DEPARTMENT OF HEALTH AND HUMAN SERVICES

ADVISORY COMMITTEE
ON
BLOOD SAFETY AND AVAILABILITY

THIRTY-FIRST MEETING

DAY 2
FRIDAY, MAY 11, 2007

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

AGENDA:

First session of the morning is closed to the public.

08:30	Annual Ethics Training for Committee	John Condray, J.D.
09:30	Doors Open - Open to the Public	
09:35	Call to Order and Roll Call	Arthur W. Bracey, M.D. Jerry A. Holmberg, Ph.D.
09:40	Status of Transfusion and Transplantation Safety Continued	Arthur W. Bracey, M.D.
	American Association of Tissue Banks (AATB)	Scott A. Brubaker, CTBS, Chief Policy Officer
	American Society for Reproductive Medicine (ASRM)	G. David Ball, Ph.D.
	American Academy of Orthopaedic Surgeons	Michael Joyce, M.D.
	Committee Discussion	Arthur W. Bracey, M.D.
10:45	Break	
11:00	United Network for Organ Sharing (UNOS)	Jay A. Fishman, M.D., Professor of Medicine, Harvard Medical School

11:30	Open Public Hearing - Ms.Ellen Heck, MT (ASCP), MA, CEBT Eye Bank Association of America	Arthur W. Bracey, M.D.
12:00	Lunch	
1:00	Status of Transfusion and Transplantation Safety Continued	Arthur W. Bracey, M.D.
	Managing Tissues in Hospitals	D. Ted Eastlund, M.D.
	Canadian Experience	Marc Germain, M.D, FRCP(C), Ph.D.
2:00	Committee Discussion	Arthur W. Bracey, M.D.
4:00	Meeting Adjournment	Arthur W. Bracey, M.D.

PARTICIPANTS:

CHAIR: DR. ARTHUR BRACEY

DR. JERRY HOLMBERG

MEMBERS:

ANN MARIE BENZINGER
JULIE BIRKOFER
GREGG BLOCHE, M.D., J.D.
WILLIAM DUFFELL Jr., Ph.D. (Absent)
ANN MARIE FINLEY
CHARLES HALEY, M.D., M.S. (Absent)
PETER KOUIDES, M.D.
ILEANA LOPEZ-PLAZA, M.D.
DAVID MATYAS, J.D.
JOHN McGUIRE (Absent)
GLENN PIERCE, M.D., Ph.D.
GLENN RAMSEY, M.D. (Absent)
SUSAN ROSEFF, M.D.
GERALD SANDLER, M.D.
LINDA THOMAS
DARRELL TRIULZI, M.D. (Absent)

NON-VOTING EX-OFFICIO MEMBERS

MATTHEW KUEHNERT, M.D.
JAY EPSTEIN, M.D.
HARVEY KLEIN, M.D. (Absent)
MICHAEL LIBBY, Commander
JAMES BOWMAN III, M.D.
ROBIN ASHTON
RUTH SOLOMON, M.D.

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P R O C E E D I N G S

(08:30 a.m.)

DR. HOLMBERG: I'd like to invite all the committee members to come to the table please. I'd like to open the meeting and call the meeting to order and also to have a roll call. Dr. Bracey?

DR. BRACEY: Present.

DR. HOLMBERG: Ms. Benzinger?

MS. BENZINGER: Present.

DR. HOLMBERG: Ms. Birkofer?

MS. BIRKOFER: Present.

DR. HOLMBERG: Dr. Bloche?

SPEAKER: -- make comments on it.

SPEAKER: Ah.

SPEAKER: Where were you? You were supposed to be ethics training.

DR. HOLMBERG: Dr. Duffell is absent. Ms. Finley?

MS. FINLEY: Here.

DR. HOLMBERG: Dr. Haley is absent. Dr. Kouides?

DR. KOUIDES: Present.

DR. HOLMBERG: Dr. Lopez-Plaza?

DR. LOPEZ-PLAZA: Present.

DR. HOLMBERG: Mr. Matyas?

MR. MATYAS: Present.

DR. HOLMBERG: Mr. McGuire is absent. Dr. Pierce?

DR. PIERCE: Present.

DR. HOLMBERG: Dr. Ramsey is absent. Dr. Roseff?

DR. ROSEFF: Here.

DR. HOLMBERG: Dr. Sandler?

DR. SANDLER: Present.

DR. HOLMBERG: Ms. Thomas?

MS. THOMAS: Present.

DR. HOLMBERG: Dr. Triulzi is absent at another commitment. Dr. Epstein?

DR. EPSTEIN: Here.

DR. HOLMBERG: Dr. Kuehnert?

DR. KUEHNERT: Here.

DR. HOLMBERG: Commander Libby?

CDR. LIBBY: Present.

DR. HOLMBERG: Mr. -- Dr. Bowman?

DR. BOWMAN: I'm here.

DR. HOLMBERG: And we have Dr. Solomon (phonetic).

DR. SOLOMON: Here.

DR. HOLMBERG: And sitting in for Dr. Burdick today is Ms. Robin Ashton (phonetic). So -- okay. Mr. Chairman we do have a forum.

DR. BRACEY: Oh, thank you.

SPEAKER: Excuse me, could you explain the policy on substitutions?

DR. HOLMBERG: On the substitutions, especially for the government, it does not specifically specify the person or the position. And with the Federal Government we have had numerous people that have other commitments later today. So for instance at this current time, Dr. Solomon is sitting in the position for the gene therapy -- gene cellular therapy and tissues, and normally Dr. Laura St. Martin will be here. She has been assigned to the committee. Also, Dr. Burdick represented HRSA yesterday, but he has also designed that Ms. Robin Ashton -- his surrogate today and in future meetings he will probably have Dr. Ortiz Rios (phonetic), the representative from

HRSA. The government employees are non-voting members.

Ms. FINLEY: Dr. Holmberg, could you ask the individuals who may be sitting in front of their name cards with someone else's name maybe to write their names in? Thanks.

DR. HOLMBERG: I think Robyn Ashton is the only one, so --

Ms BIRKOFER: Dr. Holmberg, for the SGEs, if there is a conflict where you can't attend, can they appoint someone if --

DR. HOLMBERG: No. Even with the representatives, each person, both the SGE and the representatives, have been designated by the Secretary. This situation has come up especially in the blood community trying to substitute for another person and it is not possible under the charter.

SPEAKER: Thanks.

SPEAKER: Thanks.

DR. BRACEY: Good morning. Today we continue the presentations. Yesterday we heard from the major blood organizations and today we will hear from tissue organizations as well as physician groups and other

entities dealing with tissues and transplants. Yesterday evening we did have discussions in terms of what the focus of the committee would be and in terms of its product from the specific meeting. And as such we actually have in past put together, A, a strategic plan, and B, a recommendation with the definition of biovigilance for the Secretary.

So as I see it, we have questions from the Secretary and then our response -- our responsibility to advise the Secretary. We need to hear what these presenters are saying today and then to be able to address the questions of the Secretary toward the end of that meeting. Now, to bring the newer members up to date in terms of our previous recommendations, we do have handouts that include the specific recommendations from our August '06 meeting on biovigilance. That being said, let's continue with the presentations and we'll have to keep it on a tight timeline in order to allow for a good discussion at the end of the meeting.

The first presenter today is Dr. Scott Brubaker. He is with the -- he is the chief policy officer of the American Association of Tissue Banks in McLean, Virginia.

And he will be speaking to us on the status of safety with regard to tissue banks.

MR. BRUBAKER: Thank you very much, and thank you, Jerry -- Dr. Holmberg for inviting us to speak today. And it's an honor and a privilege. Thanks. I do have too many slides for my 15 minutes, so I'm going to kind of rush through some of them.

(Slide.)

MR. BRUBAKER: And the first one is just here to show you that the title of your committee actually matches our mission. It's all about safety and making sure there is a uniform high quality and quantity sufficient to meet patient needs. We are all about accomplishing our mission and our standards, which you each have now a current copy of our 11th edition. That's our primary focus, to promote safety. But we also inspect and accredit tissue banks. It's a voluntary basis. We inspect and accredit those -- we accredit those every 3 years. We train and certify tissue bank personnel with our CTBS program and we foster education with many meetings throughout the year that are highly attended by professionals in our field and as well as regulators.

(Slide.)

MR. BRUBAKER: And we are a professional liaison for our accredited banks. And to give you an idea of who we harmonize with and work with throughout the nation and the world, you can see all of those acronyms up there. We do have active communication with them on a constant basis and I have hospitals listed there. I personally probably communicate with a hospital four times a week on different tissue issues.

(Slide.)

MR. BRUBAKER: We were founded in 1976. Members of the U.S. Navy Tissue Bank were part of that foundation. And I won't go through all of those. We have about 99 accredited tissue banks right now throughout the U.S. and Canada. They recover approximately 25,000 tissue donors; distribute about 2 million grafts every year.

(Slide.)

MR. BRUBAKER: Just -- I just want to show you one example of a standard that goes beyond federal regulations and is a requirement. And it has everything to do with algor mortis, which is the body cooling after death, and time limitations for recovery. And the

clostridium death that occurred in 2001, that recovery agency and the processor were not accredited by the AATB and went outside of that standard and that led to this incident.

(Slide.)

MR. BRUBAKER: Our standards have been used throughout the world by different regulators, as you can see, that are listed there. Dr. Noel, I know him very well, a good friend, and he -- the WHO Aide Memoirs that he mentioned yesterday, we did have a part in creating those documents as well.

(Slide.)

MR. BRUBAKER: We have our guidance documents. Of course we have standards, and to try to help banks understand how to meet those standards, we've created guidance documents. You can see the three there. Now, this last one was released recently and it doesn’t look to you probably that this might be related to a safety issue but it absolutely is. Providing service to tissue donor families, I can tell you that the BTS and DRS situations, those organizations as recovery agencies did not have these programs in place.

(Slide.)

MR. BRUBAKER: We're working on other guidance documents and they're all related to safety in some way, shape, or form and the four that are highlighted there are related to our investigation of the BTS incidents.

(Slide.)

MR. BRUBAKER: We're also working with other organizations on a uniform donor history questionnaire, so we can have one that's uniform throughout organ, tissue, and eye donation, much like the cell therapy and the blood donation industries have done recently.

(Slide.)

MR. BRUBAKER: Now, I realized yesterday, and I changed my slides and you have a new handout because we have -- I want to make sure you understand what types of tissues we cover. The FDA listing for HCTPs that are related to our tissue types are listed on the left and they are in decreasing order of actually distribution in the United States. Our designations are on the right. And again musculoskeletal includes soft tissue grafts as well -- osteoarticular. Then you have cardiac, vascular, skin and so forth. We also accredit reproductive banks,

but we only have less than a dozen who are accredited, and we have autologous and living donor surgical bone and other living donor standards as well, not just deceased donors.

(Slide.)

MR. BRUBAKER: To get an idea of distribution, we have done surveys over the years and we are performing a 3-year retrospective survey this year, so we'll have updated information for you in the future, but you can see how many grafts are distributed. And these are musculoskeletal allografts only, bone and soft tissue. And you can see the soft tissue is the very small bar there, at about 81,000 in 2003 and about 1.3 million for bone grafts. So a large majority of the tissue being distributed are bone grafts and they are highly processed, which I'll show you here in a minute.

(Slide.)

MR. BRUBAKER: One of the other things to be aware of is that many of our banks also follow GMPs because the product that they are actually distributing or manufacturing is a medical device. It's highly processed, it's demineralized bone matrix added to a carrier, some

kind of carrier and it's designated as a device.

(Slide.)

MR. BRUBAKER: I won't go over this and -- spend maybe just 10 seconds on it, but Klaus Nether presented this history yesterday and I do want to highlight though that recipient notification is something they have control of that probably no one else does in their standards, possibly ABB in their standards for their blood bank if they handle tissue.

(Slide.)

MR. BRUBAKER: We are also regulated by states, especially New York State, Florida, and California. They have their own tissue regulations. So you need to be aware of that. And they can inspect tissue banks every 3 years. The New York State and Florida State do inspect states out -- I'm sorry, tissue banks, tissue establishments outside of their state, California only inspects within the state, but they do require licensure. So there is another level of safety through these inspections and licensing agencies that are out there.

(Slide.)

MR. BRUBAKER: There -- usually when we present

at a meeting like this, FDA has presented the regs. That can take a long time because there are a lot of them. I forgot to bring my notebook up here to show you how thick the regulations are, but they are all related to safety and to controlling contamination and cross-contamination for communicable diseases. It began in 1990, and you can see all of those there and then I know the committee has a handout so I won't go into those in detail.

(Slide.)

MR. BRUBAKER: The most current ones are these that are currently effective, depending on when the tissue was recovered, before or after May 25th of 2005. But you can see that they are very extensive, and actually the structure of it does match that within standards, our standards.

(Slide.)

MR. BRUBAKER: And another thing I realized was you may be very familiar with blood donor screening and collection and so forth and testing, but for a tissue donor it's a highly involved process. Those donors don't come to us, we don't talk to them normally as -- of course if it's a disease donation, we rely on a historian, and

just getting a blood sample, finding one that's qualified, it's very labor-intensive. And that's what this picture here is supposed to depict. And it's the same for ocular donation as well. We have a lot of investigation to go through and a lot of seeking of information to gather the correct and adequate information to determine eligibility of the donor.

(Slide.)

MR. BRUBAKER: Now, 11 percent, in our last survey we performed, of all organ donors are also tissue donors. And there are reasons that the number is actually that low. I've got some of them listed there, but it is based -- you heard -- I believe Ruth mentioned yesterday the risk benefit ratio. And for organ donation it is different. You know, their donor acceptance criteria policy through the OPTN, UNOS, and AOPO standards, they are not as strict. They are working off of CDC recommendations from 1994. They don't assess the sample for plasma delusion; it's not a requirement for testing laboratories to be clear registered as CMS equivalent. And the test kits themselves need to be licensed -- screening-test approved by FDA, but we found that

compliance actually may be a little low there. And there are reasons for that too, as well though.

(Slide.)

MR. BRUBAKER: Just to briefly go over some handling of tissue -- and when I talk about highly processed, please be aware that there are disinfection processes, irradiation processes, chemical washes and soaks. There can be acid treatment if it's a demineralized product that's distributed. There are mechanical centrifugation, sonication, agitation that it can go through; lyophilization itself can reduce contamination or eliminate it. And then there can be a terminal gamma irradiation at the end, in this final package.

(Slide.)

MR. BRUBAKER: I think one of the best ways for you to understand how tissues are processed -- or I'll show you pictures, and this is demineralized bone matrix. You can see the powders in different granule sizes there that can be created and administered as pastes, putties, injectable forms and pliable pieces.

Traditional, conventional HCTPs for us would be

these chips and blocks as you can see here. And you can see all the marrow elements -- and I know one tissue bank studied showed that 99.7 percent of all the marrow elements were eliminated through their process.

(Slide.)

>R. BRUBAKER: Tissue forms today, they put pieces of bone together, almost like carpentry and woodwork, to make them stronger pieces, and that does help the patients as well, and you can see some examples here.

(Slide.)

MR. BRUBAKER: But there are grafts that are frozen, fresh, cryopreserved. Some of them can lyophilized. These may not be supplied as sterile.

(Slide.)

MR. BRUBAKER: Fresh osteochondrals of total joints for total joint replacements due to trauma and disease, those also would not be highly processed because the utility for those grafts would be compromised if you did irradiate them or if you chemically treated them.

(Slide.)

MR. BRUBAKER: Skin can be fresh, cryopreserved, lyophilized. They can be acellular products that are

freeze-dried. And you can actually even take that and cryofracture it and put it into an injectable form. And there is very much success with these products for the recipients. But some of them that are minimally processed might cause more risk than those that are highly processed.

(Slide.)

DR. BRUBAKER: Cardiac grafts are listed there. You can see the aortic heart valves, pulmonary and some patches and conduit grafts or vessels. Again, these are only disinfected and cryopreserved, so there might be some risk for those grafts compared to others.

(Slide.)

DR. BRUBAKER: Now, we talked about some information about tracking yesterday, and we performed a survey. A 100 percent of the time our banks who distribute tissue do send out an implant card. So they hope there is compliance in filling that out by the end user and sending it back to them to complete that tracing loop. No one requires that, except for Joint Commission standards. So those entities, I think, we are seeing an increase due to that.

We do -- you saw Dr. Strong's nice graphics that showed his bank was the highest at 95 percent, which was -- that is true, he is correct.

(Slide.)

MR. BRUBAKER: Information missing on the implant cards, the patient's identifier. We don't really need the name, but we'd like an identifier so that tracking can be completed at the end, but that's actually the most common piece of information that's left out. And you can see the end user types who are most noncompliant, dental offices, oral surgeons -- and these are non-Joint Commission entities, if you can think of it that day, day surgery centers and large hospitals, in that order. So there is a gap.

(Slide.)

MR. BRUBAKER: Now, I'd like to show you some recall experiences. In 1991, the HIV or the HW3 case, as we know of it, there are only five tissue grafts that were unaccounted for by hospitals during that recall situation. There were seven recipients who ended up testing positive from the 53 tissue and 4 organs that were made available. All organ recipients tested positive and three fresh

frozen minerally-processed tissues did transmit disease.

(Slide.)

MR. BRUBAKER: Now, if we jump 10 years ahead to 2001, this is the clostridium case, and at that time this bank was not accredited by AATB, but they offered this information to us now. And you can see that no tissue grafts were unaccounted for but there were only 29 that were made available. And again, these were fresh and/or frozen grafts that were -- two infections reported, one was confirmed by culture, resulted in the death, and the other one was not confirmed by culture. But he was treated and did fine.

(Slide.)

MR. BRUBAKER: Now, this recall experience is the -- is a recent one and of course the largest one ever and it's BTS-related; 28,000 tissue grafts made available from six tissue banks. And now you see almost 2,000 tissue grafts and devices that were unaccounted for by the end users and also by distributors. What was found out as a gap here was that when our banks did audit the distributors, they had SOPs in place for recall but when they were actually put to the test, they didn’t work. And

there were tracking problems. So again, this involves not just tissue grafts but tissue grafts that are kicked up into that higher level as a medical device.

There were some international -- some countries internationally who would not cooperate with the information about recipients, and you can see the other numbers there.

Again, the -- with all of this in place, 95 percent of these tissue types were highly processed that were distributed using methods that have been validated to eradicate bacteria and diminish viruses, and there have been no proven infections to date.

(Slide.)

MR. BRUBAKER: Going to the most recent recall experience I'd like to share with you is the 2006 *Chryseobacterium meningosepticum.* This was 4,805 soft tissue grafts. These were all tendons and ligaments that were distributed and recalled. And within 30 days, this bank was able to determine the disposition of 99 percent of the grafts, which is excellent when you think about the timeframe and the results. There are still only six grafts that are unaccounted for four facilities. They are

all presumed to be implanted, but those facilities could not track them to that final disposition.

There were 750 hospitals involved in this recall throughout U.S., Canada, and Mexico. And the implant card return rate was actually 74 percent for these 4,805 grafts, which is excellent.

There were two infections reported. The patients have been treated. They resolved their infections, and the grafts remain in place.

(Slide.)

MR. BRUBAKER: Now, the TTSN, you've heard a little about that, and I was hoping there would be someone who would be presenting, you know, 20 minutes just on the TTSN. We do have members from this group here who are working on this. We are in our second year of a 3-year agreement, and there is only monies allotted for 1 more year. This is something that really needs to continue. You can see the collaborative effort there is between all of those associations and federal authorities and also end user associations. That's all, again, part of the tracking issue. So this will be a database that will link all donors and tissues processed from one donor and

distributed widely by maybe a couple of banks and to link all that together to the recipients.

We are in part C right now. I am happy to say I'm a co-chair of this part of it. We are creating definitions right now for clinicians to use to hopefully if they can recognize a possible allograft-caused infection. And as you can see, we've got over the parts to go through and hopefully we will be finished by next year.

(Slide.)

MR. BRUBAKER: Now to end this, this is just an overview of the safety of tissue transplants. In the past 20 years, about 10 million tissue transplants have occurred. We don't have a true number because of the implant card return compliance rate is so low. The viral transmissions though that have occurred, the last one was in 2002, and testing today would have picked up that case; HCV NAT has now been in place by AATB for the past 2 years.

And we preceded federal regulation. That will be a requirement by fall of this year, but we've had the HIV and HCV Nucleic Acid Testing as a requirement for

accredited banks for 2 years now.

(Slide.)

MR. BRUBAKER: And you can see, early in 1990s, was the lookback testing. Again, that was a testing issue where HCV was realized. TB and HPV was over 50 years ago when that occurred, and processing was nothing like it is today, and testing nothing like today. HIV was 20 years ago and that was again testing issue, and you can see that the other diseases that we've heard about are transmitted by organs only today.

