to let Paul Beatty go through these, but the questionnaires, the medication deferral lists, the donor educational materials were evaluated by these individuals, and the questions were probed in a one-on-one laboratory setting with a trained interviewer to determine whether or not the questions were understandable and what revisions should be made.

[Slide.]

Now, I am not going to go through every single change that was made to every single question because we will be here until 10 o'clock tonight if we do that. I know that we enjoy each other's company, but perhaps not that much. But the committee members do have copies of all the questions, the revisions that were made, and the rationale for each one.

So, I am going to go over some basic features, some key features of the full-length questionnaire.

First of all, the questions all start out with a time-bounded approach. This gives the donor a frame of reference. "In the past [however long] have you done this or that?" "Between the years of X and Y, have you done this or that?"

The time frames we put into chronological order. In the current questionnaire, they are not, they are all over the map and requires basically the donors to engage in what I like to refer to as "mental time travel," which can be very confusing. So, the questions now are in chronological order from the most recent, which is 48 hours for aspirin use or something that has aspirin in it, to have you ever.

[Slide.]

We also used something called "capture questions." You might also refer to these as wide net or umbrella questions which have already been used for many years to screen donors, and it is a standard screening tool.

You want to throw out a wide net, so that you can identify donors to which that information applies, but also to which it doesn't apply. If the information doesn't apply, the donors can move on. It's a nice streamlining tool. If the donor says yes to a capture question, then, there are a series of additional questions that have to be asked to find out what part of that information applies.

It is very useful for a number of things -

medications, travel, and so forth.

The user brochure, which I will be discussing shortly, contains suggested follow-up questions for those instances in which a donor replies yes to a capture question, and the specific follow-up questions, though, could be spelled out individually by blood centers in their standard operating procedures.

[Slide.]

Here are two capture questions that are already in use. No. 14 on the AABB questionnaire. We have used this for many years. "In the past 3 years have you been outside the United States or Canada?" The purpose of this question is to identify individuals who might have traveled in an area where they could have been exposed to malaria.

We felt this was a great question. We couldn't think of a better way to reword it. We kept it.

Question 30A. This is to identify people who may have been exposed to HIV Group O. This is how it currently reads, but we felt we really want to know if they have been in Africa. That is the capture information. So, we asked them, and we have changed this, we will ask them: "Have you

ever been in Africa?"

If they say no, it takes care of travel, it takes care of residence. You can move on to the next item. But if they say yes, then, they are asked, "Did you travel there, did you live there?"

So, this is just an example of capture questions and how they are used.

[Slide.]

We have also embedded within the full-length questionnaire, some quality assurance tools. The purpose of these are to assess if the donor is paying attention, what I call are so-called surprise questions. The donor really is expecting to answer "no" to a lot of these, but if you have something in there where they have to say "yes," perhaps if they answer "no" to it inappropriately, then, the staff can pick up on that and probe with them further on, is it truly relevant information that they are trying to give or were they not paying attention.

Another kind of quality assurance tool is that the gender-based questions require specific responses from a member of the opposite sex, to there are at least three questions in the full-length questionnaire that are gender specific. It

starts out "Female donors, have you X, Y, Z," and there is a little set of instructions in parentheses that say "male donors check no."

They are not allowed to leave it blank, they are not allowed to write "not applicable." If they do those things, we have to ask, one, were they not following instructions, or, two, weren't they paying attention.

So, these are the kinds of things that are in the questionnaire for determining if the donor is with it, if you will, or with us.

[Slide.]

Now, there are many medications listed on the medication list, specific medications, most of which are FDA-deferrable medications. This has cluttered the questionnaire and also made it more difficult as questions need to be asked for blood center to incorporate that information.

[Slide.]

Question No. 10 actually is the question that deals with medications. I have just abbreviated them for you. They are actually full-length questions, a proper question with a noun and verb.

What we have determined is another

approach may be to simply say to the donor, "Please read the Medication Deferral List," which I will show you in a second. "Have you ever taken any medications on the Medication Deferral List?"

[Slide.]

Again, the committee has a copy of this, but this is what the Medical Deferral looks like, and the donor is expected to go down and look at each of these items. If they haven't taken any of them, they say "no," the screener moves on. If they say "yes," which medication, when did you take it?

If it is clear that the donor is not giving the medication list its due, the donor glances at it, says "no," it is up to the screener to give the list back to the donor and ask them to review it carefully. This is not something we want them to blow off.

So, that is the full-length questionnaire. We did not set out with a specific number of questions what we wanted it to have. It turns out that it has 48 questions, which actually is a little more than the number of numbered questions on the current questionnaire, but as you look at the full-length questionnaire, I think you can

appreciate and compared to the AABB, the current version, that is much simpler and the wording is much easier to understand.

[Slide.]

I would like to say a few words now about the abbreviated questionnaire for frequent donors.

Currently, a donor has to answer every question at every donation including things that never could have been repeated, for instance, if they had ever taken Human Derived Growth Hormone. Well, that product was not available after the early 1980s. Why do you have to keep asking that question of a donor every time they donate when, if they have said no, and it was an accurate answer, it's over, it's done.

I would like to go to the next slide and then come back to this one, if I could, please.

[Slide.]

What the abbreviated questionnaire does is that it integrates the FDA parameters. Elizabeth Callaghan has given a number of very helpful talks on what the FDA expectations were for an abbreviated questionnaire, things like what do you do if a blood center accidentally administers an abbreviation questionnaire to a donor who should

have had the full-length questionnaire, how do you handle new questions. These are examples of some of the issues that the FDA wanted us to address and we have. The committee has that.

Also, to define a frequent donor, and this is someone who has donated at least twice. One of those donations had to have been within the past six months, and both donations, at least two donations, the donor had to have been screened using the full-length questionnaire.

We chose twice because we feel that screening is an educational process. If they have been through the full-length questionnaire at least twice--and I can tell you there are millions of donors out there who have been through the full-length questionnaire now many, many, many times--if they have been through it at least twice, they have gotten the gist of the kind of information that we are seeking.

Now, if we could go back. Thank you.

[Slide.]

So, what the abbreviated questionnaire does is it eliminates the non-repeatable event questions, and it identifies recent changes, that is, since their last donation, which could not have

been any longer than six months ago, in their health, travel, and behavior, and this is where we are able to pare out a number of the questions that appear on the full-length questionnaire.

It obviously retains questions about risk-associated activities that are relevant, it uses capture questions, it is in a time-bounded format.

Basically, the abbreviated questionnaire now has 27 questions on it, and this is a significant difference from the full-length questionnaire with its 48 questions on it.

[Slide.]

The pre-screening donor educational materials. The idea of providing donors with materials before they donate originated in 1984 because there was not an HIV assay available, so donors were given written materials that contained the HIV signs and symptoms, and risk information.

The goal was to get the donor to self-defer or at least get them to ask the blood center staff about these things, so they would know whether or not to be deferred.

The educational materials in use by blood donors currently include all of this information plus information about new and potential risks, and

information about the donation process, but we had some concerns about the educational materials.

First of all, they are not uniform within the U.S. Now, blood centers do include the FDA required information on the educational materials, but there is a great deal of variability. We felt that there needed to be more emphasis on accuracy and honesty in the donor, so the second paragraph in the educational materials hits them with that please provide us with information that is honest and accurate as possible.

We tried to answer questions for donors, what is sex. Now, we will get to that in a second.

[Slide.]

Therefore, we have a new emphasis on accuracy and honesty, an emphasis on encouraging donors to ask questions. We feel this has to be a two-way interactive process, that we needed to define sexual contact, because in about 20 percent of the questions, there is a question about sexual contact or sex, and we know from the survey of design literature or survey literature, that people have very differing views of what constitutes sex.

For instance, in a 1998 JAMA article published by Sanders, et al., there was clearly 50

percent of donors or of respondees did not think that oral sex constituted sex. We know that poses a risk for transmission of a number of agents.

A fifth of the respondents did not think that anal sex was sex, and there are a number of other studies out there that we looked at, and, of course, our former president, Bill Clinton, I think helps to drive home this point. So, we do have definitions of sex listed.

We decided to go with medical jargon. To try to use street terms, we thought just would be really pushing the envelope especially with the blood drives to high schools where there are 17- and 18-year-olds although they probably know a lot more than the rest of us.

We are also recommending that the educational materials be standardized, that the blood centers can add to them, but they cannot rearrange the current format, and they cannot delete anything.

[Slide.]

The user brochures. These are brochures that have been designed to help blood centers and donor screeners learn how to use the new materials. There is one for the full-length questionnaire and

one for the abbreviated version.

It explains the concept of capture questions, which I think many blood centers already understand because they have been using them for years, but for a new screener, this is helpful information, and it offers suggested follow-up questions to any affirmative answers for capture questions.

[Slide.]

In terms of administration around the U.S., currently there is significant variation. The American Red Cross, with FDA approval in 1998, began to use the self-administered questionnaire. There was one question at the end asked by staff in order to ascertain whether the donor had any questions or there was anything they didn't understand.

In some centers, the donor uses the pencil or the pen and paper approach, answers the questions, answers the questions, and blood bank staff will either ask all of the questions again or just selected questions. In some blood centers, they just ask questions orally of donors. So, there is a fairly significant degree of variation.

[Slide.]

We are recommending that the full-length and abbreviated screening questionnaires be self-administered by blood donors for the following reasons.

[Slide.]

1. Survey literature shows that people are less likely to disclose personal information in a face-to-face interview versus a self-administered questionnaire.

2. The NCHS cognitive evaluations and the entire process was geared toward a self-administered questionnaire with the input and buy-in of our survey design experts, so we are recommending a self-administered questionnaire.

[Slide.]

Now, one of the issues that we grappled with was how we get the word out to our constituents, blood centers, and donor screeners about what we are doing, and how do we know that they support this process.

