfusion service, might have unique problems that put other patients at risk, investigators go out to investigate those.

And so you have got the three sets of requirements there that relate to this. Guidance is available, again, on line. The most recent guidance published in September of '03, final guidance. We also try to be as transparent as possible in sharing the information that we have learned from these fatality reports. And we just recently put on line our second annual fatality report. You go back three or four years, it was a presentation like this where that data was released. But, now we have a formal mechanism of releasing it on a routine basis.

So, the question we'll ask, how many fatality reports do relate to donors? The last three columns of this have been reported already on line. I had Sue Cannon, who monitors this for us, manages this

project, to look back a couple more years just to give you an indication. The reports from '03 and '04 were

reviewed by a project manager out in my group, typically an experienced blood bank or SG level person and a medical officer. '05, '06, '07 we have formed a team of medical officers that review every fatality report so that we have some assurances of a chance for that professional discussion and review. If the medical officers want more information, then the project manager goes back to the hospital or potentially sends an investigator to get more information.

On a case by case review, of all of these reports of fatalities that have a temporal association with donation, our reviewers could not find any evidence that would conclude that the act of donation contributed substantially to the donor's death. Now, within our office of epidemiology, there's a medical officer that serves on that committee. There's also a desire to trend these issues over time and look at them closely. It's difficult to do that with such small

numbers. And so looking at these numbers, there was some follow-up, follow-up discussions, and the sense

from the source plasma manufacturer who counted for most of these higher numbers in '06 and '07, after follow up examination was that there was over reporting going on. And so again, I go to both the case review, the fact that the numbers were noticed, and we did follow-up on it.

You have to go back all the way to 1987 to find a report where the evidence supported a causal relationship. In 1987, there was manual apheresis going on for source plasma collections, and in this one case, group B red cells were returned to a group O donor by accident. Those red cells actually belonged to somebody in another bed in the same facility at that time.

There was, in the interest of full disclosure, in '06, there was one whole blood donation, there was an error in hemoglobin hematocrit testing. The donor probably should have been deferred because the donor was below the cut off point for hemoglobin

hematocrit. The donor -- the death of that patient
occurred postoperatively. And these cases get very

difficult to review because there are many comorbidities. They're complex clinical cases. That's why we have a committee of three medical officers to review these. They could neither confirm nor rule out whether the donation of a slightly anemic donor may have contributed to the death postoperatively. So, that's full disclosure. You have everything we know.

Biological product deviation reports, again, critical elements. They're recording any event which may affect the safety, purity or potency of a distributed product. You identify the problem before you distribute it and you never distribute it if that problem does not get reported to us. So, it's a very distinct subset of data of problems in the manufacturing industry.

Our final guidance was in October of '06. And for many years now, you can go through our web page and see the last five years, and since each is a summary of multiple years, probably goes back more like

eight years of data, and you can see the summaries,
health summaries, of all this information.

Who must report biological product deviation reports? It's required of all manufacturers of blood and blood components. That includes licensed manufacturers, unlicensed manufacturers and transfusion services. Total reports EPDR is 38,000 to 46,000 reports that are received a year. Right now every one of those are looked at by one of two people of my group. That represents reporting from 14 to 1600 reporting establishments. Trying to bore down as we are today on blood and plasma manufacturers, I want to give you the numbers for the number of establishments that are reporting, and the total number of reports that were received, this is all from fiscal year '07. And again, this is available on our web page in much more detail.

The numbers in parentheses here are when there is a licensed manufacturer that has many establishments that work under their license. So, for example, for licensed blood establishment, while there

are reports from 235 establishments, that represented
119 licensed manufacturers. That gives you a sense of

how many reports we see. But, I have to caution you that the DBPDR system is very product center. They have to report within 45 days of discovery a deviation or event that may affect safety, purity or potency. Again, only of distributed products.

There are some reports that tangentially relate to public health. There are many, many more records that don't specifically relate to that issue. We recently -- there was a paper published about babesia, and you saw earlier in the slides that were presented, and so this workshop, the number of BPDRs that we've seen over the years that relate to babesiosis. Again, understanding that's only distributed product. So, it's a rough indicator of what's going on, but it doesn't include every case of babesiosis that may have been identified. So, recognize the limitations of the subset.

Again, just to give you a rough idea of numbers of donor suitability, lab testing,

miscellaneous, again there's a number of reports and a percentage of total reports, you can see that donor

suitability, in particular, post donation information has for years been the front runner of BPDR reports that we see. Coming in to relate directly to public health, only a small subset of those. More likely they relate to the quality of the final product.

And finally I wanted to talk a little bit about the AERS Med Watch Reporting System. We can underscore the remarks that Dr. Epstein made earlier. 606.170 requires adverse reactions to be thoroughly investigated and that records be maintained. That's in the facility where the events occur. But, there is no required adverse event reporting regarding donors or donation for nonfatal events. Fatalities have to be reported to us, not the nonfatal events. Voluntary reports may be filed by consumers or health professionals and I've provided the web page, and there are multiple submission modalities to make it very easy. But, when I check with the folks who log these in and monitor them, there have been very few voluntary

reports received having anything to do with donors.

So, it really answers the question earlier. AERS

reporting is not required. It's voluntary only, and as a voluntary system, we're seeing very few reports.

Now with no clock in sight, I have no idea how closely I am with my time frame, but I will be happy to answer questions.

DR. BRACEY: Thank you very much.

Questions from the panel or committee regarding the FDA regulations? Sounds as so though you had a very thorough presentation. Thank you very much. Our next speaker is from the committee, and it's Dr. Darrell Triulzi and he will present the AABB Standards and current status of blood donor health discovery and follow-up.

DR. TRIULZI: Thank you very much for the opportunity to speak today. I'm here with my task representing the AABB in attempting to provide some of the information that Dr. Wright requested so that we can respond to his question. And the AABB is the primary standard setting and accrediting agency for

blood banks in the US and it actually has multiple sets
of standards. The set of standards that relates to the

questions at hand today are the standards for blood bank and transfusion services. And as I sat here today, I thought maybe a word about the process by which these are set might be useful in how they relate to FDA regulations.

The AABB has a committee of volunteers for the standards for blood bank and transfusion services and it includes liaisons from FDA, CDC, et cetera. And so the intent of the liaison is so there is no conflict between AABB standards and FDA regulations. And we believe that to be the case and I'm sure Jay or the liaison will let us know if that was not the case.

However, the ABB does have additional standards to what would be FDA regulations. So, they're not identical. AABB often has, and we can cite examples, of additional standards to those that are required as regulatory by FDA.

In general, the ABB standards for transfusion services focus on donor and patient care

and safety related to blood collection and donation in transfusions. And the standards committee will also

consider impact on blood supply for developing these standards.

This is just to give you an idea of the breadth of elements that are addressed by the ABB standard quality system. We're only going to focus today on the process of standards regarding donation collection. But, there are many more, and you can see many of these overlap with what you heard from Mr. Conley, our previous speaker from FDA, and in fact, there is consort intentionally between the two organizations.

So I'm going to focus on the process control standards that address collection and production of components. And there are standards that address the requirement to provide educational information to a donor, that they have to have written documentation that they've received and understand that educational material. There's a requirement for written consent that addresses the risks of the

donation procedure as well as the list and
understanding of the tests that are going to be done

that are required for donation. And there is a notification requirement.

There are standards that address the care of donors that may include arm preparation, for instance, donor qualification, and I'll show you those, and then a number of other things that are really not relevant to today's question.

So, first regarding donor consent, which is one of the five questions we were asked, the standards that are relevant, 5.2.2 says the consent of all donors shall be obtained before donation. So, this is a requirement for ABB accreditation. That the elements of the donation procedure shall be explained to the donor in understandable terms, and that this will include information about the risks of the procedure and the test that will be provided, that the donor shall have the opportunity to ask questions have them answered and give reasonable consent for donation.

An additional standard is a prospective

donor shall be informed that there are circumstances in which infectious disease tests are not performed. And

the reason why this is important is there may be circumstances where the test cannot be performed, either the tube is broken or lost or mishandled. And the donors need to know that a -- not getting back to them doesn't mean that they tested either normal or negative for the tests that are done. So, that is specifically required to discuss with the donor.

Donor qualifications include elements that address both the safety of the donor and the safety of the recipient. So, for instance, the age of the donor is important for the safety of the collection. Blood pressure the same, pulse the same, whereas other things such as the temperature or drug therapy are for recipient safety. So, these elements encompass both donor and recipient safety. I'll just point out the medical health history questionnaire. UDHQ is also a joint effort between FDA, ABB and other relevant organizations so that there is consort and agreement in the donor health history questions.

The question about notification of donors,
the ABB does have a standard that addresses this and

requires that donor notification of abnormal findings in test results occur. And it's worded as the medical director shall establish the means to notify all donors with any medically significant abnormalities. So, the standard does not say that a donor needs to be notified of every possible thing that could be found, but only those that are medically significant. It doesn't define that. It allows the medical staff at the center to define what medically significant is and that there shall be, at the bottom, appropriate education, counselling and referral.

And there are various degrees, again, the ABB doesn't define it, but the center defines the degree to which the counseling and referrals necessary. So, for instance, a donor who is deferred due to a hemoglobin deferral will get that information at the time of the donation before they leave often by a nurse. Whereas an HIV confirmed positive test will be a face to face interview back at the blood center with

a trained personnel and or physician. So, the response
is coordinated with the degree of abnormality. The ABB

allows the center, through this standard, to define the method and intensity of the counselling and referral that's needed.

The standards also require fatality reporting in consort with FDA requirements, that fatalities related to blood donation or transfusion shall be reported to outside agencies as required and that is referring to the FDA requirements, and that adverse events related to donation, the standards, adverse events also related to donation process shall be assessed, investigated and monitored. Again, very similar to FDA regulations.

Now, the bio vigilance program will or may ultimately result in additional standards being considered about reporting those through the bio vigilance program. But, this is the standard as it exists today.

So, in conclusion, the ABB's focus is on optimizing donor patient care and safety relating to

the donation process and the transfusion process. It
is a local decision to be made by individual blood

centers whether to provide additional public health services to donors. However, if it is offered by a blood center, the standards would require that there is additional health services be incorporated to existing SOPs including the notification process for those. And I will be happy to take any questions.

DR. BRACEY: Thank you Dr. Triulzi.

Questions or comments? I've got one question, and that is, although the standard exists and applies to the ancillary tests that may be offered, what is your perspective on how often the standard is actually adhered to for those ancillary tests by the regular blood center? For example, cholesterol, et cetera.

DR. TRIULZI: Let's say a center chooses to do cholesterol testing. Then the standard is their SOPs must define how they're doing cholesterol testing and how they notify donors, what they do with the results. And so to be compliant with ABB standards, those must be present. So, if they're doing ancillary

tests and not doing those, then that would be a reason
to be cited.

DR. BRACEY: So, you're saying then that it's basically through the process of assessment.

DR. TRIULZI: Correct. Right.

DR. ISON: Is there any policy or comment on recommendations to donors about reporting illnesses for a period of time after the donation?

DR. TRIULZI: That's part of the educational material that donors would notify the blood center if they develop sickness after the event after they actually leave the physical donation process.

DR. ISON: What's that time frame that's usually recommended?

DR. TRIULZI: I think that varies from center to center and I don't think it's less to say after 24 hours you don't need to report it. I think the centers would rather get reported to anything that might be considered, and then through the investigation decide whether it's relevant or not. There's no ABB requirements that sets a time limit.

UNIDENTIFIED PARTICIPANT: Just to sort of
follow up on what Dr. Triulzi is saying, there's no

specific time line on any of the reporting. In many facilities, this is discussed and at times there's a requirement. But, we always stress longer periods for some things. Hepatitis, it's really relevant. There's no hard fast rule or requirement.

DR. BRACEY: Recognizing that the leadership of HHS has plans for Healthy People 2010 and 2020, and each of the blood centers, it's pretty much free to interpret how it would address given lab data. Has there been any communication between the HHS and the blood centers that are performing screening as to how we would best approach a healthy patient in 2010 and 2020?

DR. TRIULZI: I don't think I can answer that. Maybe someone with HHS. Do you want to?

UNIDENTIFIED PARTICIPANT: I do not believe there's been any communication with AABB about our take on those goals. I can double check that, but that's as far as I know.

UNIDENTIFIED PARTICIPANT: There are blood
centers about to undertake a very big screening program

which you will hear more about tomorrow. But, what we did was we got advice from our local Department of Health, the New York City Department of Health and we engaged experts in the New York community, cardiovascular disease and other programs. But, we have, other than looking at the website and looking at the materials in Healthy 2010, I think is what is up there now. We haven't had direct interaction.

DR. BRACEY: Thank you. Dr. Holmberg?

DR. HOLMBERG: Just to follow-up, that's one of the reasons we had asked this question, is that at the present time, we do have 2010 guidelines set up. Blood is just mentioned, I believe, once or twice in the entire 2010. And so what we're looking at is how do we develop that area? And at the present time, I do not believe that there has been any communication with AABB on this, but this is the reason for the question today.

DR. BRACEY: Thank you. Any additional

questions or comments for Dr. Triulzi? Dr. Holmberg?

DR. HOLMBERG: Just a quick question. Are

there any standardized educational materials for the donor provided by AABB?

DR. TRIULZI: There is templates, but not standardized. There's not ones that are required to be used by any individual center. So, the centers developed their educational materials.

UNIDENTIFIED PARTICIPANT: Again, there's no requirement from the standards, however, part of a questionnaire that Dr. Triulzi referred to earlier has a section on education for the donor and there is some standard material that has to be used.

DR. BRACEY: Thank you.

UNIDENTIFIED PARTICIPANT: Well, Doctor, you mentioned as far as the standards committee for developing standards for bio vigilance, is that on the docket? Or how does AABB plan to move forward on that? If there's standards right now, I think it will be 18 more months before more standards come out. And so has there been discussion as far as putting in some sort of

accreditation process for bio vigilance?

DR. TRIULZI: I have reviewed the processed

standards which will go out for public comment and I don't believe there is anything in the proposed standards that would require reporting through the bio vigilance, particularly on the donor side as it's not ready. But, I think the standards committee would consider that when the bio vigilance network is capable of receiving the reports. But, in the proposed standards, even for the next edition, that is not currently a proposed requirement. Of course, anyone in this room is welcome to respond to the proposed standards and the standards committee will consider it.

UNIDENTIFIED PARTICIPANT: I'm on staff of the committee. There isn't anything that is in the proposed standards which, as Dr. Triulzi said, they're out for comment right now. And standards would not put a new standard in until there was a system that was in place that was pretty much universally accepted because you can't have a standard for an organization that can't possibly meet it. So, it has to be a system that

everybody would be able to use.

DR. BRACEY: Questions?

UNIDENTIFIED PARTICIPANT: When you guys -- and looking at donors, basically generally individualized, individual donors, has there been any thought to looking at donor communities and how the larger health picture looks in terms of how that affects the individual donors within any given donor community? What comes to mind? For instance, is the donors along the Texas/Mexico border for plasma, source plasma?

DR. TRIULZI: Those issues tend to be regional and local. And so another one might be babesia, you know, which is a localized disease for the most part. And we leave that to the centers to define themselves. So, if you want to think about it, the ABB would be a minimum set of standards, but it wouldn't preclude a region or a blood center from adopting additional standards that may be required for a particular circumstances in their area. If they do, then the ABB standards would say how you could do that,

what would need to be required in terms of SOP.

UNIDENTIFIED PARTICIPANT: You guys see

AABB standards as a floor which could be built on regionally, for instance?

DR. TRIULZI: Right, and so there are places which may choose to do additional screening tests that are not required by AABB or ask additional donor questions.

DR. BRACEY: Question by Dr. Klein.

DR. KLEIN: I just want to get back to Dr. Holmberg's question. You mentioned that if there is reason to introduce a new standard through the AABB, one doesn't have to wait for the next cycle. There is no mechanism for introducing the standard in between cycles. So, the fact that there's nothing on the docket for the next set of standards doesn't mean even if the system came into play, that couldn't introduce a standard between issues of the standards?

DR. BRACEY: Dr. Sayers?

DR. SAYERS: This is in response to Dr. Holmberg's question about whether there were

education materials available from AABB. I'll share
this tomorrow in my presentation. When individuals at

our center go in to get their cholesterol results, they're invited to an NIH website which is abundant in its information and edification counsel that might relate to cholesterol.

DR. BRACEY: Thank you. Any other questions or comments at this time? If not, thank you, Dr. Triulzi. We're now going to the open public comment. And Dr. Holmberg, do we have any -- we have Mr. -- okay. So, first is Mr. Val Bias who is the CEO for the National Hemophilia Foundation.

MR. BIAS: NHF is the oldest and largest organization advocating for the needs of people affected by hemophilia and other bleeding disorders and now also clotting disorders. No one understands the critical importance of careful donor screening and the impact of donor health and the health of others better than the hemophiliac community. I personally am affected by severe factor 9 deficiency. I have been exposed to HIV, Hepatitis C and Hepatitis B during my

lifetime. We appreciate the contributions of those who
donate blood and plasma. It is our obligation and

concern ourselves with their health and well-being even beyond the impact to our own health.

Even so, we paid a hard price for failing to be vigilant in the past. We're not willing to pay again. We applaud the committee for taking a hard look at this critical issue if it helps us to maintain or even expand our vigilance. We'll have certain resolve as well. The safe blood plasma supply and derived products that we have today are a result of such efforts. We must not be lulled into a false sense of security with the notion that we can only do less is a slippery slope and potentially dangerous.

So, I want to applaud the community for their efforts today. We look forward to hearing the rest of the presentations and continuing to work with other agencies and organizations represented here to ensure all Americans, those who donate blood plasma and those who receive those donations, that they remain safe and healthy. Thank you very much.

DR. BRACEY: Thank you. So, we are now to
our second presenter representing the Committee of

10,000.

UNIDENTIFIED PARTICIPANT: Mr. Chairman, Dr. Holmberg, members of committee, it's always a pleasure to address this committee, one which the committee was partially responsible for its original convening through the Institute of Medicine. And I'll ask there's always been a committee like this. And it's good to come back and address you. The 1990s were a unique time, great upheaval in the blood system in the United States. And we developed a perfect storm, if you will, within which there was a critical mass of community, medical, government that led to an evolutionary period of great change. Since that, unfortunately, we have had secretaries that -- originally under Dr. Lee, the committee was very connected under Secretary Shalala, I think since 2000, the relationship between the committee and the secretary hasn't been strong. And it's affected the community's work. I think we're about to enter a

period where that's about to change again. We're very excited about it and want to develop that critical mass

that moves the recommendations, moves the inner agency approach to what happened.