(Slide.)

MR. BRUBAKER: Bacterial transmissions, there have been a few, and you can see that one tissue bank, who was unaccredited, was involved in a lot of those. They've now reached another higher level and they're accredited by the AATB, and I think they've been inspected by the FDA more than -- more detailed and under more scrutiny than any other bank in the country, and there has been no malignancy in cancer or no transmissions that way.

(Slide.)

MR. BRUBAKER: Someone talked about coding, and we are involved with the Zen (phonetic) Group in Europe,

talking -- we're part of their workshop and committee workgroup who is looking at ISBT 128 and applying it to tissues throughout Europe. So we want to maintain that communication. We have actually promoted that within the -- our banks that are accredited by forming the NATAG (phonetic) as you see there, and we've actually had 6 meetings that have occurred over the past 2 years or so and we're trying to get banks to fall into accepting that kind of coding system.

It's difficult. We have a lot of -- a variety of grafts that our banks do offer for distribution and implant. It's a little different. To code them is tough.

(Slide.)

MR. BRUBAKER: And I'm wearing black and blue today because we feel a little bit beat up and I just want to show you this slide. These are the advisory committees that we've presented at probably in the past year I think, and the CTGTAC is our assigned committee, but we only have one representative of 15 that are familiar with tissue on that group. And tissue has not actually been part of their agenda to date. The BPAC, no tissue representation. When they talked about Chagas, the -- one representative

from the CTGTAC attended BPAC for -- on our behalf I guess.

ACOT (phonetic) has had two meetings where tissue was on the agenda, and again no tissue representation. The OPOs are involved with that one. And this advisory committee now has in its charter tissue, or actually transplantation, and tissue is part of that. And we have no formal tissue representation on this committee either, so we're kind of lost I guess.

(Slide.)

MR. BRUBAKER: So my final slide here is to answer these questions that were posed. The current state of safety for conventional tissue transplantation is safe and high. Further enhancing that safety is continuing to evolve with methodologies for validating our processes and also the culture techniques that are being used to assure sterility. Areas of commonality for conventional tissues is aligned with reproductive, ocular, and organ for donation, cell therapy and blood donation for screening. However, tissue processing is not really considered in the regulatory process in the tiered risk-based approach, at least not to date. And I think that's happened in the

plasma industry. So that's something that could be looked at in the future.

And a master strategy plan may be indicated but focus group efforts are logical, like the TTSN where you have the organ tissue and ocular folks working together to try to alleviate what's happened in the past. And what's happened in the past -- someone mentioned this yesterday, almost this exact quote. We need to learn from history and apply that to what we do today and improve our processes. Thank you.

DR. BRACEY: Thank you. Questions or comments for Dr. Brubaker. I have a brief question and that is in terms of the accreditation process. What percent of tissue banks are accredited?

MR. BRUBAKER: Well, I put in a Freedom of Information request in to FDA to get a list of all of the establishments who are registered with them, so I can review that to see how many are -- we have accredited and how many are not, and what functions they perform. And we believe in -- well, I haven't had a reply back yet, so I haven't been able to do that, but I've done a manual search of just processors. And I have discovered that

there are -- you know, there's those who list processing. There are, I think, 865, but processing what type of HCTP is the question.

And when I narrow that down just by going through each one manually and looking them up, I come up with about 15 who actually processed or lyophilized bone which is our highest distribution throughout the country of any type of graft, and 13 of those are accredited by us. So we believe -- when we talk about distribution numbers, we really truly believe that 95 percent of the tissue that's distributed in the U.S. today is from accredited -- AATB-accredited banks.

DR. BRACEY: Thank you. Question, Ms. Finley?

MS. FINLEY: I had a question on I think your fourth slide. You had a line on the top that said that there was 85 percent compliance with FDA, and I didn't want to interrupt your train of thought here.

MR. BRUBAKER: Yeah, I forgot to mention that thing. I forgot to mention that, thank you.

MS. FINLEY: Could you flip back to where it was at the beginning of your presentation, please, so everyone can see it? Thank you.

MR. BRUBAKER: Yeah. I'm trying to remember which one that was. It wasn't -- that's 4.

MS. FINLEY: No.

SPEAKER: Eleventh slide.

MR. BRUBAKER: Eleventh?

MS. FINLEY: Thank you. There it is.

MR. BRUBAKER: Yes.

MS. FINLEY: What does that first line mean?

MR. BRUBAKER: That first line means -- actually, I took that right from the GTP final rule there. I mean, I'm not sure if it was in the text or the -- probably the preamble I believe, where it was stated by FDA, if you follow AATB standards already -- it didn't say if you were accredited, but if you follow our standards already, you will be 85 percent compliant with these, this new rule, which was the Good Tissue Practices final rule.

MS. FINLEY: When did that go into effect?

MR. BRUBAKER: March 25th of 2005.

MS. FINLEY: Okay. So then in effect, FDA is asking for a 15 percent greater compliance than what is already standard for AATB?

MR. BRUBAKER: I'm not sure it could be stated

that way, Ruth.

DR. BRACEY: Dr. Solomon.

DR. SOLOMON: This section is the economic analysis section of the preamble where the estimated burden on industry is estimated, and that's why the figure 85 percent of tissue banks out there, if they follow standards would already be following these CGTP rules. And the point being made is, you know, the burden is not terribly excessive.

MS. FINLEY: Okay. Thank you, may I ask you a follow-up question? I was a bit unclear as to what percentage of tissue banks are -- are the rules for tissue banks the same as for blood banks that have -- in the interstate commerce -- you -- I guess it wouldn't if you're -- if you have to meet these AATB standards. Do all tissue banks have to meet AATB standards? Do they elect to do so upon membership in AATB?

DR. SOLOMON: I'm not sure what you're asking.

MS. FINLEY: I'm asking about the -- basically the general level of compliance among tissue banks because I think that's one of the issues that was expressed privately earlier, and maybe the basis for the

biovigilance part of the tissue question we're going to answer today.

DR. SOLOMON: Well, that would be a question that our Office of Compliance could answer or Office of Regulatory Affairs, where on inspection, they determine compliance with the rules.

MS. FINLEY: Okay, but generally what percent -- I mean, do you have a rough idea of how many or -- and maybe this is a question better directed at our speaker, what percentage of tissue banks exist in the country, just general numbers, how many of them are members of AATB and follow their standards?

DR. SOLOMON: Okay, our --

MR. BRUBAKER: Well, we can only count those who are accredited, so those who are non-accredited, we don't really focus on and keep an eye on I guess. One of the things I think that comes into play with your question is that FDA doesn't license tissue banks, they license blood establishments, but tissue establishments are -- you just -- you register and you list.

MS. FINLEY: Register with the FDA, but it's optional whether you want to belong to AATB?

MR. BRUBAKER: Right, but FDA is a requirement, so you will actually have distributors who have to register if they store and distribute tissue. So that will list as performing those functions and then they will list bone, tendons, they'll list -- they'll tick the -- tick the -- on the form which ones they handle.

MS. FINLEY: What percentage do you think you represent the tissue industry? Just ballpark.

MR. BRUBAKER: With the distribution, 95 percent of all grafts distributed.

MS. FINLEY: Okay.

DR. BRACEY: I mean, I think this is a figure that's a ballpark figure, it's not an absolute figure.

MS. FINLEY: Right, I understand.

MR. BRUBAKER: But the largest banks are well known and they are accredited now by AATB.

MS. FINLEY: What percentage --

MR. BRUBAKER: So it can take years to get to that level, but --

MS. FINLEY: What percentage of the overall members of AATB are accredited?

MR. BRUBAKER: Well, the -- see, it's different.

It's terminology I think here, because we have individual members, about 1,100 individuals who sign up every year, pay dues and get breaks at our meetings for registration. So that's -- there is about 1,100 of those consistently.

MS. FINLEY: Okay.

DR. BRACEY: In the interest of time, we will take one more question from Dr. Kuehnert, or a comment, and then we will move on to the next speaker.

DR. KUEHNERT: Yeah. Well, I had a number of comments actually, I'll sort of keep them short, but just an observation about what you said about not having a home in a Committee, I mean, it looks like there is a lot of Committees that address tissue safety issues, but no one that's focused on it, and so perhaps when responsibility is diffused there is no responsibility, so that's certainly a concern.

The other thing we're just some clarifications on the slides one was with the BTS investigation. I tried to add it all up, and it look like 2000 missing somewhere, and --

SPEAKER: An inventory they were never distributed.

DR. KUEHNERT: There were an inventory never distributed, okay, thank you. The other is just a clarification on Rabies (phonetic), you had put you know, only organs, and as you all know there was an iliac vessel graft that was implanted that led to a lot of issues. And I know that that's classified as part of an organ, this piece of tissue, but from the CDC perspective we are not looking at the regulatory aspects to us, you know, it was a tissue.

So, you know, I guess I take a little bit of exception to that, but I understand what you are saying regulatory-wise that it was all involving organs, but I think, you know, I think the Committee should read the article, and the discussion section about some of the issues there because I think it's very important, and again we need to think beyond the regulatory aspects.

The question I have -- one question I have for you is about tracking. You said, for the last investigation it was a -- there was a 74 percent a tracking rate, and then you got it up to 98 percent, and I wondered if you have any idea how much time it took for each tissue bank in a hospital to get from 74 percent to 98 percent,

and if with that time they could have hired a transplantation safety officer for six months.

MR. BRUBAKER: It took 30 days, and we are hoping that that bank they've agreed to present at annual meeting their whole experience, you know, how they identified root cause for what happened, what they did in their investigation, how the recall actually didn't work so well.

DR. KUEHNERT: Yeah.

MR. BRUBAKER: We would really want to get that word out and there are agreeing to do that now which is great. They want to go into the detail and educate everyone.

DR. KUEHNERT: And because that would be very helpful because, I mean, 30 days around the clock may have been necessary because we certainly had some difficulties in reaching your users of tissues when we had to, and it's just so labor intensive as you know.

So, I guess, I should have said this yesterday, but I think there is a lot in here that Scott presented, and I, you know, I just encourage the Committee if they can during the break or something to look at the some of the articles in the discussion section that talks about some of

the tracking issues.

DR. BRACEY: Thank you. Thank you we'll move on to the next speaker. Next speaker is Dr. David Ball. Dr. Ball represents the American Society for Reproductive Medicine, and he will speak to us on their processes.

DR. BALL: Thank you, and I appreciate the invitation to be here, and depending on how this goes the next few minutes it maybe my only one, but it's certainly been interesting visiting with folks that have obviously a lot different emphasis than what we do. And maybe a quick comment on that.

It does strike me listening to these presentations last day or so, the focus of what we do, it appears to me is quite different or in some ways at least, different in what we've heard spoken about before, and that is the huge majority tissues, as I think you'll in a few minutes that we're going to talking about here are initially produced by couples were Autologous use, okay?

Now there are some exceptions of that of course which we will discuss, at least initially, I think the long effects of disease transmission is well as a potentially ethical issue comes from those embryos that were created

initially for Autologous use by a specific couple.

I'd like to point out very quickly also Sean Tipton, one of the ASRM colleagues; the Public Affairs Director is here also. So, if you have any difficult questions, I am sure he'll be happy answer.

(Laughter)

DR. BALL: Okay. Just very quickly for those of who that may not be aware, American Society for Reproductive Medicine is a professional group. It's obviously voluntary; the huge majority of programs performing ART in the country are members, as well as many outside the country. Within ASRM there are many subgroups of reproductive medicine including surgery and so forth, but our specific field is assisted reproductive technologies, and therefore the nomenclature of Society of Assisted Reproductive Technologies or SART, okay?

And within that group then we really focus on the ARTs primarily in-vitro fertilization, which includes sexually intimate couples, which actually -- of all the IVF I've done in this country, about 93 percent or higher are actually represented IVF clinics that are SART members, so I think that's an important observation.

Then of course, donation cycles, which are a big focus of the next few minutes discussion, which would include sperm, eggs, and embryos are included in this as well. For about the past three years or so the number of cycles performed in the country has -- it seems to leveled off at around 120,000 to 130,000, and that's total cycles. The actual number of donation cycles is about 10 percent of that. So, it's somewhere around 10,000 to 12,000 cycles per year.

Okay, in terms of reproductive tissues specifically of course we are talking about sperm. I see this as a bit different than the eggs and embryos, which we'll talk about in a moment because anymore in this country semen donation, sperm donation is primarily a commercial venture, and I think the reason for the semen banks really started in this country in early '70s, and as a result we are way out ahead of the development of the ARTs, which came about a decade later.

So, they've had 10 years basically that kind of organize their groups in accordance they'd been subject to a number of inspection agencies during that time, including my colleague that just spoke, Scott Brubaker in the

American Association of Tissue Banks.

Okay, but then we move onto eggs or Oocytes, and these the donors for eggs are primarily recruited, screened, and tested via ART clinics. There are some commercial agencies out there, typically they are recruiting agencies solely they'll find donors and so forth. Some will do screening questionnaires, medical histories and so forth, none as far as I know, do the actual testing, decease testing.

And then we move onto embryos, of course these are produced solely by ART programs. There are some non profit so called adoption agencies, which typically in my view are either religiously based or for some ethical reasons commonly tried to find "homes," if you will, for embryos that have been put up for donation by couples that originally produce them.

Then of course there are few storage facilities, long-term storage facilities that will take these embryos in. Typically the couple that produce them will send them to these agency or these facilities for long-term storage. And then it would not be unusual for that couple later to decide they've completed their family building perhaps

they've one or two children at home, they have those frozen embryos remaining at the long-term storage facility, and now they wish to put them up for adoption, and some of these storage facilities will do the basically donor eligibility determination on those embryos.

Okay, current oversight, this is perhaps a little bit of a defensive slide because I know in general people see our field as unregulated, I would argue that's not true. Certainly, from a medical standpoint there is a typical physician licensing that goes on in any field. But then there is another aspect here that folks typically are not aware of in that there is a federally mandated cycle reporting to Centers for Disease Control and Prevention, pardon me, this came about in the early '90s, and I think commonly is referred to as the Wyden Bill.

The bottom-line here is that every ART in the cycle -- every ART cycle in the country is required to be reported for the Centers for Disease Control for outcome monitoring. I think the primary emphasis of this was to make sure clinics are being straight forward with their claims of pregnancy rights.

Okay, this effort is actually a joint-validation

effort between Centers for Disease Control and SART. I actually happened to be the SART-Chair for that Committee that interacts with the CDC folks. On the laboratory standpoint or from the laboratory standpoint of course we have CLIA, various inspection agencies including various state agencies, which again Scott Brubaker referred to, College of American Pathologists are a common vehicle for inspection in our programs. And then some programs do use JACO (phonetic) as an inspection agency also.

In terms of both that is, laboratory and medical clinics, of course FDA since May 25 of '05 has been involved with inspecting our programs. This whole focus here at this point at least is donor eligibility determination as opposed to GTPs that is expected to be faced in sometime in the future. And then of course professional organizations oversee these clinics, and primarily that would be ASRM and SART.

Okay, so in terms specific disease prevention issues SART guidelines, there are SART guidelines for donor testing, and not to be outdone by federal agencies are particular guidelines amount to 50 pages for both sperm, eggs, and embryos.

Okay, there and in some cases they are actually quite a bit more stringent than FDA requirements, and in particular one I would cite is our recommendations at least suggest testing of recipients, I'm sorry, the recipients of donor tissues as well as the donor tissue themselves. This equates somewhat to liability issues, but also in a larger from a larger viewpoint looking towards the well-being of any children born from these donations.

FDA of course is specific for sperm, eggs, and embryos, donor eligibility determination again is the focus here. And screening, testing, and then the timeframes for these screening, testing our course is defined there.

SART has in fact about three weeks ago now requested an FDA liaison to be assigned to help us develop uniform donor questionnaires for screening of all donors. And the point here is that about a year-and-a-half ago now, our two years, when these FDA Regs. came along people were scrabbling a little bit trying to develop these screening questionnaires and so forth, and I would say primarily wind up using blood screening questionnaires as a template to go forward. But we'd like to formulize that a bit more, and have uniform screening questionnaire that's had at least

some FDA oversight available to all our SART and ART members, so that's the reason for the request for liaison.

Okay, in terms of FDA inspections themselves that this information I've picked up from a meeting towards the end of January this year, but at that point at least the information given was that ART programs across our subject to FDA Regs. as of 5/25/'05, and as of the end of January towards the end of January about 30 percent of all ART programs had in fact been inspected, at least the information I saw presented on slides it indicated that actions rates whether it's voluntary or official were similar to those in other field, bone donation, tissue donations, and so on.

Okay, areas of concerns for us in the field. And I will qualify all my statements here today by saying I am an embryologist, so I work in the lab, and on a day-to-day basis work with these patients as well as the materials themselves. So, perhaps my viewpoint on this is a little bit different, but the point here is that we do have some concerns with the false positive test results and re-entry criteria of all of the donors.

And the point here is that of course even if

there is a known positive false positive test result, these donors are excluded from donation, and at least at this point for reproductive tissue donors there are no re-entry criteria. So, even on the false positive these donors, once they're out there, they're out for good. Answer this is especially critical for egg donors and the point here is that egg donors are actually quite rare individuals quite honestly, there is not an endless supply of these folks as it could be argued there as for semen donors.

These typically are young females, not uncommonly sisters or people with infertile -- infertility issues and so forth, and of course the screening, testing, and so forth is some what labor intensive and not cheap. The point being is that it go through all the initial screening, testing, and so forth before we can use these donors to have them excluded based on a false positive test result makes it difficult for these people.

In -- on top of that besides there being limited number of donors there is also within ASRM guidelines a limited number of cycles any particular donor can donate. So, that even shrinks that potential egg donor pool more. Okay, and of course from a consumer standpoint one of the

big concerns with all of these is the extra cost that that's incurred by patients requiring donation.

I think it's quite clear most patients do pay out-of- pocket for this kind of care, and an even small increase are important to them. Okay, from an advisory -- I am sorry, from the risk estimate, I would argue in this field it's low, Gametes and embryo status as a disease vector are not known, I can tell you I've checked around the country with my colleagues, and none can cite a known example of disease transmission through an egg, or an embryo to this point in time.

And also there is some literature although on semen -- a lot of these comes from the Italian literature, but some in this country as well that is, even in couples with known to be discordant for HIV, and this would positive males, negative females, the risk of transmission with appropriate oversight, that is treatment, preventive treatment of the recipient, as well as processing of the semen sample seems to be very low. These of courser are not donation cycles, these are sexually intimate couples, but I think it serves at least as a reference of some kind to do a risk estimate from.

Okay, maybe one twist here that that some of these other fields represented at this meeting doesn't have. Some of the ethical implications I think maybe important to consider here. For example, once these embryos that are produced from these ART cycles are frozen, the best we can tell they are stable for at least decades if not centuries, okay? So, they don't really seem to have much of a shelf life here, so is not the sort of thing where, you know, after a year, or well the concerns with the donation really go away because the tissues are not viable anyway, that's not the case.

Most embryos for donations are from couples that have completed their family building. One of the twists of this if you will hear is that typically they would -- having finished their family building, they do seem to commonly have a closer tie to these frozen embryos than they would have if they had not been successful. In some ways if you will, these are kind of siblings to the children they are now taking care of is live biological specimens, if you will. So some of the emotions and psychology gets a bit interesting here I think.

Now, if the requirements for embryo donation are too restrictive the concern, of course, is that it will result in many embryos being discarded as a opposed to being donated to couples in need.

Okay, so again, this is, I think a unique twist perhaps compared to some of the other fields represented here and for what it's worth there was a RAN Study done, I think, about eight years ago now that polled ART programs across the country and the estimate at that point was there is about 500,000 frozen embryos in liquid nitrogen tanks around the country at that point.

My guess is its higher now, okay? The majority of those in that same survey, a huge majority of them, I think, it was 90 percent, 89 or 90 percent of those were for future use by the same couple that produced them, but the others obviously or at least in theory potential for donation.

Okay, well, that's all I have. I tried to keep it short.

DR. BRACEY: Thank you. Questions for Dr. Ball from the Committee? Seeing none, we thank you.

DR. BALL: Great, thank you.

DR. BRACEY: Our next speaker is Dr. Michael Joyce. Dr. Joyce is an orthopaedic surgeon with expertise in reconstruction, out of the Cleveland Clinic. He is a very active member of the American Association of Tissue Banks, and he will present on the American Academy of Orthopaedics' position regarding tissue safety.

DR. JOYCE: First of all, I would like to say, very much that the American Academy of Orthopaedic Surgeons appreciate the opportunity to interact with the advisory Committee as a user and as I have listed here, I'm one of, probably, about 10 members of the academy that have dual roles that have become very interested in tissue banking and today I'd like to just put on my orthopaedic surgeon's cap, but every now and then I'll slip into my tissue banking hat so-- make you aware of some of these conflicts.