First of all, we included what we felt were the key people, and we have discussed that already, but starting with the FDA. Alan actually has done this, so I won't reiterate the FDA involvement, but there were two representatives

ultimately who communicated informally with CBER. This was presented to the BPAC last year, and then we incorporated the input that CBER provided last fall.

[Slide.]

America's Blood Centers, the American Red Cross, American Association of Blood Banks had numerous meetings, conference calls, web postings, publications in which the task force activity was well chronicled, and in all of those, there were requests for feedback, which was provided.

[Slide.]

American Association of Blood Banks especially was very proactive in doing this.

[Slide.]

As Chair of the task force, I got to travel and see interesting and unusual places to take the gospel, if you will, of the task force, or mantra at least--gospel is probably not a good word--but our mantra at multiple national meetings, meetings in California. California is important because it collects 8 percent of the blood, and it was the Blood Centers of California that developed the first Uniform Donor Screen Questionnaire, so thereby and in particular we felt it was important.

The goal of my presentation was, first of all, to discuss our activities, but also to use the bully pulpit to get feedback about what we were doing.

[Slide.]

Finally, we also went to the blood screeners themselves. It was a small study, but yielded very important information. We went to five different blood centers and had 13 screeners evaluate the new materials for their usability, user friendliness, comprehension, and because these are the people who are on the front line interviewing donors, to try to get an idea from them how they felt the donors would respond to the materials.

We provided the data to CBER, and the ratings indicated a very, very positive response to the new materials, very high ratings, and most of the screeners who looked at these materials felt that they were a significant improvement over what they were currently using.

[Slide.]

In terms of how we are going to get the word out after the FDA, with the input of BPAC, publishes its guidance or endorsement, or however

it will communicate, puts its imprimatur on the products, the AABB will use its publications and web site to inform members about the final products, will make the materials available, will use the resources at its disposal to work with blood centers in implementing the new products.

[Slide.]

Blood centers will be responsible for obtaining and familiarizing themselves with the new materials, for developing their standard operating procedures to go with the new questionnaires, for training their staff, and assessing competency, for educating blood donors about the new approach, because this is very, very new, and have staff available to assist donors.

These are our thoughts about how the implementation should proceed.

[Slide.]

So, just to kind of wrap up, the documents that were submitted to the FDA, and which the committee now has before it, are the full-length questionnaire, the Medication Deferral List, which is the companion document to the full-length questionnaire, an abbreviated version for frequent donors, the donor educational materials, and the

user brochures for the questionnaires.

[Slide.]

I just want to once again emphasize the task force really was breaking new ground here in terms of donor screening. This is really the first time that appropriate approaches for evaluating the questions, on writing them had ever been used, and we hope that this is an approach that will continue to be used by the FDA and the AABB as they develop new questions, and that considering that questions that went into the original AABB questionnaire had not undergone field testing, did not, by and large, have the input of survey design expertise, that what the task force is putting before you today represents a significant and major improvement.

[Slide.]

I would like to thank the many task force members and after two years of hard work, I think they deserve to have their names read out loud, and I will do it in microwave version - Paul Beatty, John Boyle, Mary Chamberland, Linda Chambers, JoAnne Chiavetta, Judy Ciaraldi, Ken Clark, Kay Gregory, Jan Hamilton, Debbie Kessler, Steve Kleinman, Trish Landry, Sharyn Orton, Terry Perlin, Mary Townsend, Steve Vamvakas, Donna Whittaker,

Alan Williams, and Anita Winters.

Special thanks I would like to give to Dr. Sharyn Orton, who conducted the focus groups, George Nemo, who made the funding possible for the cognitive evaluation, Paul Beatty and John Boyle, who were our survey design experts, and to Kay Gregory and Anita Winters, who provided all the administrative and logistical support and hand-holding to get us through this project.

I would like to thank the committee for their interest, for their attention, and this concludes my presentation. Thank you.

[Applause.]

DR. NELSON: Thank you. It sounds like you did a lot of work on this.

Questions or comments?

DR. ALLEN: One comment, one question. This is fabulous, long overdue. I really applaud the process that was used and the way in which you have approached it. Fortunately, we got the materials enough in advance that we had a chance to look through, read, and review them, and I think they are fabulous.

My question. Was anything off limits?

DR. FRIDEY: Well, we would all love a

questionnaire that only had five questions on it, but the question is which ones do you eliminate. We did go to the FDA and ask if there were any specific items that we could drop, and the FDA felt that at this point in time, that we should retain all the FDA-recommended or required items, so we did, we did retain those.

DR. ALLEN: In the exact format or were you allowed to recommend changes?

DR. FRIDEY: Oh, no, we absolutely had the FDA buy in to revise those questions, to reword them, yes, absolutely.

DR. NELSON: I hate to bring up specific questions, but I have one, which is No. 46, had sexual contact with anyone who was born in or lived in Africa, and there is something about travel to Africa.

If that relates to Subgroup O, I thought the FDA had required that screening tests be sensitive to Subgroup O, and I wondered why that's in there.

DR. FRIDEY: I will let Jay answer that.

DR. EPSTEIN: We have not yet approved an HIV screening test with validated sensitivity for Group O. We have encouraged manufacturers to

submit supplements or new tests, new original submissions, but that process has been slow. There are such tests in the pipeline, but we are not there yet.

DR. NELSON: So we can drop that question as soon as you license it.

DR. EPSTEIN: Well, that has been our thinking.

DR. NELSON: Maybe you could drop it now.

DR. EPSTEIN: Well, we could revisit that. I mean when we took the position that the screens should be sensitive to Group O, it was based on the perception that there might be an expanding new epidemic, it was after the first two cases were identified in the U.S.

It is my understanding that there have not been any subsequent cases identified in the U.S., but it is also the case that surveillance may not have been kept at the same level. So, I mean we could revisit that question, but I think it is fair to--

DR. NELSON: If the tests aren't sensitive or if the tests that are being used are not, then, I certainly agree with the question, but it was my understanding that they were sensitive.

DR. EPSTEIN: The existing tests are incompletely sensitive, and they do vary.

DR. NELSON: Yes.

DR. LEW: I don't know if you are the one to ask this question, but if you could clarify. In the information in our packet, it did mention the studies that suggested a one-on-one interview was better to look at HIV risk factors, and I also understand though, indeed, that under the privacy of looking at questions yourself, that other studies have shown that you are more likely to tell the truth.

It wasn't very clear to me, though, how you all decided in the end to go with the studies just saying it is better to do it in privacy rather than looking again at the issue of doing it one-on-one, when those studies did clearly say it seemed to be more helpful.

DR. FRIDEY: First of all, I want to thank you for reading the materials, it is clear that you did. That's great. This is a study that was done at a blood center by a blood banker. It was published 10 years ago. With all respect to the author, those kinds of findings have not been reproduced in general survey literature.

It was observed in that study that, in general, first-time donors, people who donate that frequently were more likely than frequent donors to pay attention to a self-administered questionnaire, so the authors of that paper did, in fact, make that comment.

There was another study that was later done and felt that even though there was face-to-face interviewing, that they did not observe that the overall decline in HIV seroprevalence was significant, and said, in fact, that the decrease in HIV seroprevalence was likely not attributable even to direct questioning.

So, given the fact that there is a very, vary large body of literature, survey design literature, which we gave some references from directly and, in fact, cited in the project, and the fact that none of these have substantiated the 10-year-old study out of a blood center, we felt that it was appropriate to recommend a self-administered questionnaire.

DR. NELSON: I understand that the CASI, the questionnaire is read, I mean there is oral administration of the question and then computer answers, might be better than a personal interview,

but how do you deal with the issue of literacy among the donor population where somebody might check answers yes or no, but really not actually be able to read the questionnaire, and marginal literacy is perhaps more frequent in U.S. populations than is thought?

DR. FRIDEY: Well, we could hold up a sign that says, "Can you read this?"

DR. NELSON: If somebody said, "Yes" --

DR. FRIDEY: I am being a little tongue in cheek there. That was a joke. My father used to say, "There are always two floor shows, one to tell it and one to explain it."

That is an issue that I think we have to struggle with. I think that when eventually blood centers get to computer-assisted interviewing, there will be an audio portion. The video portion will be terrific for donors who are hearing impaired. There will be the capability for multiple languages. That's a long way to say I think that is probably an issue that has to be worked out, and our feeling is at this point that the blood centers should develop an approach for determining whether someone can really sit down and go through the questionnaire and answer it

themselves based on their literacy level or whether or not the blood center should administer it.

DR. NELSON: This questionnaire will be in a couple of languages, certainly Spanish and maybe Chinese?

DR. FRIDEY: The task force members are all looking forward to a long retirement somewhere in the South Pacific, but there already are approaches out there, and many blood centers have translated their current materials into Spanish and have used validation approaches for that, so we would just suggest that blood centers do the same for this.

MS. KESSLER: Debbie Kessler, New York Blood Center. I was on the task force.

About the literacy question, Joy was describing how you could pick up on problems a person would have in answering the questions based on the answer patterns, and you could always administer it orally if you did have somebody who couldn't read the questionnaire.

DR. FITZGERALD: Joy, this is really great. I just had one question on the disclaimer on what happens to your donation. How do we address the AABB standard that we have to inform

the donor that their blood sample may not be tested, is that done at the local level or is that going to be included?

DR. FRIDEY: That would be at the local level, and that actually is an issue that the Standards Committee is going to take up because it has continued to be a troubling one.

DR. HOLLINGER: Excellent, and I am glad we had all this information given to us to read.

One thing that wasn't on there, though, is the educational material, the pre-screening, if you will. Was there something on there? I guess I didn't see the pre-screening educational material. Sorry about that. That is one thing I didn't see, because I think that is really critical because there is where a lot of the perhaps self-referrals.

I see a reasonable number of patients who have had hepatitis, for example, hepatitis C, who are found to be positive and obviously when we talk to them, have histories of injection drug use, and so on, that obviously have not responded to the question.