We were the canaries in the coal mine in hemophilia and we still have great concerns about where we are. One of our concerns is reporting. And that was confirmed today as I sat and listened. And many of you who know us know that we have been pushing and cajoling for one national mandatory reporting system for about ten years. Nothing I've heard today changes that one bit. In fact, it concerns us greatly that in an economic time, at a time when we have very few precious national resources, we have all this duplicative efforts, AABB, ABC, others, that from our perspective drain the energy for one national mandatory system that includes in service training for the medical community.

I know a lot of doctors in central California, all fine practitioners, many of them ID, some family practitioner, if you ask them what AERS is,

they don't know. If you is ask them how to patch into
AERS once you explain to them that that's the adverse

event reporting system, they're curious about it, but they have no base knowledge.

And this debate is continued. But, it seems a waste of resources and efforts to have all these different systems and then spend a great deal of time, as I hear being said today, looking at how to integrate those different systems to get some consistency to the whole thing. When from our perspective, it ought to be one national system. We ought to set the objective, educate your medical community. Implement.

When I hear -- you heard my question earlier, when I hear 71,000 adverse events in the study, and yet we can't correlate that to AERS. So, we don't really know how AERS is functioning, if it's functioning well at all. We would propose it's not functioning well. And we would propose for a western democracy as important as the United States in blood, that it is curious that we haven't gone here. And for

us, it is unacceptable. How do we manage trends with
all these different systems? How do we see the red

flags that might have protected us if we had had a national system then and the flags had gone up early enough for the system to respond.

We look at some communities and see them highly at risk. Former member of your committee, Mr. Larry Allen from the sickle cell community, has sat on our board since 1998. We brought Larry in because in our look at the landscape of blood end user communities, we feel the sickle cell community is one of those most at risk if something happens again, if some unknown pathogen comes forward.

And we're not at all clear how all these different systems are going to come together and protect us. And we believe the committee should really begin to start discussing, can we create a national system? We would think, yes. What resources do we need and how can we stop doing these things in different places, that is the AABB, ABC, elsewhere, and take our resources, which as I said earlier, are

extremely limited, and shepherd them? We're coming
into a new administration. We all hopefully will be

more activist and more a partner in DHSS with the committee, the secretary, to do these things. But, I think the leadership, the push has to come here. This is the committee that's got the ability to do it, the right people at the table, the right mix at the table, and it's time, from our perspective, that we stop wasting our time. I don't mean the efforts are wasted. Please don't misinterpret us. But, that the resources are lost when we could all pull together. Everybody has to give something, everybody gets something, just like we did around AIDS blood. We all gave and take so we could kind of get to know each other and get some things done.

We need to do that again. Because the issue isn't whether it's AABB's turf or ABC's turf. The issue is the United States and how we're going to protect the end users and how we're going to prevent another problem and contain it? Because everybody agrees it's not if it will happen, it's when.

And for us, there are troubling things in
the industry. I raised a moment ago blood collection

on the Texas/Mexico border. And that's why we asked the question about when you look at donor health and wellness, are we just looking at individuals or are we looking at donor communities? Because for us, where many of those border donors are coming from, the free trade zone, the maquiladoras is one of the most polluted zones in North America.

Health care was very limited to folks to before now, its even less limited as many of these big firms are cutting back, laying people off because of the global economic situation. So, we see the need, and what I want to close with, is something those of you who know me know, this is a bit kind of like the barking dog, we have been saying for many years, we have this whole body of policies and regs. But, we do not have an overarching guidance that is a national policy that sets the objectives, sets the goals of the policy and then the regs flow from those goals. What's important as a nation in blood? What's important as a

nation with donors? What's important in reporting as a
nation? And it's high time we did this. There's not

too many of us in hemophilia left in my generation. I'm about 54 years old. You all haven't seen me in a little white because I went full blown and had to realize it's time to get my own health together, and as my T cells were dipping fast, I looked around my beautiful backyard which I landscaped and said, if I don't stop this crash, this backyard is going to become a legion of micropredators waiting to jump my butt and kill me. Luckily, everything worked well. My T cells are rebuilding.

Part of that, I think we've gotten a commitment to strongly and continually push for a national system of reporting, and above that, a national policy. So we as a nation understand why we have regulations, what we're doing and what our goals and objectives are.

It's always a pleasure to address this committee. I always appreciate being in front of you all. We take a certain pride in this committee because

of our role in the Institute of Medicine study and this
recommendation, and we think this is the only place

that's going to happen. Because you all are important members of different segments of what we call the American blood system. We haven't been leaders in this one though in terms of a national policy or reporting and we need to be. We need to look back to the gold standard and reestablish it. And thank you.

DR. BRACEY: Thank you. We are at the point for discussion. We only need to discuss issues of -- these burning issues -- Ms. Wade, do you have a comment?

MS. WADE: Yes. I just wanted to briefly just to address the gentleman's, both gentlemen's recommendations and suggestion. I first would like to say, however, that my being on this board, I feel we have done some wonderful things. Being the director of the Sickle Cell Association in Austin, of more than a decade, I'm very much aware of the plight and condition and concerns in terms of donor collection and also recipients.

Where some of you know that I lost my late
husband at the age of 46 after 28 years of wonderful

marriage. So, I'm very well aware of the limiting challenges. However, I also would like to say that, again, this committee, in my opinion, has done a remarkable and outstanding job, not only in the sickle cell community, but I would also like to address you all because not only do I advocate for not only sickle cell, but other individuals. I, myself, have been a recipient of blood donation. I'm originally from Oakland, California, received blood in 1981 on the cusp of the AIDS -- HIV awareness epidemic. So, I'm a very much aware and we appreciate that comment.

But again, I do just want to express my pleasure and delight for this outstanding board and our contribution in making a difference for all individuals, whether recipients and/or donors. And I'd just like to say that. Thank you so much.

UNIDENTIFIED PARTICIPANT: Nothing I said, I hope, was interpreted as criticism of the committee. Obviously we believe in this committee. We helped

start it. We still believe in it today or we wouldn't
be standing up here making suggestions. We think this

is the place it can happen and should happen. And I look around the table and many people I know, trust, respect and I think we're going to see an assistant secretary, even a secretary, again who is interested in blood, again wants to hear loudly the committee's recommendations. And I think what we're trying to say is gives us a roadmap and we have a critical mass. And much good came of it.

Certainly we took the hit in one way, but out of that, rather than get mad -- we got mad all right, but we got busy. And government and industry, there was a wonderful critical mass. And I think it's time to recreate that. It will be different because we're not losing people at one or two a day as we were. I think we have a chance to recreate a critical mass and I think we'll have the secretary's attention. What a golden opportunity to do even more good above the good that's already been done. This is a great committee. No question. This is where we keep coming

back to talk because we believe in what you all want to
do and want to be a part of and want to endorse it.

Thank you. I didn't mean to -- I thought we were over.

DR. BRACEY: Thank you. One of the earlier -- actually, our first presentation on babesiosis struck me as perhaps an opportunity again to have some impact on that they're developing an area in terms of the issue of recommendations vis-a-vis reporting. And so I just thought I would ask the committee if perhaps you thought it would be appropriate that we would develop some recommendations vis-a-vis reporting.

DR. ISON: Can I ask a question? From the CDC's perspective, or whoever sets the national reporting on babesia, what thresholds are used to determine what would be a reportable disease versus one that is not?

DR. DUFFELL: Well first, states have to make diseases notifiable, and I'm not sure of the exact process as far as making them nationally notifiable. But, it's an extensive process. Can't just say that

something is notifiable. It has -- if -- there is a
process that we believe involves perhaps legislative.

MS. FINLEY: I believe I did look into this, on this issue, as a matter of fact, many years ago when I was on the health -- and we believe that the recommendation is often made by CDC to the association, state, territorial, whatever, health directors, Dr. Klein, I'm sure he can fill me in. But, then they make their recommendations to state legislators who have to make it reportable in the state. However, you know, our recommendations to the secretary, we are certainly as a committee free to recommend to the secretary that he or she recommend the CDC make recommendations to the association, state, to health directors or epidemiologists, whatever organizations they are. So, this is a long standing and festering issue. I would concur with making some recommendations in that regard. I think it does. CDC is saying, look, I need you to look more into this.

DR. ISON: So another point of clarification, do we know how many states? And if so,

which states currently do require it?

DR. BRACEY: Well, I think we heard today

that we know New York requires it. But, beyond that, I

--

UNIDENTIFIED PARTICIPANT: It's multiple states. I wouldn't want to recite them off the top of my head, but it's multiple states.

DR. BRACEY: So, is the consensus of the committee that we would make some sort of recommendation vis-a-vis to enhance the current state of reporting of babesia?

DR. ISON: I think that we should first find out how many states require it. Because if a large percentage that have the highest prevalence are already requiring it, although it might be of interest to find out if a state we wouldn't expect has a case, we may be recommending something that is not usable.

DR. BRACEY: Dr. Benjamin?

DR. BENJAMIN: I'll just make a point that the bio vigilance system has 18 cases of transfusion babesia in the last three years. And at least five of

those were babesia where it occurred in a state that
doesn't have a high prevalence of babesia. So, even a

system of reporting would be optimum.

UNIDENTIFIED PARTICIPANT: At the babesia workshop, there is seven states talking about it being accepted, considering babesia. So, I'm just going to say that. The other thing is the task force, AABB is going through their TPB committee. We do have representation on that task force from the council sector because this very discussion is going on in that community. That task force.

DR. POMPER: I just wanted to make a comment as we are considering what we should require in terms of reporting. Often there has been conflict between the patient's confidentiality and the HIPPA regulations, it's not just HIPPA regulations, but even prior to that, and then communicating the information that would -- with enough detail to allow -- to permit or to avoid duplication. So, one group may encounter -- one state may encounter a case of babesia and it may have already been reported in another state.

And it's hard to discern those at times.

So, I just wanted to, at least, raise that

issue. And also I think it's germane to the question of the national reporting system which is, it's a very reasonable consideration. And so somehow there will, I think, need to be consideration of how one maintains a level of confidential reporting and yet there is enough detail to permit analysis of the cases.

DR. BRACEY: Dr. Kuehnert?

DR. KUEHNERT: I think that's a very good point because we can talk about national notifiable diseases and see if something has to be notifiable. But, that doesn't mean that that report to the Health Department is going to have that data element that says that it was transmitted by transfusion. We actually see this more often in the organ transplant segment where there has been a report to the Health Department on an organism -- disease of public health importance, and the Health Department may know, say it's positive culture in an organ donor, but they don't know that the person was an organ donor.

So, if you don't have that information,
whether it's to do with transfusion of the recipient or

blood donors, it doesn't help you unless you have that linkage. And there are issues between -- and communication between blood banks and public health. And certainly it could be improved with focused discussion about the issues.

DR. BRACEY: Ms. Finley?

MS. FINLEY: I just wanted the committee to keep in mind that it takes a while for a recommendation of mandatory reporting to come through. You're relying on 50 state legislators, and not all of them are in session every year. So, if you think that this information is important, I would strongly advise that this committee make that recommendation to the secretary and let's get the ball rolling on it because it will take a while.

DR. BRACEY: Perhaps the recommendations that were clearly not stated here, will reflect that the committee has concern regarding the increasing transfusion transmitted incidents or prevalence of

babesia and the reporting of such and would seek, would
ask the department to ensure that reporting is

optional.

MS. FINLEY: I think I'd write a little more specifically to what you wanted to do. If you want to make it mandatory, we should ask them to take this issue and take the initial steps to make it mandatory reporting. Because, you know, it's -- unfortunately, it's a very complicated and less than optimal system.

DR. KUEHNERT: Will you be suggesting that babesia overall be nationally notifiable or only transfusion transmitted babesia?

MS. FINLEY: That's the kind of thing I think I would leave to the secretary of the CDC. Getting back to my usually stated point that the fact that our job is to make recommendations, not necessarily to tell them how to do every single thing. I think the CDC secretary can work out how they want to handle that. But, your point is well taken if what you really want is the transfusion transmitted situation,

then you should --

DR. KUEHNERT: I was just making a point

just so the committee understands that the recommendation to make babesiosis nationally, notifiable, you're saying that a case -- you're asking a case of -- you're drafting that cases that are nontransfusion transmitted be notifiable.

MS. FINLEY: Do we have other infectious cases that are notifiable only as transfusion transmitted?

DR. KUEHNERT: I don't believe so.

MS. FINLEY: Do we look to the bigger question then that we need to look at transfusion transmitted infections and that those be notifiable?

DR. KUEHNERT: That is a bigger issue. Whether that could be even implemented is another issue. But, as per my previous comments about communication between Health Departments and blood centers, I think that's something that we could talk about. Because the problem is that a clinician recognizing that context, and then reporting it in that

context, as a probable transfusion transmitted disease
rather than recognizing the disease without the

association with the transfusion.

MS. FINLEY: I understand your point is very valid and I appreciate the fact you're making them. What I am concerned about though is that the committee overall understand it's not our job to sort out communication between the blood banks and the clinicians. It's our job to make recommendations to the secretary. So, from a federal policy perspective, I would think the recommendation for transfusion transmitted babesiosis, if we are, in fact, concerned about it, will be made from CDC to the national institutes, states, territorial health contractors, epidemiologists whatever. That would be the way I would write the recommendation. So, I don't want us to lose the impetus to do something that we are capable of making recommendations for because there are so many other issues out there including the 50 state legislatures.

DR. BRACEY: I think that given the caveat

of Dr. Kuehnert in terms of a linkage of particular cases to a particular origin, that that would argue

strongly for basically universal notification vis-a-vis in a particular agent, because of the linkage, may not be obvious to the end user.

And I guess in the big picture, it never -- let's put it -- I don't think -- it would not hurt the situation to request more reporting.

DR. ISON: I've had reports of babesiosis transmitted and/or potential transmission by organizations as well. So, I think limiting it to just transfusion would be a little bit too narrow.

DR. RAMSEY: One thing here about the reporting system that's voluntary for West Nile donor testing where anyone who wants to go can to the web and see, see a map of where there have been positive West Nile cases over a course of the season. Now, as a donor site, which we're talking about also, but if there would be some geographical importance in monitoring recipients or patients with the infections, transmitted infections, perhaps there should be some

thought toward some kind of system like that as well
where the blood collection agencies might consider the

possibility of pooling information like that for transmitting infectious data discovery in some national surveillance system as well.

DR. BRACEY: But, again, the basis of that is the reporting that occurs.

DR. RAMSEY: The blood center reporting to donors perhaps they're investigating transfusion infections, perhaps there should be parallel means of identifying infections.

DR. EPSTEIN: It's a little unclear to me exactly which part of the problem we're trying to solve here with notification strategies. Truly there are many emerging diseases where you want the national picture and you might want better national surveillance. You don't always get there though by having notifiable disease. You will sometimes get there by doing studies, studies of prevalence. If what we're trying to figure out is the risk to the blood safety, what you want to know is the prevalence of

infection of the donor, the transmission rate and the disease attack rate. We can get that from focused

studies in epidemic areas, even independent of knowing the national picture. And knowing the national picture will have a tendency to average things out, because one of the things we have already learned about babesiosis, like West Nile, is that it's very, very focal. So, I think that whereas reporting in general is helpful because it gives you the global perspective, in reality, what we're really trying to get at is clarifying the risk to a blood recipient. And the big pieces that I think are missing are these: Right now we don't have the right test to screen donors. The big barrier, you know, sure as having pathogen reduction, which we all hope will progress, but until that day comes, we're dependent on screening and testing. Screening by history of risk exposure doesn't work and the tests are not adequate. You know PCR is too insensitive and we have heard 95 percent in the acute patients we looked at are asymptomatic, down around 50 percent. So PCR isn't working very well. But, the

problem with antibody testing is that it's highly
nonspecific and it's also over inclusive because many

antibody positive donors aren't going to transmit. So, the central problem is that we don't have the test.

The second major problem is that the condition in the recipient goes under diagnosed. And so the door that that opens as well, we should be talking to the doctors or we should do for perhaps babesia what we did for Tolley, which is develop the standard criteria and, you know, stimulate reporting through some kind of public service announcement, dear doctor letter. That kind of thing.

But, just to close the loop here, I believe that the task group is discussing studies on linking prevalencies to donors to transmission rates in recipients. I mean, others, perhaps there are some on here, who could comment and knows what's in progress there.

So, I'm just concerned that if we simply advocate a national report requirement, it just may miss the mark. Because what we're really trying to get

at is what is the risk to donors? And that really
comes down to figuring out how endemicity affects

transmission of disease. I think we can get there, but we are not going to get there clearly by national required reports. Not that I'm against it, mind you, but keep our eye on the ball.

DR. BRACEY: Dr. Klein?

DR. KLEIN: I entirely agree with that. I think the committees today perhaps can be able to tell the secretary that we have identified this as a problem and the problem really is the lack of information. We don't know how prevalent it is. We don't know what the appropriates are and we don't know whether this is a national problem. It appears to be growing, but we don't really even know that. And so I think what the committee needs to do is recommend that a mechanism be put in place to get some of these answers. I don't know if that mechanism is national surveillance testing, which I doubt, but I think we don't have the expertise sitting around the table right now, we don't even know how many states are for it, to make that kind

of specific recommendation. But, I do think we have
both the authority and the moral imperative to say we

recognize an issue and we need to have it addressed.

DR. BRACEY: Thank you. Dr. Duffell?

DR. DUFFELL: Jay wouldn't say it, but I think I will. I think I am against it, and the reason is, I mean, from the data that we heard this morning and the occurrence rate, I think it is a topic that needs some more study. What I am thinking about is in the economy that's facing our nation from a health care standpoint, we can always add on additional burden to the industry to make mandatory certain tests. And I'm wondering about the return on investment for doing it for this particular item. Again, the occurrence rate just doesn't seem to scream out that that's exactly what's needed right now. But, I do think that Jay's proposal, looking at it from a more population based study, makes a lot of sense from making -- before burdening the industry with another set of reporting requirements.

MS. FINLEY: I would concur with Dr.

Epstein's comment mainly because the time it would take
and the uncertainty of getting full reporting because

of involving 50 state legislators a lot. It wouldn't give you the information that we need now. So, I think the goal here is to get information to not only identify the problem, but also the opportunity for a company that would come in and develop a test. I gather we don't currently have anybody who is interested. So, I would concur from that perspective.

DR. BRACEY: I sense that, as pointed out, that we aren't really certain of the impact the reporting requirement would have in the recommendation, that it would take a great amount of time. I think the committee needs to express -- my opinion is that the committee should express some concern about the lack of information regarding this entity, and as Dr. Epstein more eloquently stated, we really need to advise that the secretary support studies to answer these questions so that we can really make decisions on this particular question with a little more information at hand and less conjecture. Dr. Haley?

DR. HALEY: I'm not sure the reporting
would be a good way. My previous career, I was an

epidemiologist for county health department, before that, at CDC, and I have a great deal of experience with reporting of diseases. Most states don't actually require it, and actually the state legislature, state board of health or some other state committee would make that decision. But, the end result goes back to what Dr. Pomper said. What's going to motivate that practicing physician to pick up the phone and call the local Health Department and report a condition? It could be on the list and he might not report it just because he doesn't think to pick up the phone and make the report. He's breaking the law by not reporting it, but in most states, there are no penalties. So, what motivates the physician to make a report of a disease is that he thinks that there's something the local health department should be doing.