The message that we'd like to give the Committee is that these allografts are safe and the use of these grafts provide the opportunity to improve function, reconstruct limps, and it enhances a quality of life. The transmission of disease is a rare event. You have a

handout that actually outlines all the muscal (phonetic) transplant episodes.

Strides have been made by the federal government with the regulations and guidelines that have come out -- AATB standards and joint commission standards about what happens to these tissues in the hospital. There had been blemishes as Scott Brubaker pointed out to you that most of these, not all of them, have been with not accredited AATB banks.

The academy has come out with an advisory statement that I've actually, provided in the slides since I didn't make it as a handout, but I -- this is from December 2006, we've had an advisory statement that has been revised since the 1980's by bringing to your attention that we recommend tissue use from those accredited tissue banks only.

Also in the small print here, we implore the orthopaedic surgeons to participate in trace back and when requested to participate what has happened to their patients and so forth in the way of reporting and so forth. We have provided over the past four years a yearly scientific exhibit on patient safety and you have in your

handout this yearly updated scientific exhibit that is a foldout and again, we didn't go over in very great detail about those muscular skeletal infection instances, but they're recorded on the last page.

I point out to you that this is a combined project between the academy and myself and Scott Brubaker, AATB. We've come out with a pamphlet about what that can be passed out to patients about bone and tissue transplantation as a combined project between the academy and AATB. AATB is voluntary standards, things can be part of AATB, and we were just delighted in 1993 that the government in their regulations made the interim rule; eventually the final rule and then we've had current good tissue practices that has evolved over the past four years.

A lot of investment at the time and we thank Dr. Solomon from a user's perspective for these regulations which is essentially the role of the land and they're not voluntary as AATB is, but they are the rule, and they've been implemented, since May of 2005. We know which banks do, do tissues so forth through registration and donor eligibility.

Recently, in February the guidelines came out concerning donor eligibility outlining things, and then a couple of key points that I like to bring to your attention, a lot of work in a document that if you pull it up on the web each and every page has the term “nonbinding” for all the years that have gone into this and so forth, it’s quite interesting, if an orthopaedic surgeon brings this up, is this really a rule, is this a guideline, is this a mandate, what are the regulations and on each and every page, it says “nonbinding” and I understand why, but my orthopaedic colleagues probably do not.

In this we have essentially guideline recommendations for NAT testing HIV and Hepatitis C for donors recovered after August 28, 2007, six month implementation of this guideline and it’s not really technically it’s guideline recommendation, but in essence it’s a mandated NAT, HIV, Hepatitis C for these particular donors that are recovered and we, the academy is just happy with that, it makes the tissues safer. There had been window periods of time mentioned here.

This requirement for NAT has been in vogue since March 9, 2005 for AATB accredited tissue banks, and then we look about, what about inventory. These tissues are stored for usually two years, some of them were stored up to five years, and inventory has not been addressed neither by AATB nor by these more current guidelines. For AATB issues, usually the most tissues that I use for tumor and adult reconstruction would pass that time, but I just bring to your attention that it doesn't address inventory.

So if I as an orthopaedic surgeon want to make sure that it's not tested, I have to look at the label, okay, and I ask my colleagues, how many of them look at the label. So they trust their tissue banker, but when issues come up then at times they don't trust their tissue banker. We try to teach in our pamphlet that you need to know your tissue banker. If you're going to order tissue, know your tissue banker.

The problem is most of the time the hospitals order the tissue and the orthopaedic surgeon may or may not have significant involvement. The joint commission is essentially the only organization that has come out to actually make rules that are concrete. They are not part

of the federal government, but obviously each and every major institution wants to be joint commission accredited.

I bring to your attention that there is a mandate. This has been in vogue since July of 2005 that those little cards that come with the tissue we're supposed to send them back as a mandate, but the best we can do is 70-75 percent and I would ask (inaudible) that which major hospital system has been nailed for a violation about not sending those cards back. It's miniscule for what they're looking at, but at least it is a start in trying to do tissue tracing.

The member of the Committee AABB of tissue and then we have written and my colleagues mostly I've reviewed this and supplied suggestions and there is an emphasis on centralization in a hospital about how tissue is handled. It comes into the hospital, people have to look at the package, is the package intact, has it -- or has been frozen in transportation and so forth logged in and so forth.

Dr. Eastlund will go over that. Dr. Eastlund is a little bit aberrant just like I'm an aberrant as an orthopaedic surgeon knowing about tissues. He's a blood

banker who knows about tissues and tissue regulation and about tissue use because he used to be a tissue banker and he probably still is a tissue banker and is actively involved in this, but not all blood bankers at a small community hospital or even a mid level hospital has much knowledge about musculoskeletal tissue. Even at my place, we are decentralized, okay.

Heaven forbid if you tell the CEO of the hospital if he wants a human heart valve that he has to go through the blood bank. The cardiovascular division handles their cardiovascular allografts, same way with the plastic surgery people, same way with me with musculoskeletal, and we have a medical director for each and every type of area, but truly even though we're under the division transplantation, we are decentralized not centralized and our blood bank doesn't want to have anything to do with it.

Full time equivalent dollars give us something -- give us education and so forth, so there is two different ways to handle it. When it's handled, there is a centralized fashion I think that's a very good thing to change major systems that maybe a challenge. The master

strategy I shared with you that for tissues now, we're doing that testing. Interestingly, this was a blood iron D project back in 1999.

The licensed test came out in 2002. We had problems using a living donor test. We went to the test companies and asked for cadaveric testing. They eventually came out with that. Most of the banks started to do NAT testing; AATB mandated it in March 2005. Now, for organs, if you're in a system in the Cleveland Clinic does NAT testing for OPO, a five-hour turnaround time.

That's great, they have ready access and an essentially most of the organ donors are NAT tested at least locally in North Eastern Ohio, but that's not the rule for a lot of other OPOs that don't quite have that access, so there is going to be a certain times where we have problems. We have a lot of tests out there, we have screening tests, we have diagnostic tests, we have tests for living donors, we got tests that have been validated for cadaveric serum and there maybe discordant results and late discovery, the organs are implanted, tissue goes off the tissue bank, a NAT test is done and lo and behold is NAT positive, what are the organ people going to do?

You can imagine the pressure involved. We don't really want NAT testing if we can't get it upfront and sometimes there is conflicts between organs and tissues and with that particular topic. If you are as a Committee trying to paint a broad stroke, you're going to have to be cautious and you're going to have to be cautious because if you look at blood, blood is out there, we have millions of units, okay.

Now, if you look at tissues, tissues are seldom in short supply. Maybe, the bone-tendon-bones, but organs we all know are in short supply, so if we restrict there will be and declined donors and so forth on a possible false negative test we run into problems. Concerning guidelines, another point that neither AATB or the guidelines address is recreational drug use crack and crack cocaine. Dr. Gocke published a study that of a couple of thousand donors in this particular situation these were donors that were recovered, they were squeaky clean at least on forums and everything else than they did the serology and he found that there were 10 percent positive serology that they had to decline the donor.

Just because they checked off that yes, they did use crack cocaine, or crack or cocaine, but not IV drug abuse, so in this particular situation, lot of the banks have gotten smart, they asked that question, they declined the donor, but there is no rule out there that says that we can't use a recreational drug user. He certainly has much more risk. It's a social history issue with regards to things.

The other thing that the donor eligibility guidelines don't address is who makes these gray zone decisions. The -- I'll put my medical director hat on, when I was at Case Western Reserve University, we had a gentleman in ladies clothes, painted toe nails and so forth, okay. Now, he went through on donor screening and so forth fine and dandy. Serology tests at that time, fine and dandy, but the organ people, you know, we needed him were as recovered.

I declined him because of a social index factor; we sometimes call that lowlife index. Maybe, I'm not being politically correct, but he has potential high-risk behavior, but is not outlined in public health service guidelines. I declined him another tissue bank when I

hadn’t procured him -- recovered him. So who makes those decisions, well, it would be nice if an MD made those decisions.

Right now, the guidelines say that the patient -- the person who makes those decisions are someone who is trained and has appropriate training to make those decisions, but not needing to be an MD or DO, if you are AATB accredited you have the requirement to have a medical director and he makes those decisions, and then we look at who participates in AATB. We have a physicians’ counsel, we have 97, I believe, accredited tissue banks.

Some of the accredited tissue banks have two or three medical directors, MTF, CryoLife and so forth have multiple medical directors. At an AATB meeting at the physicians’ council we see about 30 of them. We have two-thirds of medical directors that are not interacting, continuing in educations and so forth with us. There are no guidelines about who makes these particular decisions concerning training.

I as an orthopaedic surgeon am board certified, reaccredited, I do trauma every four years, I have to get my ATLS reaccredited, I’m certified to the hilt about what

I do in clinical practice. People who were making judgments about release of tissue are well trained. However, where are they with continuing education, where are they with requirements and so forth with that. So we come up with how safe is the tissue that I'm using. We have -- Mike Strong presented the data and I quote that I won't go into detail, but the tissue donor is at least 10 times more at risk to having positive serology.

This is a tissue donor that tissue screening was fine. We went ahead and did the blood test. We already recovered the tissue; we already spent money 10 times more than a blood donor that we're going to discover that particular donor. Point out to you that the blood poll is a repeat donor poll, and obviously cadaveric donors are a one-time issue.

How safe is the tissue, it depends on the processing the tissue bank. We can have aseptic procured tissue that's washed, they can get rid off some of the Staph epi, some of the other bacteria that we have preprocessing cultures, that is, aseptic tissue, it's not sterile tissue. We can have aseptic tissue that's processed, has some positive cultures on it and go ahead

and irradiate it, but it’s never terminally sterilized that’s still aseptic tissue.

We can have processed tissue washed and the matter washed out and so forth and irradiate it, irradiate it usually to 12 kilogray to 18 kilogray and people have validation studies that indeed that is sterilized tissue one times ten to the minus six, one in a million chance that it may harbor bacteria. Then we have chemically treated grafts, RTI BioCleanse is an example of this and again they put sterile tissue, but we have another technique that actually states that they can kill viruses.

The BioCleanse people, number 4 will also say that they are viracidal, but high-dose 50 kilogray, it’s a question whether we can deal with the prions at that level. It’s interesting when you take a piece of tissue out of the bag, this is a bone-tendon-bone, one of my colleagues said, “Hey, it smelled like hydrogen sulfide” and actually, they -- you know, the nurses raised so much problems in the OR, he elected not to use that one, take another one out of the bank, just because of the smell.

Now, it’s a residual and even if it smells, it’s actually very sterilized graft. He wasn’t prepared

knowledge-wise or whatever that that's the type of graft that it gets with that. It's a good graft, so we have claims of sterility. Claims can be one in a thousand or one in a million. The federal government regulations allow us to make those statements.

The package labeling is confusing to the orthopaedic surgeon. If I implanted a soft tissue graft in you or you had a bone tumor and I replaced your distal femur, wouldn't you like to have a graft that had a risk of one in a million chance of having a bacterial or fungal infection than one in a thousand? It's up to you.

But, as we look at these labels, I bring to your attention that this is bone-tendon-bone and it says "R" on it, it means that it's been irradiated and that's sterile and so they will have a claim that this is sterile tissue on to ten to the minus six, one in a million.

This says this is aseptically processed, but passes USP 71 for sterility. Is this a sterile graft or not? I won't challenge you; this is aseptic processing that per validation meets the requirement of USP 71. It is not one in a million; this is not sterilized tissue

that I'm just bringing to your attention on how confusing that it can be.

This is mineralized bone matrix; this is another one that is aseptic, not truly sterilized, and terminal sterilization. It's a cortical stripe as you look at this, you know, again, it meets the definitions of the federal government USP for sterility, but it's not one in a million, not the typical graft that you are looking at fascia lata. This one had preprocessing cultures that was treated with preprocessing treatment of radiation, but not terminal radiation that you could ever call it sterile, and then this is a fresh graft.

I'm sorry, a fresh graft meaning that it has viable cartilage and the cartilage has been preserved with DMSO. It hasn't been irradiated, but again it carries a label of sterility, but this is an aseptic graft, this is aseptic process graft. It is not what we would label in our mind, if I look at a thermal rod and they tell me that it's sterile; I can't say that -- that this piece of graft has the same sterility as that metal rod that I'm going to put in a patient. So, it's little bit confusing for the orthopaedic surgeon.

This one sort of tells me that it has been processed a septic technique and it's not really truly sterilized. But I would tell you that label is valid because they've validated their sterility to one to the ten to the minus third, where you can see the confusion here. And then we have manufactured tissue that is so sterile and true that's the type of graft that is the same as the metal road that I was describing.

So, label-wise if what we've irradiated that should say so and it does, bacteria just means fungus and for sterility bacteria and fungus it doesn't include the viruses in that definition, I have alluded to the fact that BioCleanse will claim virucidal activity and the current technique to 50 kilogray will claim to virucidal capacity as well. Some companies use terminal radiation and if they do that then it's truly a sterile graft.

The demineralized bone product are processed in hydrochloric acid and peroxide and there has been no transmission of disease ever reported with those particular grafts, but just to meet requirements of sterility we are now irradiating demineralized bone from some companies. The question is just how well this

demineralized bone perform in contrast to how it performed before it was irradiated. We, as orthopaedic surgeons, are not provided feedbacks about the difference on those two types of demineralized bone piece.

So, one could say, hey as an orthopaedic surgeon I'm confused. Could we possibly have a White Paper on this particular topic about what -- you know, how safe are these grafts? We're bombarded by the companies left and right about, "My graft is better," we as an orthopaedic community are confused. I'm not confused, but to educate people in a good proper technique makes it quite difficult and just how sterile are these grafts? We don't really know.

The BTS was mentioned, I bring to your attention that AATB has upgraded their scrutiny over their tissue banks and over the recovery folk, but if recovery folks lie and they go-ahead and sent in someone else's blood and they don't get informed constantly, lie about and so forth, those things are very hard to check-up on unless you're there minute by minute with those folks. But increased scrutiny has happened through AATB concerning those credit tissue banks that have recovery folk's that

are separate from their bank proper.

FDA was prompt in their response to this, but there may easily be other BTS entities out there. It certainly created some loss of faith in tissue banking for the user. So, the user, the hospital systems have said, well, this was a funeral home situation we’re not going to take any tissue from funeral homes, because they are uncontrolled settings. Now, most tissue banks have excellent parameters for recovery in funeral homes there is excellent guidelines and requirements from AATB and I as a tissue banker involved with tissue banks and so forth I don’t have problems using tissue from funeral homes as long as it comes from AATB accredited tissue bank.

But oftentimes hospital systems will say, we're not taking tissues from funeral homes. And that creates little bit of grief because most tissue banks do procure and recover and funeral homes, but it’s very controlled setting, not like the BTS type situation. But lo and behold, there were credit tissue banks that were involved with recovery with BTS. The scrutiny has -- went up significantly through increased requirements AATB, my compliments.

The orthopaedic surgeon is fearful about positive cultures and so forth. I remind people that on the back table after two hours I can take a swab and have a positive culture just from the back table the instruments and so forth. Cultures in the hospital are kept only to three to five days. Tissue bank cultures are validated for seven to 14 days.

So, we've got orthopaedic surgeons swapping tissues, sending-off cultures, getting false contaminants and then what do you do with those results? You go to a couple of colonies, do I treat the patient, this is tissue that has had multiple negative cultures, what are we doing in the operating room? There are named orthopaedic surgeons in sports medicine -- much greyer hair than mine that will get up in public in their meetings and say that is malpractice if you don't culture the tissue, okay? This is the message of some of my colleagues are giving people.

So, when you get this one colony the tissue bank goes back looks at it for the scrutiny and the tissue banks do a good job, the report back and say hey there were none of positive cultures for that even on the

preprocessing cultures. So, we don't need to culture tissue in the operating room. But to make a science out of it and so forth it would be wise to have an advisory statement that tissue banks with -- refer us not to do that, we used to culture when we did a total joint replacement, we used to culture the joint. Virgin Total Hip, total joint culture positive swap whatever I do with that.

Orthopaedic surgeons have learned that that's a waste of money, waste of time we don't do that any more. We used to culture all open fractures in the emergency room. People got sued when they didn't do that. Now, two decades later that's not a requirement. We don't cultures open fractures in the emergency room, times have changed. This is another issue that we need to have a change in concept in paradigm for the orthopaedic surgeon.

But who is going to step up to the plate and say you don't need to culture that particular graft, because of the information that's out there. I'm part of the TTSN project, I hope Dr. Fishman goes into a little bit more detail, I'm on the tissue side, I have that privilege and as a three-year project you've heard a little bit about

it, you have a member on your Committee Dr. Cooner to that has done yeoman's job in arranging speakers this and that and it’s interesting he has given some of us -- clinicians some responsibility. But it’s a well-organized project through, you know, was rewarded this contract.

We have made it through part A, we are trying to get a uniform donor number for both tissues and organs that you can -- that all donors would be recorded in a database on a website protected and secured. So we know who the donors are and we know where the organs and tissues came from and so forth.

Part B, is that if you’ll implant this the ideal situation would be, I need to go ahead and do an implantation. Before the case I go on the website and I bring up a data and the graft that I have here in front of me, I login this universal donor number or a number that will link me with the universal donor number and I will get immediate print information on that particular graft that is not involved in the quarantine or recall or whatever.

And then -- then I can go ahead and use it and then I -- instead of the donor cards that have to be

mailed in that are not being mailed in, for me to use that graft I have to log in to Part B, security systems telling who the recipient is and so forth that we have the absolute tracking, tracing ability with this.

Part C is also doing adverse events and one of my personal goals is to login the lower-level of concerns, the concerns that we never get to MedWatch. But if we have enough of them than they would add up and people would scrutinize over those. The other thing is that we need to know if you have a combined organ and tissue donor we already know the organs had been implanted. It'll be wise to know what happened to those organ recipients.

So we have examples in 1991 with HIV and where we have three -- the donor was in 1985 not recognized until 1981. We knew the organs -- all four organs were HIV deaths related and so forth, but the tissue world never caught up to that information. So we had three people with soft tissue graft and -- I'm sorry, two soft tissue grafts, one bone transmission of HIV.

We should have been smarter to pick that up earlier. If we knew the organs sort of converted to HIV we shouldn't have released the tissue.

So do we learn anything? So 2002, the Portland donor this is a 2000 type situation where the donor was procured in 2000, so it is hepatitis C, this is before NAT testing. But again we have organ recipients sure of converting with still tissue released and issues of communication. The TTSN project is trying to bridge the gap in communication with this.

And then we have other situations that had no tissue associated with them, rabies, lymphocytic choriomeningitis case. I just asked the question; hey, would the tissue people be notified that organ recipients died of rabies and choriomeningitis in that particular situation. So we need to know what happens to the organ donors. There was no reporting back up until about one year to UNOS. There is no mandatory testing of organ recipient that costs money. However, oftentimes if we only know at three or four months before tissue was released, it would be most helpful as a safety.

It’s essentially another biological marker, serological test. Problem is cost, permission, data collection and communication, I'm trying to do that. We need, as a tissue community, know what happened to the

organ recipient. This advisory committee has a huge task. I bring to you their attention; I'm talking about the grafts that are considered tissue, 361 items, okay? What about devices, are we any -- demineralized bone paste with a carrier is a device. There's tissue engineering, I would predict that instead of talking about some grafts in a bottle, we're going to talk about tissue engineered grafts. Those are going to be devices.

I bring to your attention that for meniscal transplantation we have a collagen matrix because it's dead tissue. It's not counted as a xenograft even though orthopedically, science-wise, they'd count it as a xenograft. But this is tissue transplantation; this is something that the advisory committee has to appreciate that may fall into your lap. Not only the "blood, tissues and organs," but we're talking about devices that have tissue associated with them.

We have no real information about whether these DBMs really work, when you radiate, do they have problem with osteoinduction. Can the surgeon compare DBMs, no. In the ASTM, we have yet to be able to get even a document, a guideline, about how to test for

osteoinduction. Do these grafts stretch out? Mike Strong had mentioned about nonunion and fractures of large grafts, late rejection. There's very little database out there about information and the outcomes.

We have a good model, we have a human model. We need to know what happens to these grafts. There needs to be a national database about outcomes. I'm not going to go into blood safety; you have the slides on that. But I'd just bring to your attention a couple of points. In a major hospital system, there should be a medical anemia pre-operative workup program that if patient could benefit from epogen, erythropoietin, recombinant erythropoietin. I, as an orthopedic surgeon, shouldn't write them a prescription for an injection of Epogen once every three weeks and their hematocrit goes sky high, and then they have deep vein thrombosis or a stroke. It should be medically managed. These patients should be able to go to medical clinic.