A lot of that is because this concern about putting an X or having an X put in a box, that is going to be there for a long period of time

on a record about this, have you ever had sex with a prostitute or a variety of other things. I mean people don't like to see that. It is one thing they don't like to have on there even though they might answer it otherwise.

We often have to just tell many of them who come in, look, I don't have to put it in your chart, I am not going to put it there, but it's important for us in terms of talking to you about a variety of other things, at which time many of them will say, well, okay, you know, and then they will give that piece of information.

I have been impressed with that particular difficulty in answering these kind of behavioral questions. Sometimes you could get that out in the educational material, which really explains why these questions are important about even once, and things like this, so they could self-defer ahead of time.

But that is the only concern I have with some of the questions is that they do have some powerful things that keep people from answering, I think, honestly.

DR. FRIDEY: I agree, and the survey literature does, in fact, support that, and if you

are talking about methods of administration, that is something that the donor sits down and does themselves, they are more likely to answer truthfully than if it's in a face-to-face format.

We do try to assure donors that the information is confidential. That is getting to be a tougher sell, I think, these days, but blood centers have to have systems that are secure and do, and communicate that to blood donors, so that they will feel more comfortable answering these kinds of questions.

DR. NELSON: Thank you.

DR. FRIDEY: Thank you very much.

DR. NELSON: Paul Beatty.

UDHQ Cognitive Studies

DR. BEATTY: I sort of walked into this process kind of like in the middle of the session, so I think it was really nice to have the introduction that Alan and Joy provided.

I am actually going to now talk about something a lot smaller than the whole scope of things that they talked about, a pretty small part of the process although an intensive one, and only about one major product really. The questionnaire itself is what I am going to spend most of my time

talking about.

You will also notice as I go through this that I will be talking more about what we found that wasn't so great rather than what was good, and that is not because that was the overwhelming stuff that we found. Actually, we found that the evidence was very positive about this instrument and about the questionnaire.

The idea behind cognitive testing is really to poke and prod and push this thing until we find out what goes wrong with it and where it breaks, so that is going to be more what I am going to be talking about.

Fortunately, the things that we found are generally pretty fixable.

[Slide.]

The task force, at the point that I came in on this had already revised the questionnaire based on a review of regulations, principles, the questionnaire design, information from focus groups, and all that, but the evaluation stage that we came in had to address some remaining questions, and we had to figure out, well, what is the best way to evaluate, how easy this thing is to understand, what is the quality of material that it

generates, what is the validity of the responses, and all that, and what the task force decided to do was employ cognitive interviewing.

At the National Center for Health Statistics, this is what our group does full time, evaluate survey questionnaires primarily to find out the strengths and weaknesses of each of them, but what is cognitive interviewing?

[Slide.]

It is a process that has been developed about 15 years ago where questionnaire design specialists conduct one-on-one interviews with people who are typical respondents of a questionnaire.

They administer the questionnaire as it originally appears, so mode is an important factor there. This was given as self-administered instrument, so we had the people that participated in our study fill it out by themselves first.

Then, the investigative part is where we probe the interpretation of the answers and what they think questions mean. That helps to explore various things - comprehension problems, difficulty of what they are trying to recall, various response biases, inappropriate answer categories although

that wasn't so much of a concern with this one because the answer categories were basically yes and no, so they seemed to work pretty well.

It is not the only technique that is used to develop questionnaires and to evaluate their quality. Focus groups have been mentioned, and they can play an important role. Actually field pre-tests of questionnaires that are exactly the same as someone going through the process without this intensive probing can also be important.

But this technique seems to work best when you are at sort of middle point, where you have the basic content figured out, but there are still some tweaking of the actual wording that needs to be developed. So, it's sort of something that falls in the middle.

[Slide.]

Let's make it a little more specific. This is one of the questions that we looked at. "In the past 12 months, have you had sexual contact with a person who has had hepatitis?"

They would answer that question by themselves first. Then, we would use probes to explore several possible things, like how do people interpret what we mean by sexual contact. We would

use probes to explore whether they know anyone who has hepatitis, what sort of contact did they have with this person, what time frame they are thinking about while they are answering, to basically take their answer that they give us, which is a short yes or no, and then get a more expanded, long-term answer that we use to evaluate the validity.

So, when we get either a yes or a no, this longer and extended narrative is what we use to evaluate the quality of what they have given us.

The interviews are tape recorded, they are very textually rich, transcribed, and they are analyzed largely qualitatively, although some quantitative techniques can be used with certain caveats that I will get to in a minute.

[Slide.]

These interviews are pretty labor-intensive. We worked on this for about six months of actually interviewing and analyzing these data with a fairly small sample. We only talked with 35 people, which is about the same or maybe slightly larger than most of the studies that we do.

Now, the participants are selected, so that they are relevant to the topic of interest, but you shouldn't take that to mean that we are

considering this to be a representative sample in any sense.

We are not trying to infer the exact extent of a problem in some population. What we are trying to do, instead, is to understand what is likely to be a problem and then to develop a basis for understanding why that is likely to be a problem.

The extent is something that you really have to go somewhere else to figure out, but we can usually, when we do this properly, figure out what it is exactly that is going on in people's minds, and then point that back to something that is wrong with the question itself.

[Slide.]

The people we talk to in this study, we did it in three rounds where we had a chance to actually conduct about 12 interviews per round, and then regroup, rethink what we learned, and then talked to some different people.

The first round, we decided to go for people who had never donated blood, but were eligible to do so as far as they knew. Hopefully, that group is representative--representative is a funny word--but those people are common of the type

of people who would be first-time users of this questionnaire, they have no experience with it, they are relatively naive.

Some of these terms, concepts, and ideas, they have never seen before. The whole process might seem alien to them. So, we want to get them really kind of on the ground floor. The problem with that is that it misses a lot of things. In an evaluation of this type, we get a lot of people who answer the questions "no," because a lot of the things we are asking about are quite rare.

We want to get also people who answer the questions "yes," because if you only are evaluating the veracity of "no" responses, you are really missing a big part of the puzzle. So, that is kind of what the second round is all about.

We looked for people who had been actually deferred from donating whole blood on at least one occasion.

Then, the third category after that was sort of a catch-all to fill in the gaps. We has some evidence or some reasons to believe that younger participants might be interpreting some of the questions differently. We weren't sure that we had really adequately hit people how had lower

education levels, so we wanted to fill in some gaps there, and we also used the third round to address the quality of the abbreviated version of the questionnaire.

[Slide.]

Thirty-five total interviews came out 12, 12, and 11 per round, and what did we learn?

[Slide.]

One of the real challenges of this instrument, I think, is that it has to balance thoroughness and simplicity. On the one hand, you need the questions to be not so simple that they are open to misinterpretation because that way, they could fail to stimulate memories, but questions that are overly thorough, even though they might address all these sources of ambiguity, could be tedious and may reduce the overall motivation. What do you do to balance that out?

[Slide.]

Well, it is important to keep in mind that many of the nuances that questions are really designed to get at, like hitting a definition really hard to make sure they understand exactly what it means, for example, clotting factor concentrates only apply to a very small number of

people, so if you are making a question that is for the, I don't know, let's just say 1 percent that that applies to, you are really forcing everyone else to be dragged through this process that can be quite long and involving.

One alternative that you have is you have to remember that this questionnaire is unlike a survey questionnaire in a lot of ways. It doesn't have to stand entirely by itself. It can be supplemented by the pre-screening materials, the educational stuff, and also are guidelines for people who ask questions that there can be additional information to help them clarify, like, well, I might have had clotting factor concentrates, but I am not sure. If you provide staff at centers with definitional guidance, that is perhaps way and a more efficient way to help them clarify what they are getting at.

[Slide.]

Burden is something that a lot of survey questionnaire designers completely fail to think about, and it was actually a very serious concern in all the deliberations of this task force, which is I think really to their credit.

[Slide.]

Sometimes we found that there were attempts to make the questions a little too compact, that had actual larger ramifications. One example was feeling well as opposed to a question that said feeling healthy and well. Well, that seems like that is basically the same thing, but when you interview people in depth, you find that when you just say "well," a lot of them think you are talking about a more holistic sense of their mental and possibly physical well-being, but they don't always focus in on what you are really thinking about.

Now, I am not sure that that actually means that someone would say if they had the flu, that they are feeling well, because they are in a good state of mind, but it opened up a little ambiguity that didn't really need to be there. Just by adding the word "healthy," you could make a lot of that go away. So, this sort of minor tweaking really helped to make a difference.

Another issue, terms "even once," there was talk about taking them out. A lot of people said, well, you know, the question was clear enough, I didn't need that to clarify it for me, you know, it was kind of insulting, and so on.

Actually, though, "even once" can be important for a small group of people because that is sort of an out that people take.

You know, I might have done this sort of thing at one time, but that is not what I am anymore, that is not what I am all about, that is not the way I think, that is not the way I am, and therefore, they think that is the larger truth, and they can use that as a basis to justify their answer of no, I never did that, because admitting that you did it once, that would be kind of not really indicative of what they are all about.

So, it really doesn't make a lot of sense to take that out. The burden that it creates is really not significant. Keeping it in there actually can make a definite improvement. We have seen plenty of evidence in the social sciences that people do make such inferences about what they can get away with because it doesn't really apply to them.

So, the principle, dropping a few words sometimes doesn't significantly reduce the burden, but can create complications. There are times when that is not the right approach.

[Slide.]

Other examples of minor tweaking of wording. This was one example where just a few minor changes, I mean the question was basically all right, but a simple fix could have a little bit of an impact.

"In the past four weeks, have you had any shots or vaccinations?" It is not that it is not clear, but sometimes it seemed like people thought too much about vaccination and really failed to think about other things that could qualify as shots.

One person was very remarkable in this case. They had actually had a shot of cortisone in their foot on the way to the interview where we talked to them, and answered the question "no," and only in probing in depth, well, wait a minute, you mentioned that you just had a shot, and that was this morning, doesn't that count? And they are like, oh, my gosh, I was thinking totally about vaccinations, which you can see sort of why that would happen. It talks about shots or vaccinations. That kind of looms large in the brain, overwhelms potentially other interpretations that you might have of that.