And so my question, were I still in my position as an epidemiologist, I would be asking, what would I do in response to Dr. Pomper's report of a case

of babesiosis? Well, I probably would fill out a form
that the CDC gave me. I wouldn't do it myself, my

public health nurse would do it. And maybe that form is designed in a way that asks about prior transfusion or prior or blood donation or organ transplant, maybe it doesn't. Maybe the form doesn't have that on there. But, basically for us, it would be to fill out a form. And then nowadays, I send electronic copy of that to the state health department and from there to the CDC.

So, the essential action is what's going to motivate the doctor to pick up the phone and call the local health department? And I think with babesiosis, if they make the connection that they think it's transfusion related, the current laws are such that most states would require that it be reported even though it's not required to give a name. Anything that is potentially of a public health consequence is supposed to be reported. If it's not transfusion related, maybe they'd pick up the phone and report it, maybe they wouldn't today. Maybe the local health department will do something with that report, maybe

they wouldn't. It's difficult. But, I agree with what
Dr. Epstein said, what we need to do is to find what

information we want and then go for that information.

And I'm not sure that just putting it on the list of reportable diseases is going to get us there.

DR. BRACEY: Thank you.

DR. KUEHNERT: I agree with that.

DR. HALEY: You better.

DR. KUEHNERT: And I think that it's important, it is important for public health that we raise awareness about the association of babesiosis with transfusion and potentially transfer specifically. And you know, I think this speaks to a broad array of diseases where we need to do a review in public health to look at what's on the forms and how they relate, where there are data elements that relate this disease to transfusion. And I think that would be a very important suggestion whether it came from here or elsewhere. I'll indicate that fact.

The other thing I wanted to just encourage the committee to do is think a step ahead. I think the

babesia workshop was well summarized here. But, I think we got the sense, I did, and I got the sense that

we have a good idea that it's a big problem as a transfusion transmitted disease. Perhaps one of the larger problems concerning infectious disease transmission that we have in transfusion. So, if we do these studies, and it turns out it's as we think it is, it's a growing problem, perhaps just in some locals it's a growing problem, what will be done about it? And the issue really goes back to screening. And whether there are screening tests that are suitable.

So, I mean, I think we're going to start to take this issue on, we need to think about what else, what other obstacles there are besides just understanding the problem, what are the obstacles of actually implementing it and prevention, and that gets to encouraging industry to develop a suitable test for actually, in this case, actually, there are multiple species of babesia that cause this problem, suitable tests that could be used to intervene.

DR. BRACEY: Dr. Epstein?

DR. EPSTEIN: So, I drafted some candidate
language.

DR. BRACEY: Good. I was about to appoint you to a subcommittee to do so.

DR. EPSTEIN: I'll try this. The committee recognizes -- and this is really following Dr. Klein's concept, the committee recognizes an apparent increase in transfusion transmitted babesiosis as a blood safety concern, and say tissue transplantation concern. Given the significant health risk of babesiosis and the current lack of accurate scientific information on the transfusion and transplantation risk of babesiosis, the committee recommends that the secretary support efforts to determine the population and donor prevalence of babesiosis, its transmissibility by transfusion and transplantation and potential damage.

DR. BRACEY: Sounds good to me. Further discussion?

MS. FINLEY: I was going to make a motion.

DR. HOLMBERG: I like that other interventions because I think it's clear that pathogen

reduction was a possibility. And so, you know, I think
this is one area where we need to go concurrently down

the road. We may not, you know, what's going to get us there first? The screening test or a pathogen reduction? Probably the screening test before we get pathogen reduction. But, we don't know. Once again, I think that it's something that we put forward to the secretary for recommendation. Maybe we need to put in parentheses or examples there for the intervention. I don't know, or whether that would be understood. But, I think that it may send another message if the committee desires to send a message on pathogen reduction.

DR. ISON: I think recognizing that pathogen reduction isn't an option for organ transplantation. So, I think I would be supportive of having one of the options recognizing this is an issue beyond just transfusion. And that's our purview today.

DR. BRACEY: So, you want to add an EG? Is that okay with the committee? EG screening? Pathogen reduction has to point out the options. Is there a

motion?

MS. FINLEY: How do you want it written up

so we can look at it?

DR. BRACEY: We can do it after lunch.

After hearing the discussion in the morning, I thought we really needed to think about babesia. And then the rest of what will be important to us we'll hear this afternoon in terms of donor safety. And so a motion for lunch? We are adjourned for lunch. We'll regroup in one hour. So, that will be at quarter to 2:00.

(Luncheon recess was taken.)

DR. BRACEY: Welcome back after hopefully a very tasty and healthy lunch. Mrs. Birkofer, Julie Birkofer, is joining us. She had some mandatory meetings of her association, but was able to clear that and is now joining us.

Our next speaker is Dr. Richard Davey.

Dr. Richard Davey is the director of transfusion medicine at the Methodist Hospital in Houston and he's held a number of very important positions in the blood banking world including as chief medical officer and

vice president of medical cares and New York Blood
Center. Dr. Davey will present for us blood plasma

centers as a potential community health resources. Dr. Davey?

DR. DAVEY: Thank you, Dr. Bracey, Dr. Holmberg and the committee and I appreciate the opportunity to speak with you today about the simple topic of committee deliberations at this time is how can we look at blood centers and hospital blood banks as more than just places to donate blood and blood components, which is probably their key function. But, can they serve our community as health resources? Can blood donors be not only enticed, but encouraged to participate in the blood center, blood -- hospital blood bank, not only because it helps, but perhaps there's some health benefits for them participating also.

So what I'd like to do with my time is go over this typical blood collection data, which you have already heard. I'll touch on a bit about the issue of 16 year old donors who we're going to hear more about

probably tomorrow also. Then look at some health
benefits of donation itself. Can we look at the issue

of iron depletion from a positive standpoint of certain donor groups? Then we'll touch a little bit on required health screening tests, some of the low hanging fruit that we can take advantage of in our donation process, especially blood pressure monitoring and determination of hemoglobin.

We'll then look a little bit about some of abstractional screening tests which have been considered, and in some instances, implemented, in blood centers around the country, cholesterol, PSA, C-reactive protein, glucose, A1c. I'd like to also review very briefly an experience we have at the New York blood center with genetic screening for genetic markers of hemochromatosis and then very briefly again, since others will be speaking on this, talk about some of the issues that come up with some of these opportunities for blood donors, and that is, whose going to pay for it? The logistics and liability issues. Is this really an effective way for the

community to look at overall community health? Does
this have an impact on donations? Our blood centers

may want to see, but if they're going to invest costs and effort and manpower in additional testing, they may want to see some benefit in donations. And can we pin that down? And then again, medical follow-up on the issue of who is going to take responsibility for some of these tests.

So, again just by way of review, the latest data which we heard earlier this morning about the total collections around the country is about 16.2 units, which is a nice increase from 2004 to 2006. In other words, seeing that the available red cell units are over 15 million and the transfusion units are over 14 million units. There have been over 9 million successful donors. That's a lot of blood donors with 2.7 million first time donors, 6.8 million repeat donors with an average of 1.7 donations per donor.

So, that's a lot of donors. But, still we have a blood shortage in blood supply. We have to be careful with our donors. We have to make sure that

when we're trying to find ways to increase the blood supply, and before we get into some of the ultimate

screen tests, I just want to touch on some issues that we might have about expanding our donor base and some concerns that we must look at when we do that.

This is a little bit about 16 year old donors. It's permitted now in at least 22 states. I think that Dr. Strong mentioned volunteers at their center, they have been doing this for like 30 years, they have about 4700 to 5000 usable units from 16 years olds a year. And that translates into about 200,000 units nationally. There are issues with 16 year old donors. There are increases we see in referral and reaction rates. Who gives consent? Who gets test results? All of these issues have to be worked out on a state by state basis if we're going to use 16 year old donors.

The Red Cross data, again I think we'll hear again a little about tomorrow, looking at 16 year old donors from the Red Cross system, from March of '05 to February of '06, they reported 145,000 units from 16

and 17 year olds, 133,000 plus units from 18 and 19
year olds and over one and a half million units from

older donors. Complications were high, as we might expect, but they were definitely higher in each respective age group, as you're going to see, 10.7, 8.3 and 2.8 percent with the younger age groups having considerably higher reaction rates than the older donors.

If we look at data in more graphic form, you can see it quite dramatically that the incidence of loss of consciousness, short, long, prolonged recovery and presyncope with loss of consciousness and injury that the 16 and 17 year old, and 18 and 19 year old groups had considerable higher reaction rates than the older donors. We look at it in a slightly different way by first time donors, repeat donors, male donors and female donors, you see the same trend where younger donors clearly have a higher reaction rate, and serious reaction rate, than older donors. So, what should we do about this ethical issue? Do we need to deal with it in terms of younger donors? Probably we do. I

think as Dr. Strong indicated, there are ways to
address this problem. And I think those of us, and

most of us in the blood center world that are employing 16 year old donors, need to kind of take some special steps to make sure that this reaction rate is better managed.

Some of those steps I have noted on this slide. You can increase the number of staff at high school drives. Certainly talking to the high school kids about blood donation before the fact, a little bit of education goes a long way. Drinking and eating before donation is good I think for all blood donors, and no doubt for 16 and 17 year olds also. I think we know in certain of these drives, older donors, if somebody faints, everyone faints. So, having a private resting place for donors that feel a little woozy is a good idea. Get them out of the main flow so if they have a fainting spell, they're not going to trigger mass fainting in the high school gym. Also, further and further into the field of apheresis, having balanced fluid replacement for all donors, including

younger donors, may be a good idea.

So, this is by way of, I think, we have to

be careful in our enthusiasm to increase our donor base that we take care of our donors, and in this case, take special care of our younger donors who are at greater risk for some of these reactions.

So, what about a blood center to be another player in community health? If we look at the data, we can see that over 35,000 people donate blood every day in the US. And, of course, many, many more internationally. That's a lot of folks interacting with the health care system, 35,000 a day. So, our thinking is that screening and referral programs for certain required interventions as well as optional interventions, and actually, strengthen the role of the blood center in the community and as a resource of community health. This is good PR for the blood center. It's a good thing to do for community health. I think blood centers can promote themselves as actual purveyors of good health as well as good feeling. And that can be a real positive incentive for people to

show up.

And we might even look at it again by way

of before we get to some of the testing, is donation itself beneficial to health? There are couple studies out there that suggest that perhaps donation itself for certain groups may actually be beneficial. The thinking is that through blood donation, we lower our body iron and lower iron may protect heart disease, by in theory, lower oxygenation of chlorophyll. So, there was a study done by Meyers, et al. in Kansas City published in Transfusion a few years ago, in which they looked at two groups. Their study group were defined as frequent donors, they looked at 1500 adults who donated more than one unit per year for at least three years. Their control group, they called casual donors, which is the same number, only donated only one unit over a three year period. And they surveyed over 2000 people for over ten years looking at their cardiovascular event rate, and the frequent donors, the ones that donated more frequently, had a significantly lower rate of cardiovascular events than the casual

donors. You can see 6.3 percent versus 10.5 percent, which is a significant difference. This study is not a

robust study. It hasn't been reported in -- it hasn't been repeated in great detail, but it's suggestive that in this particular study, that blood donation may indeed have some benefit in terms of cardiovascular health.

A more extensive study was done out of Dartmouth where they again postulated that there might be iron catalyzed free radical oxidative stress, and by reducing body iron, it's going to be a positive health benefit. They pointed out that there is an increase of myocardial infarction in women following menopause with the rates of MI increased earlier in men than in women. And that reducing iron influence clinical outcome in patients with symptomatic peripheral arterial disease. This was big study. It was six year study. They looked at over 1200 patients. I'm sure many of you are aware of this study. There was a two and a half year minimum follow-up and they looked at ages -- a wide age range from 43 to 87. About 630, 640 patients in each

arm, the one arm, the study arm group had a unit
phlebotomy every six months during that period of

study. The control group had no phlebotomy at all, and the end point was all-cause mortality plus nonfatal MI and stroke. And the results, just in the brief summary, showed that there really was no significant difference when the whole group was looked at in total. But, the study group showing a trend toward improvement in terms of all-cause mortality, MI and stroke over the control group, but neither finding reached statistical significance. However, the younger, looked at different age segments and found that results analyzed for younger patients only, those ages 33 to 61, that there was significant findings. There was a reduction in all-cause mortality and a reduction in mortality where it's nonfatal MI stroke. You can see.

So, the conclusions of this particular study, and this is just a tentative conclusion, I think it benefited -- also dove tails with the study out in Kansas City, was that iron depletion may benefit men and post menopausal women. And we have to emphasize

the word may. And, of course, in this particular instance, more studies are needed. I think it's

premature for us to go out and promote blood donation as really helpful in terms of cardiovascular risk, but the data are provocative, they're there, and I think more studies could be beneficial if indeed this benefit can be panned out in those particular donor segments.

So, if we look at health benefits in the standard donation process, they're pretty substantial. As was pointed out earlier, the health history questionnaire is not only to protect the recipient, but to protect the donor. And the health history questions, the ones of those of you that donated blood, it's not a long inquisition, there's been a lot of improvement with the new donor history questionnaire, but these questions can really trigger a donor to understand his or her risks and certain disease categories. With proper education of our colleagues to manage this questionnaire so that they can handle questions from the donors, this can be a very helpful initial screen on a donor's health. I think what we'll

find throughout this particular discussion and the ones
that follows, is that education of the staff is

critical. The staff has to know how to deal with donor questions, has to know how to deal with follow-up on lab results, contacting donors, understanding what some of these test results mean so that the donors can benefit more properly concerning some of these interventions.

Blood pressure, we'll talk a little bit more about that in a minute. As I said, there's some low hanging fruit out there. We have to take the blood pressure. 33,000 people every day get their blood pressure measured in our blood centers. Some are rejected, some with high blood pressure are accepted, depending on where their blood pressure measurements lie, as you will see in a few minutes. Hemoglobin determination, we'll hear more about that in a bit. We'll touch on that also. Pulse rate irregularity, we check on that. Again, it depends on our screeners to make sure they understand what the pulse rate irregularity means. But, it's also every day in a

larger blood center when one might pick up an irregular pulse. And this requires medical intervention and

medical understanding. An irregular pulse can lead to a proper and cardiac intervention. So, we can't dismiss pulse rate irregularity. Temperature, of course, an elevated temperature is a trigger and infectious disease screening tests. These are the tests that are both required and recommended for blood donors, I think I captioned them right. I don't know if I missed them, but it's a range of testing donors perform so that they can donate blood, a unit of blood for the safety for recipients. But, these tests aren't helpful. Our donors often come in with asymptomatic infections. They're unaware of some of these viral diseases that they may be harboring, and even though this information may or may not be welcome by any means, it's certainly useful to have our donors screened, recognized, counselled and treated for diseases that are picked up on these transfusion transmitted diseases, no question.

This is just, again, a slide which we have

seen showing there is great improvement in terms of
post transfusion hepatitis. Certainly for a number of

reasons, some of which relate to questions, most of which relate to improved screening technologies and more sensitive screening tests as we go down the road.

So, let's talk a little bit more about blood pressure. In the New York blood center, when I was there, we did have a hypertension screening referral program. We know that blood pressure contributes to a range of cardiovascular diseases and effective treatments do exist. The deferral criteria for blood pressure is 180 over 100. Anybody with blood pressure measurements over that is deferred. But, you can donate with a blood pressure of 175 over 95 and be okay. It's acceptable for some of you to walk in and donate blood with that. In either case, it's a golden opportunity for a blood center to say, either thank you for the donation, but this is an issue which you need to attend to, or we can't take your blood today because your blood pressure is too high. This is an issue which you should attend do.

I'm afraid in too many instances these
days, we find blood centers say, thank you for the

blood, or we can't take you. Good-bye. And there just isn't enough attention to this critical health point that can be managed in terms of our screening process. Up in New York, we think and incorporated an early lab report program where we had our donors screened for blood pressure, and a relationship with one of our local hospitals where there was a clinic, the idea was we referred this hypertensive patient to their medical clinic. They would get expedited treatment at the clinic and the blood center would get back data from the clinic, cumulative data on how our donors are doing in terms of blood pressure maintenance. Win both for the hospital, the donors and the blood center.

We found in the screening program, and I think these data I think are reasonably -- I think broad data might be applicable to a number of different blood donor scenarios, but in terms of the screening program, out of 5400 donors evaluated, about 7 percent, 365 were found to be hypertensive. You can see the

breakdown between stage one, stage two and stage three
hypertension. The different percentages and raw

numbers of donors that fell in each category. This is not an incidental problem. These were hypertensive donors that no matter where they were, stage one, two or three, could benefit from the blood center saying, you have this issue, we can take your blood, thank you very much, but this is what you need to do to follow-up. I think in most of these instances, you will see what the blood center can do is give information and refer to a primary physician. Give information and refer to a clinic. It's rare that a blood center would want to get to managing hypertension. I don't think a medical director would particularly want to do that. But, it's a good opportunity for referral to a hospital, to the private physician for medical management. And hypertension is clearly one of the best ways you can do that.

Actually, I think the results of the New York program were that they have a -- tell these folks, invite them in to attend the clinic. Actually attending the

hospital clinic was not accepted very robustly. But,
they did want to go to their private physician, let me

take care of this with my private doctor. And that was a treatment of choice. But, the referral with the clinic, while I think was a good idea, really didn't pay off too well for the clinic or the blood center. But, I think the patient or the donors really did achieve the real benefit by having hypertension identified and properly taken care of.

What do we mean by deferrals? For sure, donors see deferral a most major consequence in terms of our percentage in numbers of deferrals. This, again, was a study done by the New York Blood Center where the deferrals for hemoglobin were, percent of collections, 6.1, percent of deferrals, almost 38 percent. 33,000 deferrals a year in one blood center alone was for low hemoglobin. 92.7 percent of those deferrals were women. You can see that of a thousand deferrals of hemoglobin levels, a bit surprisingly, when we broke down, 12.4, 11.5, you can there, was significant numbers of donors, almost all

women, who were really quite anemic when they showed up
to donate blood. So, there's another opportunity for

the blood center to say, this is an issue, this is what it means, this is what you should do to address this. Depending maybe on the severity of the hemoglobin that's determined or not. But, again, information is key. Training of the phlebotomist is also key. We know that in terms of iron supplementation, which is a big issue that's been talked about in separate seminars, and quite to an extensive degree, couple slides about it, we know that men and women differ considerably in terms of their iron requirement, their iron stores. Women lose iron through pregnancy and iron deficiency is clearly much more common in women than in men. But, can we pass out iron to everyone? Probably not. There are risks of iron supplementation, risks of treating anemia in the blood center. Blood centers probably shouldn't get into treating anemia, but they clearly get into replacing iron loss from the donation. Risk of iron supplementation, missing a GI neoplasm, worsening hereditary hemochromatosis, iron

poisoning, et cetera. Now, currently iron has been
touted as being a bit more safe than ferrous sulphate,

ferrous gluconate, not sure, but there is some thought, it's pure elemental iron, is less of a poison risk for children as well as identify effects for those who take the iron. There has been some debate about that. Supplemental iron is promoted as a preferred iron supplement if you're on supplemental iron.