And if you have less blood use, then there's going to be much more safety as I outlined. I am a tumor doc, I have cases that sometimes like liver transplant people, it embarrasses me at times where I'm told that

there’s antibodies. When I'm told once the patient has already started to be operated on, where is the check and balance. In orthopedic surgery, now we have this thing that is called a timeout. So we are not likely to operate on the wrong limb, wrong patient, because we have a timeout.

Here’s another issue that I think needs to be protected in a hospital scenario. Not safety intrinsic to that unit of blood, but safety to how it’s used, and attention needs to be directed to that. The other point that I was going to make very briefly is that I have a patient who really needs blood, an old timer and so forth. How long does it take to get him a unit of blood on the floor, is there a type in cross or type in screen in the bank? And I can tell you there was times that it may take hours.

Okay, and for scrutiny and wise, I -- in participating with the joint commission, I have asked them, why don’t you scrutinize or have some data information in the hospital? How long does it take when someone writes an order that they finally get transfused another safety issue. Thank you for the privilege.

SPEAKER: Thank you, we will take one or two questions from the committee. Dr. Holmberg.

DR. HOLMBERG: You know, you commented about the problem with getting the cards returned, and with the TTSN, that problem won't go away. But part of the timeout, could the question of has the card been filled out be part of that check time or when we get to the TTSN, has that information been entered?

DR. JOYCE: Your point is well taken. But -- and why not, it’s a matter of practice and habit, and number of your physicians; you know how hard it is to change behavior.

SPEAKER: Just one question, and that is do you see a role for -- in the hospital for a tissue committee and well there’s transfusion committee in some hospitals. What about some medical staff function that gains control?

DR. JOYCE: The guidelines that are -- have been written by AABB, my compliments to them about this guideline book. And Ted Eastlund will tell you about a, actually handbook that is going to come out, advocates that. And if you're ahead of the curve, and I was going to show pictures of our tissue bank that we’ve already

fulfilled over the past 14 years, a lot of these requirements, if you headed the curve, you already have a committee, but most hospitals do not.

SPEAKER: Thanks, Dr. Solomon has a question.

DR. SOLOMON: Dr. Joyce, thank you for your interesting and provocative talk. And you raised a number of important questions which could take a lot of time to answer right now. So we might discuss them offline. But I just like to mention about our guidance documents versus rules. There's nothing specific about this. For tissue, this applies across the board for all FDA guidances, basically their recommendations to help you comply with the regulations.

And basically, the rule would -- our tissue rule says to adequately and appropriately reduce the risk of a particular, let's say HIV infection. You have to screen and test the donor. And then, the guidance tells you what is -- what we believe is adequate and appropriate testing to do. And all guidances, of course, say at the beginning that if you have an alternate method that will meet the rule, you're welcome to use that, but discuss with FDA.

And I don't believe at this point there is a

more sensitive test than the NAT test. So I think you'd be hard pressed to come up with something that could also -- could meet the rules as well as what the guidance recommends. Also, I'd like to mention that FDA is considering having a public discussion of some of the issues you've raised in terms of what is sterile, and what are different processing methods and their claims et cetera. I can't really say more but beyond the lookout for an FR notice on that.

SPEAKER: Thank you, in the interest of time, can we just have -- just -- are your questions --

SPEAKER: It's not a question, it's a comment.

SPEAKER: Comment, okay, all right.

SPEAKER: I'll make it brief.

SPEAKER: Just keep it brief, thank you.

SPEAKER: I think what we've heard this morning is really again lack of evidence based decision making.

SPEAKER: Yes.

SPEAKER: I think, you know, as a person who knows blood, I don't know about transmission and oocytes that I'm hearing about today, or transmission in bone, how it's different. So as we go forward, and we have to make

decisions about what has commonality with blood and how should we apply regulations and standards of safety. It's very, very different. You don't want to exclude an organ donor --

SPEAKER: Right.

SPEAKER: -- because of something that we know in blood -- we don't know in organs, what is transmissible or in tissue. So I think it's very complex. As the more I hear, the more complex this becomes, and the more careful I think we have to be about not excluding people on the basis of information we don't have.

Dr. BRACEY: All right, then last comment from Ms. Thomas.

MS. THOMAS: Just a question. I wanted to thank you Dr. Joyce, but I did have just a quick question. You had mentioned earlier in your presentation that transmission of disease is rare. And I would just like to know how rare. Thank you.

DR. JOYCE: There are over a million musculoskeletal allografts a year, and I'm addressing only musculoskeletal allografts. And at the Boot's workshop, if I recall right, that were in 100th percent range of the

chance of transmission of disease that has been documented and proven over the years. Dr. Coonert has helped put together some of that data that was stated at the Boot's workshop. Thank you.

SPEAKER: Thank you.

DR. JOYCE: I was just going to say that what was done at the -- this 2005 organ and tissue safety workshop as we took the number of investigations that we did, and then divided by the number of allografts that were, you know, distributed during those years and came up with a number. And I think it's not a number that I would want to repeat because I don't think it's accurate.

SPEAKER: We need more data. So with that, why don't we take a break and return in 10 minutes -- after.

(Recess)

SPEAKER: Good.

DR. BRACEY: The proceedings --

SPEAKER: -- didn't do it, so --

DR. BRACEY: -- our next speaker is Dr. Fishman, one second here, Dr. Fishman is the director of Transplant, Infectious Disease and Compromised Host Program at the Massachusetts general hospital. Dr.

Fishman will present today the United Network of Organ Sharing, UNOS' perspective on transplantation safety, thank you Dr. Fishman.

DR. FISHMAN: Well, thank you very much for inviting me. First, a couple of disclaimers. Although I work closely with UNOS I am an infectious disease specialist and in that regard, probably reflect the infectious disease community that's involved in transplantation closely, and I wouldn't want to affect any policy decisions at UNOS. There are people better qualified to speak directly to UNOS here; Walter Graham, the executive director is here and Joyce Hager who is our point person for reporting of disease transmissions is also here.

I also thought that I should spend two seconds since organs have in multiple presentations been pointed at as whatever I say doesn't apply to organs as almost an excluded group, and there's a reason for that, and I put it all on a board there, just so it'd be here for the record, but I thought I would mention a couple of key things that differentiate organs from much of the rest of allograft if you will, including blood transmission. It

probably most closely relates to blood, but there are a couple of things.

Organ transplants are in general vascularized viable tissue, which means they are a superb media for transmission of infection, particularly viral pathogens. The second thing is there is a short timeline for screening, in that, they have to be used within hours of donor availability for cadaveric or deceased donor, which means its screening technology has to live to the organ life.

The next is that many of the assays which are used routinely in blood screening are not approved, FDA approved, for use for single donors in organs. That means that assays are more happenstance and are not necessarily agreed upon in advance. As you probably know, organ safety is regulated by Health and Human Services, not by the Food and Drug Administration, so there is a disconnect there. And the -- perhaps the most important feature of organ transplantation is that the recipient is an immunocompromised host by definition, which is to say that to prevent rejection of the graft, they are given drugs to block immune function.

The end result of that is infection, which might not occur in a normal individual, is amplified in the immunocompromised transplant recipient, which means they are sentinels for infections that won't affect other patient populations. Therefore, what we see in organs is a better mirror of what is actually happening, not necessarily an advantageous mirror, but a better mirror than are potentially other grafts that go to other types of recipients.

So I start with the bad news. Recent -- April 23, 2007, a new virus causes transplant deaths in Australia, and I follow it a little bit according to the way it was reported, so these are news reports. A previously unknown virus has killed three organ transplant patients in Australia; they received organs; a liver and two kidneys from the same donor, they analyzed the organs and found little pieces of a virus related to Lymphocytic Choriomeningitis or LCMV, a rodent virus, which obviously wasn't a new virus, that occasionally infects people and is linked with disease in organ transplant patients.

Three recipients, ages 63, 64, and 44 received the liver and kidneys of a 57-year-old organ donor who

died of a brain hemorrhage and therefore manifested no signs of disease in December 2006, and then the disclaimer returning to Australia from an extended stay in Europe. So clearly, it was the fault of the Europeans and not the Australians.

(Laughter)

DR. FISHMAN: Confusion. Victoria's acting health -- Chief health officer told the Australian broadcasting Company that the virus does not pose a risk to the community, because it was not believed to be an infectious disease, but the conclusions were correct. The transplant program saves many hundreds of lives every year, this is a one off or at least a rare event, introduction of tests for the new virus will be discussed and then the more tests that are done the longer the delay in transplanting the organ.

If someone is terminally ill, waiting for an organ, you don't want to delay that procedure to undertake tests that may not be properly validated yet or tests that are to look for an extremely rare event. It is not in fact, as I've already alluded to, and has been alluded to by the previous speakers, that rare, it certainly is

uncommon, but I should mention a number of similar events that have occurred in the United States and elsewhere.

So we've had a number of outbreaks, two in the United States of LCMV infection associated with hamsters and rodents primarily associated with nine deaths. You may've read in the newspapers about rabies virus, with two known outbreaks; one in Germany, one in the United States, and five deaths including one when a piece of vascular graft was used after the transplants had been completed. West Nile virus was most common in 2002 to 2003 with four infections and one death in the organ recipients, a number with encephalitis including flaccid paralysis in two individuals.

There was a more recent outbreak in Texas, I believe, in 2006, nine affected individuals, four deaths, and four episodes of flaccid paralysis. So these are not benign transmission. Two deaths due to Chagas disease transmission with organs and herpes simplex virus, which you all know as "cold sores" has also been associated as recently as last year in Boston with a number of deaths despite knowing what the pathogen was. So these are unusual, I should say, very unusual events, but they do

occur.

So the response would be let's screen every donor for everything or not. So what are we talking about numerically? And this is a question that's come up. About 8,000 diseased donors each year with 28,000 transplanted solid organs, a very long list of people waiting for grafts. As I mentioned, all receive immune suppression to prevent immunologic graft rejection. Almost 7,000 Americans die each year waiting for a transplant. Organs must be used within four to 24 hours after procurement, and therefore testing and screening must be available for individual organ donors on a 24/7 basis.

As you've heard, organs are lifesaving, so false positive assays have an adverse effect that is not true of any other group of allografts; we can't just discard organs. Testing is different than for blood products, there is no batch testing, there's no time to wait, and the assays are not necessarily approved for individual organ screening. So how much more infection do we see? The data available suggests that transmission is four to five times -- my guess is that it's significantly greater

than that, more likely in a solid organ transplant recipient than in normal individuals.

Improved diagnostic assays don't necessarily work, and we are seeing a broader array of pathogens due to broader social and geographic backgrounds of our organ donors. What types of infection do we see? Just about everything. Why is it? A lot of it's just bad luck. If somebody has a bacteremia or fungi -- bacterial or fungal infection at the time of procurement, it may not be detected despite the fact that we're doing routine cultures until after implantation has occurred. This was -- some slides from a couple of months ago of a transmission of Chagas disease after cardiac transplantation. So lest you think this is a rare -- that rare an event we’re -- only two of these, the Chagas disease transplantation, but the patients did indeed die.

What has been reported to UNOS; there is a group, and I will come back to it later, called "the disease transmission advisory group," but infectious transmissions and malignancies are required to be transmitted to UNOS or to the OPTN and reported, so that we have some baseline epidemiology. This is what we've

seen in about the last year since this mandated reporting has been going on, and the data have been collected. What you see here are endemic fungi, bacteria, parasites, viruses, and a variety of other pathogens, it is -- just about covers the whole spectrum.

But these again, are rare events. For solid organ transplantation, screening means something perhaps a little different than it will for many tissues. There is a social issue -- history specifically aimed at excluding high-risk behaviors related to the possible transmission of HIV and secondarily hepatitis C. Blood and urine cultures are done, but of course, those results are generally not available until after implantation. And then there are a variety of serologies that are done to exclude common infections or to risk stratify donors. For example, we routinely implant tissues from people infected with cytomegalovirus and we develop a prophylactic strategy to go along with that.

I'm going to focus on two aspects of screening, and I'm happy to take questions along the way, but first is detection, which is how well do the assays work, and the second is communication about which you've heard a lot

from previous speakers. In terms of detection, how available are the assays, do they have the sensitivity needed to exclude risk, do they have specificity, can they be done quickly, and do we have the money to do them?

In terms of communication, as you've heard, we need to -- communication in multiple directions, we need communication about an organ from an organ bank, or from a procurement organization, we need backwards communication if an event has occurred in a recipient, so that recipients of other organs and tissues from the same donor can be notified, because that has a clinical impact in terms of lifesaving therapies. So the timeline for those kinds of communications, should be hours not days, that means filling out a form and putting it in an envelope and mailing it off to somebody doesn't work very well.

The information must be accurate, and it must also connect to public health authorities as well as care providers so that investigations about outbreaks can be done by the people equipped to do those kinds of investigations. It is worth remembering, and those of you in the blood banking arena know this better than I do that serologies are not perfect; they may remain negative it --

during acute infection, often up to weeks after infection so that a seronegative person for, for example, hepatitis C, might have hepatitis C and you just are detecting the antibody response, not the virus. Antigen test and nucleic acid tests are waved around as being highly useful, we'll talk about that again in a second. They are highly sensitive false positive assays are not rare, and they're not available for all pathogens; they're also not perfect.

What are the imperfections? Recent cases of West Nile Virus, blood testing on the donor was negative, because the blood samples were degraded and the PCR assays were negative, while the tissues were positive in the recipients. In the cases of lymphocytic choriomeningitis virus in which I was involved and Dr. Kuehnert was involved in the investigation, we were never able to demonstrate the presence of virus in donor blood or tissues even after developing specific primers for the strain of virus that caused the infection. That is to say the level of viral infection was so low as to never be detectable in the donor although it was transmitted to four recipients and detected in the hamster that seemed to

have caused all the trouble in the first place.

Therefore, nucleic acid testing, I'm a big advocate, it's not perfect. Recent cases of rabies, there was no history of a bad exposure, until after the recipients had become ill. The further problem of which assays are the correct assays, West Nile virus being a very good example. And I use West Nile virus, because the CDC maps are the best. First of all, back in 1997, all the various encephalitis viruses were where they were supposed to be, which is to say the Japanese encephalitis virus was in Japan, St. Louis was in St. Louis, West Nile was in West Nile, everything was good, and everybody could be color-coded. Something went wrong, so in 1999, we had a few states with West Nile virus, this -- these are not political maps by the way, this is not red and blue.

(Laughter)

DR. FISHMAN: By 2004 --

SPEAKER: Yeah.

DR. FISHMAN: -- this is what the West Nile map looked for -- we don't know what was going on in Washington, but it had spread across the entire United States rather quickly, obviously within three to four

years, which would've meant we would've had -- have West Nile virus testing in place by 2000, and we didn't of course, and therefore what happens? Well, as you go forward, of course, West Nile seropositivity changes, and the incidence of West Nile virus infection drops.

So is West Nile the right thing to be testing for, because it caused some fatalities back in 2002, and a small cluster in 2006, or should we be looking at other viruses that we know are around the world, and that we know are likely to be transmitted eventually to transplant recipients, but just haven't made it yet, and the fact that you can't pronounce the viruses doesn’t matter, they’ll still be on the exam at the end.

So we need rapid assays of high sensitivity with the acknowledgement that no test will prevent transmission of infection a 100 percent of the time. We need rapid communication of data for all types of allografts and between all types of allografts all via central repository and a tracking system so that we can track back and forth from organ donor to organ recipient. I’ve mentioned some of the initials. DTAG is a subcommittee of the operations committee of UNOS, the Disease Transmission Advisory

Group, which is the advisory group that reviews reports of disease transmission to UNOS.

What is reported is mandated by policy 4.0, but the only absolute exclusion criteria for organ donors is HIV, which means there is a lot of latitude in terms of what happens with other organs, this is the -- reflects the nature of the evolution of transplantation as much as it does, the fact that this is lifesaving surgery and there are some -- (inaudible) area for negotiation.

You've heard from a number of people about TTSN, the Transplant Transmission Sentinel Network, which is the CDC derived and UNOS established web based reporting system under development right now. The concept is this, we need to go in both directions, that means, we have a donor who has an infection. If we recognize that infection later, we need to communicate it to the clinical centers. If we recognize that clinical syndrome in a recipient, we need to be able to backtrack and report to all the people that may have received any grafts from that individual.

As was pointed out earlier by Scott Brubaker, the problem with this is that tissues in particular can be

processed and divided and spread out over many areas. Therefore, we need to know where every tissue went and who got an implant. You've heard a little bit about the various parts of it that each -- in part A, that every donor would have a unique tissue identifier. In part B, we have a system to track each tissue all the way through to the recipient. In part C, we have the back information system, notification system for adverse events, where you can say "My patient has infection x, y, z," or I can say, "My patient has meningitis, my patient has encephalitis or hepatitis, does anybody else who got an organ from the same donor have a similar syndrome?"

So it's going to be reported based on specific microbiology, or not based on microbiology as much as a syndrome. Part D was the idea that we notify appropriate regulatory authorities, both for investigation and for -- to -- for mandated reporting and part E is a forward looking education program to say you have West Nile in your area now, you should be testing for it even though it's not mandated, or similar types of information. So it is a communication system in many sense of the word.

As has been said, a lot of work has gone into

this, this is the front page of the TTSN network, it does exist, you're able to search and link to organs, allografts or various type tissues et cetera, numbers, so that virtual numbers are all stored in one data set that is confidentially protected. What are the problems? Well, TTSN is not yet completed, there's no agreement on an appropriate screening paradigm, so you may've heard overall that we're screening for a lot of different potential pathogens, but of course, we don't know day to day, which are necessarily the best ones to screen for and what is the best test.

Compliance is not mandated, you've heard about cards that get sent back. Well, we don't even have cards in the organ community, but even though we're supposed to have mandated compliance of reporting, it doesn't always occur. Once TTSN is finished, it is a demonstration project in many senses of the imagination, so there is no funding, there is no mechanism which will mandate implementation of TTSN nationally. So the -- all the good things you've heard about TTSN and the communication, all the organs, all the tissues, et cetera, all the eyes will be left still hanging unless somebody pays to have it

implemented in the mandates compliance. It will become irrelevant if it's not funded. And screening of solid organ donors can't be folded into a screening paradigm, developed for blood or tissue screening, as the issues while closely related are distinct for the reasons I mentioned earlier.

So the lessons are that new pathogens can be detected using molecular and immunologic techniques, sensitivity is not yet perfect, but is improving. Infection is amplified in transplant recipients with immune suppression, so the risk is greater than in the general population and that we need the rapid coordination of information amongst appropriate authorities and clinical care providers. So what are the lessons? Well, there are a lot of lessons and you all know them better than I do, we need resources for outbreak investigations, we need reference labs that are available to everyone for rapid access to evaluate our recipients, we need to be proactive in pathogen discovery technology, so that we know what’s coming, and I showed you West Nile went through the entire United States in four years, and it's taken a while to get all the assays up and running.

We need to mandate reporting of specified infections and clinical syndromes, we might think about a system for archiving of specimens from old donors, for future epidemiologic investigations, something which Health Canada is by the way piloting, and we need to perform cost effectiveness analyses and collect data to answer the question that was asked earlier about decisions regarding implementations of new screening tests and I will stop there, thank you very much for including me in your session.

DR. BRACEY: Thank you. Questions from the committee? Dr. Kuehnert?

DR. KUEHNERT: It was an excellent presentation, I think it filled a lot of the gaps that existed maybe perhaps in the committee members' minds, I just want to clarify one thing. You mentioned regulated by HHS and specifically --

DR. BRACEY: I knew I was going to get in trouble for that --

DR. KUEHNERT: But specifically, I think maybe you meant HRSA for organs, okay --

DR. BRACEY: Yes, I’m sure I meant HRSA.

(Laughter)

DR. KUEHNERT: And the other thing --

DR. BRACEY: You can tell I work for the government, right?

DR. KUEHNERT: I'm the one wearing the uniform, so don't worry.

DR. BRACEY: Yeah.

DR. KUEHNERT: SO the other thing I just wanted to touch on was -- and Scott Brubaker mentioned this before, is the difference in deferral criteria, and he gave the example of a donor that had a history of crack cocaine use, IV drug use, could you just sort of explain to the Committee like what happens when such a donor becomes available, and who makes that sort of a decision, because I know for organs, it's really more of a judgment situation.

DR. BRACEY: So just to take one step further back, each organ procurement organization has related, but slightly distinct social history forms, you have to recall of course, that the social history is often taken from family members who're under a lot of stress. So the information that you may get may be excellent or may not

be, but it's nobody's fault, these particular screening strategies -- therefore, you may get information that somebody's an IV drug abuser or not, various other -- so there are gaps in that kind of screening, which are backed up of course, by microbiologic screening techniques.