Again, maybe these are not huge things to

have lost, but you never know, and it is easy to solve this problem. The principle that you invoke to fix it is that you say, well, "vaccinations or" and then you give this other half of it more weight, "any other kind of shot," emphasizing that there are really multiple ways this could come into play. It is a simple fix, it really costs you nothing, and it has the potential to solve a definitely identified error.

[Slide.]

Some of the questions that were originally on the instrument were quite compounded, linking many, many things, and so all the questions that we dealt with were much shorter that we actually tested, but some of them still had some compounded things that didn't make a whole lot of sense.

"Had an ear or skin piercing including acupuncture." When you are trying to get a question that is easy for people to answer and has a really appropriate frame of reference that you don't have to scan their entire memories, but can think about something quite specific to come up with an answer, this is a little too much.

I mean a tongue piercing and acupuncture are not in the same universe of activities, and

people pointed that out to us. Even more so in the next question that we have. "Had an accidental needlestick or come into contact with someone else's blood." One participant remarked, you know, "Oh, my God, you are talking about cleaning my granddaughter's knee and stepping on a hypodermic needle in the same question," like what's that all about.

Are the consequences of doing this really severe? Probably not for a large group of people, but it can seem strange, and strangeness has another problem, as well, because it really has sort of a subtle and insidious impact on how seriously they take the whole process.

If you are asking questions that are just absurd, they think you don't really know what you are talking about, and they don't take you as seriously. You can also get them from a purely cognitive standpoint to have their attention gravitate towards one aspect or the other. So, they hear skin piercing, they don't hear acupuncture.

Again, maybe acupuncture is not that important, but if it is, you might as well separate it out. The same thing with accidental

needlestick, coming into contact with someone else's blood, we thought was probably worth a question of its own.

DR. NELSON: Just as an aside, we took out acupuncture at the last meeting.

DR. BEATTY: But you get the principle anyway.

DR. NELSON: We have simplified the question.

DR. BEATTY: Good principle, good thing to do.

By the way, these are all minor things.

This is kind of some good news. False positives are really much more common that false negatives, which is really in the direction that you would hope to find things. All the pushing and prodding and trying to find mistakes that we could come up with generated a few false positives and very few false negatives.

The false positives that we did come up with really fell into two categories, one, more conceptual, and the other involving time frame and dating.

An example of a conceptual false positive is, "Have you taken aspirin or anything that has

aspirin in it." We had a lot of reports of people bringing in ibuprofen, acetaminophen, things that if you have a follow-up with them at all are not that difficult to find out that that is what they are talking about.

In the time frame example, it is more about a process called "forward telescoping" where something that actually occurred longer ago than the reference period you are talking about, somehow gets imported into the time frame you are talking about.

So, say, for example, 14 months ago this happened. You say "yes" to the question. Why does that happen? Well, it is really the same thing for both. When you have people think through this question and what it is getting at, they scan their memory for anything that seems to be relevant and anything that could possibly apply to it, and things that are close, but not quite there can get tagged. They don't literally go back in time until they hit the 12 months period and then say, oh, that's enough, I am going to stop. They think for events usually first and then try to date them. If they are close, they get stuck in the memory and sometimes get reported.

The same thing for the conceptual stuff. Did I have anything? Well, they probably think medications first and pain relievers, oh, yeah I did have one of those, it was acetaminophen. Again, with even a minuscule amount of follow-up, that's not that difficult to find that that sort of thing is happening, and much more common than the alternative, which is what we would like.

[Slide.]

Sometimes in spite of our best efforts, it is not really a problem with the question, but people just have incomplete knowledge. "Have you come into contact with the blood or saliva of a person who has hepatitis?"

Well, the thought process that someone might go through to answer a question such as that is, first, to think broadly, do I know anybody who has hepatitis, and they might say "no" at that point and then that is simple, they don't really worry about the other nuances of the question, that's enough for them to make the judgment necessary to answer, or maybe they do, and they don't think they have had that type of contact, and that is where they have to kind of work through the implications of the exact wording a little bit

more.

But sometimes they just don't know. I mean, well, yeah, I do have a friend with hepatitis. Did we have any saliva contact? Well, I mean they are over at my house a lot. We have parties. We share wine glasses perhaps. It is just hard to tell, so they make the best estimated guess that they can.

One thing they do is they bring in a sort of an assessment of potential risk, and they think, well, what is the real chance that this could have happened.

Another example is had sex with a male who has ever had sex with another male. They can make general assumptions about what they think their partner is like. Like one person said, oh, I am sure that he had never had sex with another male, he is the most homophobe person of all, but sometimes that doesn't tell you necessarily anything.

So, you have to realize realistically what you are getting. You are getting reasonable inferences about what is likely to have been the case, not a total 100 percent accurate screening of everything that could have ever happened to them.

[Slide.]

Some concepts we found were just inherently difficult. Joy invoked the name of Bill Clinton on this one, and many of our participants did also. When you talk about sex, what does it mean, intercourse or other activities such as oral sex?

It was very clear in talking to people that their definitions of what "have sex" included varies quite a bit. Some included things other than intercourse, and some people didn't, but the tendency, and it was probably more so this way than we expected, was for people to be inclusive.

The reason that they did is because they thought, well, pragmatically, I know what you are trying to find out, you are trying to find out about risk. I recognize that this is a screening instrument, and if there is any doubt, it should be included in there.

There were exceptions, some of which we saw for sure happening and others that we just realized could happen. It could be that young people think differently, and there are also some people who would reject that whole argument I just made because they would say that oral sex is not

risky, to therefore, it is not of any concern to you, it is not of any concern to this question. So, there is some potential room for error there.

Note, though, that most people don't have to go through that big debate with themselves about what the meaning of "have sex" is. A lot of people we talked to said, "I didn't even think about it, I haven't had any sexual contact with anyone in over a year."

Other people said, "Well, I have been married for 20 years, and I am pretty confident we have both been faithful, so I didn't even really think about it. Whether oral sex counts or not is totally irrelevant to me." There is a more global sort of judgment that is invoked instead, but for some people that is not the case, and you have to sort of work with them.

[Slide.]

Sometimes the problems are not entirely with the wording of the question, but can do it the way they are presented visually. We didn't use what was in any sense a final version of the way this instrument should look. We did a mock-up of it ourselves, and sometimes the way that we mocked it up had some problems.

For example, the time frame was often forgotten. We had people answer questions that were in a long series invoking things that happened in the last 12 months, like had a tattoo applied, and they would answer yes, not because they had had a tattoo in the past 12 months, but because they had had one 10 years ago.

The point there is that you can have perfect questions, but there is still another step. You have to make sure it looks appropriate and in a way that is easy for them to make sense of. They are going to use the organization of it physically and visually to make sense of it and understand the details. So, that is an important step that shouldn't be ignored.

[Slide.]

I mentioned that one of the things we were trying to do was get people who answer both yes and no to some questions. That is hard to do. You can't really ask people these questions in advance to screen them or you have kind of blown the question before they even get into the room.

You have to have people who are hearing the question kind of for the first time. That is largely what the point of this thing is. On the

other hand, it is hard to get people to get enough variety in all these answers.

So, what can we do? To do a really high end, ultimate gold standard validity test, what you would do is find people that you knew from some other source for sure fill in some of these categories, like you know that they have Chagas' disease, but they don't know that you know that, so that way you get them.

You know in advance they should answer yes, and then you can evaluate the quality of their answer. In most cases, that is simply not feasible to do. That would be extremely expensive, extremely time-consuming.

At some point, it would be great if people actually did that. In lieu of that, we have devised a sort of towards the end of the study, something that might help a little bit, the use of vignettes that sort of artificially expand the variety of experiences that people have to think about while answering.

Here is one example. Kim has a boyfriend who has used a needle to inject illegal drugs at least once. They have not had sexual intercourse, although they have had oral sex together. I am

trying to paint a picture of someone that is kind of on the cusp, playing on their ambiguities, maybe this should be a yes, maybe this should be a no, what do you think. It might help us understand more about the way people are interpreting questions for situations that there is extremely little chance that we would actually pick up in a sample of 35 people.

[Slide.]

That is not an ideal test. I mean it is still hypothetical and it doesn't rely on their own autobiographical memory, but it does at least require them to go through their thought processes of answering the question. It requires them to absorb the words that we are asking them to think through a situation and apply this text of this question to this situation, and at least it's close than a totally hypothetical do you think this should count, do you think this definition includes this.

The vignette responses tended to echo what we had already found, that they were very conservative in their answers. They included things that--I say conservative--what I really mean is that their interpretations were very broad. If

there was any doubt at all they should be included, they tended to stick it in.

Is that a perfect test? No, it is not, but it does tend to indicate that there is a sort of pragmatic component to question interpretation, that they are trying to figure out what it is that you want and why you want it, which also does come back to the issue of the educational materials, and their importance is not only as a pre-screener to tell them the order of the major things that you should be looking out for, but to give them more of an input into what the process is all about, why this matters, why you should care, why you need to think about these things and answer them accurately, because that is an important component of how they make sense of what you are asking them.

[Slide.]

So, to wrap up, the questionnaire that we tested was very much on target in terms of balancing simplicity and thoroughness. It made things about as simple as you reasonably could with maintaining the integrity of the information that it needed to capture.

The lion's share of errors that we found, and we tried hard to find errors, were false

positives, much more common than false negatives. The things that we did find were minor, really fell into three categories of ways that you could solve them.

One is by supplemental materials, either definitions provided afterwards for that small group that might have questions or doubts about what something means, minor wording changes which we recommended, and the splitting of questions occasionally where it must made a little more sense to separate concepts that were linked and might have been a little confusing that way.

DR. NELSON: Thank you very much. It was a very clear presentation.