There is a study out of Brittingham in which the idea was not to treat anemia, this particular study is someone with low hemoglobin, they were deferred or counselled about seeing their doctor for work up, for the anemia, see what is the problem. Their idea in this particular study was to replace the iron that was lost in that particular donation. If you're only replacing the iron lost in a particular donation, you're not treating anemia, you're replacing iron from that donation. So, in phase one, as you can see, of 200 men and 200 women, young women, given carbonyl iron, 100 milligrams a day for 56 days, in their initial study, they had aggressive follow-up with

nurses. And with that particular pilot study, they had some good results, a number of successful donations

increased 50 percent over control. That was a number of years ago.

So, they thought, let's increase this study to a study that's more equitable to day to day blood banking. So, they went to over a thousand, tested in a blood center operational mode, and in this case, the main difference was there was no intensive nursing follow-up, the donors were mailed an invitation, a questionnaire, they donated blood and then picked up their iron and there was no real follow up aggressively with that group.

And in this case, no change was found in the study control versus control. So, I think there is a conclusion that can be drawn from this particular study, is that iron supplementation, iron replacement with the iron lost in blood donation can work. It can keep women in the blood supply. It can be a benefit for their health probably. But, it does require more than just passing out the iron and saying, take the

iron and good luck. You really need to have more
aggressive, minimal staff time, nursing time. And that

could be a bit of a problem.

Now we'll hear more from Dr. Bryant in a subsequent lecture. There is really not too much about donor health, but I'll take the opportunity to just make a kind of a pitch to consider if we're going to consider anemia and hemoglobin determinations for our blood donors, we probably ought to think about reevaluating the cut off in men and women. And this has been discussed at length, and I only have one slide on it. But, right now as we know, the cut off for both men and women is 12.4-grams per deciliter for men and women. Men and women are different. The CDC criteria for anemia in adults is 12 for women and 13.6 for men. We know now that 50 to 60 percent of whole blood donors are deferred for hemoglobin, and almost all of them are women. So, one solution is to change the cut off. There's a lot of discussion we could have about that. But, change the cut off could be more reflective of the physiologic differences between normal values for

hemoglobin in men and women. And perhaps that change
can be lowering the cut off for women to twelve and

raising it for men to 13.5. At the moment, I think you have heard this from others, we seem to be accepting anemic males and rejecting normal females with the cut off we have right now. We could also predict this, changing these cut offs, we can limit the donations to three per year. I don't think that would help. I don't think that would hurt our blood supply very much. There are not too many women that donate more than three times a year. The fact that we're keeping those women in the blood supply and not losing them, I think, would outweigh any loss from the women giving four or five times a year. And some estimates that the yield for some of these changes would be substantial, perhaps a half million or so a year. And we might do a benefit treating them a bit more appropriately in terms of what their hemoglobin cut off values and supplementing their iron for the donation.

So, that's most the tests that we're doing already. We can make a lot of progress just with

hypertension screening and attention and hemoglobin

screening and attention as well as going to donor

questionnaire and the other screening tests that we do. But, there are other screening tests and procedures that are amenable to donation process that have been tried in various blood centers with fairly reasonable success. Cholesterol, iron supplementation we have touched on, PSA testing, C-reactive protein determination, glucose, hemoglobin A1c, and I think, in general, I don't want to talk about specific, is blood donation is a great opportunity to just convey a plethora of different health information to our donors. And I think Johnson & Johnson prepared, a year ago, had a great instrument where a donor, while he or she was waiting to know, could fill out a questionnaire, run it through an instrument, get a quick little profile on cardiovascular risks and other important health information. Very useful. Again, great opportunity. 35,000 a day can learn about their health.

We'll talk a bit about genetic screening in a study that was done for hemochromatosis. And for

total cholesterol, a number of blood centers do total
cholesterol. We do it in my institution. It's a test

that we can do without having to have the donor be fasting. Obviously blood centers don't want donors coming in donating blood if they're fasting. You need to have donors who are hydrated, had a meal, had breakfast. You don't want to do a fasting test on blood donors. So, you want to see if we can find an array of tests that don't require fasting or a fasting situation until they ask them to come back for specialized testing. It's an inexpensive test. It only costs three bucks to have it done. It's useful, and in our institution, we send a letter with -- a thank you letter with blood type and cholesterol values, with some information on cholesterol. If it's above a certain number, I get called and I call the donor specifically if it's sufficiently high to require medical intervention for a person.

This can trigger, of course, with proper education and training from our staff, a more extensive fasting lipid profile which can be done by their

private physician.

PSA testing. I know of one center that is

doing this, that's been a pioneer in many of these efforts to increase the health opportunities for donors. This is a pretty controversial stand alone screening test. In terms of what is normal, that varies with age. Some folks in an Oklahoma Blood Institute, use 4.0 as a cut off. But, that can vary with age. That's probably too high for a young man and too low for an old man. There's variability in tests. I think we're running probably more into liability issues with PSA, a cancer detecting test that can be implicating cancer. There are many reasons for PSA, but cancer is the bad one. So, there are liability issues to consider. The New York blood centers would shy away from doing prostate PSA testing especially without a concomitant vigilant exam by a physician, which blood center regulators don't want to do that. So, I think that we're not going to look at this. I think OBI charges -- they give this opportunity to their male donors, they charge \$15 a pop. So, they

don't do this for free. That's a \$15 test. But, in
talking the folks at OBI, they have a great response to

this. Male donors take advantage of this. And again, with proper information and proper hand outs to these male donors, you can probably get away with this and provide some benefit.

C-reactive protein, high sensitivity, a variety of issues. As you know, it's a nonspecific measure of inflammation and it's been promoted more and more aggressively recently as an indicator of cardiovascular disease. The American Heart Institute has identified three risk groups, lower risk, average group, and high risk with C-reactive protein numbers, as you can see. But, they are not recommending -- the heart cardiac people, they're not particularly recommending this as a basic screening. This is a screening if you're in a group that might be of higher risk of cardiovascular disease, either by age or by other parameters, but as basic screening test, probably not. So, again, of all the items, I think they're the ones that are probably ...

Glucose. Here's one that is I think is
much more amenable to aggressive blood center

intervention. I think we -- at least I learned, we really should always get a fasting glucose to make any determinations. Well, apparently that's not the case. My colleagues from diabetes and some of these related fields say that nonfasting glucose and the numbers can vary, let's say above 160, is important. It's important to check out a number that high with referral and perhaps a fasting study. So that screening donors, even nonfasting donors for glucose can really get us some good mileage. Another test which could be either a follow up test or as a primary screening test would be hemoglobin A1c. Again, controversial as a screening test, but clearly hemoglobin A1c, I don't know if you can see this chart, but it measures the longer term exposure of hemoglobin through elevated glucose screen and tends to give you a longer term idea of blood glucose levels in a particular donor. Again, as a primary screening test, it's probably a bit expensive. OBI thinks they can do the hemoglobin A1c for about

seven to \$10. That's a reasonable number that most
blood centers cannot absorb. So, perhaps a fasting

glucose, which is a much less extensive study with referral, and perhaps even more of an A1c testing at that point may be a more reasonable option.

I've mentioned the overall blood institute a couple of times in this particular talk. They have been very aggressive in promoting blood donation as a health benefit for their donors. They have a heart check program where they tell their donors, come on back with fasting, in a fasting situation, and for \$75, we will do this panel of tests for you, blood pressure, hemoglobin A1c, total cholesterol, a complete fasting lipid panel, serum ferritin and C-reactive protein. If you look at their website, they did a lot of information on this. This is not just on how -- they have pages and pages of information for the donor about what all these tests mean. What the findings indicate and what they should do about it. So, this is a program which has been a moderate success. It's very hard to ask them, can you quantitate, does this result

in increased blood donations? And that's really hard
to think about. But, they do feel it's increased the

community good will. Blood centers in Oklahoma City, I think, is viewed as not just a place to donate blood and help others, which is certainly good, but it's also a place where they care about your health. And they're going to give you options, either this heart screen or PSA testing and add to your personal health and well being also.

Hereditary hemochromatosis, genetic screening is starting to be used, it's been with us for years. We know hereditary hemochromatosis is amenable for genetic screening. Most cases, this is just the time frame of total body iron through the years to someone with hereditary hemochromatosis. What we're finding, and what has been known now for a number of years, is most cases are linking to the mutation of the HFE gene, and one in 200 folks are homozygous to the most highly implicated mutation for that particular gene which is the C282Y mutation. But, we know the prevalence of the disease is much lower. However,

blood centers are particularly interested in this

because the treatment for hereditary hemochromatosis is

phlebotomy, is donation. We know now through a waiver situation for blood that's been donated by someone with hemochromatosis passes out of the screening test to be used in the general blood supply. So, the thinking has been, can we identify hemochromatosis donors, recruit them to be frequent donors, and this benefits them for their disease, benefit the blood supply with increased donation. NIH, they have had a very aggressive program with known patients of hemochromatosis, 14 percent from patients with hemochromatosis, which is probably the most successful and aggressive program in America.

In New York, there is a thought to let's screen regular blood donors for this gene. See if we can identify enough blood donors which is kind of interesting, and actually identify enough donors to participate in the blood donation process. We can offset the cost of the screening program. Well, we found some good news. The genetic screening program was accepted under informed consent by about 85 percent

of those approached. And that means that genetic screening was performed on almost 5,000 donors. The

genotyping results were consistent with the population. We did offer free iron testing to all folks with one of the mutations. But, the overall response to this program was suboptimal. Only 50 of these patients actually returned for iron studies, only one donor actually had elevated iron, and that donor decided to go to his personal physician. So this was an expensive, interesting study, but it did result in some donors understanding their disease risks more completely. But, it did not result in us getting particularly more blood in the door. Certainly it's a lot cheaper and that's what has been employed by those who were open to this possibility. So, I think we'll hear more about this from others. But, there are issues with adopting some of these special screening programs.

Who's going to take medical responsibility?

I think in most instances, it's okay for the blood center to assume these responsibilities. We're not

asking medical directors to be interventionists, treat
hypertension, treat diabetes, to treat someone with an

elevated CRP or PSA. What we are asking the blood centers to do is be responsible for making sure that donors who have these tests performed are informed and their staff knows how to manage this information and inform donors properly either through letters or hand outs or test results. This is clearly in a red zone, we have the doctor, medical director call the donor and counsel them. I think there are ways we can discharge our responsibilities without putting ourselves at increased liability. As mentioned earlier this morning, you really need to -- you're going to embark on one of these specialized screening programs, you get proper SOPs in place, you know what you're doing, how you're managing it, how the information is being conveyed, how you're managing these donors. Liability is an issue that you have to bring up with your risk management people. But, I think it's minimal except maybe with PSA. Most instances, you're moving to get informed consent if you're going to be doing external,

not required tests. How to pay for it, obviously, it's
a big issue. Who's going to pay for these tests?

Glucose and hypertension screening is free. Glucose is free -- not free. There's low cost options that blood centers can take. Again in Oklahoma they are looking for health department support, the donor support the blood donors can get in the community from donors. Especially if it's pitched that we're doing this to increase community health. This is a good thing when we are in our community. You can pitch in by supporting these. But, cost is an issue and blood centers don't want to incur this cost if they're not going to increase blood donations in the door or increase community feasibility.

So, at least one possible scenario that I think might work is a test that we can really recommend for clear focus is blood pressure with aggressive follow-up for high blood pressure in our donors and proper referral. Hemoglobin with referral of anemic donors to their personal physician and/or replacement of iron in donors that successfully donated, especially

young women. Perhaps followed up with anemic donors if
you wish with complete blood count and ferritin levels,

or the other way around. Cholesterol testing, total cholesterol testing, and easy, inexpensive intervention that can lead with proper referral to a fasting lipid panel and perhaps a C-reactive protein or homocystine determinations. And nonfasting glucose levels, if they're elevated above a number that you would choose, 160 or 200, then again, a referral is in order. Take care of your donor. Make sure that he or she gets to the doctor, gets a fasting glucose done and maybe then hemoglobin A1c. And some of these screen tests can be reversed if you wish. But, these four I think are easy. This is, again, low hanging fruit. This is where we can intervene and make sure our donors know that we care about their health as well.

Final slide, I think what we can state for our donors is we give them a mini health assessment. If they have abnormal screening tests, required or not required, they're going to get aggressive follow-up and counselling. Additional tests, personal community

health benefit can be offered, especially cholesterol
and glucose. Need to back it up with proper

educational activities. Our target is better community health and hopefully more engaged donors. There are confounding issues, but they can be managed. So, I think it's a great opportunity for blood centers and I appreciate it.

DR. BRACEY: Thank you, Dr. Davey. Any questions or comments from the committee?

DR. ISON: I have two questions. Clearly this is something that will give out a benefit potentially, and is implemental since you can go to a lot of pharmacies. The two questions that I have, there have been surveys of individuals that are potential donors to see if they even want this test offered? And number 2, has there been any studies looking at impact on donation? Especially, is it more repeated donations or is it just going to have a bunch of people come in for one type of testing and never come back again?

DR. DAVEY: Those are great questions I

think from my understanding, the studies on whether
this results in increased donations are not

substantial. Those data just aren't there. The anecdotal evidence from OBI, from the New York Blood Center, is yeah, we like it. This a great thing. We appreciate you're doing this. It's helped us out. But, if that's translated into more donations, it's hard to tease that out. We know it creates good will, but does it create more donations? And I'm not sure. And your other question was?

DR. ISON: Have you surveyed patients to see if they even want this?

DR. DAVEY: Another good question. We did have survey with cholesterol testing, but there were three groups. One group had no interaction from the blood center, one group had an e-mail letter saying, please donate blood, and the third group said, please donate blood, we'll give you a free cholesterol test. The two groups where the blood center intervened with e-mails or e-mails plus cholesterol, both had increased donations. But, they weren't -- they were both above

no interaction. So, in that particular study,
actually, offering a cholesterol test didn't seem to

make a lot of difference. It just was an added incentive I think for people to show up.

DR. BRACEY: Questions for Dr. Davey?

DR. KOUIDES: The setting you study you quoted I think is from your place, your blood center. I have a follow-up to the Brooklyn Hospital. Did you also collect the data of what proportion of donors that did not have any insurance and, you know, assumed those who didn't, you know, you alluded to that some people still, they went to Brooklyn Hospital, they also to their private doctor, but I guess what I am asking is, maybe there's another proportion of donors that do not have any insurance? Because this kind of build up, the point I want to make is, you don't necessarily want to be using the centers to be surrogates in that sense, or we have a crisis of 40 million without insurance, another 40 million probably who are underinsured who probably can't afford a co-pay now for these lab tests. And if that's the case, that's a great potential that

they would be more likely to use this center for those purposes. And I'd be curious to know what is the

proportion of such donors who don't have insurance?

DR. DAVEY: I don't have an answer for that. I think in terms of the study with the Brooklyn Blood Center, the agreement with the hospital, and Debbie will correct me if I'm wrong, was that they will provide care pro bono and probably through state support or something. And so that the option was there for our donors to get free care for their hypertension. Most of those donors we did survey had private doctors and they said, we prefer to do it that way. But, we did offer that option. It just wasn't taken up by many of our donors.

DR. KOUIDES: I just want to make a comment that it does appear you made some good arguments in terms of screening, but some could argue, PSA, this is controversial, but as far as some of these kind of referred to as stand alone hypertension, blood pressure monitoring, blood pressure and cholesterol, they naturally stand alone, I think the problem we have to

kind of deal with if you're looking to, you know,
support the role of these centers, this may just

contribute to the fragmentation, because I think in many ways, you may be sending the wrong message. Again, this is coming from a hematologist and board certified internist, you may be sending wrong message to patients that, oh, I went to give blood and I saw that my cholesterol is high. I guess I have to watch my weight, and they're perhaps 200, 300-pounds. I guess my blood pressure is high, but I don't have to stop smoking. So, all this can be done in a vacuum, I guess, you can send detailed letters, but it doesn't take away from the need to really have a day keeper or someone overseeing this. I mean, there's too much fragmentation period that could happen in this type of situation. I mean, you're not also looking at weight reduction, you're not looking at smoking reduction. Some of those are far more important in many ways than some of these other --

DR. BRACEY: I think that's the issue with the Healthy People for 2010, 2020 comes up, and we'll

hear more about that tomorrow. Because I agree, that
all together, I think is an important consideration.

DR. KLEIN: This may be relevant to 2020.

The problem that I don't have numbers on the uninsured, but the problem really is that you do get particularly young blood donors who come in and you tell them that their blood pressure is elevated. And perhaps they do want to see a physician. You can give them a physician's name, you can give them a clinic's name, but not only do they not have their own personal physician, they don't have any insurance. So, another thing, you know you have identified an actual problem. They can do nothing about it. The blood center is not about to become a medical care facility. It identifies the issue, it refers. But, that leads to an ethical problem.

DR. DAVEY: I think your points, which are good ones, if there is a possibility for entry into the medical system when a key indicator is out of line, either blood pressure or high glucose, giving someone that information with some way to get an entry into the

health care system is better than not having done anything at all.

DR. BRACEY: Another question, in terms of the potential educational piece, which I think Dr. Kouides was referring to, such as smoking cessation and weight, et cetera, in your program, was that weaved into professional medical educators? Because there is a science to education of patients about medical conditions. So, I'm wondering, was the blood center kind of a stand alone or do you use resources or exactly how did you approach the educational piece?

DR. DAVEY: Mostly the education was done through blood center physicians and blood center personnel. Nurses and doctors were trained specifically in dealing with some of this information, high cholesterol, high blood pressure, what this means. So, it's our own staff that we can manage most efficiently there. In terms again with our referral, to one specific hospital, we partnered very closely with physicians at that hospital so that they were able to kind of understand how these donors are identified

and perhaps the best way to deal with their particular
problem. But, in terms of the wider community, we let

the patients deal with their own private physician.

DR. BRACEY: Dr. Kuehnert?

DR. KUEHNERT: I was going to ask if there's ever been an examination of whether there's higher deferral rates associated with donors that might have incentives for this sort of testing?

DR. DAVEY: Higher deferral rates?