The -- I earn my keep largely by answering the question that you just asked, which is we have a patient who was in jail recently, do you want to use the organs? Well, if you have somebody who's dying and the serology is negative for HIV, you may decide to use the heart from that person with informed consent. You will tell the family or the recipient, "I have a heart that I'm going to give you, but there is a potential problem, are you willing?" And of course, in that lifesaving situation, somebody will often take it. We generally get away with it, our microbiologic screening is pretty good. We may in fact take organs that we know are infected.

For example, with hepatitis c, for somebody who will die within a day without a new liver so that we have a lot of latitude, but the reason is because of lifesaving technology. Now, we don't do that in general for kidneys, we -- very rarely, because there are other technologies to

sustain life in the need -- when you need a kidney transplant. So that I think it's a very important question and where you have the latitude it is made by the clinical center in which the organ is to be implanted.

DR. KUEHNERT: And just to emphasize that point you made, it's also their judgment to say, "Well, we need the heart, we need the liver, well, why not take the kidneys too." I wonder how they -- how people -- different people make that differential judgment on whether they -- the kidneys are sort of coming with it, why not transplant those too --

DR. BRACEY: Well, each --

DR. KUEHNERT: Well, you know, they -- like you said, those patients could be on dialysis, let’s hold off, given the risk.

DR. HOLMBERG: And the other point that I’m sure everyone here knows, but I’ll just mention is that each organ is allocated separately. So that unless you’re asking for a liver, kidney or some combination, the patients are listed through OPTN, through UNOS as individual recipients and the organs are shared across wide geographic areas. It may be for example, that I

wouldn’t accept a heart for one of my recipients, but somebody in a neighboring community might, that is the -- that’s the appropriate nature of the judgment call that’s made.

DR. BRACEY: Thank you Dr. Holmberg?

DR. HOLMBERG: Yeah, thank you Dr. Fishman. You made a fantastic comment about the sentinel -- the organ donor being the sentinel parameter here, and I think that we really need to spend a little time on that, but one of the things as far as the TTSN is that I noticed that there were two different number systems, so currently, there’s no agreement, consensus on what numbering system to use, and it sounds like also that for a period of time there’s going to have to be cross referencing.

DR. FISHMAN: Well, in fact, it was addressed more directly than that, in that there are numbering systems that exist for each of the types of allografts, so for eyes and for tissues and for organs, but at different organizations or at different places. For example, it may be that tissues have -- that one tissue bank has their own numbering system. The way to make everyone buy into this system and to facilitate its use is that each donor will

get a single number, but that would be linked to all the other numbers that might be generated, so that if you get a tissue graft, it might have one number on it, but if you go into the computer, that computer will pull up for you the number that is -- applies to the donor, so each donor has a single number, but all of the subsequent tissues from that may or may not -- all be linked in cyber space.

DR. HOLMBERG: Okay. The other question I have is regarding testing. Now, are most organ donors, are they tested by a diagnostic test or a blood screening test?

DR. FISHMAN: Yes.

DR. HOLMBERG: And I raise that question, because I think with tissues we have another issue and that is that I don’t believe that all screening tests are approved for cadaveric samples.

DR. FISHMAN: It’s -- the reason I say that is it's obviously a mix. So that there are tests, the serologic tests that are used are approved for organ donor screening. They are generally also approved for tissue procurement screening. However, when we get to the nucleic acid test level, most of those are approved for

blood banking and/or for tissues, but not necessarily for organs, they weren't designed for single organ donors necessarily. So that there's some variability, and it depends on the individual test. For example, for West Nile testing, there are multiple manufacturers and their tests have different approvals for different types of specific indications.

SPEAKER: Could I --

DR. BRACEY: Dr. Solomon (phonetic) --

DR. SoLOMON: -- back please, all of the current FDA licensed NAT tests are approved for organ donor screening, it -- that's what it says in the package insert, that organ donors can be screened with all the FDA license NAT tests.

DR. FISHMAN: According -- I don't want to disagree, because I know you're the source here for this information. But according to the manufacturers, for West Nile testing, that's not necessarily the case. So there is some communication issue. You're probably completely correct, but the manufacturers don't necessarily know it, because they haven't filed the paperwork for organ screening. So I just mentioned that there are

communication issues that may have to be carried through in terms of what's approved for what.

DR. BRACEY: Thank you. We will then move to the open -- oh, yes, Dr. McCurty.

DR. McCURDY: I've kind of lost track with what the end point was, but one of the two original contracts for the development of NAT testing was specified for organ donors, and the idea was, when it started out, that this would be a single tube test, it would be doable by technicians who are not specially trained for NAT testing, and it could be done in the middle of the night or any time. I don't know how this turned out with the approval process, but that was the original goal of one of the two contracts that was -- Gen-Probe was the contract winner in those.

SPEAKER: I couldn't say whether the laboratories that do the tests are open 24 hours, I really don't know that.

DR. McCURDY: The idea was that it would be any hospital laboratory. In other words, a hospital laboratory, it was -- in a hospital it was doing transplants, it would have 24/7 coverage of the

laboratory. They have 24/7 coverage of the blood bank, the chemistry lab and others and this was a test that was meant to be designed or being done by the midnight tech the night shift, if necessary.

SPEAKER: I'd like to, if I can, move to the open public hearing section. We have statements by three presenters. The first is Ms. Ellen Heck from the Eye Bank Association of America, Ms. Heck is director of the University of Texas transplant services for the Lions eye bank.

MS. HECK: Thank you very much. As he said, I am a director of a transplant center in Texas, and it is a tissue and eye center, but I'm here today to represent the EBAA, and I appreciate this opportunity to talk to you. Last night I heard a talk on listening, and I think it's been very apropos to what I've been doing today, which is listening, and I find that there are a great deal of similarities between the things that I've listened to on blood and organs and certainly on eyes and tissues, but there are a great deal of differences as well.

I'd like to give you, before I get into those, a little bit of background though about the EBAA and its

member eye banks if I can. The EBAA -- let me see if I've got this figured out. Here we go, thank you. The EBAA was formed in 1961, and it represents 98 percent of all the eye banks in the United States with additional members worldwide. The EBAA published its first standards in 1981 based on scientific research and information specific to eye banking and to corneal and scleral transplantation.

These standards have been reviewed and administered and changed as progress has come along in our industry and as medical needs have changed over the years. The Board that meets twice a year on this is comprised of renowned corneal surgeons, experienced eye bank professionals and a number of advisors in various areas who contribute their expertise on the relevant issues that address the safety and effectiveness of ocular tissue for delivery for transplantation.

EBAA through its standards has been a leader in the field in testing for HIV, which was implemented in 1986, and I think was the first implementation in the tissue industry for that, followed closely by implementation of testing for hepatitis B and hepatitis C. We've really had very little infection since 1987, in fact

there've been no reported cases of transmission of systemic disease since the -- since that time, which we think coincides well with our medical standards. Now, there were some talk about rabies, and I'd like to spend a minute to talk about that, because, while you can take a Texan out of Texas, but you can't take the Texan out of a Texas person. So that was in Texas that the rabies occurred with the organs and later with the vessel.

And I think that standards and certainly FDA regulations should get some credit here, because those -- that donor was referred to us as the tissue and eye bank in that area and was declined based on the screening criteria that had been implemented by both the EBAA and the AATB and the FDA regulations. So there are safeguards that do appear to be working in some cases, and we were -- we could not accept that donor based on the history of presentation to the emergency room even though at that initial time, we did not know about the rabies, we did know about the mental disorientation, the possibility of encephalitis, the high temperature, things like that which obviously made it -- this would not be a donor acceptable to enter into our donor pool. So there are some safety

guidelines already in place that do seem to be working.

Also I think it's important, because Dr. Joyce referred to this earlier about how a donor is deferred and who makes that deferral or acceptance decision to think about eye banking a little bit differently than you think about tissue banking, because retrieval of a -- of corneas or whole eyes is much less invasive and therefore much less risky to the person doing it than spending five or six hours recovering extensive muscular skeletal tissue, which we want to concerned, I think in safety, not only about the recipient of the transplant, but also about the personnel who conducts the retrieval of the transplant.

So with an eye donor, you might go out and retrieve the cornea or retrieve the eye, and then do a more extensive investigation of the medical social history and get your testing results after you have completed this retrieval, because it takes only a matter of an hour or less to do this, and then you can -- and it certainly is not as expensive and time consuming as it is to go out and retrieve a muscular skeletal tissue if you retrieve an entire -- sites that are consented for, so this is -- some differences that we obviously find that are notable.

The other thing that I think is interesting is to note that in the 35,000 to 40,000 transplants per year, we have approximately two tenths percent primary graft failure. So not only is it an issue of infection, but it's also an issue of function and the corneas function very, very well. They function very, very well, I think in large part, because they are retrieved very soon after death and they are also implanted very soon after death, and this is another area where unlike muscular skeletal grafts or skin grafts, we don’t have the leisure time that they have with 14 -- waiting on 14-day microbiology or other testing results to get these corneas transplanted, because although the cornea procedures are scheduled surgeries, they’re usually done within four days of the time the tissue is actually retrieved, and I think this something to do with the very success rate we see in corneal transplants, which is virtually 90 percent of them are successful and restore functional vision to the individuals who receive the transplants.

And now I’ve gotten way off of what I was going to say, but I think those are the issues that in the listening to that I’ve heard today. EBAA would find it

unethical and irresponsible not to continually review and carefully consider all scientific and medical evidence and documentation in establishing future standards and regulations for ocular tissue. And we'd like to use the Chagas and West Nile virus examples here, because recently, we've looked at the literature, and the Chagas, except for the few examples that were noted here just a moment ago, a majority of that has been in south America, and so if we were practicing eye banking in south America, we might feel differently, but in the United States, we don't seem to see any -- we've -- even in south America where they have had Chagas organs transplanted, not even all of the heart and kidney recipients have received -- have converted and had Chagas disease, and there've been no reports of Chagas disease transmitted from those corneas.

So we think that there's some difference based on the systemic immunosuppression of organ recipients versus those of corneal patients, which as I said earlier are generally -- otherwise healthy individuals that undergo a scheduled procedure which doesn't require systemic immunosuppression, and therefore they're probably

much less likely to contract host-sequestered agent even if it were to be present in this relatively avascular4 tissue. And there again we have some differences between organs because this is such an avascular tissue.

Now we -- Scott talked about the processing and the radiation that things that you could do to sterilize tissues, and obviously that is not an option that we have with corneas. But the avascular nature of the cornea is somewhat protective and the actual procedures involved in the cornea retrieval are not nearly as invasive and do not lend themselves as easily to contamination or cross-contamination as you might see with a more extensive surgery of bone removal, which can be quite complicated at times.

Given the lack of evidence of a high-risk of disease transmission and the likelihood of false positive test results with adding new tests such as Chagas and West Nile virus, we think that a level -- a very screening strategy and testing evaluation would seem prudent. Premature implementation of testing regime to lead to significant discards of healthy tissue based on false positive testing even have some unknown risk factor.

West Nile virus offers a good model for this. For the FDA guidance document now requires screening, not testing, for a disease that would have a higher probability in the United States than Chagas disease. And here I have to deviate for just a moment because on our -- we've been getting a lot of rain down in Texas followed -- we had droughts for a couple of years; it was just terrible.

And I noticed the slide where only Mike Strong's State didn't have the West Nile virus and that has to have been from the rain because I just heard that mosquitoes from rain don't carry West Niles; it's mosquitoes who find stagnant water. So, they're saying to us in Texas that they're washing out all of our mosquitoes with West Nile with all this rain we've had, which is great. We'll take it.

So maybe we -- you know, maybe the FDA was even preemptive in their understanding of the West Nile by not -- requiring testing at this point. Potential donors who have Chagas disease may exhibit symptoms of fever, headaches, malaise, flu, rashes and lymphadenopathy. And this kind of a medical history would, just like the rabies

history that I previously alluded to, cause must more investigation and the individual would be highly unlikely to ever be eligible for donation for transplant purposes.

These screening criteria do work. They're not infallible just as testing is not infallible, but they are certainly leading us in a direction which gets us to what I think is the most important part, and that's that these are patients who we want to give back their sight. Certainly, we're not life saving as the organ people mentioned to us, but we are very definitely life restoring.

And so we think that if you recognize -- though we recognize and share your concerns about emerging infectious diseases, we would support recommendations that are based on risk and risk benefit of the individual tissue. The FDA model would seem to support this with their recent leukocyte-rich versus other types of tissue. Not all tissues have the same disease risk or associated infection potential. And we are pleased with the fact that FDA has recommended that.

We believe individual assessment would produce a safe system of regulation, which can be applied

epidemiologically in statistically analyzed problem, or the lack of a problem, and would provide us with a safety without inappropriately constraining transplantation medicine.

We urge the Committee to weight tissues on an individual disease basis and the known individual nature of risk as well as the individual potential of the tissue to carry this risk. Thank you all very much.

DR. BRACEY: Thank you. In the interest of time, I'd like to move on to the next speaker who we have listed as Dr. Barbie Whitaker. Dr. Whitaker is known to many in the room. She is very active in the AABB's program for biovigilance.

DR. WHITAKER: Good morning. My name is Barbie Whitaker. I'm the director of the Center for Data and Special Programs with AABB. Over the past 10 months AABB has participated in the inter-organizational task force for biovigilance, which includes both government and private representation.

We've agreed over this time that there are certain attributes for a national biovigilance system including that it should be a voluntary reporting system,

that it be non-punitive, confidential and web-based, and that there should be in the near future a pilot hemovigilance system developed to test the feasibility of collecting this type of data, much of which we discussed here today or yesterday.

The pilot system should be focused on five serious untoward consequences of transfusion and four significant events, but it should allow and encourage reporting of other types of reactions. The Committee has recommended that the ISBT working party's adverse event definitions be used provided that they create no major contradictions with definitions commonly used in the U.S. and that the MERS-TM system be used for definition and classification of events. And we heard the MERS-TM system described last August I believe at this meeting.

I'd like to make a few comments based on our experiences over the past 10 months. Without a doubt there are many things that we in the United States can learn from other country's hemovigilance, and as they develop biovigilance systems. However, the U.S. is unlike any other model. The U.S. does not have a unified national healthcare system. The government does not pay

for the delivery of blood or tissue or transplantation services.

We have a public/private healthcare delivery model, which is why a shared public/private model for biovigilance is a logical solution. There are two examples that come to mind. The TTSN, which is the joint effort between the CDC, and UNOS and it's resident outside the government, and the stem cell therapeutic outcomes database funded by the CW Bill Young Cell Transplant Program within HRSA and resident at the Center for International Blood and Marrow Transplant Research.

Secondly, the system must be flexible. It must be nimble enough to react to the changing clinical practice and epidemiological environment. If it becomes apparent that an emerging pathogen or a particular clinical problem warrants a special question or alert, the system must be facile enough to accommodate a software change.

We've talked about evidence-based medicine. This would be the opportunity to collect the evidence. For example, if we'd had a system that collected data on (inaudible) cases, we might've been able to insert a new

field on -- a new field to follow up on donor's sex imparity. Any government funded software system requiring approval by OMB for every software change or question change, which is often a five-month timeframe, might restrict this responsiveness.

Yesterday and today we've heard about the National Healthcare Safety Network from CDC touted as a likely comparison for a potential biovigilance system. We agree that the transactional basis for the system is comparable to what we'd like to see developed and that there are many positive features to the system; however, there are some things to keep in mind when making good -- the comparison.

The NHSN tracks nosocomial infections. These are directly related to the length of patient-hospital stays and therefore a significant financial concern for hospitals, insurers and CMS. Because of the financial component of nosocomial infections, infection safety officer exists in many hospitals nationwide and their presence supports data entry into NHSN.

While we support the similar concept of a transfusion safety officer like in Canada, unfortunately

we don’t perceive that a comparable model would work for biovigilance. For what we proposed to monitor via hemo or biovigilance system, we are unlikely to show with the numbers and types of reactions that any of this will save a hospital enough money to justify the time and effort.

Lastly, we should not collect data for data sake. One of the problems with some hemovigilance systems is that they function to collect nice, but historical, data that doesn’t make a difference. We don’t have the time or the funding or, to put it bluntly, the lives for that. The data now comes from a biovigilance system must be accessible to hospitals and to clinicians, the people who can make the difference in the lives of the patients.

We have to support the analytical tools to change clinical practice, to improve transfusion and transplantation services quality in real time, not after the fact. We would like to see a biovigilance system that reflects the public/private commitment to quality transfusion and transplantation medicine that we see in this room that can react nimbly to a changing environment and that can get the data, outcomes and analysis to the responsible parties within the government and especially

to the clinicians who affects the lives of patients everyday. Thank you.

DR. BRACEY: Thank you, Dr. Whitaker. We'll move ahead then to our last presenter who is Mr. Corey Dubin of the Committee of Ten Thousand.

MR. DUBIN: Thank you, Mr. Chairman. I won't waste anybody's time with introducing myself. We recently became aware of an instance where a hemophilia client who had a hip replacement and cadaver bone was kneaded, two months later was informed that that cadaver bone was HIV infected. As far as our internal looking into the matter goes, not only was he not informed for two months, but there was -- as far as we know to this point there was no reporting under the adverse events reporting system.

We're deeply troubled by this. And some of you know, due to the joint damage associated with hemophilia, we require quite a bit of joint surgery, and cadaver bone in some instances becomes a part of that. We're also seeing more liver transplantation due to the Hepatitis-C associated problems in hemophilia. And now that we're up to three institutions in the United States that will transplant HIV infected persons with hemophilia liver

transplants.

So, we're greatly concerned by this. And we got to say we do not understand the use of the words bio and hemovigilance in a system that is not mandatory. How do we know what's going on out there? We talked with doctors who don't even understand what AERS is, more or less that they should report an adverse event. So if we're really talking about hemo and biovigilance, why do we keep falling back on non-mandatory reporting?

It boggles our mind, and we've seen even outside of hemophilia, but this is a very tangible instance in hemophilia that's got our attentions, and we're asking more and more questions. So we come back to the issue of voluntary reporting, given our history and all that we've seen doesn't seem to be the way. And we would really urge secretary, the ASH, the Committee to really ask the question, is voluntary reporting to the adverse event system really going to get the job done when we have so many parameters to cover.

And we'd like to come down very strongly for mandatory reporting. Earlier somebody had **Huxley** up there learning from history. What the heck are we doing not

requiring reporting. We're not learning from history in that way. We're ignoring history, and we're going to get hurt again. It may not be us, but that doesn't matter. For us the importance is to really understand history and design programs that are going to guarantee that the FDA knows what's going on out there, and that the government and private structure for blood and transplantation medicine know what's going on.

And in tissue, it occurs to us, something we don't deal with a lot, that it's been a bit of a "cowboy" private enterprise. And that these new companies have gotten out ahead of the government, and the government scrambling to get caught up, which makes us think even more that mandatory reporting is the way to go.

Thank you, Mr. Chairman.

DR. BRACEY: Thank you, Mr. Dubin. We will take a break for lunch in the interest of allowing us to complete the task that we have. I ask that we reconvene at 1:00, so if you can compress your lunch by 10 minutes or so. Thank you.

(Recess)

SPEAKER: We'd like to reconvene. It turns out

that there is a question from Dr. Kuehnert to Ms. Heck regarding her presentation. Dr. Kuehnert, he's running away.

DR. Kuehnert: Heading for the hills?

SPEAKER: Heading for the doors. So Dr. Kuehnert, your question?

DR. Kuehnert: I -- well, I just wanted to commend EBAA for having adverse event reporting system in place already. And I think you said that, but I just wanted to emphasize that. But that there are some real challenges, and, you know, I'll just use this as an opportunity to just comment that from all the other speakers, I mean, I think we've seen where disasters happen. But we're -- what we're not appreciating is where we probably dodge some bullets too.

You know, there happened to be donor screened out because of various social issues, and therefore didn't donate tissues. But there have been some that like for instance, with LCMV, I believe, where it was just the family's preference not to donate tissues. Otherwise, we had -- would have had a far more complicated situation. In fact, in that particular situation, corneas were

procured and implanted.

And it was very, very difficult to -- which probably isn't reflected in (italics) The New England Journal paper, to follow those patients because they were implanted in Algeria. And so I just wondered if you could comment on some of the challenges of adverse event reporting, particularly when corneas are exported, how often that happens, and what challenges that presents.

DR. HECK: I thank you, Dr. Kuehnert. Well, with corneas, of course, we have an advantage because we're not tracking thousands of products like you might be from one tissue donor. However, with corneas we generally know to whom they're -- if they're going to be transplanted in the United States, we generally know to whom they are going to be transplanted before they ever leave the eye bank, which is a very different scenario from a lot of transplantation.