DR. ALLEN: You obviously addressed well, I think, the question basically of aspirin. Did you get a sense as you asked people about other products that contained aspirin, I mean are they aware that the standard cold medications, you know, these sort of wastebasket medications that are over the counter often contain aspirin products? Was there that degree of sophistication or is there a potential problem with missing some of these?

DR. BEATTY: It was varied, but I think it was clear that not everyone knew whether all

medications that they had, had aspirin in them at some time. We found people that said things that probably did have aspirin in them and didn't report them. Most people answer in a more global level, that, you know, I haven't had anything that could possibly apply, medicine of any type, I don't take it, I don't like it, I try to avoid it.

I think, if I am remembering, the time frame for that was pretty recent, as well. We weren't thinking about even 30 days, we are talking about a couple days, so most people could be ruled out on that basis.

That is another good example, though, of what do you do about it. You would find that there are potentially some mistakes. You could provide a huge list of anything that could include it, but is that really worth it?

I mean the answer is that if someone has any doubts, you encourage them to talk about their doubts if they have them, and you have a list available if they need them, that might contain some examples, and you sort of prompt that way.

The question itself is probably as good as it could possibly be.

DR. FITZGERALD: In your survey, it was

Question 31 and on the card it is Question 30, and the response to one of the individuals brought out something I am not sure we thought about or the task force may not have thought about.

Question 30 says, "Were you a member of the U.S. military or civilian military employee or dependent of a member of the U.S. military and then in 31, one of your respondents was the spouse of a civilian employee on a base, and added up her time on the base because she lived on the economy and it didn't add up to six months.

But what we are losing there is that the importance of that question is the availability of purchasing beef from the commissary and eating it during that period of time, and civilian employees on DoD installations overseas have access to the commissary, so we are missing a group of dependents of people in that question.

So, I just needed you all to go back and look at that aspect of that question because it doesn't matter how long she was on the base because she probably went to the commissary and bought groceries on those brief periods that she was there.

DR. FRIDEY: If I could just briefly

address that, that kind of discussion did take place with the task force members, like a contractor, somebody who comes onto the base to do some work and might eat there, how do you deal with that.

We did actually recommend ultimately some different wording to the FDA because about this time that all this was going on, there were some new variant CJD questions that were being floated, there was a draft guidance out there, so we did make this recommendation that the wording be such that it does capture that kind of information.

I think the FDA did choose in the guidance that's the final guidance to retain their original wording, but it was something that was discussed.

DR. KLEINMAN: That was very nice, Paul. I just thought of something even though I was involved during this process, I hadn't thought of, and that is, we tended to say that we wanted to make the questionnaire simpler and more comprehensible to persons, to interviewees, and in the way we equated those two terms in our mind, simpler and more easily comprehended, but I don't think those two are the same, because I think actually what we found in the process--and you can

correct me if I am wrong--is that our real goal was to make it more easily comprehended, so that people really understood what the questions were.

I am not sure that resulted in the questionnaire necessarily being simpler, i.e., being shorter, but hopefully, it is less ambiguous. I think if we use the word "simpler" we are using a word that is subject to a lot of interpretation, and I think it might be easier to think of this as trying to make a questionnaire where the intent of the questions would be clearer to the people who are reading it, because I am not sure that we wound up with a document that is any simpler.

DR. BEATTY: Yes, I think that is absolutely right, and that was something that I tried to kind of put forth there. Sometimes simpler is less comprehensible because it doesn't give you enough information to make sense of what you have.

DR. FRIDEY: Actually, when we launched this project, I gave a number of talks at AABB meetings, and I tried to prepare the membership for the fact--membership being blood banks--that we were not necessarily going to end up with a questionnaire that was shorter with every question

very brief, and so I was trying to introduce that concept to the membership that you cannot necessarily have simple and comprehensive together in the same thing.

Actually, I thought of them as more kind of mutually exclusive terms, so actually, with all respect to Dr. Kleinman, it was a concept that was introduced early on to AABB members, so that they would understand that the final product was not, in fact, going to be a five-question document, and clearly, we tried to balance things out, so that we could get at the information, but in a way that the person being screened would know what we were trying to get at.

DR. KLEIN: I guess this just illustrates how difficult it is to do things, because I think I don't qualify as an illiterate person, I mean I obviously can understand concepts, and yet I somehow went through this process thinking that although we were trying to make it more--obviously, we weren't going to do a five-question questionnaire, I think we knew that, but that somehow it seemed there was some sort of equation between more comprehensive and simpler, and there is to some extent, but I think, as the cognitive

studies pointed out, you can oversimplify and then lose the comprehension.

I think Paul said it much better than I did, that there is a balance between the two, but I think ultimately, you don't necessarily wind up with a document that if you now bring it out to people, that people will say, gee, I thought your purpose was to simplify this, this doesn't seem any simpler to me than it was before.

I think you may get that reaction even despite the fact that you have tried to prepare people for that.

DR. NELSON: One comment back there.

DR. LUCY: I am Dr. Charles Lucy. I am an occupational environmental medicine doctor. I wanted to echo one comment and then make another comment. I have had a lot of experience with screening tests.

With truckdriver physicals, I have found in many years of practice that many of the drivers do not spend enough time answering the questions that are meant to screen them for the Department of Transportation's required physical exams and questionnaires.

Only upon questioning by a physician do

they admit that they have been hospitalized or they have had problems or things like that, so I think with any questionnaire you still have a problem of checking the data. How can you do that?

I think one area that has been explored by other people for informed consent is the use of interactive media laboratories that allow a process that is interactive and can be tailored at the patient level depending on their education and what their concerns are.

So, I think this is an excellent approach to a questionnaire. I think in the future, as you do move into a computer-assisted device, it gives you the opportunity perhaps to design an instrument that is educational, as you say, that is tailored to help the person understand what the questions mean, that perhaps can be changed, so that questions are programmed to be asked if a positive is received at a screening or a grab bag level, et cetera.

I might just make that suggestion that interactive media is one way to get the person involved and may help clarify some of the things you are looking at, and may allow you to do such things as self-verification, so you know the person

understands the instrument and you know the person has attempted to answer truthfully, for instance.

DR. NELSON: Thank you.

Judy Ciaraldi from the FDA.

FDA Status of Review of AABB Task Force UDHQ

MS. CIARALDI: Good evening, everyone, and thank you so much for staying on. I have to start out with letting you know that I was going to tease Alan Williams, my division director, about his effect on a crowd and his ability to clear a room when I noticed that as soon as he got up, everybody left, just about everybody. The most important people are here.

[Slide.]

I am going to give you a brief overview of how we are conducting the review of the AABB Uniform Donor History Questionnaire. I am going to follow with some review comments, comments from the preliminary review. Now, we haven't completed analyzing all of the documents and going over all of the comments, so these will only be preliminary comments and it will not be complete.

I will also list the proposed mechanisms that we are discussing for implementing the donor history questionnaire. Before I get any further, I

want to remind you that I am only talking about the review of the questionnaire used to screen whole blood donors and plateletpheresis, plasmapheresis donors, the donors for transfusable blood components.

As you know after today's talk, these donors also donate recovered plasma. We are going to use the same general review process for the donor history questionnaire that is submitted by the source plasma industry, but we don't have that yet, and we will use this particular review process when it is submitted.

[Slide.]

The process stated by assembling a work group that identified the scope of the review and selected a cadre of reviewers with a variety of backgrounds and expertise. The reviewers were given three weeks to complete the review, and they were to have their comments in to me by the end of May, and everyone that provided comments back did have that.

We are currently compiling the reviewers' comments and we are going to be evaluating them. When that is done, we will prepare a written response and send it back to the AABB Task Force

informing them of our findings.

The working group facilitating the review process consists of Dr. Williams, Dr. Orton, Elizabeth Callaghan, Jennifer Thomas, who is the Associate Director for Policy for the Office of Compliance and Biologics Quality, and me.

Because Drs. Williams and Orton and I were all on the task force, we could not be on the reviewer cadre. Ms. Thomas and Ms. Callaghan were both part of the review cadre.

[Slide.]

This is a list of the documents that were sent to each of the reviewers. I am not going to go over it because Dr. Fridey already did, but I will show you what they got.

So, it was a yeoman's job and our hats went off to them.

[Slide.]

We asked the reviewers to keep in mind the following questions, so that they could focus their review. Is the content of the questions and the accompanying documents consistent with our regulations and our recommendations? Is the rationale for the revisions appropriate? Is the proposed format for the questionnaire acceptable?

So the user brochures provide adequate instructions for donor screening personnel, and are there any other issues that still need to be addressed, any concerns that they want us to let the task force know about?

[Slide.]

These are the hard-working reviewer cadre, the individuals that are on the reviewer cadre who kindly agreed to participate in this project.

On the lefthand side, we have reviewers from within the FDA. They represent the Division of Blood Applications, Division of Emerging Transfusion Transmitted Diseases, and the immediate Office of the Director for the Office of Blood Research and Review.

We also have the Office Compliance and Biologics Quality represented, as well as the Office of Regulatory Affairs.

On the right side are consultant reviewers that we had representing the interest of industry both from the donor center side and the patient side. These people provided personal opinions, their ideas and their concerns on the guidance document.

I think you will recognize the names of

current and ex-BPAC members, but their participation were as experts in the industry, and not as BPAC members. Of the 12 reviewers, 10 have submitted comments, one that submitted no comments at all, she didn't have any comments, and there was one that has not turned in their comments to me yet, and you know who you are. I also know where you live, so I will come and get those soon.

[Slide.]

We are still compiling the comments, but in general, the reviewers thought that the questions were consistent with the FDA regulations and recommendation, the rationale for the revisions and the studies were appropriate. The proposed format was acceptable, the accompanying documents were simple, and I am sorry to use that word now, but that was their word, but they captured the important issues.

The abbreviated questionnaire seems to be acceptable for repeat donors and possibly even a desirable option, and they felt that the documents will improve the donor interviews and streamline the interview process.