DR. KUEHNERT: That are associated with these efforts to try to attract people for cholesterol or --

DR. DAVEY: We don't have those data. I don't think, again, it's very clear how many donors we get to walk in the door because that particular program is in place. So, I'm not sure that's exactly how -- but that's information we want to get the donor in the door and get screened, but they do not get something better for their health. They may as part of their consent program, but now in terms of deferral data --

UNIDENTIFIED PARTICIPANT: I can answer

that question. There was not a high deferral rate for people who received cholesterol. I think that we are

still to this day not doing it in a fashion that is consistent. It's offered at some drives, but not all drives. People get it one time, they don't get it the next time. So, the program that Dr. Jones' blood center will present to you tomorrow is completely different. And we'll be able to look into some of these questions that you're asking including who has insurance. I don't want to spoil the fun. But, we'll be able to look into some of these questions in better depth.

DR. BRACEY: You have patiently been waiting to comment or question.

UNIDENTIFIED PARTICIPANT: I'd like to respond to that question about market surveys. Blood institution centers have a very slow day on Mondays, the plasma donations. They offered cholesterol panels for all who would donate on Monday mornings. Monday, and now it's one of their busiest days. Many people will vote with their feet in the real world. The

confirmation is the life line. We have all heard CT
scans for \$139. They did a prototype survey in

Wisconsin and three variables, cholesterol, C- reactive protein and blood sugar. They priced it \$89 trying to return at least their costs in that trial. They had such a response, they now dropped it to a national campaign of \$79. This means that people are really moving toward personal wellness information and are willing to pay more than one would expect, but modify their behavior. In fact, that's been one of my chief actions, standing in blood donations, seeing the population altruistically, we assume. You take a health and wellness criteria, both of them, and, in fact, if you could price it economically enough, you could attract huge increases in after donations. So, I'm just saying, people do respond to health and wellness information.

DR. BRACEY: Thank you. I think we better move on.

UNIDENTIFIED PARTICIPANT: Quick question.
If somebody comes in having been motivated by hearing

about availability of the tests, and then they're
deferred just based on the questionnaire, let's say,

so, they haven't taken the blood yet, is the center still obligated to give the tests?

DR. DAVEY: No, I don't think so. If they're deferred, in most instances, unless in certain instance like OBI where they charge 15 bucks for PSA, that's a point that could be offered in most instances. No.

DR. BRACEY: We better move on so we can stay on schedule, or a little ahead of schedule actually. The next speaker is Dr. Ron Domen. Dr. Domen is professor and associate dean of the Penn State College of Medicine. And he has been very active in transfusion medicine for many years and he will speak to us today on the informed consent process.

DR. DOMEN: Thank, you Dr. Bracey for inviting me here today to talk about informed consent for blood donation before the committee. I would like to disclose that I have nothing to disclose. I have no conflicts of interest, financial rewards coming. And I

owe special thanks to two colleagues over the years who
have provided me with education in this area as well as

coauthorship, Dr. Martin Smith, Department of Bioethics and Dr. Kathleen Sazama. I'm going to talk about the legal and ethical concepts underlying the doctrine of informed consent defining what the elements of the informed consent processes are, analyze the informed consent process as it applies to blood donations and to review the current studies that are out there relating to informed consent of all donations.

Some have suggested alternatives to the term informed consent, and you can see a listing there that I have put together as well as what I've heard from other people. Informed acceptance, informed agreement, decision making, informed authorization, informed permission, informed choice, donor consent statement is what we have on our history form where I currently work in that we have the donor sign it, and some have suggested a written statement of others. I'll return to that a little bit later and go back over that.

Informed consent in this country goes back
quite a ways, particularly owing to a 1914 case where

surgery was performed against the patient's expressed wishes while that patient was under anesthesia. The patient expressly said that she did not want to have surgery performed, but a tumor was found and surgery was performed. And she successfully sued the surgeon because there were complications that resulted from that.

In 1957, the duty to disclose, IE, inform, risks and alternatives prior to medical interventions was detailing the landmark case involving Stanford University at that time. And the judge indicated that full disclosure of facts is necessary to an informed consent. And this is where the term inform actually became embedded in the consent program, from that 1957 case.

Over the ensuing years, there were a number of cases, but particularly in 1972, there were three landmark cases that were litigated that one upheld the duty to disclose risk and alternatives, also upheld a

patient's right of self decision and the exercise of
choice and obligation to inform patients in

understandable language and terms. And throughout this, while these are dealing with patients, the implication is this is anybody that's undergoing some sort of intervention, and I equate the term patient with donor as well.

The ethical basis for informed consent goes back to the 1947 initiative with the Nuremberg Code where informed consent was indicated as applied to research subjects, and the first tenant of the Nuremberg Code states voluntary consent of human subjects is absolutely essential. Following up on that, in 1964 the Declaration of Helsinki stated that subjects must be volunteers and inform participants in the research project. And more recently in the United States, in 1979 we had the Belmont Report which sort of laid the foundation for human subjects protection and their current institutional uses. The AMA Code of Medical Ethics, as most of us are aware, has been around for a long time. It was initially formulated

around 1847, and obviously updated a lot over the
years, and the current AMA Code of Ethics contains a

very detailed and information upon informed consent in medical interventions. So, they very much do uphold the concept of informed consent in health care.

Now, the ethical principles underlying informed consent can be divided into four main areas, autonomy, beneficence, confidentiality and privacy and justice. Autonomy is respect for a person's individual decision making capacity, their freedom of choice, freedom of will. Beneficence is the process of benefiting others, minimizing harm in those individuals. Confidentiality and privacy is concerned with protection from unwanted intrusions happening to that individual and justice is being treated appropriately and fairly.

A lot of emphasis probably uphold the concept that autonomy is probably one of the main ethical tenants associated with the informed consent process. And respecting a person's autonomy obligates us, being the health care professional, to basically

uphold these truths. To tell the truth, to respect the
privacy of others and to protect confidentiality or

their confidential information, to obtain consent for intervention, to help others make important decisions. So, we foster their ability to make decisions that affect them, making sure we disclose all the appropriate information and insure that the person understands what's being asked of them and that it's being asked voluntarily. In other words, we treat others as ends and not means of.

I think most of the ethical literature will withhold that the major elements of informed consent are disclosure, comprehension, voluntarism, competence and consent. So, disclosing the information to the person, to the patient, to the donor, sharing all the risks, benefits and any alternatives that exist.

Comprehension is the ability to understand the information and give the opportunity for the person to ask questions. Voluntarism is the individual's freedom in making those decisions without coercion, and competence is their ability to make decisions and then

finally consent. You're giving consent or refusing consent and being allowed to make that decision.

Now, specifically related to blood donor informed consent, 1941 started a major blood program in this country and that was under the auspices of the American Red Cross formed at the beginning of World War II. And at that point, every donor was required to sign what was actually termed a release before they could donate blood. And this release was a record that the individual was going to donate blood at his or her own risk with the intent that everyone involved in the collecting, testing, transfusion activity was absolved from any liability or responsibility to the donor. There was nothing in there regarding risk or benefits or any other testing that might be done.

The AMA Code of Medical Ethics is, as far as blood donor informed consent, is concerned only with cord blood donors in the sense that they stipulate that normal clamping of the umbilical cord should be followed in order to avoid health risks to the infant and that informed consent must be obtained from the

parents. The AMA Code, as I mentioned earlier, is very clear on the use of informed consent in general in the

health care profession.

The AABB Code of Ethics, the last revision in 1997, indicates that institutions should develop and/or support policies that prevent or eliminate the exploitation of donors and opposes those measures that adversely affect their health. It does not specifically mention the term informed consent. The International Society of Blood Transfusion Code of Ethics, last formulated in 2000, does mention donor informed consent and indicated donors should be advised of the risks associated with the procedure, the donor's health and safety must be protected. Any procedures relating to the administration to the donor of any substance for increasing the concentration of specific blood components should be in compliance with internationally accepted standards.

Now the AABB standards themselves, and the latest edition, talks about donor consent in this form. They don't mention informed, but it's implied, I think,

in the statement. I have underlined some of the major
elements relating to informed consent. So,

understanding knowledge about the risks, the tests that are going to be performed, opportunity to ask questions, and then finally the opportunity to either give or refuse consent for donation. So, the major elements I think are detailed there, but it's not very specific as to how that should look in the final form.

Now, again getting back to some of the terminology, Nuremberg Code mentioned voluntary consent. And the person involved should have knowledge, comprehension of the elements of the subject matter involved as to be able to make an understanding and enlightened decision. Again, use of the term voluntary consent with the major elements underlying informed consent are detailed there.

The actual term informed consent, as you know, is a humorously recognized and accepted term and the elements are all well defined as I pointed out earlier. And all other terms, in my personal opinion, are simply skirting around the issue of what

constitutes informed versus consent. And this leaves
too many loopholes for possible interpretation. We

know what informed is, we know what consent is, and the two have been linked together since 1957.

Obviously when it comes to blood donation, the type of informed consent that will be used is probably going to differ based on whether you're donating whole blood or components, apheresis components or whether the donor is given stimulatory medications to promote one cell type over another for the collection process and also for cord blood.

Risks Associated with donation. I think we're all familiar with the risk of whole blood donation, it's been detailed by others in discussions today. I won't be spending much time on that. There's a number of things that we typically talk about that are mentioned, I don't think most of us miss when you talk about which risk of donation, obviously some of these are rare, and I guess you can debate how much detail you want to get into this. But, we also know that -- but as I learned today that the 39 reported

deaths in the last three years apparently are not
currently related to blood donation upon further

investigation, so, I'm not sure what this number means.

Apheresis collections, you can have unstimulated donors, and they also have reactions potentially associated with them. The immediate reactions, I think, we're pretty familiar with. Some of the long-term reactions we may not be as familiar with or have as much knowledge on the incidence of these kinds of reactions. The stimulated donors, again, you're giving drugs in the setting of DCSF, for example, stimulate granulocyte production. Giving other drugs to stimulate potential self proliferation. Again, we don't know what some of the long-term effects of giving some drugs are, but we do know they do have potential serious side effects.

Cord blood donors are a special category here. Parental consent is what's primarily sought because, obviously, the parent is the guardian of the baby in this case. And again, we don't know what the long-term risks are associated with cord blood

donation. It appears to be safe, but there haven't
been a lot of studies looking at this today. And I

think this is the kind of information that needs to be part of the consent process.

Now, what do we currently know about the informed consent process in blood donation?

Principally there have three studies that have been performed directly related to the blood donation. The first study by Sugarman, et al in 2002 was in cord blood donors. And here the mothers were surveyed after giving birth, and after signing consent forms to donate their baby's cord blood, and he found that there is really a surprising lack of comprehension by those mothers in several areas related to that study of cord blood donation.

Another study out of Scandinavia in 2003 looked at some elements of the informed consent process for blood donation and demonstrated that how information is presented to donors can affect their level of understanding. They use particular terminology like, immunological window period, and

obviously donors aren't necessarily going to understand that. But, I don't know what information was actually

imparted to donors that maybe they should have understood that. But, they also found that information presented to donors could have been better presented.

And finally, the last study in 2008 that I was associated with found that whole blood donors do not fully comprehend the risk of the donation process, and how often and how the information is presented may be important. I want to look at that study in a little bit more detail. And this is a study that we surveyed whole blood donors and we ended up with 849 usable surveys. The donor's self assessment and comprehension of donor information, and then we actually quizzed the donors on the level of their comprehension. Prior to donation, donors read two handouts. This is fairly typical of most blood centers. One hand out was important information for blood donors about the blood donation process, risk eligibility, HIV information and those kinds of things.

At that time, we were also doing part of

the West Nile Virus Research Testing Protocol, so there was a separate information sheet related to that

testing that was also presented to the donors. Donors then filled out the donor form and there was questions on the donor form about past and present medical conditions, about their drug use, living in certain countries, et cetera.

And then the donors met privately with the blood center staff. And here they had their blood pressure checked, pulse, hematocrit testing, they were verbally asked the questions and then the donor then signed the consent form or statement on the history form. Section one of our survey, and the donors did this after they went through the whole donation process and donated, section one was just gathering demographic information. Section two was their self assessment of the content and comprehension of the donor information that was just presented to them. And in section three, they were quizzed on their comprehension.

There were 21 possible points on this. They got one point per correct response. And some of

the questions were, for example, the following are
reasons the person may not be eligible to donate, and

then check all that apply. And there would be several things in that question for them to check. Or possible risk of donating blood for a donor are, and then check all that apply.

The demographic information you can see there, the average age, the male female breakdown, first time donor, content, 6.7 percent of this group, and we can see the repeat donors, how often they repeated. Almost half had a high school education and the other half had college or higher education. 97.5 percent of the donors are generally satisfied with the content and the length of the information, except, as no surprise, the repeat donors felt the length was too long as compared to the first time donors. And that was a significant difference. 96.5 percent of the donors agree, or strongly agreed, that they fully comprehended the risk and benefits of the blood donation process. But, interestingly, the ones that indicated -- the 40 percent that indicated strongly

agreed had a higher quiz score compared to those who simply agreed. And that was significant. We found

that greater than 90 percent of our donors comprehended that the aspect of living in certain countries or being on certain medications affected their eligibility to donate. And dizziness is a risk of donation and they seemed to understand the AIDS related information and questions, which was encouraging, and that fainting is a risk of donation.

Less than 50 percent of donors fully comprehended the West Nile Virus research study, which is surprising. A whole separate information sheet on that. Potential donors deferral registry placement was not understood by donors, that they could end up with positive infectious disease blood test from the donation process. And that is pretty much how we worded it, so I'm not sure exactly where the donors we were looking at, that may not be worded exactly right, but we were getting after false positive testing concerns there, not that they actually donated and ended up with a positive -- real positive test. And

they didn't seem to understand the referral to a
physician for medical risk evaluation was a risk of

coming in and donating, that they could potentially be referred to a physician for follow-up for something.

In between the 90 and 50 percentile, slightly a few of the examples, there were -- they felt as their level of comprehension. So, most of them understand that they'd probably have bruising risk, their arm would be sore. Not too many of them seemed to understand how many days you could go between donations and things like fatigue and blood pressure eligibility and criteria.

So, I think some of the questions raised by this study as well as the other two studies is, can we do a better job of informing donors about all the risks associated with the donation process? And what method and approaches, are best to ensure donors can comprehend the risk of the donation process? I think from a legal and ethical standpoint, there's certainly sufficient justification for a robust informed consent process. And that's been firmly established in the

literature and practice. You have reviewed studies
that actually examined the informed consent process in

blood donation. And these studies actually raised questions about how well donors are informed of the donation risk and donation process in general. So, I think we need additional studies on informed consent in the process in blood donation. The current state of the art probably needs to be studied in detail and defined as to what is the current state of the art and to look for best practices out there and have those disseminated to those of us in transfusion medicine.

Perhaps then expanding through the formation of national recommendations and guidelines as to what should constitute informed consent for blood donation and what that process should look like. Obviously, we don't want to slow down the donation process all that much, so I think there needs to be maybe new ways of looking at it in a donation process and using different technology available to make sure the donors are comprehending the information.

Establishment of The National Donor

Registry, I think, has been talked about to collect safety and adverse events in all types of donors so

that we have a much clearer picture across the country as to what the risks and benefits are for apheresis donations or HSC donations are. As part of this process, I think we can -- it kind of means we want to think about a donor bill of rights as what we're asking them to do and how we're going to support them.

So, I think the voluntary donation of tissue organs by healthy individuals is certainly an altruistic act and we really have a moral duty and obligation to protect the donors from harm and to make sure that they understand what's being asked of them. And with that, I'll take any questions.

DR. BRACEY: Thank you Dr. Domen. We'll open up for questions. Dr. Epstein?

DR. EPSTEIN: Thank you. This is very illuminating. One question in my mind is how does this compare to informed consent in medicine in general? Are there any comparators available? To be placed on a drug, being offered elective surgery, et cetera, et

cetera, et cetera, because it may be that with all the deficiencies you pointed out, it could be light years

ahead of informed consent in medicine in general.

DR. DOMEN: There's a number of studies in the informed consent process in general in patient care, hospital settings. And the results are generally abysmal. They're not all abysmal, but there's room for improvement. So, I think it's an issue.

DR. BRACEY: Dr. Pomper?

DR. POMPER: Yes. In keeping with what Dr. Epstein raised, I wanted to ask, as a donor, I would be in the statistically significant, as you repeat donate, you don't want to go through this process again where it becomes repetitive. And also, in my involvement with ethical discussions with my colleagues, occasionally I receive some push back, especially on the subject of informed consent. So with that lead in, my question is, is there a statute of limitations on informed consent or, this just in general, do you know of a practice standard of -- if somebody goes through a good, efficient informed consent process to donate,

then would it need to be repeated each time one donates
or could one return and say, I have given my informed

consent, I've heard these issues in the past and I'm okay? Do you think that would be a benefit or a hinderance to the process?

DR. DOMEN: No, I think that's actually -- you know, there are standards, but there are practices that support that. For time informed consent, the time of maybe a year. And even with the AABB, I think supports as far as informed consent for transfusion, will support the concept that you need one informed consent for that hospitalization, or from that treatment site. So, somebody going through treatment for leukemia, you know, you only need one informed consent for transfusion for the whole treatment cycle that they're going through, for example. And the same could be held true for somebody undergoing apheresis platelet collections. You do one really good informed consent, and then maybe you do that every six months or a year. And whole blood, I think there's probably ways we could probably figure out. It doesn't need to be an

onerous process every time somebody comes in.

DR. POMPER: I've received that question at

times from folks caring for patients that tend to have repeated discharges, admissions and now the day hospital admissions, things like this, where each time a person is discharged, their informed consent is invalidated. So, those same disease processes, they need to repeat the informed consent when nothing really has changed. So, I thought, at least to me, it's similar with a donation process where a lot of the risks that were listed seemed to have been there for a while. So, but, in fact, the question of what's magic about 365 days has been brought to me. Like why one year, six months is a person not capable of understanding the risk than say, what is the time limit for that? I'm not trying to be argumentative, but I appreciate your comments on this.

DR. DOMEN: I don't know that anybody knows what the magic number is. They pick a number and that's kind of what they go by. Our hospital policy is, if I recall correctly, is every three months, they

do a repeat informed consent. But, we have been able
to adjust that in our apheresis center for red cell

exchange patients, do it every once a year. So, those people are coming in on a regular basis.

UNIDENTIFIED PARTICIPANT: How much of the result is due to memory as opposed to actually understanding what was said? That's the first question. The second one is related, and that is, is there a difference among those who are first time donors and those who have donated seven times in terms of having heard those results? And I'm looking at a questionnaire, and I have the paper here, your last question five says possible risks. If one reads this and is asked correctly, is that people may not see as a risk of donation or donating blood obtaining a positive infectious disease is not a risk of the donation. Or a referral to a physician is not a risk of donation. So, they may not have understood the question.

DR. DOMEN: In looking back, there may have been somewhat a misunderstanding on their part. But, there is data going back early in the HIV period in the

late eighties and early nineties, where people actually
did think that they could get HIV if they donated

blood. And there was about a 25 percent of blood donors, at least in some surveys, that indicated that they thought that was a risk of donating. So, I'm not sure where -- how the people are answering those questions are thinking of false positives or true test.