So that allows us to initially begin our tracking process a little bit more preemptively than it does with tissue. The only thing that's put on the shelves, so to speak, is the sclera. And basically from one donor you should only have a maximum of eight pieces

of sclera. So again, we have a smaller tracking problem than with most of the tissue. We have had very good compliance. And I, as a tissue banker, I can speak to this from two different aspects.

The corneal adverse reaction in implantation records, and utilization outcome follow-up from our cornea physicians is very, very high. We get 90 plus percent of that back on a routine basis. It has been more difficult to get that kind of compliance right from our orthopedic surgeons, and our burn surgeons, and our plastic surgeons, and so forth for the other tissues that we provide because there are so many of them.

And they don't get them specifically, except for the larger musculoskeletal grafts. They don't get them specifically for one patient necessarily. They have them available, they go in, they take a box off the shelf, and that makes a big difference. But with corneas, the tracking has been very good. Now, out of the country, that becomes a much more difficult issue. And we have had some problems tracking those that have gone to other countries. We are trying to do that, our program accounts for that. But again, once they leave the United States,

we have very little control over that.

And unless there are some sort of WHO or other intervention to get a more standardized reporting form, we're going to have that. Physicians also, in other countries, have a reluctance to report a problem because they're going to be afraid that then we won't send them anything the next time they ask for it. And that's an issue that I think we have throughout transplant.

SPEAKER: About what percentage are exported, of corneas?

DR. HECK: Well, that percentage dropped a little bit this year, and so I'm kind of reluctant to quote a figure. But we do export what -- at about 10,000 corneas. Not that many this year, previously about 10,000 corneas had been going outside the country, I'd say probably now maybe seven to eight thousand. And that number may be dropping again as we're having more needs in the United States for corneas, and less cornea donation.

SPEAKER: That's about 15 or 20 percent?

DR. HECK: Yes.

SPEAKER: Yeah, thanks. Thank you very much.

SPEAKER: Yes, Dr. Solomon.

DR. SOLOMON: Ellen, could you comment on the fact that eye banks are really a one-stop shop in terms of you send out -- do you send out the recovery person from the eye bank, and it's all contained, there aren't various agencies involved?

DR. HECK: Basically, that's true. Most eye banks prefer to retrieve their own corneal tissue, there are few where a tissue bank or an organ bank may recover tissue for the eye bank. One of the things that you have to remember, and I may have mentioned this earlier, is that it's simple to retrieve, and then we can take a closer look at it. So even though we retrieve it, particularly if they have signed a consent that says it can be used for research as well as transplant, we may retrieve it and then do more in-depth evaluation.

And because of the nature of the retrieval we're able to do it at more sites with less restrictions. For instance, you could actually recover or retrieve a whole eye or a cornea donation in a patient's room if you could constrain traffic flow in that environment for the amount of time that you were doing it. You could do it in a funeral home as well, you could do it in an operating

room. So there's a variety of different flexibilities there that you have because of the nature of the recovery that don't apply to tissues.

SPEAKER: I believe Dr. Holmberg also had a question. Well, Dr. BlOCHE has a question.

DR. BLOCHE: Go ahead first, and then I'll follow you.

DR. HOLMBERG: Well, I'm glad that we have this opportunity to ask you questions, Ms. Heck. You made mention in your presentation about the situation where the body of the individual, that was then later to have transmitted the rabies, was refused by your facility. And it appears to me that the OPOs and the tissue banks can pick and choose. And so it can -- it sounds to me like there's different criteria for acceptance. Is that the case?

DR. HECK: Well, there's very different criteria for acceptance between organs and tissues. And I think that was alluded to by the, you know, speaker earlier. It's a very different situation. We actually have less ability to pick and choose, if you will, because we are regulated, as you know, by the Food and Drug

Administration who has a guidance, who has a regulation and a guidance document for us on donor eligibility.

So we are going to be screening out those cases which come under, as I mentioned before, people who have high unexplained temperatures, who have various signs of disorientation and things like that that can't be accounted for. So those are going to fall outside our criteria. Whereas, if you think it's gone, in encephalitis case, for instance in an organ transplant, they may be willing to take that risk and feel that they'll treat the patient to overcome it, and it's a reasonable risk given the situation. But it's not a reasonable risk for us.

SPEAKER: Then, Dr. Bloche.

DR. BLoche: I'd be interested in what other countries besides, I think you said Algeria, the corneas are exported to? And what are the allocation principles? Is it a matter of bidding and -- where the pricing is most advantageous or are there other allocation principles?

DR. HECK: Well, that's an interesting question. Actually the pricing isn't advantageous for exportation of corneas. And I could start trying to name the countries

to which they go, but it would go all over the map, from Europe to Asia to South America, you pick it, it practically goes everywhere. It's how that allocation process works.

I mentioned earlier that corneal surgery was a scheduled surgery. Unfortunately, donor death is not. So we get corneas for surgeries on Monday, Tuesday, and Wednesday, and some doctors will operate on Thursday. But Monday, Tuesday, and Wednesday are the high days for corneal transplantation.

So if the death and the screening criteria and the testing criteria that we go through doesn't allow for the donor to fall into those three or four days within about four days after death. We have a more difficult time utilizing those corneas in the United States sometimes, and those then are made available outside the States.

DR. BLOCHE: And how are those, how does that allocation occur?

MS. HECK: Well, it really occurs by contact from a bank or a physician in the country that to one of the banks here in the United States, and the allocation is

made strictly on availability. If it's there, it goes; if it's not, it doesn't.

DR. BLOCHE: But when an informer who knows somebody and who gives a call, kinds of fashion, or are there formula or protocols for this allocation?

MS. HECK: Well, most of it is related to established networks. They know people who have export tissue available. Export tissue is coordinated through three or four major outlets here in the United States. We might send a cornea from Dallas for instance to Seattle to one of the -- to the eye bank up there, who has a distribution network with Japan.

DR. BLOCHE: Are there protocols posted on the web or in any other public setting that layout how this occurs?

MS. HECK: Not that I am aware of. But if in the eye bank accreditation process, they examine our allocation of tissue as part of our accreditation, it must be on a first come first serve basis. And so that that's the only way that I know of that you could actually document the allocation.

And that's first come first serve in the United

States and then it goes outside. It's part of our mission driven statement that we are a 501 (c)(3) and it's really not a for-profit entity, so it is not like we hold an auction for these.

DR. BLOCHE: But is it -- when a cornea is shipped abroad, is there -- I assume there is some sort of transfer of money meant to cover costs, right?

MS. HECK: Yes, there is, and sometimes it does cover cost and sometimes it doesn't. The majority -- I think, the majority of us feel that our mission is to restore sight, and so if we have a cornea that that we can place in some country that can't pay for it, if they are going to pay the shipping, and they are not going to cover the rest of the charges, we're still going to ship it to them, because that's what our mission is.

DR. BRACEY: Okay, if we could move on then to the next speaker. The next speaker is Dr. Ted Eastlund. He has been the Medical Director of Transfusion Services, Therapeutic Apheresis, and Stem Cell Collection at the University of Minnesota Medical Center. He has been very active in tissue banking, serving as the past president of the ATB. He will speak to us on managing tissues in

hospitals. Dr. Eastlund.

DR. EASTLUND: Good afternoon. I've been a blood transfusion service medical director for about 11 years, and prior to that for about 16 years, a regional blood center medical director, and also for about 11 years a regional tissue services' medical director.

So I have been involved with a lot of things that we have been talking about. And as a hospital blood bank medical director, I am well versed with all the elements of a blood transfusion service. And it seems to me that I am here to talk to you about the elements of a blood bank in a hospital, and how it relates to the hospital's handling of tissues.

Because more and more we are realizing that all the elements of how blood is handled in a hospital is how it should be handled for tissues also. And I'll spend a lot of time on that.

So I plan to start because if some of your questions are written questions about the similarities between tissues and blood, I'll talk very briefly about clinical use and risks, that's been covered a lot the last two days.

And then we will go into hospital handling of tissues and how we are currently, actively, working on getting hospitals to handle tissues more safely in a more reliable way. And it seems that it is a lot more than just problems with traceability in hospitals.

And I'll emphasize that the problem is that hospitals handling tissues aren't incorporating all the elements of a blood transfusion service, particularly, regarding evaluating adverse reactions about overall medical overview of the service. Things like abilities to do look back investigations and things like that.

This is a 1989 slide that I had comparing organ tissue and blood transplantation. The basic similarities as you can see as far as -- what's missing from here is things like public support is necessary for all, donor recruitment, donor screening, exam, and testing, hospital blood bank is not involved or hospital blood bank model isn't included in all this.

Including the investigation, adverse outcomes, all these things that we'll talk about soon. This is the basic steps from donor on the way to the recipient not in the hospital, but in the Regional Blood Center and in the

Regional Blood Bank -- I'm sorry, tissue bank that these are suppliers of tissue on the right and supplier of blood on the left.

So in both, if you look to the left the blood center requires and needs volunteer donation. The risk of disease transmission is 5 to 25 times higher if it is a paid donor. Medical history, social history, risk factor, exclusionary factors to make sure that you reduce that risk in the public from 10 to 50 times before you do blood testing and further eligibility.

There are differences, permanent exclusions if you are a man who had sex with a man is permanent in blood, whereas in tissue banking, it is a 5-year deferral or I should say exclusion.

Physical exam is much different. There is some checking for tracks, for blood donors, but there is a more full examination of the body in a diseased donor tissue situation. Confidential exclusion option for a blood donor does not exist, of course, for the diseased donor, that's aseptic collection.

And the cadaver tissue collection that includes bacterial testing of all the tissues that is removed at

the time prior to processing. Infectious disease test is very similar, and as you heard, we're doing HCV RNA and HIV RNA.

And about 50 percent approximately of cadaver tissue donors, have autopsies are reviewed before any tissue is distributed. Now, the manufacturing side of it is much different.

There is component production, of course, and processing, (inaudible) reduction for blood, even bacterial testing for platelets, and it is very different for cadaver tissue making the precise type of tissue product the component of the bones that are divided into small pieces, cleaned all the blood, and fat is taken out, often times they are treated with things like peroxide, antibiotics, alcohols, and as you may have heard already, solvent detergents and gamma radiation, a number of things that's in manufacturing. Now there are some other similarities, the blood banks, regional blood centers and the regional tissue banks also do adverse reaction evaluation and initiate recalls and look backs, and they do quite a good job.

Now blood transfusion services on the left here

in hospitals is listed, the very basic elements, vendor qualification that is to make sure that the supplier of blood is supplying blood from an FDA approved bank in high-quality, incoming inspections, storage, record keeping, matching and selection, releasing from storage, and at that time for instance if you have platelet concentrates, you do a test for bacteria, the preparation, filling, pooling, investigating adverse outcomes, conducting recalls and look back investigations. Now, all those steps are basic elements.

On the right is -- is what we have in hospital tissue services now, mainly a rudimentary beginning of vendor tissue supplier qualification, incoming inspections and logging in, storage record-keeping, matching and selection, releasing from the storage, preparation in the OR and the implant of the actual tissue. What's largely missing is experience or well-designed plans and procedures for investigating adverse outcome, conducting recalls and look back investigation.

In addition, the hospital tissue services, as we've already discussed don't have recognized medical directors or the cognitive transfusion committees for

overview of the whole service. There is also similarities in the tissues and the organs, and the blood regarding disease transmission.

You see on the top here a bunch of diseases that are similar in all three groups. Certain viruses, bacteria, CMV, and next is a group that is common for blood transfusion on the left, West Nile, Toxo, Parvo, Chagas, malaria, GVHD and on the right same diseases in organs. Below that you see the diseases, rabbis, malignancy, TB, Herpes simplex virus, from tissues and also form organs and then underneath that is other -- it includes other diseases that have been transmitted. Not a complete list but at least that shows in groupings what -- what diseases are transmitted in comparison with each other.

Now in general, the prevalence of disease transmitted through tissues is really unknown, but we all feel fairly confident that it’s quite low, particularly in a majority of the tissues transplanted today. The biggest concern is tissues that have not been well treated with disinfectants or sterilants, tissues that must be transplanted when they are in the fresh state, and

therefore can be basically be temporarily treated with antibiotics only.

More studies are needed prospectively, and even retrospectively about what the prevalence and incidence of these diseases -- that these diseases are in the United States and also studies of how some of these diseases arrive. For instance we'll talk about the bacterial diseases that have occurred in some patients. Largely these have been in the tissues before processing. The donor was healthy and well prior to death, he was not infected, but -- or somewhere is around twenty -- 10-20 percent of the tissues recovered end up with bacteria on it.

The translocation of bacteria from the intestine through the body occurs after death, and we have requirements about recovering tissues within certain number of hours, but this translocation does occur and yet there is not enough scientific data really to -- too much or know much about this. In the living human there is much more information, but in the -- the dead person there isn't.

Now the common clinical uses we talked about

some already, and I'll just list these with the diseases that have been transmitted. The corneas, the bacteria, fungus - hepatitis B, rabies - CJD malignancy, the bone - HIV HCV HTLV tuberculosis and bacteria. The relatively lightly processed tendons, HIV, HCV and bacteria; the heart valves that are viable cryo-preserved in DMSO, bacteria and yeast for sure, and it seems like some old cases of tuberculosis.

The other tissues that are transplanted and the diseases are listed here. You'll see cartilage with bacteria, skin with bacteria and HIV, pericardium with bacteria, dura mater with CJD and blood vessels with HCV and rabies. There is a difference as far as ability for these tissues to transmit, and you can see how I have listed on the left the non-viable tissues, the most common tissues transplanted including bone, do not need living cells, and as a result they can be sterilized and a large portion of the bone transplants are sterilized where as some are not. Some are heavily or lightly disinfected and that's about all. Whereas the viable tissues cannot be as heavily disinfected or sterilized and that includes heart valves, corneas, articular cartilage and skin.

I want to go now with -- where some of the origins of the microbe came from according to the types of infections that have occurred from tissues. First of all, newly infected donors in the seronegative window phase have transmitted disease. We've probably heard about some of these in the last two days or so. There has been cases of hepatitis C both from frozen tendons and saphenous veins.

As far as HIV has occurred, also especially with the famous case in 1985 we'll briefly mention. There has also been donors that were newly infected that were not adequately diagnosed at the time of death. And one of them was a patient who died of a -- what was thought to be a toxic drug overdose, when it was actually a toxic shock syndrome from group A streptococcus. Event that fresh artery we were taking about was wrongly diagnosed at the time of the death. It was thought to be a cocaine overdose when it was actually rabies because of similarities in hypertension, MI status, epilepticus, things like that that can occur and it was hard to tell the difference between cocaine overdose and rabies.

And of course with brain death you can have a

104 fever, so it all kind of fits in those kind of -- that one patient. Now the demonstrations of seronegative patients who transmitted the disease are amongst cases of HIV and (inaudible) HIV. I think for time we better not go too much into this. But just briefly, in 1985 when the HIV test was came about, the seronegative window then was about 45 days or so. And this shows you -- the dotted line, the IGM level of the antibody, and then the IGG, and the newer tests now can pick it up since 1992 around 20 or 21 days or so.

So this patient who was shot in the head and became a organ and tissue donor in 1985 was in that seronegative window and he donated, and as a result, transmitted HIV through organs, tendons, and femoral heads. Not through freeze-dried tendons that -- or not through freeze-dried bone or irradiated dura. Six recipients of -- I think about 50 or so recipients were not able to be located because of again, poor records in hospitals, and the same thing occurred only with very much smaller numbers of unfound recipients was the case we talked about in the year 2000, organ and tissue donor where lung and kidneys recipients were infected. The

corneas did not infect patients, but a year later or a half year later, HCV infection developed in saphenous veins and tibialis tendon and that was reported to a tissue bank, but the tissue bank said the donor was negative therefore it must not have been the tissue.

Then as you can see here on the time lines after the right, in 2002, the tissue bank who had most of the bones from the body of the donor processed then in March of 2002 and in April or so gave tendons to patient and within a short time the patients developed hepatitis C.

This tissue bank though looked carefully and decided we better look and see if this could have been the donor and ended up evaluating with help from CDC and showing that the donor actually was seronegative but had HCV RNA in the blood. And so as a result there was a large look back investigation and two recipients or one -- I'm not sure, were not found. 32 recipients were tested, five of 27 were HCV RNA positive, including 303 bone tendon bone recipients for a knee surgery. So it's another example of seronegative donor that was infected and the look back show that the traceability in hospitals was not a 100 percent.

Now different type and source of infection is when the endogenous contamination of tissues occurs after the donor has died, coming out of the intestines or who knows where, and infects the tissues. It doesn't infect the tissues, it colonies the tissues, and that's what all the process is done to eliminate those -- those bacteria. But sometimes it has still been there, it's failed in lightly processed tissues, failed to be eradicated and has been shown with fresh cartilage with a 21-year-old man who died from clostridium infection in November of 2001 from fresh cartilage that was only exposed to antibiotics.

It's also been shown in the frozen tendon recipients and in cornea recipients, and example for instance cornea is one of the fresh tissues that is basically stored in antibiotic solutions. So any of the bacteria that was there or is might not always be eliminated. And every year including this past year they have reports of unusually named yeast that infect patients from the corneas, because antibiotics are not perfect. So the normal bacteria and yeast that are in humans can persist at times and infect patients through tissues when the tissues are not heavily treated, disinfected strongly

or sterilized.

The other type of sources of infections is unusual bacteria acquired from the tissue bank environment during processing. There is a recent example that has been -- I think Scott mentioned. And also contaminated Hanks' balanced salt solution was used as a washing reagent for pericardium. There was an unusual bacteria in all those bottles when they washed the pericardium. The Pericardium is used as a dura replacement and several kids got osumalytis (phonetic) and meningitis. So there is plenty of examples of lack of traceability in these different kinds of cases and I would like to -- try to move on to the traceability issues.

The lack of traceability in hospitals was first really noticed in 1990 or so when the first HIV case occurred. After that the profession decided to try to implement standards in hospitals. The American Red Cross did it in '92, 1993 or 1994, AABB and AATB did, and developed hospital standards, but they don't necessarily always affect the hospitals when the standards are by blood banks. So the American Association of Tissue Banks then went to JCAHO, then the Joint Commission to ask them

to look at the way hospital blood banks handle blood. All those elements, and see if they couldn't be -- that we can put those into JCAHO standards and have some teeth, especially if they are handled by labs or by blood banks, and they did that.

It wasn't recognized though or realized that the standards didn't apply to ORs for a long time. In the fall of '04 one of the technical committees of the joint commission recognized because of recent infections that -- they needed some standards that improved. And as a result in the year 2005 they applied new standards that included operating rooms and hospitals and surgical centers.

That really made a big change that we're feeling right now. Since then there has been so much improvement and so much recognition that the hospital tissue services need to establish themselves as a thorough service and more and more people are realizing it should include the elements of blood banks.

Problems that were seen in about 1994 and 1995 are listed here. Tissues were then, and are now mostly handled in operating rooms, occasionally in blood banks; problems where -- when you looked at blood banks you saw

hardly any problems but when it was in the operating rooms serious problems in the over half. No tracking mechanisms at all in some ORs and this is 10 years ago, partial tracking in others, no temperature monitoring on weekends lack of alarms on freezers, no temperatures monitored at all, alarms not checked for response and for the freeze-dried tissues, no knowledge about what the limit should be about temperatures, acceptability, or monitoring or them either. So there wasn't much improvement since, even the late 80s when I did some surveys then. And some of the problems are illustrated just recently when I visited the hospital. To trace and track, you need record-keeping, and they don't always have them. And so several hospitals told me we can do it though if we go to billing, billing will allow that.

Hospitals do billing directly, that is they generate the billing, the ORs do I mean, for tissues and so they can track and trace but it's not within their control of doing that. But billing doesn't seem like a good way to do it. Now hospital tissue services -- this is the way I define it, it's the hospital entity that acquires storage and -- stores and provides an adequate,

safe and effective supply of tissue autografts and allografts and it ensures cost-effective and clinically appropriate use. If it sounds familiar that's basically what hospital blood transfusion services does. The main components of a transfusion system and a tissue system are really alike. We have tissues and blood suppliers. Again, the tissue system we also have tissue distributors that have an impact with storing temporarily between the tissue bank and the hospital, and we have end users mainly hospitals. We've gone through already with the tissue and blood suppliers the different functions they have, tissue distributors, obtained from a tissue bank store and then sell it to the hospitals. Now, the end users or hospitals, I won't take the time to go through those elements right now, but I've separated these elements with a dotted line here to show you which ones are routinely done, not necessarily correctly done on the top, that is qualifying tissue suppliers, inspections, record-keeping storage, selection of the tissue end preparation on the OR. But if you ask, well it's hard to know what you would find if you ask about what is your basic responsibility? Is it to provide a safe effective tissue in the OR or not?