Before I go any further, I want to say that these opinions and the opinions on the next

two slides are those of the cadre of the reviewers, and not my opinions or the opinions of the FDA.

[Slide.]

Now, the reviewers still had some ideas that they felt still needed to be addressed. They felt that there were some limitations in the cognitive studies. A few examples of these were that the individuals in the focus groups and in the cognitive study groups do not represent all the minorities especially those for whom English was a second language. They didn't see that that evidence was there in the report.

Also, they observed that the testing was done on individual questions, and not on the format, the whole tool of the Uniform Donor History Questionnaire. They felt that terms needed to be defined and written in a language that the donors will understand.

They felt that there was a little too much medical terminology, specifically phrases like "prescribed by a physician" and "apheresis device."

They felt that the user brochure needed to explain when accompanying documents should be used. For example, they weren't sure if the educational material sheet should be used for abbreviated

questionnaires.

They also felt that the user brochures need to contain more information about what to do with donor responses. The user brochures do not describe how to document follow-up responses in a standardized manner.

In addition, the users are referred to their own SOP for whether or not a donor is acceptable depending on the responses they give, and the reviewers felt that properly the user brochure said make some of those decisions.

Lastly, it wasn't clear from the user brochure if the donor was to complete the whole questionnaire even if they were deferred on a question early in the questionnaire.

[Slide.]

They also felt that there were some limitations on the Medication Deferral List. For instance, they felt that donors will provide information only on the medications that are on the list while there may be other medications that donors are taking that may defer them.

They also felt that the donors may be taking the medications for the conditions that are different than the conditions that are listed on

the Medical Deferral List, and therefore, not volunteer that they are taking that specific medication.

They also felt that the educational material was difficult to read. They felt it was hard to get through all the different fonts and the organization of the material, and one reviewer recommended that the educational material sheet be revised in plain language.

They also noticed that the information on the educational sheet was not exactly in the same order as the information provided in the questionnaires, and they felt that if the donors were to read it and then to go to the questionnaire, they might get confused.

Now, in the rationale, one of the questions that asked for contact with saliva by kissing, explained in the rationale that this was due because of exposure to hepatitis, this was to detect somebody who had been exposed for hepatitis.

The reviewer felt that this wasn't an adequate question to detect all incidents of hepatitis because there are other ways of getting exposed, such as the fecal-oral route. So, this is one of the responses that we will have to look at

closely because this is one that we recommended to the task force in our letter last year be included in the questionnaire, so our working group will look hard at this to decide which way we go on it.

Also, in the rationale, they stated that they eliminated the question off the questionnaire about asking the donor if they understood the questions and if they had any other--the questions that were asked to them and the information that was presented, and had all their questions been answered or did they have any other questions.

They stated that they removed this because it was part of the donor consent statement, and the reviewers felt that they could not make this judgment, they didn't know whether to agree with it or not, because there weren't any donor consent statements that were included in the review packet for the FDA.

Lastly, they were concerned a little bit about the abbreviated questionnaire. The user brochure states that the abbreviated questionnaire will be used only after the donors have been screened with the full-length questionnaire two times.

Some of the biological product deviation

reports that have come in to FDA has shown that there are considerable numbers of postdonation information reports that come in to CBER, that are due to information that is gathered on the third donation or even later, and if those questions are eliminated from the abbreviated questionnaire, there may be a group of donors that are missed.

They weren't sure if the abbreviated questionnaire would be given to current repeat donors in the donor center once the whole tool is implemented in a blood center or would once the whole tool is implemented, would repeat donors start getting the new questionnaire and then eventually step down to the abbreviated. That information wasn't explained.

[Slide.]

Previously, we reviewed the UDHQ from AABB when it was sent in, and we provided comments back to them, however, we did not review a final document, but the AABB published the new questionnaire as being FDA approved.

Our Chief Counsels have informed us that we can no longer do it this way, so we are evaluating some alternative mechanisms for implementing the donor history questionnaire, the

new revised one.

One mechanism that we are looking at is to have a prior approval supplement submitted by a licensed applicant that we would review and approve.

Another possible mechanism is to prepare our own questions and list them in a guidance, similar to what we did with the '93 HIV guidance.

Another possibility is to adopt the industry standard, in other words, the AABB questionnaire, in a guidance document, similar to what we did with the ISBT-128, uniform labeling guidelines.

I am not going to go into any detail in any of these because they are still being discussed internally, and in the end, we may even decide to do something that is not listed on this slide.

[Slide.]

To conclude, this is where we are going. We are going to complete compiling the reviewers' comments, and we hope to have this done sometime in July. Then, we will prepare a written response to send back to the AABB Task Force, and we hope to have that out the month after.

After AABB has addressed our comments and

have sent them in to us, we will give them back to the reviewers. I have informed the cadre that their job is not over yet, so they will get the response back, and they will determine if all of the concerns have been addressed.

Of course, we don't know this date, because it will be on AABB's timeline. In the meantime, we will determine which mechanism we will use to implement the questionnaire, and if it is determined that we need to publish guidance document, we hope to have that out by September.

Thank you very much for your attention.

DR. NELSON: Thank you, Judy.

Questions? Yes, Mary.

DR. CHAMBERLAND: Judy, thanks for your comments.

Just a question for my education here, too, in terms of the feedback that is going to be given to AABB, I guess I have to say I am just not familiar with sort of the format that that might take.

For example, will it include every reviewer's comments on filtered, so you get their raw data, so to speak. Then, I have to imagine there must be some intermediary step where FDA

staff, some of whom are on the Review Committee, but supplemented by additional folks who have all the regulatory and all that information, that they provide, if you will, sort of like a comment on the comments, and some sort of final summary of what it is that you need to do either that would be required to be done, would be recommended but not required.

Could you speak to that a little bit, about what to expect for feedback and its format?

MS. CIARALDI: Sure. What we will do, and it will be the working group of the five or six individuals I had up on an earlier slide, with input from our General Counsel and Dr. Epstein and his group, as well.

We are going to look over the comments. Some of the comments were given to us, I didn't include them in here. For instance, one reviewer wanted us to recompound all the questions, which is something that we know because some of us are reviewers and some of us were on the task force, is not optimal, it is not desirable.

So, that would be a comment that our working group would decide that we probably would not forward on to the AABB Task Force as a valid

comment. So, basically, we are looking for ones that are comments that really need to be addressed, that we feel are--I don't want to use the word valid, but do raise concerns where revisions are needed or issues need to be brought up.

So, we are not judging the right or wrong of the comments because all the comments were made in good faith, but there are some cases where some of the comments were probably made outside of some additional knowledge.

DR. CHAMBERLAND: So, will there be a set of recommendations or requirements? I guess I am just not sure. I mean this could go on indefinitely, and Joy said the task force is waiting for its vacation on some exotic isle.

You make it very clear. I mean there are some things that probably will be not negotiable, but there might be others that would be. As I said, we could continue to exchange drafts ad infinitum. How do we put some closure to this?

MS. CIARALDI: It is our desire not to go back and forth. What we will do will be similar to what we do with what we call a complete response letter. In it, we address what we call, in the case of a review, it is called a deficiency, in

here it will be called an observation, things that we have picked up during our review.

Then, we will go ahead and come back and say something like FDA recommends you do this or please give us some additional information, so we can make a determination if this is valid.

So, in some cases, we may ask for additional information, and in some cases, we may ask for revision. It may be a combination of both, but we definitely will give them some guidance on how they should address it.

Alan, I saw that you were up, I am sorry.

DR. WILLIAMS: You answered most of it, Judy. I guess the one comment I have, the one new word I learned since joining the agency, is vetting. What we do is discuss everything internally. I suspect what goes back will be a unified opinion from the agency, incorporating what we feel are the most relevant comments, and certainly would not want to hinder progress in this area.

DR. NELSON: Thank you.

I would like to move to the Open Public Hearing.

Celso Bianco from America's Blood Centers.

Hopefully, we can have some brief statements at this point.

DR. BIANCO: The committee has received the statement, the audience, too, so I would like to read only the last paragraph of the statement from America's Blood Centers.

I am Celso Bianco. I am with America's Blood Centers.

ABC urges this committee to support the task force recommendation that all new donor screening questions undergo vigorous validation procedures to assure that they are both sensitive and specific to the transfusion risk they are intended to address.

The donor screening document being used today is a hodgepodge of questions that have evolved over time. These questions have not been evaluated for efficacy or efficiency. The result is a screening tool that includes many complex multi-part questions that are confusing to donors and screening personnel alike.

Prime examples are the recently promulgated questions to identify persons at risk of CJD because of international travel and questions now under consideration by FDA to

identify donors at risk for exposure of zono via xenotransplantation.

ABC urges FDA and this committee to require validation of all new questions and to submit them to a forum, such as the Interagency Task Force to redesign the blood donor screening questionnaire.

Thank you.

DR. NELSON: Thank you, Celso.

Dr. Rita Reik from the American Red Cross.

DR. REIK: Good evening. I am Rita Reik, Senior Medical Officer at the American Red Cross. I would like to thank you for the opportunity to speak to the committee regarding the Uniform Donor History Questionnaire.

I am somewhat of a cognitive quality control check for those of you who are staying paying attention because some of you probably realize that I am not the Red Cross representative on the task force. Dr. Linda Chambers actually represented the Red Cross, but she was unable to make it, so I am here in her stead.

I would be very happy to read this very brief statement into the record.

In late March, AABB submitted their

recommendations for a revised Uniform Donor History Questionnaire to the FDA. This submission was, as you know, the culmination of a two-year effort by AABB and the Uniform Donor History Questionnaire Task Force to examine all possibilities for strengthening the questionnaire.

The American Red Cross is currently evaluating the Uniform Donor History Questionnaire and its operational implications, and we are pleased to have the opportunity to emphasize our support of both the AABB submission today and the process used in the redesign of the Uniform Donor History Questionnaire.