UNIDENTIFIED PARTICIPANT: But, the first two questions I'm really interested in, did preparation based on the number of times people have been given information and their accuracy in reporting, in other words, it's a memory problem as opposed to a comprehension problem?

DR. DOMEN: Well, that would be hard to tease out, I think, whether it's memory or comprehension.

UNIDENTIFIED PARTICIPANT: You can do it by the number of times people have heard it.

DR. BRACEY: Comment from Dr. Holmberg.

DR. HOLMBERG: I was very intrigued by the comment about a donor bill of rights. What would that

look like?

DR. DOMEN: Well, there is one or two

references. There is an actual suggested donor bill of rights. It might look like that, we are going to do everything possible to inform you of all risks and benefits and we're going to make sure that you get your test results and things are explained to you. And there's a whole -- we're going to treat you with respect, you know, and sort of that.

DR. HOLMBERG: I'm glad to hear that respect part. I think, the study a few years ago, especially with Hispanic donors, that came out very loud and clear. What brought them back was respect.

DR. BRACEY: One of the interesting questions that often in the medical world, the printed document serves simply to document the process that has taken place. But, informed consent is considered something between two individuals, one with knowledge imparting knowledge to those who would be having the therapy. Is your assessment of informed consent for blood donors that, what is the process, the prevalent

process? It's generally a process of reading and signing the document or a process whereby the

information is imparted from one knowledgeable source to another?

DR. DOMEN: In my experience, and this is in spending five years in the blood center as well as ten plus years in a hospital program, is that we rely a lot on handing them information sheets to read.

Whatever is detailed in there, we expect them to read it and understand it. That's not always the case, and in particular, by repeat donors who are tired of

looking at it, don't look at it anymore. And so it

depends on how you present it. And I think a lot of

times we don't even look necessarily at what their

language level is, what grade level it is. Those

things are written for, perhaps, can you understand it?

Do we even know that the person can read for one thing?

So, there are things that perhaps during the interview

session used to be picked up and handled better. And

I'm not sure how well they're doing that, the nurses

are doing the hematocrit and blood pressure and are,

you know, are they really taking some important time to
make sure that the donor comprehends and has questions

and asks them and so forth. I think there are areas that it's not just signing a sheet of the paper, but it's making sure there is some dialogue. That's the important thing that goes on, and that they understand it.

UNIDENTIFIED PARTICIPANT: I did want to mention that in the AAPP unified donor history test, or donor history form, there were specific things there to pick up comprehension and retention, and trigger those kinds of conversations. But, the question I wanted to ask is, I was looking at your numbers of what people remembered or comprehended, and the critical things, the comprehension rate was pretty good, and some of the other things were around 50 percent or something. How do you determine what's good enough? When do we know we're there and what we're doing is where we want to be? And as you mentioned, compared to some other kinds of informed consent, like medical procedures, this is pretty good.

DR. DOMEN: I would say we probably have done a good job in some areas informing donors, and

they seem, it's been similar with HIV, they seem to have a pretty decent understanding of that. But, I'm not sure how well they understand the other things on the bottom of those lists. The fact, that they come and donate today, they may end up with a medical referral is going to cost them money potentially or that they might get a false positive infectious disease test which is then going to cost them money, additional testing and sometimes they actually come back and say, who's going to pay for this? You referred me to a physician. Why do I have to -- you know, this kind of -- they're very concerned about this, but I'm not sure we're doing a great job informing them up front about these.

DR. BRACEY: Perhaps one more comment before we take our break. Dr. Sayers?

DR. SAYERS: I don't want this to sound as if I'm disinterested in informed consent, I think they really are very important. But, do we know of any

instances where blood programs have been successfully
sued because donors alleged harm attributable to the

fact the informed consent was inadequate in preparing them for the experience?

DR. DOMEN: I don't have any direct information on that. I don't think there's been enough studies done in this area to elicit some of that data as far as, you know, what people actually do in the informed consent.

DR. BRACEY: Thank you, Dr. Domen. Why don't we take a 15 minute break and then we'll reconvene.

(A brief recess was taken.)

DR. BRACEY: We would like to move onto our next talk and presentation. We're moving onto our next talk. Dr. Bryant is so patiently waiting. Committee members, please back to the table. Let's reconvene. Our next talk is from Dr. Barbara Bryant, and the last time I saw Dr. Bryant was in September at a similar venue just before Hurricane Ike hit the gulf coast. And we were both impressed and impacted by that in a

major way. But, Dr. Bryant is an associate professor
for pathology and associate director of the blood bank

at the University of Texas in Galveston which was impacted in a major way. And she's done much work in this area of great importance and she's published and also imparted information to other expert bodies on identification and management of iron in donors. So, Dr. Bryant.

DR. BRYANT: Thank you, Dr. Bracey and the committee for asking me to speak today. I'm going to talk about the identification of iron status and its management in blood donors. So, iron deficiency in first time and repeat blood donors is a real issue in transfusion medicine, and as you heard earlier today, iron is an essential element lost with each blood donation. Men lose about 242-milligrams and women about 217. And the normal iron source for men is a thousand milligrams, but only 350 milligrams in women.

So, in order for a donor to compensate for iron loss during donating blood, iron has to be localized from body's iron stores and has to be

increased in absorption diet. So, this balance can be difficult to maintain, especially in premenopausal

females and regular blood donors since there's ongoing blood loss. Now, the consequences of iron deficiency in donors is decreased iron stores leading to decreased hemoglobin values and then donor deferral.

Additionally, this iron anemia is not treated and symptoms of iron deficiency include fatigue, difficulty with concentration, pica, we'll talk about in a second.

So, the need for giving replacement iron for blood donors has been acknowledged with very much debate in the literature. There's several successful short term studies, less than a year. Iron is usually only given to premenopausal females. There's no long-term study and few studies include males or postmenopausal females.

So, at NIH, we have a protocol called iron replacement or iron replacement in blood donors. And this is an NIH protocol. In the background is eight to 12 percent of all of our whole blood donations, donors

that have been included from individual deferral for
low hemoglobin. So, we set off to do a three year

study. We thought we had a thousand low hemoglobin donors, and 500 control donors. Now, the low hemoglobin donors we put in this category based on the capillary finger stick sample, and then the control donors who are donors who have never had a low hemoglobin and they're not currently taking iron.

The goals of the study was to analyze the cause of those low hemoglobin, quantitate the prevalence of iron deficiency, study the long-term effects of blood donation on donors' hemoglobin and iron stores, and evaluate the safety, efficacy and practicality of distributing oral iron to determine how this affected the donor pool.

So, donors who were enrolled in the protocol were asked a series of questions. We were wanting to know about previous deferrals, do they have any history of anemia, have they ever been treated for anemia? Or family history, family history of GI bleeding or personal history of GI bleeding, family

history of GI cancers and the like. Testing was
performed on these donors. A CBC was done, so we had

venous hemoglobin samples compared to capillary samples and also iron studies, which is ferritin saturation, transferrin and serum iron. And then occasionally, depending on results, we may run a hemoglobin electrophoresis.

So, just a few definitions before I get going with the results. The normal rate, and I use ferritin to determine iron deficiency and depletion. Ferritin is an easy test. It's cheap, I get results back. There are other tests that I can run, but ferritin seems to give just about the best answer I can get in a short period of time. We do acknowledge that ferritin in an acute phase reaction can be elevated at times.

However, when you look at the full picture, a person who has a falsely elevated or elevated ferritin due to inflammatory process, it's a localism. So, we use ferritin to determine the deficiency and depletion. So, the normal range of ferritin for a

woman is nine to 100 mcgs per liter and we determine
iron deficiency, ferritin less than nine, iron

depletion, we pick nine to 19. And iron replete was a ferritin greater than 20.

For men, the normal range is 18 to 370. So iron deficiency is a ferritin less than 18, depleted, 19 to 29, and replete greater than 30. Now, I'll acknowledge here that I use the depleted range for both men and women that was pretty narrow. I wanted to be very conservative. A lot of people used depleted all the way up to ferritin 50. But, I wanted to keep it nice and narrow for this study. So, I'm going to report the results for a 30 month period from January '06 to July '08. We had 891 low finger stick hemoglobin donors. Eighty-six percent were female with a mean hemoglobin of 11.8. The remainder were men with hemoglobin levels of -- a mean level of 11.9. Of the 406 control donors, now, remember these are donors who pass the hemoglobin screen, 36 percent were female and the mean hemoglobin was 13.7, and 64 percent were male, mean hemoglobin of 14.9.

So, this shows the donor demographics of
our two groups, low hemoglobin group, and the control

group. So, the low hemoglobin group was predominantly female compared to the control group. The women were younger in the low hemoglobin group compared to the control group. There were more males in the control group, and as far as race, the breakdown of race, there were more Caucasians in the control group and more African-Americans in the low hemoglobin group.

Number of first time donors, I have to say, we had 31 percent were first time donors in the low hemoglobin group compared to only 12 percent in the control group. However, this question about first time donations related to donations at NIH. So, they may have had 31 percent. They may have donated in other locations prior to coming to NIH. And also the prior number of donations before they were placed in the low hemoglobin group was almost eleven for women and 30 for men.

So, overall, the results showed in the low hemoglobin group that women, 32 percent were iron

depleted and 22 percent were iron deficient. Of the
males in the low hemoglobin group, 10 percent were iron

depleted and 53 percent were iron deficient, which kind of makes sense. By the time a man has a hemoglobin less than 12.5, he's basically in the anemic range. So, you do expect to see more iron deficiency in the men in the low hemoglobin group.

So, we broke these statistics down to take a look by different hemoglobin levels. So, this is based on the finger stick hemoglobin level and this is in women. So, the greater 12.5, which would be the women in the control group, as you can see, ten percent and iron deficient, 30 percent iron depleted. Now, if you'll note at the bottom, venous hemoglobin greater than 12.5. I wanted to know how this correlated to finger stick. So, in the group that had finger stick hemoglobin greater than -- greater than or equal to 12.5, 81 percent of them did have a venous hemoglobin greater than 12.5. Now, in the twelve to 12.4 category, 14 percent were iron deficient, 35 percent were iron depleted. If you look at the bottom, 56

percent of those donors had a venous hemoglobin greater than or equal to 12.5. However, the finger sticks

showed between twelve and 12.4.

So, it shows that especially in this range, that the finger stick hemoglobin -- you can almost flip a coin as to whether or not that really correlated to the venous hemoglobin. In the 11.5 and 11.9 range, 23 percent of the women were iron deficient and 29 percent were iron depleted. And as you can see, in the less than 11.5 grams hemoglobin, it's 40 percent iron deficient, 27 percent iron depleted.

Now, in the men, I broke it out just a little bit further. I took a look hemoglobins greater than or equal to 13.5. So 14 percent were -- I'm sorry, 19 percent were iron deficient. And in the group of 13 to 13.4, again, my control donors, 25 percent were iron deficient, small end of, and also the 12.5 to 12.9 range, 56 percent were iron deficient. In the twelve to 12.4 range, 46 percent were iron deficient and twelve percent were iron depleted, and in the men with hemoglobins less than twelve, 63 percent

were iron deficient.

Now, I have this slide here to remind me to

talk about pica. We asked questions about pica when we did the screening, and pica is a craving for a non-nutritive substance. The classic one associates with iron deficiency is crushed ice. These people consume large volumes of crushed ice. I have many donors tell me about sneaking ice during the night, having stop on the way to work to get more ice. I had several donors tell me best ice in the NIH clinical center -- the funny thing, they're all the same machines, is hidden up on the fifth floor. I had donors reporting that they ate frozen lettuce. I had a donor that eats coal. I had several donors that ate dirt. Raw pasta. I had a school teacher that consumed large amounts of chalk when the kids were at recess. And, of course, we have Argo starch as another.

When we gave donors that had pica iron, it's very interesting. The cravings appear -- well, first of all, they decrease within five to ten days and between ten to 14 days were totally gone. Restless leg

syndrome is also associated with iron deficiency anemia. And it has been reported in blood donors.

This is secondary restless leg, not primary. It seems that iron deficiency or depletion can cause or exacerbate restless leg syndrome.

Now, it's thought because of the decreased central nervous system iron, especially in the substantia nigra may be responsible. But, basically the low iron stores, they're actually -- they compromised iron management or produce or exacerbate -- -- reduce iron levels from restless leg syndrome. So we asked patients about this, and it's very interesting. Some of our patients reported no improvement once placed on iron. But, those that did took about six weeks to two months before the symptoms got much better. This was -- between the pica and the restless leg syndrome, if you can improve someone's life, they're not having restless leg syndrome at night and they're not chewing ice all day long, they're very happy people.

So, we took a look at the association of

finger stick hemoglobin levels and pica and restless
leg syndrome in women. In women and men. But, for

women, you'll notice at the hemoglobin levels less than 11.5, it was 14 percent reported pica and 16 percent report restless leg syndrome symptoms. And this was statistically significant. And it approached significance if you just took the whole group of women that had hemoglobin levels less than 12.5 just for pica.

And for men, if they were iron deficient, pica was present in 18 percent and restless leg was present in 17 percent. In the depleted category, pica was present in 7 percent. I'm sorry. That was wrong. Again I'm sorry. I'm looking at the association of pica and restless leg based on iron statuses as opposed to just hemoglobin.

Now, for the men, for pica, it was associated with a hemoglobin level less than twelve. Eleven percent of the male donors reported pica. And the other one -- that was not statistically significant. And overall, pica has been seen in 6.4

percent in men with hemoglobins than 12.5. When you looked at the iron status in men, nothing was really

statistically significant.

So, in our study, we wanted to see the effect of giving oral iron, being dispensed from the blood bank, what type of effect that would have. So, we gave donors ferrous sulphate or ferrous gluconate, 325 milligrams. We gave them a 60 pack of iron and we gave the tablets -- instructed them to take it once a day for 60 days and then return to the blood bank. Now, ferrous sulphate 325 milligrams is 65 milligrams elemental iron, and gluconate 325-milligrams is 38 milligrams of elemental iron. We also gave ferrous sulphate first as the first line, and those that were intolerant to sulphate or had a previous history of intolerance to sulphate would get gluconate. These tablets were packaged in blister packs. So, they were child resistant. They were difficult to open. Most of my donors indicated it was adult resistant as well, they had to take scissors to open them. That was actually my biggest complaint, how those things were

packaged.

We saw overall 71 percent compliance taking

iron tablets. Initially 82 percent were given ferrous sulphate with the other 18 percent reporting intolerance. Again, they had had a previous history -- generally it was females taking it during pregnancy and they weren't interested in taking sulphates again. An additional 18 percent developed intolerance and were switched to gluconate. I only had 2.8 percent of donors that were intolerant to both the sulphate and the gluconate. Most common complaint is GI discomfort, specifically constipation.

So, I want to spend a few minutes on this slide. This shows the effect of iron therapy in the low finger stick hemoglobin donors. Now, you'll first note the finger stick, that is the peak line. Remember the average finger stick is 11.8, 11.9. So, this is the number of visits. These donors took the iron, returned and continued to donating blood. And we gave them additional iron after each donation. So, finger stick hemoglobin went up to -- about a gram or more and

then maintained -- it became stable throughout the
donation history because they continued to get iron

with each blood donation.

The venous hemoglobin followed along as well. The RDW, red cell distribution width, it actually went up first and then went back down into the normal range. And you would expect that because these donors had iron deficient or iron depleted red cells. So, when we gave iron, they started making nice new plump red cells. So, where you would expect the RDW to be. The MCV was low in most donors or on the low side of normal. As we gave iron, the MCV increased and stabilized in the normal range. And the ferritin, which was very low to begin it, increased, went up through the donation and then kind of stabilized out. As you can see, it didn't really go too extremely high. This is 50 up here. So, on average, stayed in a range about maybe up to 40 and kind of hovered around 30.

Now, in the study, we gave iron to blood donors who came in with a low finger stick hemoglobin, and then we got the lab results. And there were donors

in our study that had low finger stick hemoglobin levels, but they were not iron depleted or deficient.

So, we wanted to see what would happen to these donors. These donors continued to take the iron. We wanted to see what would happen. In other words, would we overdose them in iron? What would we cause their ferritin levels to do? Could you harm these donors? Every time they're coming in, I'm running a lab. So, I have a wonderful set of data to look at broken out by apheresis male, apheresis female, whole blood male, whole blood female. As you can imagine, the top line is the male and the bottom lines are the women. And again, remember, we started around 11.8, 11.9. We gave them iron, and this is each subsequent blood donation when they came in, and they had been taking their iron. As you can see, even though they weren't iron depleted or deficient by the definitions we used, their hemoglobins jumped up about 1 gram and then pretty much remained stable.

Now, the ferritin levels the same thing.

Remember these folks did not have iron depletion or

deficiency. So, their iron, their ferritin levels are
in the normal range. We gave them iron -- gave them

the iron. It bumped up a little bit, came down. This probably -- this fourth visit was associated with some a little less compliant, but they pretty much maintained. No one had a ferritin level that kept going up and increasing.

Now, this set of slides shows what happens to the control donors if they don't get iron. The way we set this study up was that a control donor would not get iron unless they became iron deficient. We're not going to treat iron depletion. We're just going to wait and see what happens. So, graph A shows what happened to control donors without iron therapy. So, the first donation, they had ferritins on average around 60 and then second donation it just keeps on going downhill. The second graph shows the group of donors, control donors on their first donation were found to be iron deficient and we put on iron and their ferritin level goes up and then just kind of stays in this range here. The third graph shows donors that

were started on iron on their second blood donation and
were found to be iron deficient. Same type of graph,

and this is on the third visit and fourth visit. This is what happens when the donors continued to donate and they don't take iron. In the average interval between donations, there was about three and a half, almost four months. I think it was about three and a half. Three months, three weeks. So, in the study, no donors were found to have ferritin and transferrin saturation levels suggestive of hemochromatosis. And this is a issue of giving iron to blood donors. You don't want to give iron to someone who has hemochromatosis. So, just by using the ferritin as a screen, we didn't find anybody that had levels suggesting hemochromatosis. There were no malignancies reported or detected during the study, and all donors with iron deficiency got a copy of their lab results to take to their primary care physician.

One of the big concerns in this study is that we would possibly give iron to a massive condition in which iron deficiency was a hallmark for, that

condition, specifically colorectal cancer. And we
asked a whole lot of questions and picked up -- I'll

show you some of the serious medical conditions we did pick up by asking the questions. But I wanted to show the age related SEER incidence rates for colorectal cancer per 100,000 population. This group is SEER data 1998 to 2002. So, if you'll look right here in the male, the chance of colorectal cancer incidence is .5 per thousand at about age 54, and that increases to three per thousand at age 74. So, the likelihood that a low hemoglobin in a repeat male donor is due to colon cancer is extremely low. So, therefore, the likelihood of masking it is even lower.