Certainly, it’s an unnecessary thought that broadly they are very, very, worried about patients and want to do the best job at all times. But I think more of -- in the blood transfusion service with transfusion committees working with the physicians using blood we’re more willing and able to say that we are here to assure a safe and effective blood supply and some one should -- for tissues also. And the biggest deficiency I see is the investigation of the worst outcomes, the response to look back investigations, peer approval and review -- I should say peer review of tissues and how they are used and appropriateness of use, medical staff overview of appropriateness, and medical director function.

Excuse me, wrong slide. I think I’ll pass up on telling you the expertise of hospital blood banks, because I am repeating myself. But I’ve listed them here and these are the things that I say needed to be applied to the tissue services within hospitals. So currently, I'll repeat one more time that there has been a fairly good performance in operating rooms and in hospitals where storage and improved traceability since JCAHO put it -- gave us part of -- then Trent Commission (phonetic) gave

its new standards and 2005, currently the tissue services meets requirements of surgeons well. It has quality programs within hospitals and it's starting to meet the JCAHO requirements much better. But there are -- there are deficiencies in the other areas that we've mentioned.

Next is the investigation of adverse outcomes. The adverse outcome investigation that is infections, is basically first of all is to evaluate whether the infection arose from the patient and that's where the orthopedic surgeon comes in or other physicians involved. Second, is to decide whether the infection could have arise -- arose in the hospital. There is no need to just give this report to the supplier without going through that filter.

Similar things occur in blood banks. When a report of an infection such as hepatitis B or HIV would occur and be reported to the blood bank medical director, the medical director doesn't just pass it on to the supplier, of the regional blood bank. There is an investigation to decide did that recipient have hemophilia, were the injecting blood users. Was there a reason for it other than the source from the blood itself?

And when there has been some evaluation then you are -- at that time ready tell the blood bank who supplied the blood, that it could have been from the blood that was transfused. Likewise, there needs to be an initial filter to jointly decide is that possible that the tissues could have caused this infection and then report it to the tissue supplier.

In blood transfusion, its simple, the physician and patient are involved with the initial infection as reported to the blood bank and then reported to the blood supplier. For tissues, it’s a little bit more obscure as far as who and when and where the reporting goes. The surgeon and patient are involved of course, the surgeon needs to decide, could this bacteria have been from a tissue or was it an ordinary infection?

Generally though, the surgeon doesn’t think of an entity in the blood bank -- in the hospital to report it to. You know, he got the tissues in, or someone did in the operating room freezer and use it, does he tell the nurse in the operating room, does he tell hospital infection control, and in general, I think most surgeons would take the enderon, as you can see on the right there

in the light black lines, going directly to the supplier or to the tissue bank, at least that happens, in my experience.

But I say the surgeons should be reporting this to the hospital tissue services that should be operated like a blood transfusion service. There should be a full investigation. The tissue distributor may and may not be involved or may and may not be told, I'm not sure what's the right thing to do, but certainly early on the tissue bank supplier should be told and involved with this.

Tissue distributors sometimes store tissues for months and months and months, and it could have an impact on the quality of the tissue if the storage is not right or the package integrity is missing and could even have some impact potentially of infectivity of the tissue. The transplant surgeons has responsibilities, Mike Joyce spoke a lot of this, but I think the hospitals, just like they do for blood, have a responsibility to make sure that hospital physicians are educated about the risks of the blood transfusions and tissue grafts.

They should be told, as we do tell our physicians about blood transfusion risks every other year

formally in materials -- what should -- they should do if they have a recently diagnosed patient with an infection? For instance, if you have HIV or hepatitis you should make sure you report that if that's within six months of the tissue graft. If you have a West Nile virus infection within four weeks of a fresh viable graft you should report it. If you develop CJD, within say three decades, who has a memory though that lasts that long, of these tissue grafts, you should report it.

If you have a fungal infection, using a heart valve for instance, that's multifocal disseminated of embolic origin within three years of the graft you should report that, because they sit without symptoms for a year or two, these fungal infections, without showing up. If you have a deep bacterial graft site with a certain characteristic, of course you should report that right away, and you should report if there is unusual graft failures, noninfectious complications. And user physicians need to be reminded of these things, and in writing on a regular basis.

Now, to work on these tissue issues in hospitals the Americans -- the AABB has developed a Tissue Committee

with representatives from the Joint Commission FDA, EBA, AATB, the Armed Forces, Blood Group, AAOS with Dr. Joyce on it, and CDC, it has done a number of things on helping in the area of hospital tissue services. It conducted a survey where the tissues are handled in hospitals. It's developed some guidelines, it’s in the process of a handbook development. It has had, and is performing audio conferences and updating standards of the AABB and a number of educational programs.

The survey was conducted in, I think, 2005 and showed that of 402 hospitals, 76 percent of them stored tissues entirely in the operating rooms but -- in about 50 percent the blood banks had some role, varying from just storage or total full control of tissues. The guideline book was designed to give guidance temporarily until more publications were available in educational programs on how to comply with the JCAHO, the joint commission, new standards and it dealt with these issues that we’ve talked about. Oversight responsibility must be there, obtaining tissue grafts, supplier qualification, inspection and documentation on receipt, these are the chapters that are in this booklet.

Now, traceability and record-keeping, storage of tissues, investigating adverse outcomes and handling tissue recalls and withdrawals. In addition, this and our other published materials will discuss these other areas about medical review, medical involvement, tissue committee involvement, our transfusion committee equivalents. For instance, AABB has standards about roles of blood bank physician overview, approval of procedures, approval of deviations from procedures, being involved with the actual use of the blood, developing this consent procedures, determining indications and evaluating adverse outcomes.

So we have some proposed roles of a medical director of a tissue service which are not well published and are certainly not in operation at this time, that are very similar and given those in your handout, very similar to that based on a hospital blood bank medical director responsibility. In addition, we are proposing guidelines for hospitals to develop tissue transplantation overview committees that are based on the required AABB requirements for an overview blood transfusion utilization committee.

So reviewing practices, to review adverse outcomes, to develop and maintain appropriateness guidelines and do peer review of appropriateness, review regulatory and accreditation reports, and reports of the quality assurance and activities of the tissue service.

On summary, the risk of disease transmission from tissues is really low and it’s mainly in the fresh less processed tissues. There are many areas of improvement that are needed inside the hospital regarding handling of tissues. The elements of a blood transfusion service in hospitals should be mimicked for tissue service, and implementing the existing AATB, AABB, and the Joint Commission requirements will make transplants much safer in the future. And I see that happening right now, thanks to the Joint Commission’s standards that they made broader in 2005.

Now regarding the state of safety of tissues, the risk is very low, these are my answers to your questions that were in writing, and it’s mainly associated with the lesser process graft, there's commonalities. We mentioned about diseases that are of human origin. My own suggestions to improve safety, one of them is to require

all the elements of a transfusion service in the hospital for tissues, they must be present whether they are in the OR or the blood bank, they don't have to be in the blood bank.

But all of these elements must be present in order for the system to work appropriately. That does include medical director involvement and also to develop a system that's dealing with, I think, some of your topics that you had these last -- few meetings of yours. A system of recognizing and managing tissue related infections. Most important resources that I see are needed at this time, are again, identification of infections by surgeons and by hospitals, and improving the investigations at the hospitals of the reported infections excluding hospital acquisition and then reporting it to the tissue banks.

And reporting, and trending, and tracking at a national level if there was a system of -- of having the system starting at the beginning with the doctor, the surgeons and investigation in the hospital, then report it to the tissue banks in a very ethereal (phonetic), manner and then tracking it throughout the system.

Then you'd have data to be able to improve the problem of disease transmission and tissues, thank you very much.

DR. BRACEY: Thank you Dr. Eastlund, that's a wonderful review. Questions from the committee? Dr. Roseff?

DR. ROSEFF: I have two questions. First, how many people do you think it takes in your blood bank to be assigned to doing tissue management?

DR. EASTLUND: At the Beaumont Hospital in Michigan we have one full-time person, and they've been doing that for 11 years, and a part -- the medical directors service both blood and tissues.

DR. ROSEFF: And the other question is, you've implemented this a long time ago, but what kinds of cultural, and I guess, historical issues arose at the blood bank start taking control of tissue out of the OR at the surgeons purview?

DR. EASTLUND: The social and cultural issues are being shown this year and last year more than ever before, because it is now the disease is really occurring where hospital staff in the operating room are realizing

this is too much for them. That's probably the most common thing. The second most common is these are good things to do and we are going to do them. And they are trying hard but they feel a bit incompetent about it. And they are frequently asking, how can I do this, am I doing it right?

And that's the status right now, regional meeting that we are having in the Twin Cities, that's the common thing is, I want to know, is this the way, am I doing it right? They don't have a leadership that's helping them. And I think the most important social issue is the issue of taking away a service that they have liked doing, some haven't liked it, but they feel and dedication to make sure that the tissue is there and it's right and I've worked with the doctors directly, and they don't see it, real easy how they can give that up.

It's not a 100 percent, large number of them are saying we want to get rid of this, period. And we see even the blood bank as once we know how to do it. So there is a mixed response there. But there is a strong degree of professionalism that in the operating rooms that it's not easy to overcome and it's not necessary to

overcome it. It's just that they need to do things a lot more in detail and many of them are just realizing that.

DR. BRACEY: Thank you. There are no more -- we do have a question. Yes, Ms. Benzinger?

MS. BENZINGER: Yes, I have a question/comment. I like to make a statement about the transplanting surgeon’s responsibilities, and how they need to be diligent in recognizing after four weeks, six months and decades. I would like anecdotally to say surgeon basically doesn’t see that patient after a successful surgery. Then I think that you’re -- part of this is leaving out the patient responsibility and the education of the patient going in, that they carry a responsibility of notifying the physician in charge of their care of the fact that they've had this type of a surgery requiring the grafts and things.

So I feel like the patient is being left out of here in bearing some of the responsibility of notification. Because again, that surgeon is not going to be there, probably in three years, or ten years, or you know, how many decades ago when it comes to having an illness show.

DR. BRACEY: That's a good point in a system with multiple caretakers. In the interest of time, we would like to move onto our next speaker, if you don't mind, and that is Dr. Germain. Dr. Germain comes to us from Canada, where he is trained as a medical microbiologist and he will share with us the Canadian Experience in transfusion and transplantation safety. And Dr. Germain is the vice-president of Human Tissues of Hema-Quebec.

DR. GERMAIN: Good afternoon, and thank you. I would like to thank the committee for giving me the opportunity to share with you the Canadian Experience, and those are very important issues. I have to warn you, however, that my talk is going to be tainted by much more so by the Quebec Experience, because that's where I come from and I have a little bit more details to tell you about in that regard. But I tried as much as I can to cover the whole country of Canada.

So the first question that was put to us, Speaker, was to discuss the current state of safety both in transfusion and transplantation of cells, tissues, and organs. Regarding transfusion, I am not going to spend

too much time here because I am assuming that at least for some of you, you have some knowledge of the blood system in Canada, so I will be brief.

Basically, in Canada, there are two transfusion agency providing blood and blood products to the population; one is Hema-Quebec, and that's my organization. We are serving the population of Quebec, about 25 percent of the total population of Canada, and the other organization is Canadian Blood Services.

And there two organizations have the exclusive role of providing blood and blood products for the whole country, two organizations that are also members of ABC as you have probably heard yesterday.

We operate under very strict regulations put forth by our regulators; we abide with the standards set forth by the ABB. We have strict licensing requirements very much like there is in the United States for transfusion agency.

A point that I want to make and I know that some of you are also somewhat familiar with this; in Canada, and especially in Quebec, we are fortunate to have in place a very proactive surveillance system for adverse

events to transfusion, and Quebec actually is one -- was at the forefront of this initiative, but it now has a spread across the country with various degrees of implantation in the various provinces, but we have a centralized repository of data for surveillance of adverse events to transfusion.

This means, depending on the region or the province, this means that we have dedicated personnel that has the task of being on the alert for looking for these reactions. For example in Quebec, we have transfusion safety officers in the major hospitals that provide blood banking services, and that has been a very interesting tool for us in order to assess safety. We manage risk very diligently; both organizations have committees, that assess various risks, composed of international experts, at least one of them is in this room today.

The incidence and the prevalence of infectious disease in our donor population is very low, actually somewhat lower compared to the rates that are seen in the United States. So all in all, I think it is fair to claim that blood in Canada is as safe as can be, and I think that for us it really serves as a benchmark to evaluate

the safety of other biological products such as cells, tissues, and organs.

So what about CTOs, I will start first by talking about the regulatory environment in Canada in that regard. I will go relatively quickly because hearing the other presentations, I realized that it is a system that is very similar to what is in place in the U.S.

In Canada, the role of regulating healthcare products including blood, blood products, but also, more recently, cells, tissues, and organs falls to Health Canada, which is basically the equivalent of the Food and Drugs Administration in the U.S., and therefore, Health Canada has been quite active in that regard.

The main difference compared to regulations for blood and blood products is probably one of timing. It is fairly recently that Health Canada has taken an active role in regulating cells, tissues, and organs at least in comparison with blood.

So basically, the first step that they took was too ask an organization, the Canadian Standards Organization to come up with standards relating to the procurement, processing, and transplantation of cells,

tissues, and organs.

Canadian Standards Association is an organization that specializes in writing up standards in various fields of the industry, including in the healthcare industry, and basically, they are very good at getting experts together and come up with standards that can be applied in the field.

So that process was started in 2000, and after only two, three years, the first standards were published that covered various areas of cells, tissues, and organs transplantation. One of these standards had a set of general standards that applied to all cells, tissues, and organs, and subsets were dealing with the specifics, for example, for organs, or tissues, or eye tissues, et cetera.

These standards when they were published were still voluntary. It was not enforced at the time of their publication, and the last point that I want to mention, obviously, the standards are very similar to other existing standards, for example -- or regulations, for example the 80b standards or the CFRs.

Health Canada really wanted to base their

regulatory framework on these standards and it is a process that takes a while. In the meantime, they didn't want to just wait for that, and so what they did in 2003 was to issue, what they call, a directive, which is, if you wish, one step below the full regulatory framework.

And that directive was basically an excerpt of most of the dispositions included in the CSA standards, and that directive had force of law, if you wish, and covered the whole spectrum of donor, of cells, tissues, and organs from donor procurement assessment down to distribution.

This was not, however, the full regulatory framework. There were still some things missing and you will see that it was added a bit later. Now, once the directive was published, Health Canada embarked into what they call a national review. Basically, it meant that they went after all of the cells, tissues, and organ establishments that they knew about and asked them to provide documentation as to their level of compliance with the directive.

Once they received that information, they then started to audit all of these establishments and I don't

remember the exact figures, but it was more than a hundred, if I recall. And basically, that first audit was targeted almost exclusively on issues around donor qualification and donor testing and not addressing the full scope of what is delineated in the standards.

And this was done only within Canada, they did not audit external establishments elsewhere in other countries.

Now, the true regulatory framework is what they call their Phase 1 and basically it is a reprise of what was in the directive, but with a more regulatory flavor if you wish. For example, they were more precise in terms of labeling requirements. Registration is not a requirement for any establishment dealing with cells, tissues, and organs; that wasn't obviously, not part of the standards. So a registration mechanism very much as you have here in the U.S.

It is interesting to note also that these regulations directly refer to the standards and that is why they call it standard based regulation. The advantage of doing it this way is that whenever the standards are modified by consensus by the community of peers and

experts in the fields, automatically the regulations should follow pace because they refer directly to the standards.

It is also interesting to note that some parts of the standards did not find their way in the regulations and that is basically because in some areas of healthcare, especially one in for things that happen at the hospital level, the Health Canada does not have authority. I already talked about the registration mechanism. I think it is important also to mention, and you'll see a bit later why I stressed this point, that establishments that are not in Canada, but that provide tissues, cells, or organs -- I'm sorry, not organs, but cells and tissues, foreign establishments that distribute in Canada should also be registered with Health Canada.

There are some exclusions in this regulatory framework, at least at this phase of this first round. Heart valves, for example, are considered medical devices. It is planned that eventually they will also fall under CTO regs. In terms of timelines, the proposed regulatory framework was published a little bit more than a year ago, up for comments for a certain period. There has been

delay in getting them published officially, but I've been told that they should become -- they should be published basically any day right now. And it is going to be a mention that the establishments will have six months to become in full compliance with these regulations.

And the Phase II will include some more precise -- the Phase II of this regulatory framework, which will happen in the next few years, will have some more precise dispositions regarding surveillance and adverse reactions reporting and also, like I said earlier, they will include tissues that are not currently falling under CTO regs.

Now, that's telling you what the regulatory status of CTOs is in Canada, but doesn’t say much of what actually is going on in the field and this is going to be the next part of my talk. So, I have to explain for those of you who are not familiar with the way the healthcare system works in Canada. The federal government has a role in terms of regulating the industry for blood cells, tissues, organs. However, the actual provision of services of healthcare services including organ donation, cells, tissue, and organ services is up to the provincial government.

So that for organs, most of the major provinces have their own programs that are run by the provinces. For tissues, it is, I think -- upfront, it is important to know that there are basically very few comprehensive tissue banks in Canada with quite small volumes and you will see a slide showing that later. But in comparison to the U.S., even taking into account the differences in the size of the populations, the infrastructure in terms of tissue banking is basically very, very poor. We have quite a few surgical bone banks that something that has somewhat disappeared from what I understand in the States over the last decade or so, bit still in Canada, quite a few hospitals rely on surgical bone banking to provide bone tissues for their orthopedic patients.

We have several eye banks that are all quite small and my understanding is that they function on very limited resources. All of our tissue banks with one exception and that is the bank -- the tissue bank that we operate at Héma-Québec, my organization, all of the other tissue banks are hospital based. And also all of these are obviously not for profit and only the few major tissue banks are -- have some sort of accreditation and basically

right now the only accreditation that we can have in Canada is the AATB accreditation, and only a few banks in Canada have that.

This is to give you a flavor of the scope of tissue banking in Canada. You'll see based on the numbers of donors procured on a yearly basis that it's really minimal, and there are basically two -- three major tissue banks or larger tissue banks, and these are multi-tissue banks operating in the country.

The situation in Ontario was interesting, because Trillium Gift of Life is the organ donation organization, but they also have the mandate of providing tissue services to the province. However, they are in the very early stage of their development, and they still have quite a few small tissue banks, each of them dealing with specific tissues.

Now, what are the current challenges for us in terms of tissue banking in Canada? First of all -- and that was quite obvious after Health Canada went around and audited the various tissue banks. The regulatory compliance of at least the smaller tissue banks is a major challenge.

And in fact, after this first round of audits, quite a few of those banks basically decided to shut down, and some of them -- for some of them the tissues were put in quarantine until they got their act together. So that's clearly a challenge for us. Donor testing, the availability of screening test adapted to CTL donors -- we've heard about that today.

I'm not going to spend much time, except to say that in Canada -- and believe it or not, that I work in an organization that screens a thousand donors daily. And we are not able to provide the services needed to screen tissue donors according to standards and regulations, and we have to send our samples to the U.S. to do that. And basically, all the major banks in Canada do that, so that's an issue for us.

A major point for us, and that's why it's really crucial for us to know what's happening in the U.S. It's that currently the supply of tissues in Canada is very heavily relying on tissues coming from American tissue banks. And we estimate that up to 90 percent of tissues used in Canada come from the American providers.

And that's also -- that's in part because we

don’t have the capacity to procure and process tissues, and also we don’t have the capacity to manufacture more specialized products such as freeze-dried bone even, demineralized bone, which are very much in use, especially in the field of orthopedics.

Because we don’t have that capacity to procure and process, we obviously don’t have the capacity to meet the full donation potential for tissue donors. I would argue -- and that point has also been made by other speakers today, that we have issues with the great diversity of methods that are used to process tissues.

At least in comparison with blood, and I can make that comparison, because that’s an activity that I’ve been involved with. It’s quite remarkable that there is such a diverse -- there are so many different ways in which tissues can be treated, and with the resulting levels of risk that may very much vary, depending on the methods that you use.

And I must say that I also find that there is a lack of standardization that even for the basic manufacturing processes you can find either in the literature, or by talking to colleagues across the world.

Traceability and surveillance are also issues, and I'll get back to that in the later part of -- the final part of my talk.

I'm going to talk -- explain briefly how we try to tackle this in our part of Canada and Quebec. Just briefly -- again, like I said, Héma-Québec provides blood and blood products in the province we've been in existence since 1998. In 2001 -- so it's fairly recent -- basically, the Minister of Health at the time gave us the mandate to also take charge of cell and tissue banking.