Those of us in the blood industry have received considerable feedback from our donors over the years regarding the design of our donor history questionnaire. They tell us they find the questions to be confusing, time consuming, and too numerous. In addition, frequent donors object to the need to answer the same questions repeatedly at each donation.

So, we believe that this is a very important first step in improving the Health History Questionnaire, and we call it a first step because the Red Cross also believes that ongoing

evaluation of the questionnaire will be an integral part of the process.

FDA and the blood industry will continue to encounter new or potential threats to the safety of the blood supply. When these threats become known, the first consideration will be determining whether a donor might have been exposed. Traditionally, a primary method used to make that determination has been to add a new question to the Health History Questionnaire.

The donation process is becoming increasingly more complex. For example, donor deferral policies have expanded as we have become aware of the potential for transmission of emerging diseases. As a result, there are more questions than ever.

In addition, the nation's demographics are changing, and we now recruit donors from a multitude of different cultures for which English is a second language. While it is feasible to offer translations of the donor questionnaire, we must keep in mind that a translation is more likely to result in an accurate answer if we start with the simplest English version possible.

Also, having the briefest, simplest

questionnaire is desirable in that donors are more likely to return if we minimize their time investment relative to donation.

In conclusion, the ARC believes that BPAC, FDA, and the industry have a unique opportunity here to advance the collection process to a new level. With the approval of the improved questionnaire would also come the opportunity to institute a process for ensuring the value-added of future questions.

Therefore, we urge BPAC, FDA, and the blood industry to adopt the following as guiding principles for the process of crafting the donor questionnaire: simplicity, uniformity, effectiveness and efficiency. To that end, when determining whether to add or revise donor questions, the FDA should:

1. Ensure that the questions are understandable and effective prior to including them in the final FDA regulations or guidances. Of course, it seems best to do this by piloting the questions on persons who have characteristics similar to our donors.

2. Recognize that ensuring clarity of the questions optimizes the chance for accuracy in

responses and that is just as important as ensuring accuracy in any other part of the blood product manufacturing process.

3. Adopt new questions only after determining that the existing questions cannot provide the answers and cannot be modified to do so.

4. Add new questions only after determining that they will not negative affect the ability to obtain precise answers to previously existing questions.

We look forward to continuing working on a process that we hope will establish an important set of guiding principles for future revisions.

Thank you for your attention.

DR. NELSON: Thank you very much.

Jan Hamilton.

DR. HAMILTON: This statement has already been provided to the committee. I am Jan Hamilton. I am with ZLB Plasma Services, and I am speaking on behalf of PPTA Source.

It is a relatively long statement, I would say, but I am going to read the whole thing.

DR. NELSON: Is there a way you could summarize it given that it will be included in the

record?

DR. HAMILTON: No, but I will shorten it, which is a bit different.

When you are given five minutes, it's pretty concise, to begin with, so I will just start a couple paragraphs down.

The source plasma industry supports the overall task force objective of simplifying the current questionnaire. The proposed questionnaire and supporting documents are intended to enhance blood and source plasma safety by making the screening process more effective in capturing relevant donor qualifying information.

Due to differences in the collection practices for the blood and source plasma, a subcommittee of the task force was organized by PPTA to revise the screening documents for source plasma donors. Although the majority of source plasma questions are identical to the blood industry questions, specific revisions were made to conform to source plasma screening requirements. A separate source plasma screening system proposal, including specifically tailored donor screening documents, will be submitted for review and approval by the FDA.

The source plasma screening documents include both the full-length questionnaire and abbreviated questionnaire. The abbreviated questionnaire is proposed for use with donors who have previously been questioned using the full-length questionnaire and donate frequently, as defined as at least once in a 30-day period.

The full-length questionnaire will be administered each year at the time of the donor's annual physical examination, which is not a requirement for blood donors.

The source plasma abbreviated questionnaire and high-risk poster were tested in cognitive interview studies by the National Center for Health Statistics. In addition, the questions that were revised to meet plasma sourcing requirements were also tested.

To this end, the source plasma screening documents have been tested for donor comprehension. Currently, the results of the research study are under review and the appropriate revisions are being completed on the proposed screening documents. PPTA plans to submit the source plasma proposal to FDA in July 2002.

PPTA appreciates the opportunity to

participate in this important industrywide effort to improve the donor screening process. We look forward to continued participation with the FDA and the blood industry on this and other initiatives.

DR. NELSON: Thank you very much.

The next speaker, Dr. Paul Cumming.

DR. CUMMING: I am Paul Cumming. I am president of Talisman, Limited. We are a manufacturer of software, multimedia, audio/video donor interviewing software financed, in significant part recent by the National Heart, Lung, and Blood Institute, and George Nemo, guiding it.

I did not come here prepared to make remarks, but was convinced I should do so. First, I would like to compliment the committee. I think they did superb work given the conditions under which they were doing it, and their limits on resources and everything else. It is very expensive work to do, speaking as someone who has done it for a long time, and I have nothing but compliments for the committee.

Talking to people here, many people are unaware of what it is we are doing and the fact that it is an FDA priority, part of the five point

plan, and it was financed by NIH, so we should be aware of it. Our effort has gone into the software and into publications.

The work, I will refer to as just other places that can find more information as opposed to going into it and generally what it is. First, the information is presented in terms of the first study, was presented to this committee back in 1999. It was done in conjunction with the Hoxworth Blood Center, and was a pilot study.

It was presented more recently in the December 2001 issue of Transfusion. Again, it was Dr. Zuck. We had about 400 donors. It was largely donor satisfaction information.

Since then, the technology has been expanded, and we have learned our lessons. It is now applied in the Mississippi Valley Regional Blood Center out in Davenport, Iowa, running in eight or nine centers, and we are looking at extending applications there, and another large Midwestern blood center.

The technology is officially known as Audio/Video Computer-Assisted Self-Interviewing. It runs on computers and has an audio portion through earphones for privacy. It uses Touch

Screen to avoid donor problems with keyboards and keyboard kinds of errors that go in with some other kinds of CASI technology, and it uses extensively color. It has a color picture to explain or try to explain the question, as well as the audio and the text on screen.

The results, which are on our web site, the newer work at Mississippi Valley, and I think we have interviewed something like 10,000, something in excess of 10,000 donors now, and we have repeated the studies at Hoxworth plus extended them to other things, and that is available in the form of presentations we have made to the AABB and the FDA, and it is on the web site.

The system is known as the Quality Donor System. The people who have done most of the data collection and presentation are Dr. Louis Katz from Mississippi Valley and Lauri Rozinski.

The studies in general show that donors prefer the Audio/Video Computer-Assisted Technology by a factor of at least 4 to 1, and that over face-to-face interviewing. They say, among other things, that the screening questions are clearer, they can understand them better, that they will be honest in their responses, and they are more likely

to donate again.

Staff studies we have done of staff satisfaction show similar kinds of things where the staff prefer them and believe the donors will be more honest with the technologies than they will be with face-to-face interviewing.

Staff savings in times is in the range of four or five minutes per donation. An omissions and error study that Katz and Rozinski did showed a 60 percent decline in those factors.

The information can all be found on our web site, which talismanlimited.com, all spelled out, and I can give people more complete information afterward, more precise reference. I thought it was important to communicate that.

Thank you.

DR. NELSON: Thank you.

Are we ready to discuss the questions, Alan?

Questions for the Committee and Committee Discussion

DR. WILLIAMS: Question 1. Does the committee believe that the revised Uniform Donor History Questionnaire proposed by the Task Force is suitable to screen donors of allogeneic whole blood

and blood components for transfusion?

DR. NELSON: Discussion or let's vote.

DR. DiMICHELE: I just wanted to ask, initially, when you asked that question, I thought we were kind of voting on the final version, but this isn't obviously the final version, so exactly how do you want us to comment on that?

DR. WILLIAMS: I think given that it's an ongoing process with some interaction still to be conducted between the Task Force and the FDA, it would be probably most relevant to use the concept that we do arrive at a final FDA--I hesitate which word to use, but FDA-compatible version of the questionnaire, and that is what we are addressing the question to.

I think given the content, you might also separately consider issues, such as self-administration and other factors on which you might want to comment separately, but what we are looking for is conceptually whether the field can make the change from the existing documents, which are non-standardized to what we hope would be a standardized document as shown here today.

DR. NELSON: Your idea was that once a final document was arrived at, this would be a

mandated questionnaire by the FDA? As I understand it, the content of what is asked is mandated, but how they ask it, blood centers are able to come up with any sort of way to do this.

DR. WILLIAMS: I think "mandated" probably isn't the right term. For instance, if a guidance is a mechanism, it would be recommended, and centers are free to use alternate approaches. If those approaches are less restrictive or otherwise substantially different than what is contained in the guidance, they would have to apply under a prior approval supplement for changes to their license, but that wouldn't necessarily mean that everyone has to use this questionnaire. There are avenues for variations.

I would add to that, that if there are changes proposed, that particularly changes in wording and content of the questionnaire, that it would be reasonable to expect that cognitive studies, at least up to the quality of those discussed so far, would be part of that process.

DR. STUVER: So, if this version or something close to it, it becomes recommended or not necessarily required by the FDA, will the expectation be that it is going to be a self-

administered instrument, or will there be flexibility as to whether it could be given orally or depending upon the literacy of the donor?

DR. WILLIAMS: There has been discussion about the relative merits of self-administration versus audio CASI versus face-to-face. I think I would take the position that that scientific debate has yet to be fully held.

There are literature which support arguments in both directions. The studies which actually have been conducted on the blood donor population are few with small numbers, and mostly they are extrapolations from other studies that have been done either in high risk populations or the general population.

As I mentioned in the introduction, there is a guidance document in the field for comments, and we expect that there will be arguments addressing that, supported by the scientific literature, and we, in fact, cited some in the guidance document itself, defining a similar position.

So, I think that discussion still needs to be held in depth.