Actually, our program encourages PCP evaluation for more severe anemia rather than telling them to return in a few days. One of the concerns in donor situations in donors with low hemoglobin are screened, they're sent away and said to come back in a few days or wait a week or two and no additional information is given to donors especially if they're severely anemic. So, we were actually following these

lab results very closely. And by doing so, we actually probably picked up conditions that we know had been

missed by their primary care physicians or that the patients were unaware of. In our study, we picked up two instances of upper GI bleeding due to gastritis. Both of these were picked up in the question about, do you have black tarry stools? Both of the donors indicated they did and didn't understand what that was all about.

I had two donors, and now I have more as the study has gone on, in which we've picked up vitamin B12 deficiencies because as we treated these donors with iron and their MCVs corrected and their iron deficiency went away, their MCVs went to 103, 104 and we ran B12 and folate levels and were able to give them the information to take to their primary care physician. Both of them had vitamin B12 deficiency. We also picked up a case of thyrotoxicosis that had been undiagnosed. This patient actually presented with a low MCV and it was interesting. We did run hemoglobin treatments on her and her A2 was elevated.

And hemoglobin A2 can be elevated due to
thyrotoxicosis. And actually, we brought her back in

and we talked to her a little bit more. It was obvious seeing her a week later, her symptoms were very, very clear when we saw her. So, she actually had labs. We gave her copies of her labs, sent her to the doctor. He couldn't see her until the next day, and then she actually had a full blow thyrotoxicosis event and ended up in the emergency room holding our papers. And the doctor said it saved him about four hours worth of work up. So anyway, no donors in our study were found to have cancer or hemochromatosis.

So, in summary, blood centers are confronted with ongoing challenges of iron deficiency in blood donors both preexisting iron deficiency and the resultant iron deficiency from donating blood. And these donors are altruistic. They come to give the gift of life and this is an opportunity to give something back of value to the donors. Iron replacement is cheap, it's safe. It's an effective method of preventing iron deficiency in donors. The

advantages to donors is it results in more productive
blood donations. It enhances donor well being by

preventing symptomatic iron depletion and deficiency.

And it has increased overall donor satisfaction. The advantages to the donor center of establishing a program such as this is that it decreases donor deferral for low hemoglobin values. It improves donor retention. It's cheaper to retain your donors than it is to recruit a new one. Studies show to recruit a new donor costs 50 to \$400. So, it's a win win situation.

However, I will tell you, it is important to have medical oversight in a program such as this so that you can refer donors who need to be seen by physicians to their proper care physician. Primary care physician. Blood centers have the responsibility of maintaining these issues to maintain issues to maintain suitable blood supply and ensure donor health. So, in summary, in our study, we saw 54 percent females, 63 percent of the males in the low hemoglobin group that were iron depleted or deficient. And in the control group, 40 percent of the males and 40 of the

females had iron deficiency.

So, what would I recommend? I think the

diplomatic recommendation would be administer a two month supply of oral iron tablets to all women with hemoglobins less than 12.5. Keeping in mind that women, 12.5 is a fairly high number for women, and a lot of women are in the normal range, less than 12.5. Our normal range at NIH is 11.5 to 15.1 normal hemoglobin for a woman. But, the leading cause of iron deficiency in a woman is menstrual blood loss followed by the second one, a far second, was routine blood donations.

However, in men, the leading cause of hemoglobin less than twelve is multiple previous donations. So, if a man has a history of previous blood donations and his hemoglobin is less than 12.5, if you gave him a two month supply of oral iron and he didn't respond when he came back in 60 days, then you want to refer him to a primary care physician. Any male that's a first time donor shows up with a hemoglobin less than 12.5, you give him iron, but I

would refer him to his primary care physician because
he is, at this point, iron -- he does have anemia

because his hemoglobin is 12.5. And males with a hemoglobin of less than twelve and females less than ten need to be referred to their primary care physician anyway.

Now, evidence based recommendations, based on the study supports routinely administering a two month supply of oral iron tablets to all whole blood donors, a 60 day pack of iron, if you absorb the average amount of iron every day in a two month period, you take all 60 tablets, you'll have absorbed approximately 238 milligrams of iron. And figure in every blood donation about a 240 milligram iron loss, this is the trade-off. They give us blood, we give them a pack of iron. Of course, the concern is that you give iron to someone with hemochromatosis, so it would -- you want to verify a non hemochromatosis status by at least a single ferritin level.

I'd like to acknowledge the team that I work with at NIH, Susan Leitman, Yu Ying Yah, Julie

Hopkins, Sarah Arceo, and Dr. Klein and as well as all
our blood donors.

DR. BRACEY: Thank you, Dr. Bryant. One of the things that I noted that, I guess if I got the figures right, we're only looking at anemia aside from other markers of disease. It looks like you found one in 200 individuals that had apparently healthy -- that had medical problems. Are there any other studies that looked at anemia? What's the rate of finding disease in apparently healthy donors and other studies of iron?

DR. BRYANT: I know there have been a few studies, such as colorectal cancer, I believe, that basically says, you know, you're just not going to pick up disease by hemoglobin screening in the donor. You're just not going to see it that often. Remember, the donors come in feeling well, they're healthy. So, we have this elite population of healthy feeling people, but I'm not aware of any data that actually shows numbers at this point.

DR. KOUIDES: Dr. Bryant, thank you very much. Interesting. Regarding your health

questionnaire, did you ask any identifying

characteristics of menorrhagia such as changing tampon

or pad every two hours or passing blood -- having clots the size of a quarters?

DR. BRYANT: Absolutely. We asked -- I should have mentioned, we asked a lot of questions about the OB history, the GYN history, and as you know, people will give you the most amazing answer. No, perfectly normal, but I have menstrual periods lasting twelve days, changing pads and tampons every two hours for most of those days, but assure you they pass clots no bigger than a golf ball. And I sent many a woman to an OB/GYN. I'm going to tell you, this type of study makes you feel really good as a doctor. You can fix a lot of things. But, to send a woman to a doctor that's been having this problem all her life and thought it normal because her mother and her sister told her it's normal? This problem gets resolved, I am truly a goddess for doing this.

DR. KOUIDES: That would be interesting, if you haven't done this already, to look at the

correlation of clinical details with their blood type.

What grabbed me, most people know, women -- other side

of the coin here, this is a common problem, five percent of women during reproductive cycle will report heavy periods. And a woman had a normal gynecological exam, certainly doesn't probably correlate with all these patients, I know that you have a fair number of African-American women probably with fibroids. If you look at your Caucasians, you may have 600 Caucasians here with 50 cases of Von Willebrand because at least eleven studies today have been published and, one of the studies have shown about 13 percent prevalence of Von Willebrand in women with menorrhagia with normal gynecological exam. It would be interesting to follow up with those women to see if they had hemostasis testing for Von Willebrand and especially African-American women.

DR. BRYANT: I'm so glad you brought that up. This is something I'm very interested in and I really hope to at least pick up on Von Willebrand disease. That would make the study for me. And I had

two donors which I thought for sure, this is a -- this
history in particular, it was classic. I knew for sure

I picked up Von Willebrand. And actually ran testing at NIH and they were fine. But, we were able to send that patient to the OB/GYN. Now, one was O and one was A.

DR. KOUIDES: In your group of Caucasian women, 600 here, did you see any correlation?

DR. BRYANT: I'll have to go back and look.

DR. KOUIDES: That would be very interesting. The last point, you may have uncovered hemochromatosis, perhaps in part because of the fact that many of these were repeat donors, they had over ten to 15 prior donations, and in some cases that may be enough that the iron then at this point where they didn't really have increased ferritin at that point. Because with 900 Caucasians, you should probably have three --

DR. BRYANT: Exactly. One in 200. It's interesting because we thought, what if we had a hemoglobin that had just been donated, a hundred units

or whatever, and we had a lot of hundred plus donor
unit donors in this group, what if I give them iron?

We really need to see what happens to their ferritin. I reviewed all the labs on all of these expecting maybe sooner or later I may have someone I gave iron to and their ferritin would jump from 18 up to 100. That's why. So, it never happened. I never saw it. So, if they did -- that would be interesting. No one goes around giving iron replacement to people that have hemochromatosis. I don't know what I would expect in their iron level if I gave a 60 pack of iron to someone who had hemochromatosis. Would I harm them? Would they come back for another blood donation? I assume they absorbed more iron through their GI tract, but what would their ferritin really do? Nobody ever really looked at that. Anyway, I didn't see that.

DR. KOUIDES: Do you have any questions about details of cognitive ferritin? The reason I ask is that there's a study published looking at adolescent females where they showed that they had cognitive impairment they correlated with iron deficiency.

Obviously, your age here was 18 or higher. Subsequent studies are interesting particularly in adolescents

being run in the donor pool. There could be negative impact, perhaps iron deficiency and correlated with decreased cognitive function.

DR. BRYANT: Donors actually reported feeling so much better and some said they had trouble concentrating. They were putting their heads down in the afternoon. They weren't getting their work done and that they felt they could think better, they had more energy. It was a very rewarding study to do.

Donors reported being energetic and being able to go home and one donor said, I lost 20-pounds since I started iron. But, instead they didn't collapse on the couch, they had more energy, they went to the gym, they got memberships. Donors reported overall better -- well, much better including concentration, energy, able to play with their kids. That type of thing.

DR. BRACEY: We have time maybe for one more question. Dr. Ison?

DR. ISON: The age, the median mean is in

the forties or fifties, what's the splay of that age?

Did you have sufficient numbers of older individuals

that you would expect to have a higher prevalence of colon cancer?

DR. BRYANT: We had more than a few donors that are over the age of 60. I don't have the numbers in front of me right now. But, the age range was 18 to 82. I will say that I had in the low hemoglobin group, most of them are premenopausal females, and the ones right around menopause for the reasons that we talked about. But, yes, I had quite a few older donors in my study.

DR. ISON: I think it would just be interesting to kind of look at that issue because a very small number that may be less reassuring that you didn't pick up.

DR. BRACEY: We'll move on to open public comment.

UNIDENTIFIED PARTICIPANT: I'm a very active volunteer for the Committee of 10000, and so I'm happy to see you talking about women in the blood

supply. Because I have been coming to these meetings
for 15 years and wondering why you aren't targeting

women with the message. I myself had donated on multiple occasions. First time I remember being tired, waited a while, went back. I went back, took my blood. I went back, they didn't take my blood. I went back, I brought people with me. Like the time before, they didn't take my blood, they took other people's blood. They thought they had been kind because I brought them, they wouldn't take mine.

What I find is that the message to women doesn't come out clearly come back. I've talked to friends of mine and said, are you going to go donate? And they said, no, they don't want my blood because they think that when they donate, they are determined to be on the anemic side and the blood isn't taken. They think they are not supposed to come back and they weren't going to be able to donate. So, I really just wish we would make a message clear at the time of deferral that today you may not be able to donate. Tomorrow you may be eligible. Please come back, try

again. We want your blood unless you have a reason to
be deferred. And I think that's part of why the first

time donors -- a lot of first time donors, because I think after the first time, you get the nerve to go, you go, they say no. You think they, oh, they don't want me, there's something wrong and don't go back. So, that's where I wish they would just make the message very clear. Because I think that without spending any more money than to create the message and deliver the message, I think that we will increase the blood supply quite a bit. Thank you.

DR. KLEIN: We'll be happy to take your blood.

DR. BRACEY: We're going to open this up to committee discussion. I'd like to start that by revisiting the questions from the department, the assistant secretary, and we will hear more about health screening tomorrow, and again, one of the things that I'm hoping is to see is how what we do fits into the 2020 picture. But, I think we should begin the discussion on the first question, and that is, is the

current status of informed consent of blood and plasma
donation adequate to protect donors? We've heard an

excellent presentation from Dr. Domen, so I would open up that question for the committee's discussion. I think Dr. Sayers framed it nicely with a comment that there haven't been any lawsuit, legal challenges to date related to this. Actually, it's interesting. It seems like the history of informed consent in part is based upon legal challenges. At any rate, I'll just open up the question to the committee for discussion.

DR. ISON: Well, as a challenge, I'm not sure that that's a valid reason for informed consent just because there hasn't been a lawsuit. Really what we're trying to do is impart information and make sure that the patients are understanding what they're about to go through. And I think that really our goal should be a hundred percent comprehension of patients that are undergoing this procedure. I don't think we'd be happy if it's a surgery, but I don't think we'd be happy with someone consenting for surgery if they didn't really understand what they were getting at.

That being said, you know, from the data
that's presented, I'm not sure we're doing a terrible

job. But, perhaps more research needs to go into what would facilitate better understanding of these issues.

And then I think the second issue that was raised about the need to re-consent these patients I think is a very valid thing to think about. If we really get a robust consenting process, is it something we can have some sort of term limit or time limit for? Especially since those patients are voluntarily coming in, so theoretically, they know what they're getting themselves into. They're coming back for a second.

DR. BRACEY: One thing that struck me as we were -- as we reviewed the data in terms of the briefing materials, et cetera, it seems that we continued to acquire information about the hazards associated with blood donation. And in a sense, it's a moving target and I just wonder, are -- so, how do we keep, you know, the person that's facing that intervention up to date with us? I'd raise that for someone that might be in the blood community. As we

acquire more information of that, you know, benchmark
data on the frequency of the events, is that being too

specific or is that an issue as we acquire new information, the ability of us to get it to the donors?

DR. KLEIN: First let me say that I think it's very difficult to answer the first question, because as many of you know, informed consent documentation differs from center to center, and differ quite dramatically. In addition to which, the way it's administered, it differs from center to center. So, I don't think we really know what the current status is. Aren't your questions involved -- I'm sorry.

DR. BRACEY: My question is --

DR. KLEIN: Oh, yes. The data, again, I think you run into the age old problem of what is relevant to tell a blood donor? Do we inform the blood donor that there have been 39 deaths reported to the FDA, but none of them have been associated with donation? Again, I think you have to report with a reasonable person who would want to know about donating blood. That's not usually in great detail what the

statistics might tell you. And again, I don't think we
have to look at guidelines of doing that.

DR. BRACEY: Now, it seems that the AABB is addressing the potential of having a guideline. So, if the committee, or is there a group within the committee or the industry, if you will, that's trying to make the guidelines -- develop uniform guidelines for the consent process? Dr. Kessler, did you mention that there was some activity in that regard or is that solely for questions for donor acceptability?

DR. KESSLER: I think what was mentioned was what was in this current standard which was just kind of an overview. But, there isn't any attempt on the standard committee to make that more specific. The other thing is that for the donor history form for the AABB, unified donor history form, in our working with FDA to create it, a number of things have been put into the donor educational material, and then the donor is asked did they read and understand the educational material? And then for most centers, although this can vary from center to center, the actual words within the

consent is pretty brief. But, it's based on all the
information that's in the educational materials which

is easy to update, getting back to your first question, about how do we keep current? You can always throw stuff into the educational materials.

However, having said that, that is a lot of information in those donor educational materials and a lot of things that we want the donors to read and to understand, not just related to consent. And I only, my concern in hearing some of this conversation is throwing more information at donors to understand and know about before they donate. They don't read it now. They kind of glaze over when they see it.

DR. BRACEY: Mr. Matyas?

MR. MATYAS: I'm in -- even as a lawyer, in full agreement. Lawsuits are not necessarily an indicator of whether or not the people are getting enough informed consent. The question is, do we have enough information as to what the donors believe -- do they believe they have enough information? And isn't that really left then to the AABB and ABC then to the

centers themselves to be figuring that and determining
that out since it is a national mandate as to exactly

what the informed consent is?

DR. ISON: My question is, can there be a national mandate with differences in state law, particularly relevant to testing? Currently HIV requirements for consent is very different state to state from this point. So, can we have a national standard or is that something that has to be based on state to state?

DR. BRACEY: Dr. Triulzi?

DR. TRIULZI: I think the ABB standards are meant to be a mandate to have the elements of informed consent. It doesn't give you the wording. It doesn't want to be that descriptive of the wording that has to be used. But, I think the standards are meant to provide what elements should be in there. I don't think this process is badly broken on the donor side. I think it's, in general, a low risk process to begin with. That doesn't mean there isn't some room for improvement. If you compare it to the recipient side,

there's no comparison. And so I don't think we want to
disassemble a process and rebuild. I also think we

want to make sure that we don't put something in that turns more donors off and we actually lose donors over the process. If it were badly broken, we might consider that. But, I don't think that's the case. So, I think moderation is probably the right tone to address that.

DR. BRACEY: Dr. Lopez-Plaza?

DR. LOPEZ-PLAZA: I want to make one comment. We may improve areas of consent. Probably one first example we have any consent. We need to look into the people who are actually obtaining that consent. Might it be sufficient as the implementation goes that has been presented so as we look to improve it? We have to consider that factor.

DR. BRACEY: So, the framework is there and it's not really a broken process. But, perhaps there's room for development of tools such as best practices to be shared from a facility. Would that be a fair assessment? Dr. Epstein?

DR. EPSTEIN: When will -- well, I'm just
going by the observation, looking at the outcome of

this study by Dr. Domen, that was discussed in detail, where we put effort, we have gotten results. And what I am talking about is that since the 1980s, we put a great deal of effort in trying to ensure that the donors understand the risk factors that could make their blood unsafe for a recipient. And those types of factual matters, the donors seem to get.

If you then look at the things the donor didn't get so well, they kind of correlate with level of complexity. Donors understood that they might faint. Simple. Donors tended not to understand that their name might go on a deferral registry or there might be complications of getting a false positive test result. It seemed to me that those -- that category of comprehension issues clustered with higher levels of complexity. And I think the fact that, as you know, the AIDS factor is pretty complicated too. We spent decades trying to get it right and we simply have not invested the effort to ensure that our communications

with donors are adequate in the areas of potential harm
for the donor.

So, I think, you know, you sort of get what you pay for is what's really going on here and that the underlying confounder is complexity of the information. When we talked about the donor history questionnaire, in order to validate the uniform donor history questionnaire, focus groups were utilized in the collaboration between the blood organization and the FDA to really look at issues like attention and comprehension. And nothing like that, to my knowledge, has really been done with the communicating of risk to the donor. So, I just think the output reflects the relative investment. And that shouldn't be a big surprise. But, all of that leaves open the question of how much should we invest? Because I think we have to understand that as an investment. That's my take on this, is that we have gotten pay off where we can invest in it.

DR. BRACEY: Dr. Pomper?

DR. POMPER: Some of the material we were

reviewing does cover something different than the
informed consent, which is slightly different, which is

how safe is the process or are there medical conditions or problems that we might be causing donors because of the donation process? It sounds like we don't understand those as well. So, I mean, to provide informed consent, we do need to understand what the problems are and some of these seem to be emerging. The iron is pretty interesting that way. So, it's at least for me difficult to say. Or I tried to ask, is the question more to the point of, is blood donation relatively safe? Or are we going to limit it to are we providing adequate informed consent? I say it's relatively safe, but are there conditions for which we're not adequately impressing donors on? Are we telling them about iatrogenic iron deficiency? And if we're not, it's probably because we're not quite sure what the outcome of that is. So, I'm just trying to get a handle on the two issues.

DR. BRACEY: The primary focus of this is on the process of -- the consenting process information

that's imparted on the donor as to whether current approaches are adequate. So, then --

DR. POMPER: Okay.

DR. BRACEY: So then the consensus of the committee, I'm trying to sense the consensus of the committee, I mean, as a whole, are you comfortable with the current process as it exists or as Dr. Epstein suggested? Is this something that we really should invest more time and effort to better understand? Dr. Kouides?

DR. KOUIDES: The presentation of Dr. Bryant suggests that the consent process should also include an emphasis on iatrogenic iron deficiency and anemia. Iron deficiency/anemia.

DR. BRACEY: There clearly is iron loss associated with the process, yes, indeed.

DR. KOUIDES: In other words, it seemed to overlook or generally overlooked in the consent process. There are other consent forms, specifically in Red Cross, about iron deficiency.

DR. BENJAMIN: I couldn't tell you that. I

don't think so.

DR. BRACEY: No, at least in the forms --

not Red Cross forms, but forms I have seen that local -- in my area, there's nothing that addresses that. So, I guess it raises the question of, you know, exactly what information needs to be imparted that we know about in this statement? Again, within reason because, again, with informed consent, you don't cover every absolute point. But, I think clearly that there's enough issues there for iron. Dr. Benjamin?

DR. BENJAMIN: I hate to add another level of complexity to this, but do we want to address the range of consent, 16 year old as well?

DR. BRACEY: Yes, that is an issue because often, again, just from the local experience, someone may donate by virtue of a drive and state law. But, then, you know, other issues come up. So, I think that is an important area to consider, considering that we're drawing about 14, 15 percent of donors in that group. So, I guess what I am sensing is that -- and correct me if I have the wrong interpretation, but the

consent process is, it works to a degree. But, it
could -- it does need to be further assessed and the

question of how much information needs to be given to the donor, the question of the method of delivery of the information to the donor is its efficacy. Those are -- those are at least two of the questions that currently exist and could potentially improve the process if we knew more about the best methods for, A, what needs to be delivered and what is the method for delivery? Would that be a point of consensus for the committee. Dr. Klein?

DR. KLEIN: I just want to say that I know this is the secretary's job to make recommendations, the secretary, I tend to agree with Dr. Triulzi, that the process is not badly broken, but clearly it could be done better. So, it seems to me that rather than ask the secretary to take action or provide resources and perhaps it would be advised to the blood collecting organizations that the informed consent process is grown up over the years in a nonscientific fashion. And perhaps that ought to be looked at both for the

content of what the blood donors are being advised
about and about the process of doing that. The

appropriate validation of questions in a scientific manner that have been used in donor questionnaire.

DR. BRACEY: Dr. Duffell? Do you have a question?

DR. DUFFELL: I think the thing that was a little troubling to me in discussion today was I sense apparent inconsistency in the way informed consent is done across the nation. When I think of a patient in Georgia versus a patient in Seattle, Washington the risks are appreciably different. So, I find that a little troubling because that means there's somebody that might be getting more information than me as a result. So, what I think about is, Jay, is studies produced for human subjects of basic elements of informed consent. And where I am going with this, I'm wondering maybe to pick up on Harvey's comment, should not one of these organizations come up and define what those basic elements of informed consent are? Because I know at Gambro, we address differences between

states. We do a multi center trial, we don't have
problems making sure that all 50 states where the

studies are done have basic elements of informed consent. The language may be slightly different, but the elements are all touched on or addressed. So, I guess my bottom comment for here is, I think the inconsistency is what I am troubled by. I'd like to see some sort of basic elements maybe driven by outside organizations.

DR. BRACEY: Ms. Finley?

MS. FINLEY: I'm wondering whether these issues regarding the informed consent document which are based to some extent on regulations are more appropriately addressed if we are asking blood collection organizations to make changes or suggesting changes are needed? I'm just wondering whether this committee -- or whether that falls under the --

DR. BRACEY: Again, the issue from the perspective of this committee would be, as I see it, to advise the secretary to apply adequate resources to what is perceived as the problem. So, we as the

committee would not determine what those specific questions are, nor complete invalidation of those

questions. But, we could certainly advise as to whether or not we think the process is adequate. Dr. Holmberg?

DR. HOLMBERG: Let me just turn my comment in here about whether it's appropriate for this committee or for BPAC. If it's not a regulatory issue, it's appropriate for this committee. If you're suggesting that this needs to be law, and that it needs to be put in regulation, then it clearly should be discussed at BPAC. But, what I am hearing, actually Dr. Pomper, and Charles and Dr. Klein making the comments, it sounds like what you're saying is that the whole -- we're learning more and more about the process and that maybe some of the risk factors were not clearly identified. Over the years we have a clearer picture now. And what we're really encouraging is the the accredited facilities, bodies to take a look at developing or expanding informed consent to include other areas such as the iron loss.

And let me just comment about the iron

loss. I don't have a big comment on this, but I do get

telephone calls from individuals, and I can tell you that I do get calls from elderly people that say, why wasn't I ever told about iron loss in donations? And what kind of follow-up is being done? And you know, you just challenge anybody to go out there and look at the different websites and how much risk factors are really identified on the websites. You always hear comments that, you know, blood donation is completely safe and no harm and all that. And generally speaking, you know, you're right. There is no -- there is very little harm associated with blood donation. But, there are potential risks in donating blood. And according to Dr. Bryant's data, anybody that donates blood over a series of time, donated according to what AABB permits.

DR. BRACEY: Ms. Finley?

MS. FINLEY: Has FDA looked at this issue?

Have they had complaints? What's the status from a regulatory perspective? Because this is going to affect how we write our recommendation.

DR. EPSTEIN: First, I don't know about
complaints. I'm not aware of complaints. Maybe Gill

is aware of complaints, but I'm not. But, first to clarify the regulatory landscape, current regulations do not address informed consent for whole blood donation. It only addresses it for source plasma donation. There it's well specified. Somebody just gave me a section. 640.61 Informed Consent. (Reads.)

But, that's just source plasma. The regs are silent on whole blood. However, in the November 8, 2007 proposed rules for donor eligibility, we proposed a requirement for a donor's written statement of understanding. Again, this comes back to Dr. Domen's comment on multiple formulations of consent or assent, or whatever you want to call it. All right. So, what we said here is that in order to review, the donor has been informed of and the donor understands the procedure and the education material, the collecting establishment shall be required to provide a written statement to the donor using appropriate language and literacy level and taking into account any known

disabilities to read and sign before phlebotomy is
performed. This data has to be written in clear and

understandable terminology and not include language that would waive any of the donor's legal rights. The document will provide the following information as described. And it goes on to talk about information provided to the donor.

So, we are involved in this. But as they say, for whole blood, it's not current regulation. What it begs the question of is what would be an acceptable statement?

MS. FINLEY: Yeah.

DR. EPSTEIN: And there I think that the situation is that for investigational studies, it's generally been the responsibility of the local IRB, that the FDA has not required a standard consent, and clearly when you're dealing with clinical trials, the nature of the trial, they vary from trial to trial, if you can understand that. When it comes to the donor questionnaire, the standard or uniform donor history questionnaire is used voluntarily. You don't mandate

that it be standard. Because what we recognize is that
there may be more than one way to deliver information.

So, I think it's an open question whether it's an FDA role to require a standardized instrument for informed consent. I don't think we're there now. There's a requirement for informed consent for source plasma. We have proposed such a statement of understanding for whole blood and it's -- we don't currently standardize it or require that it be standardized.

MS. FINLEY: In reality, this question is really about whether we need to standardize that?

DR. EPSTEIN: I'm not sure that's the only question.

DR. BRACEY: I'm not sure that's what the question is. Again, I think that we -- I haven't heard discussion at this level of generating regulations regarding this. We're just simply looking at the process. I think what we have said is that rather than make a recommendation, I know we're responding to the secretary, but really, the recommendation would go to those other bodies that have the ability to assess the

process and that currently have standards associated
with the process. The consent process.

MS. FINLEY: Well, I guess I would disagree a little bit and say that that issue is already on the table. I think we should find a way to see if we can come up with a consensus and address it. If ultimately we think FDA follow the other way, regarding some kind of minimum standard document, call it whatever you want, but if the issue here is that we really want iron deficiency highlighted in the informed consent, we are not seeing it consistently across the board. Or that patients don't understand it. And we think there could be better language. Should we go to AABB or one of the other groups and ask them to propose something or do we suggest it? As a committee, we have to give the secretary some response here.

DR. BRACEY: I understand. But, I think the issue, again, is whether we want to be as specific as stating specific examples as iron deficiency rather than revisiting the process in general. Because then I think we really are moving in the direction of

questions that are more pertinent to the FDA.

MS. FINLEY: We can recommend or we can

support the concept that the department review the need for a standardized document for whole blood donation which may further address concerns illuminated here about the iron deficiency.

DR. BRACEY: We can talk about those things. That's a good point. Dr. St. Martin?

DR. ST. MARTIN: I was going to comment. This seems quite similar to the issues that the organ community wrestled with in living donor transplants and living donation where they -- the organ transplant community took it upon themselves to develop model elements of consent. So, it wasn't a federal process, although they participated in some of the development, but it was really driven by the organ community in recognition of the serious risks. And there some very serious risks identified in living donation as well as some unknown long-term risks. But, it was the organ community driven process and they also are in the process of developing a donor bill of rights

specifically to living donations. So, whether we need something at a federal level, I'm not certain or if

it's something that we can work with the community to develop something similar. I think that might be a good approach.

DR. BRACEY: Dr. Epstein?

DR. EPSTEIN: I just want to come back to Dr. Pomper's comment because I think it lies at the heart of this discussion, which is to separate this question of whether informed consent is adequate into the two bins. Is it inadequate because of scope or is it inadequate because of, you know, effective delivery? And we need to first deal with the issue of scope, which is I think what prompted Dr. Kouides to focus on iron. Are there other elements of the risk of donation that are inadequately delineated here? And I think that the issue -- we're focusing on the issue of process, which is fine, but there really is the first issue which is are we telling donors about the right things? And that gets to threshold questions about what the risks are. Are they significant enough to

inform? I mean, should you inform a donor of a one in
a million risk? Or are we just worried about one in a

thousand risk? How to you factor in insignificance?

So, I think we shouldn't bypass that discussion. My personal feeling is that donors are not adequately informed about the risks of repeat donation. And that includes iron deficiency.

DR. ISON: Which I think would be an important issue to bring up since one of the things that's on the table is potentially extending the time period between the consent process. So, I do think that that's actually a very important point to think about. If you're going to consent someone once a year, here's sufficient information and to allow them to be aware if they donate every few months, or maximum frequency, they may develop a complication.

DR. BRACEY: So, what I hear is that, again, the discussion is moving in the direction of there are uncertainties about the efficacy or the amount or the scope of information that we're providing. The bottom line is that we as a

committee -- the sense I have is that we feel that this
needs -- this is an area that needs to be revisited and

rethought? Would that be -- we're not -- I would think the committee would not be complacent with where we are today in the consent process and we would want to further evaluate it? Dr. Pomper?

DR. POMPER: I just tried to put this together, so it's just sort of a stepping off point, but I think, first of all, I think that just to try to write this down, that blood donation appears to be a very safe process from what we heard about today. There are some risks, however, overall. I think the gestalt is that blood donation is very safe. However, as in the informed consent process has vastly improved over the past several decades, I'm just thinking that as informed consent is continuously improved, there has been brought to our attention, or that we are aware, as this process is improved, it's expected that there will be emerging new risk considered about the process that I think will continue. Some of these new risks will either be delineated or not, but may have to do with

repeat blood donation, so forth. But, the extent of the effect of these risks on donors is not known. They

just appear as concerns. I'm not sure what to do from there other than we do know we have donors who donate many, many times.

DR. BRACEY: Dr. Klein?

DR. KLEIN: For those who donate, donors consented to every single donation. It's not a question of extending the period between notification and informed consent. But, again, it seems to me that virtually every informed consent process or blood donation contains the elements of informed consent if you thought about Dr. Domen's slides and in the AABB standard. So, really it isn't the element of consent, but I think it is, as Dr. Epstein suggested, the content or the scope. I think that's part one.

Part two, I think, that we have never validated the content in terms of understanding of the blood donor, its content, the way we have validated the questions on the questionnaire. So, it seems to me that perhaps the response to the secretary would be

that we have identified these two areas, and again, I believe that the recommendation should go to the blood

community which, after all, has put together standards and a lot of materials that they should undertake to do this validation of both the content and the clarity of the content rather than to ask the secretary to take action in this area.

DR. BRACEY: Dr. Ramsey? You had a comment?

DR. RAMSEY: You touched on this, as I was thinking about this, I recognize that blood donation is not research, but it's an element in their own research. This is a framework, the IRB framework for approved -- before the framework is consent for the -- whatever is researched, and so one would think this might be if blood donation was a brand new process we just invented today, what would we want to have informed consent about from a person under going this procedure? And as you mentioned, IRB it's really up to the local IRB in terms of how that process works. But, there is a fairly formal requirement for informed

consent. So, maybe -- don't know. It's not
recognized, not exactly analysis, but seems -- it

certainly seems like I agree with some of the discussion. There seems to me to be more of attention to this area from the organizations that are involved in it.

UNIDENTIFIED PARTICIPANT: I would go with what you said. I agree with Dr. Klein, Dr. St. Martin. I think the community has been responsible. We have models that's worked in the past. I agree with Dr. Triulzi's point. Moderation. And I think, you know, we should look to the experts in the community and not necessarily have governmental mandate on this issue.

DR. BRACEY: So, I think then the consensus is that we would not look to, as you say, the government for a solution on this issue. We would really have a recommendation that would encourage the industry to address the areas of concern, or uncertainty, I should say, and is that the consensus then?

UNIDENTIFIED PARTICIPANT: And report back.

DR. BRACEY: And we would have moderation

in terms of our approach to the consent question?

MS. FINLEY: I don't concur with that approach. But, I have to say, first of all, I'm not convinced there's really a problem here. But, secondly, if there are concerns about it, I would think we could write some kind of a recommendation that doesn't mandate the FDA promulgate regulation or suggest the FDA should do it. But, we're doing that. There's been some comments raised in this 2007 document that we feel needs further evaluation. We hope perhaps that there would be some cooperative efforts by AABB in the blood collection organizations and FDA to address the concerns. Would that be an approach?

DR. BRACEY: This is an approach, but I'm not sensing that's the consensus of the committee. Dr. Kuehnert?

DR. KUEHNERT: Just from listening to this, I can't see why this shouldn't be just an extension of the donor assessment process including the effort to

make a uniform donor history questionnaire. So, if
it's sort of couched in those terms instead of just

saying, this is something for the industry or blood community to take care of, I mean, that's not true for the uniformed donor history questionnaire. That's been a real collaborative process. I would just describe this as being an extension of that process.

MS. FINLEY: I like that.

DR. BRACEY: So, would that be in the -- would that be okay with the committee then? From the perspective of an extension of the DHQ process? Dr. Epstein?

DR. EPSTEIN: Yeah. I think a recommendation along the lines of encourage the secretary to support, you know, government/private sector cooperation oriented toward standardizing and validating informed consent documents and procedures for blood and plasma donation.

DR. BRACEY: So, then --

DR. EPSTEIN: The other angle on this, sort of following Ms. Finley's comment, if the FDA were to

finalize a recommendation -- I'm sorry, the proposed
requirement for written statement of understanding, we

would almost necessarily be issuing guidance which we would develop a few notes and comments. So, we end up at the same place. It's just that the uncertainty is whether this element of the proposed rule will or will not be finalized.

UNIDENTIFIED PARTICIPANT: I just have a little concern. I would just have a little concern about creating standard language which would need to be validated. Because there are state requirements, there are local requirements, there are our own internal counsel's requirements about what's the appropriate way to saying something. So, that would be a little hard to mandate for an organization who feel it's their place.

DR. EPSTEIN: Along those same lines, I see we have representatives here from PPTA who live with this issue and have been a little quiet. Do you have a requirement? And how do you manage the issue of standardization and validation?

UNIDENTIFIED PARTICIPANT: I have been
listening curiously because I think since 1975,

probably it's been a requirement for uniform consent in plasma donors, and of course, one of the risks at that time was the manual procedure. So, there was a lot more risk. But, it has carried over. And a few years ago, FDA published a guidance to go along with its regulations and it was putting together the reviewer check list that had been used for several years. So there's very standard elements that are in the informed consent. However, the informed consent is a legal document. I agree with Debbie Kessler completely. I think to try to completely standardize it like they have with DHQ would be very problematic because I think each company is different. Each day there are different requirements. And we were going to mention, Josh probably already mentioned, informed consent in the presentation.

DR. BRACEY: So, we're getting at the hour of the adjournment, toward that hour. What I would like to do is to see if I could get a volunteer from

the committee who would be willing to pen a draft
recommendation incorporating the notion of public

private partnership, the scope of the content and also addressing scope and content, the need for validating the consent process. Is there a volunteer? Dr. Pomper is volunteered. So, Dr. Pomper, if you could work on that, we'll look forward to seeing a draft tomorrow.

DR. POMPER: Happy to.

DR. BRACEY: With that, we'll reconvene tomorrow at at 8:30 and we'll hear a number of other topics related to donor management. Thank you.

(Hearing concluded at 5:15 p.m.)

State of Maryland,

City of Baltimore, to wit:

I, Louisa B. McIntire-Brooks, a Notary
Public of the State of Maryland, Anne Arundel County,
do hereby certify that the within-named proceedings
took place before me at the time and place herein set
out.

I further certify that the proceedings were
recorded stenographically by me and this transcript
is a true record of the proceedings.

I further certify that I am not of counsel
to any of the parties, nor an employee of counsel,
nor related to any of the parties, nor in any way
interested in the outcome of this action.

As witnessed my hand and notarial seal this
2nd day of January, 2009.

Louisa B. McIntire-Brooks

Notary Public

My commission expires:

November 30, 2011

State of Maryland

City of Baltimore, to wit:

I, PAULA J. ELIOPOULOS a Notary Public of the State of Maryland, City of Baltimore, do hereby certify that the within-named witness personally appeared before me at the time and place herein set out, and after having been duly sworn by me, according to law, was examined by counsel.

I further certify that the examination was recorded stenographically by me and this transcript is a true record of the proceedings.

I further certify that I am not of counsel to any of the parties, nor in any way interested in the outcome of this action.

As witness my hand and notarial seal this
17th day of December, 2008.

PAULA J. ELIOPOULOS

Notary Public

My Commission Expires:

June 15, 2012