DR. NELSON: Through the REDS study, you

and colleagues have done a lot of case control, calling back of donors, and tried to get an understanding, particularly of donors who turn out to have markers as to whether or not the issue was that they didn't understand the question, or the issue was that they did understand the question, but didn't give the information candidly.

Can you assess what the proportion of the problem was with those who turn up to have markers that should have been screened out as to how much is misunderstanding and how much is actually not being candid?

DR. WILLIAMS: There are some data to address that particularly with the CDC-sponsored studies of HIV seropositive donors, the reasons for their screening responses really are across the board.

I would say that process has a validation concern of its own, and that being face to face with an individual, it is very difficult for someone, you know, obviously faced with some sort of misrepresentation to say, well, yes, I lied. It is a lot easier to say that I didn't understand the question thoroughly.

So, the data are out there. It is a

proportion. I hesitate to give that proportion.

DR. NELSON: At least it is some of the problem.

DR. ALLEN: Going back to the issue of implementation once the process on developing the questionnaire is completed, is it FDA's anticipation that licensed blood centers will come back and work out a mechanism through perhaps changes to their standard operating procedure for implementing this?

DR. WILLIAMS: That will, in fact, be a critical component. It wasn't discussed explicitly, but portions of the questionnaire use capture questions to identify a certain population which will be subject to more detailed questions, and some of that will have to be contained in the center's SOP, correct.

DR. NELSON: Theoretically, the REDS study will continue, which as I recall the REDS study has like a 10 percent resample or something of donors, isn't that right?

DR. WILLIAMS: It depends which component is being referred. There is a survey component which has captured data with respect to behavioral risk, and then there are other components, some of

which capture the entire database for markers and donor demographics, and so forth.

Probably the most relevant aspect is the survey component and which we can actually assess behavioral information. Ideally, the best way to test something like this is in a pre/post sort of study with a phased implementation, and you could survey a pre/post population or comparable parallel populations, and get some idea of what is going on.

But because the outcomes are very rare, those type of data are very difficult to measure.

DR. HOLLINGER: Alan, once this gets to the point where it could be implemented, since it has gone through all the organizations, and so on, do you perceive that there would be a problem of having what you started out to have, which is a universal uniform at least donor history from all the blood banks and blood organizations, that there would be then slight changes that would go on there, and if so, where do you perceive these occurring? What do you see these as a problem?

So, when a donor goes into a blood bank, no matter where they go, at least this portion here would be identical.

DR. WILLIAMS: I think that is the goal,

to have the major components of the questionnaire, certainly the FDA recommended and required elements be standardized. I think because transfusion medicine is medical practice, there will always be a wish for some local options, and those will be always part of the process submitted to FDA for review.

So, I suspect there will be some variation center to center. What you have to be careful of is that things aren't tagged onto the questionnaire that actually begin to compromise what has been tested as a unified package. That is the down side to making changes.

Whether or not sites will use it as is without changes remains to be seen, but we have already seen with the source plasma components, that they have split off, and I think appropriately, looked at areas that are more relevant to their donors and which they would like to define different areas of emphasis or methods.

DR. DiMICHELE: I just wanted to ask regarding this issue of self-administration versus not, on the committee was an ethicist. I know we have talked a lot about which way to do it vis-a-vis getting the most effective history, but was

there sort of an ethical response to this in terms of patient rights and sort of the ethics of administering very personal questionnaires, and how they are best done, was there any opinion there?

I just bring this to the group, was there any opinion that was rendered by the ethicist on the panel?

DR. WILLIAMS: I prefer to defer to Joy on that question.

DR. FRIDEY: I think the issue of asking personal questions is one that has been discussed for a number of years. The HIV questions dealing with males having sex with other males, or people who may have had sex with someone has been a topic of discussion for a number of years.

Those questions were issued in 1992, and there has been ongoing concern about that, but on the other hand, we are trying to identify people who may have these risk factors, and how do you get at that without just out and out saying it.

The ethicist on the committee did not render an opinion about the fact that we are asking such personal questions, because I think there is a general recognition that we really need to.

DR. DiMICHELE: My question is not so much

that we are asking them, because, of course, we have to ask them, but just in terms of the way it is done. I mean the ethicist rendered no opinion in terms of one way or the other, is that correct?

DR. FRIDEY: When you say "the way it is done"--

DR. DiMICHELE: Like, in other words, self-administered or interview-administered. I mean that is probably the biggest difference.

DR. NELSON: At one point, I remember they had--before there were specific questions--the person was given a card with a list of deferred conditions, and the person could then--the question would be, "Do you fit into any of these categories," and the person, theoretically, they could say guess without identifying that they were a drug user or that they had sex with another man.

I don't know if that is still part of the scenario.

DR. FRIDEY: To directly address your question, yes, that is on the educational materials. Except for the FDA liaisons, the Task Force was unanimous in its opinion that it should be a self-administered questionnaire, and that included the ethicist that was on the task force.

DR. DiMICHELE: Thank you.

DR. CHAMBERLAND: Joy, but always with the understanding that if the donor preferred an oral administration--

DR. FRIDEY: Right, there was always that option, absolutely.

DR. CHAMBERLAND: So, it would never be denied.

DR. FRIDEY: That's correct, if someone wanted an oral one, they could.

DR. NELSON: Are we ready to vote on this first question? I guess it's a yes or no. We are voting on when the final Uniform Donor History Questionnaire is agreed upon and developed, is it or will it not be suitable, and it will probably be very similar to what we have.

DR. SMALLWOOD: Are there any oppositions to this question?

[No response.]

DR. SMALLWOOD: Are there any abstentions?

[No response.]

DR. SMALLWOOD: Then, it would be a unanimous yes. Thank you.

DR. WILLIAMS: The second question. What additional comments does the committee have on:

(a) the validation process of the Uniform Donor History Questionnaire as revised; and (b) the specific content of the Uniform Donor History Questionnaire questions?

DR. DiMICHELE: I would just say that I think I would echo some of the comments that were made in the open hearing regarding the ongoing validation of whatever instrument is used, that it needs to have an ongoing evaluation process in the field.

DR. HOLLINGER: I have some questions, if I could, and they probably are answered, and there are probably answers to them, but I wanted to just run through them as I saw them, if I might have the opportunity.

The question about aspirin or aspirin product. Of course, that can be a real problem anymore because so many people are taking aspirin for cardiovascular events, et cetera, so a lot of people are on aspirin, but it doesn't include the other nonsteroidals - ibuprofen, Advil, Relafen, Motrin, et cetera, which also equally can cause platelet dysfunction.

It is a question we have to ask all of our patients before we are going to do a biopsy on

them. We also ask them not to take them for at least seven to 10 days before we do a biopsy for that reason, because we do bleeding times on most of them. Invariably, their bleeding time--not invariably--but sometimes their bleeding times will be elevated, and they are on Motrin or ibuprofen, and so on.

This also goes over to Celebrex and Vioxx, but not anywhere into the same realm as you find with the other nonsteroidals.

I know the question is asked primarily I guess because of its effect on the platelets--and correct me if I am wrong, Toby--or are we talking about because when they draw the blood, they are worried about bruising and things like this, which is it?

DR. SIMON: It is the effect on the platelets because if the person has been on aspirin, they can still donate, you just cannot use them as an exclusive source of platelets. So, their platelets can still be used in a pool, and it relates to the irreversible effect of aspirin versus the other drugs that you are talking about that have a reversible effect.

So, it has been consensus of scientific

medical opinion that it is not necessary to exclude platelets as a single source, platelets from those who are on these other drugs.

DR. HOLLINGER: So, they could actually be a plateletpheresis donor also if they were on these other drugs, if that is what they were coming in for?

DR. SIMON: Well, I believe that is the case. I think some centers may have individualized rules on that, but at least it is my understanding that AABB, FDA, up until now, you could be.

DR. FRIDEY: Many blood centers, and actually if there is anyone here to whom this does not apply, have very extensive lists of aspirin-containing comments. I know that our blood center does, I know the American Red Cross does, the DoD does, so that if a donor says, gee, I did take something yesterday, and I am not sure if it had aspirin in it or not, we can help them out because we have a list.

So, that is one way to address the concern that you have. At our blood center also, we do have a separate question that we ask donors, plateletapheresis donors, to try to find out if they have taken a nonsteroidal anti-inflammatory

because at our center, we don't want that person to be a plateletapheresis donor.

I can't speak for other organizations, so I would have to ask my colleagues in the American Red Cross and ABC to get up and address that.

DR. SIMON: There isn't good literature on it actually, even under the aspirin, the old studies done in the seventies, I think upon which things were based, showed that after 72 hours, you couldn't tell a difference.

DR. HOLLINGER: And this would include Ticlid and Plavix and the other things which cause an irreversible change to those platelets, as well.

DR. SIMON: I don't think they have been studied.

DR. HOLLINGER: Oh, they have been studied.

DR. SIMON: But not as plateletapheresis donors, to my knowledge.

DR. HOLLINGER: That, I don't know.

DR. BIANCO: Maybe this will help a little bit. After the explanation that Toby gave, the only donor that is important to defer is the apheresis donors, because that is a full platelet donor.

The apheresis donor is recruited in a different way, is a scheduled donor, and so that donor is recruited by telemarketing or has already made an appointment, is a donor that has already donated red cells.

Nobody puts on a machine a donor that didn't have at least some experience in the donation, and that is the first thing that the person that is talking with the donor will say, "Remember, for the next couple of days or in the next three days, you are not going to take any aspirin before you come to the appointment to make your donation."

So, it is rare that an apheresis donor will say yes to any of those questions because it's a different population, is recruited with a lot of care. The donor is going to sit on a chair for a couple of hours for the process, and you want a full platelet dose to do well.

DR. HOLLINGER: There is a couple other questions. I found the Questions 34 and 19 to be confusing about this, where it says, "Males, check no," or "Females, check no." I understand one is asking about male donors, the other asking about female donors, but it is that parenthesis which