In terms of stem cells, I'm not going to spend a lot of time, but we offer some services. We recently started the public cord blood bank, it is still in the early phases of the development, but we are currently the only cord blood bank in the province, public cord blood bank in the province. We also have a bone marrow donor registry, and we also offer some services for preserving autologous bone marrow.

In our province, as in other province across the country, organs are dealt with with a separate organization and it's called "Quebec Transplant." We obviously have close ties with them, especially when we

have to deal with organ donors who are also tissue donors. And there are two hospital-based eye banks in existence right now.

So right now in our province we are the only multi-tissue bank. The -- there are a few remaining hospital-based tissue banks, mostly surgical bank and bone banks obviously. And it is likely that these banks will cease their activities once we're up and running, and once that -- they find out that they cannot comply with the upcoming regulations.

We are still, however, in the very early phase of our development in terms of volume, but also diversity of products. It is planned that very soon -- this year actually, the two eye banks will come under our jurisdiction, and therefore we will take over these activities also. And the situation in Quebec is very similar to elsewhere in Canada, that is, the majority of tissues still come from abroad.

In some cases, we don't have any tissue. For example, there is currently quite a severe shortage of tendons, and that's true across Canada, also skin. So we really have to get our act together for those tissues. So

I'll go briefly over this, but over the last couple of years we have been very active in putting together our tissue program.

We put up a new facility where we could procure and process tissue. We obtained the AATB accreditation, the medical device license for heart valves. And one interesting and very important project for us is also to start acting as the exclusive importer and distributor of human tissues for transplantation in our province. This model exists for blood products.

All products derived for blood are currently distributed exclusively through the two agencies, Héma-Québec and CBS in Canada. We would like to apply exactly the same model to tissues. The advantage of doing this -- the first advantage being one of safety.

Under the new regulations, the importers of tissues will have the responsibility of making sure that the source establishment is duly registered with Health Canada, and that they comply with the regulations. Currently, the hospitals directly import those tissues from the U.S. vendors. They don't have the possibility, the capacity to evaluate those vendors.

We do that on a regular basis for blood-derived products, and we would like to apply the same model for tissue products. So we're starting this year with a pilot project with one of the major hospitals in Montreal, and hope that this will fan out across the province. This is just to show you the new facility; this is not only the tissue establishment.

We also have a blood -- the blood establishment there. We had to put up clean-room facilities to procure donors and process tissues. Now, I suppose that the answer to the second question, which is, "What are the areas of commonality with blood products themselves and human tissues and organs?" is quite -- well, I suppose your answer will sound obvious.

We definitely think that they have a lot in common, and that's why we decided that in our own organization we would be not only ready, but anxious to do that, because blood, cells, tissues have a lot in common. First in terms of quality we have to go with the standards, regulations, good manufacturing practices. This was already in place for blood.

In terms of safety, the processes for qualifying

donors, for testing donors are very similar. We're familiar with look-back, traceback investigations, all reasons that you've heard before from other speakers. Traceability -- we have an objective of putting in place this year the ISBT 128 Standard for blood -- for lay-by components for blood.

We are planning to do the same eventually for tissues. And there are some other advantages, and I'm going quickly over those, but we already have the infrastructure in place to assist us in developing this new area of activity. At the same time, there are some challenges, new challenges that we need to face in this field.

It's obviously not the same donor population, so we need to become familiar with this activity. Technically, there are some new skills that we need to acquire. The issue of bacterial contamination is one that we have obviously for blood, but it's very different, and again you've heard examples of that today. It's very different for tissues.

And as I said, there is -- in my view there is still a lot to be learned in those regards. We have to

become familiar with clean-room environments. Validation is a major challenge, because as I said, there are not too many guidelines out there to tell us how we should validate the processes that are used to transform our tissues. And we also need to deal with new customers at the hospital level.

Finally, is there a scientific clinical evidence to support a need for master strategy, for transfusion and transplantation, safety? I think that regardless of where tissues are processed, I'm not advocating that all tissue banks should be housed in a transfusion agency. But regardless of that, I think it makes sense to view these activities on the same basis.

In terms of standards and regulation -- and that's basically the current status report of what is happening right now in Canada. I think in terms of standards and regulations, with -- we are at par with what is in place with blood. The standards are there, the regulatory framework will allow us to make sure that we can verify compliance through these regulations.

However, there are still some issues. Donor screening, I think, is also something that has been taken

care of by putting in place these regulations. And at least for blood and tissues, this is a given. However, as I mentioned, for donor testing there are still some issues that need to be resolved in terms of the access to tests that are specifically designed for cadaveric donors, for example.

Control of bacterial contamination, as I said, is still an issue for us. In terms of self sufficiency, we're doing quite good for blood and blood products. The only area where we're not totally self sufficient is with plasma-derived products. That is not at all the same situation, and that's true across all Canada. We are certainly not self sufficient for tissues for transplantation.

Control of importations -- as I said right now, hospitals are free to get their tissues from anywhere they like. And to us we think this is a threat to the safety of patients in terms of being able to have a good assessment of the safety of those tissues, and also their traceability. And finally, traceability and surveillance, there are some clear deficiencies in those regards.

And in fact, we had a meeting about 10 days ago

in Montreal where the Hemovigilance Committee -- which is reporting to our Health Minister and has the mandate of looking over the blood system as a whole, not only Héma-Québec as a transfusion agency, but also at the surveillance that is conducted -- this committee was convened to discuss the current safety of human tissues in Quebec.

And the main talking points are basically those that you've heard from Dr. Eastlund. First of all, there is no surveillance system in place. Compared to blood it's basically -- it's actually zero right now. Nothing is being done actively in terms of surveilling adverse events to cells, tissue, and organs.

There is a need -- before we put something in place, there is clearly a need to agree between ourselves as to what should be the data elements for doing that surveillance or clearly the case definitions. There are clearly some challenges. It's interesting to hear the notion that in fact it's true some of these events can happen years after the transplantation. How are we going to tackle this?

But for us, it's quite obvious that all of this

could probably be very easily put in place by tapping into the existing hemo-vigilance system, and adding this task to what is currently being done for blood and blood products.

Finally, traceability is also deficient in our system, and the situation is basically the same as what you've just heard from Dr. Eastlund. And we also feel that hospital blood banks have all that they need to tackle this task of ensuring, tracking, and recordkeeping for tissues transplanted in their institutions.

In conclusion, I think it's fair to say that cells, tissues have become regulatory products with specification, quite similar to that of blood products. We think in our case that we have the expertise to tackle this new challenge. Blood components are mature regulatory products, whereas in the case of CTOs, they are still in their early regulatory mode.

And getting them on par, I think, is some -- is an opportunity that has to be taken in the best interest of our patients. And with this, I'll be happy to take your questions.

DR. BRACEY: Thank you, Dr. Germain. Questions

or comments from the committee? Dr. Holmberg?

DR. HOLMBERG: I wear another hat in my job, and that is with the readiness and preparedness, and one of the things that I am very concerned about in our country is the amount of skin that is available. Are you importing a lot of skin from the United States?

DR. GERMAIN: Well, we are not -- in our province, I am not aware that we are doing that, and I think it's basically because we cannot find skin on the U.S. market. If there is, I'd be glad to know because it happens that sometimes that we have request that we cannot fulfill. Fortunately in our part of the country, recently we didn't have any major disasters that put up at risk for that, but it's not a usual practice to the best of my knowledge.

DR. HOLMBERG: Okay. And I have another question. Realizing that 80 to 90 percent of your products comes from the United States, are you involved in the technical advisory group of the ISBT 128?

DR. GERMAIN: Well, as I said, ISBT 128 for blood that's being basically put in place as we speak, for tissues I am occasionally sitting on the committee that is

looking at this at the AATB, so we keep an eye on that project. And it's our intention to -- to get there as soon as possible, as feasible.

DR. HOLMBERG: Well, I guess in -- this is question for, maybe, Scott, if Scott still in the room here. And that is that I know that the AATB is part of the technical advisory group, and since you are a member of AATB, would this be a standard of AATB that all their facilities would go with this same numbering system?

DR. GERMAIN: Well, I think, and I am speaking for Scott here, he will be in a better position to answer it. I think AATB is pushing hard to get tissue banks to adopt a single standard. I don't think their naming ISBT 128, but they are probably thinking very hard about it, right Scott?

MR. BRUBAKER: We want to expose our banks to it, so they could be educated and understand how the systems works or can work. You know, labeling changes, the number changes need to be go through detailed validations, you know, it has to do with patient safety obviously that the graft would be -- will be tracked and like they can do now, which is they have excellent systems

in place due to our standards for many years.

So to change that is something that's -- it's a very big change, and you have to buy in to the how this can be better, and to prove that it's better, the ISBT or I should say the ICCBBA folks who developed ISBT 128 have been helping with our four- and five-hour long meetings, couple of times a years that we hold our these meetings in conjunction with our spring, and other annual meeting. And it's difficult for them to apply that system to all of the different types of grafts that our banks do produce.

It's been a real challenge for them to apply their system. You know, we -- we heard originally that the UK implemented the system in just a few months period of time, but their grafts they provide from their tissue banks are, you know, a set number that are very small. You know, coming from a large bank in the U.S., they may have 400 grafts of different types and sizes that they need to classify into the ISBT 128 system. It's very difficult. So we want -- we're in an education role, and it's been two years so far, and there is more positive attitude towards it now.

DR. BRACEY: Ms. Finley?

MS. FINLEY: Thank you very much for your presentation, and also for your focus on the self sufficiency issues. We've encountered this in the past going back at least 12 years in terms IVIG and anti-hemophilia products. And I was curious as to what steps the Canadian government has taken to achieve greater self sufficiency during that time period for blood derived products, plasma products, and tissues, and organs?

DR. GERMAIN: You want me to discuss specifically IVIG or at least -- but the right product?

MS. FINLEY: I am sure there are people in the audience who would love to hear you discuss IVIG, but -- but if you can talk just in general about the others to the extent that you can, I would appreciate it.

DR. GERMAIN: Yeah, there was a -- recently, and I was not part of that consensus conferences, but that that there was I think a year ago a consensus conference in Canada to discuss the issue of self sustainability for blood derived products, and the main issue being IVIG. And I don't want to misquote the panel for the conference, but basically in the end the recommendations was to decrease our level of reliance on U.S. source plasma,

recognizing that it was not probably not possible, and also probably not necessary to achieve full self sufficiency for a variety of reasons, one of them being that there is a lot of plasma available on the market, but at least some level of self sufficiency or increased self sufficiency would be -- would be desirable, and in fact both blood organizations in the country have started to work on plans to achieve that -- you know, achieve a certain increase in self sufficiency.

For tissues, basically there hasn’t been a similar exercise, but it’s quite obvious that at least for those products that are in short supply everywhere, we will definitely increase, the need to increase our degree of self sufficiency skin, heart values, tendons, et cetera, and the tissue banks that are currently operating are trying to achieve that, but there is no -- there is no such thing as a national plan to get there.

There is, however, and maybe it’s my opportunity to mention that there is an organization at the national level which is called the Canadian Counsel for Donation and Transplantation, which advices -- it’s a bit similar to your group, I should -- I probably would think so.

This group, the CCDT, advices the federal and provincial authorities as to what should be done to improve CTO services in Canada, and I am part of that group, and I'm chairing the tissue committee. And as obviously one of the very specific recommendations that we are going to make to our politicians is to make sure that we are going to be in a position to supply at least the products that are not easily available on the international market.

MS. FINLEY: Thank you.

DR. BRACEY: Given the time and the need for us to develop a recommendation for the assistant secretary, I'd like to go ahead and move into the discussion phase now. What we have done -- we have -- I can use this mic. For the sake of those who are new to the committee, the recommendation that came out of the August 2006 meeting is posted here. Specifically, whereas promoting the safety of the U.S. blood supply's principle activity, the advisory committee inclusion of efforts to improve organ and other tissue safety and availability also need to be considerably recommended to the secretary that the secretary coordinate federal actions and programs for support and facilitate by a vigilance in partnership with

initiatives of the private sector.

By a vigilance is defined as a comprehensive and integrated national patient safety program to collect, analyze and report on the outcomes of collection, and transfusion and/or transplantation of blood components derivatives, cells, tissues, and organs. Program should be an outcome driven. Sorry, -- the program should be outcome driven with I'll use the -- can you help me -- yeah. I'll just read from the -- the program should be outcome driven with the objectives of providing early warning systems of safety issues, exchanging of safety information, and promoting education and the application of evidence for practice improvement.

Formation of an HHS and PHS biovigilance taskforce would be an important step for identification of the vision, goals, and processes needed to advance these objectives. This task group should participate with private sector efforts, including the AABB inter-organizational taskforce on biovigilance to advance public health in this effort.

The HHS -- so in essence that was the recommendation, and in fact the action from the secretary

was to form that particular task group. So what we're faced with today is we have a series of questions and those questions were posed to us from the secretary. So we have a draft, which is in essence a working draft, and there are two versions. And in essence this is -- the idea is to get the momentum rolling and we will make adding as needed. But, basically, the draft that we offer, Dr. Kuehnert and I, and other -- and Dr. Holmberg have been working on this, is the following. The HHS ACBSA heard presentations on the status of safety systems for transfusion, transplantation -- sorry, transfusion, tissue banking, and transplantation from major blood collectors, accrediting agencies, and practicing physicians in its May 2007 meeting.

The committee was impressed by the number of common issues facing these activities and the opportunity for a process improvement. Whereas, the assistant secretary for health accepted the committee's August 2006 recommendation to pursue Biovigilance by expanding the role of the committee's oversight in its new charter and by establishing a PHS biovigilance task group. The assistant secretary request additional input from HHS

ACBSA.

The committee responds to the following question posed by the assistant secretary. One, is there an opportunity to lay out a process for transfusion and transplantation safety for the future? The answer or the response being yes, there is a need to develop processes to enhance quality improvement in transfusion medicine and transplantation. While transfusion medicine laboratory processes function at a high safety level, there is a great need to enhance and further develop quality systems in tissue banking and transplantation.

Recognizing the difficulty in acquiring some tissues and organs a careful risk benefit analysis should serve as the foundation of such quality systems. Two, is there scientific evidence to support the need for a master strategy? Yes. While the literature is in need of expansion, available infectious disease transmission and error reports substantiate the need for quality improvement noting the benefit risk profile differs between transfusion, tissue, and transplant recipients. All patients treated with these modalities have potential for acquiring life-threatening infections if infectious

disease screening is flawed or emerging unknown diseases evolve unchecked over time.

Non-infectious hazards with potential for implant/transplant failure through host rejection or graft failure due to faulty preparation processing or testing are also important hazards in this patient population. Three, what should be the scope (rubric) of a master strategy? Recipient -- one, recipient outcome surveillance (biovigilance system). A, identify all donors using common identification numbers linked to biological products that are uniquely identified. B, trace all biologic products to the clinical user and recipient. C, recognize transmissible events resulting in adverse outcome, including sub. one infection agents, sub. two malignancies. Sub. three toxins.

D, build communication network to share data from users and to disseminate data to users. E, allow efficient trace forward and trace back algorithms across all product types. F, given large gaps at the user level need healthcare based programs to coordinate adverse event reporting. Two -- actually, two, there is a need for new approaches to emerging infection -- sorry, infectious

disease monitoring including informatic tools and evidence-based research.

Three, other strategic plan elements should include (can be developed at subsequent meetings) donor recruitment, b, donor screening, c, research coordination, d, emergency preparedness. Under question four, what are the areas of commonality with blood products, core blood, progenerative cells, and bone marrow tissues and organs? And what we offer here in essence are these elements, donor recruitment availability, donor screening, collection, infectious disease testing, transport, much of what we've seen on the various slides, storage, processing, labeling, traceability, surveillance, outcomes analysis, adverse event reporting.

Five, how best should this be done with the stakeholders? How do we begin? Develop a forum for -- well, we need to change that -- develop a forum for development of common priorities using evidence-based decision making. Stake holders should include regulators, accrediting agencies, manufacturers, clinicians, and recipients. This considerable regulatory overlap, the efforts of OBRR, OCGT -- OCTGT, HRSA should be coordinated

within the department.

These efforts need to be public-private partnerships with transparency, collaboration, and data sharing, but the task of biovigilance is inherently a public health mission and government-based origin, and structure of the system should reflect that premise. And under d, which is not really flashed out much, it says what resources are needed, and, basically, what are the estimated costs. And we have increased appropriations from FDA. Now, we do have comments. Well, first -- the first comment was from Jay Epstein who is not here. And under the first question which is question one, is there an opportunity to lay out a process. His specific comments -- let me get those.

Ms. FINLEY: Excuse me, Dr. Bracey. Did you say there were two versions of this? Because I have one, my colleagues don't have any, and what you're reading is not the one that we have. And some of us have some difficulty with distance.

DR. BRACEY: Oh, I'm sorry. This actually, it's a merged version. The version that you have has been modified, adding comments from others. Comments from --

Ms. FINLEY: -- question, sir, okay. So this is the one that we need.

Dr. BRACEY: This is not a merged document.

Ms. Finley: Okay. Would it be possible, first, to get a copy of this, it's for reviewing it.

DR. BRACEY: Can we get a copy? One -- the specific comments that were made Jay Epstein, under number one, is there an opportunity to lay out a process for transfusion and transplantation safety for the future. His comments were, yes, correctable gaps exist. Safety reporting, evidence-based practice linked to out comes, rapid traceability, tools are available, EGIT informatics and web-based tools.

Under number two, in terms of is there scientific evidence to support the need for a master strategy? His comments were, yes. If the issues in different domains have overlapping significance, especially infectious diseases, example of blood and cell therapy, organs with many common threats. He, basically, had no other significant complication -- comments under that.

Ms. FINLEY: Complications -- you are a

physician.

DR. BRACEY: No significant comments on the rest of the -- of what was submitted. So, again, this is just a framework so we can begin to discuss what the committee wishes to -- how to respond to the question, because yesterday, part of the issue was -- well, would we recreate the questions. And I think recognizing the importance of the fact that, a, we've established within the department that there is -- there will be a biovigilance activity. Our discussion, yesterday afternoon, was in essence to flush out something that the assistant secretary could grasp, something he put his arms around, something at the 5 to 10,000 foot level, rather than at the 30,000 level, which is the strategic level because we've done that in our preceding meetings. Now, Matt, actually, had done a pyramid. You want to go over your pyramid, Matt?

Dr. Kuehnert: So, basically, this is what I was referring to yesterday, it's that, kind of in order to get to the top you have to have the lower foundation layers. And I think this is pretty much all mentioned in what actually Jim Bauman came up with independently concerning

what are some of the elements of a biovigilance program which I guess sort of strengthened my confidence, I knew we're on the right track, and it also matches what we had as priorities in the 2005 Organ and Tissue Safety Workshop, which is, basically, the first foundation to have a common donor identification number which exist for organs, but does not exist for tissues. Although, I want to quickly add that there are unique donor IDs assigned, but they just don't -- they're linked up to different tissue IDs during processing, and when it finally gets to the users so that the user doesn't see that donor ID necessarily. So that donor ID should carry all the way through to the user environment, to the clinician, the same thing as, once that's established to have tracking to the recipient.

The third level having adverse event recognition that is clinician or user generated. And there is a number of different terms for a -- for the user whether the consignee or -- consignee, or the user, or the clinician, but basically that's what we're talking about, it is finally the person who puts the tissue in. And that's -- and also added to that, I think was a very good

comment was the recipient themselves also have some responsibility for recognizing adverse events. And, perhaps, reminding the clinician that an event needs to be inputted into the system.

The next being element that's important once these others are established is to have communication to the user about other related adverse events, perhaps linked to the same donor, or perhaps just associated with general public health threats. And then the final thing, final top of the pyramid being system education being a really important aspect of this work. The system really can't work until everybody all along the various elements of the system are aware of the system and understand what they need to do to participate. And, you know, that maybe under education that also is -- gets into what we talked about as far as mandatory aspects or standards which would compel participants to use the system, and that's -- that's basically it. But I think that -- I know this is too small for anyone to read, so -- I think that under number three all these statements are basically incorporated in that. Thanks.

Dr. HOLMBERG: If I can add another question to

you, what you presented, Matt. We heard from both Dr. Klein last week -- I mean yesterday regarding that this was a PHS public health issue and that he also said that he felt that this was a mandatory requirement if I remember correctly what he was saying. I think we heard from the patient community this morning about -- again they were emphasizing in the mandatory reporting and participation. I just want to throw that out to the committee. I think that's something that the committee needs to discuss. AABB has made their statement saying that it should be a voluntary non-punitive, but I think that the rest of the committee needs to comment on that.

Dr. Kuehnert: Well, let me just say one thing in -- just before discussion is that, you know, it doesn't have to be all or none. You know, there can be aspects of it that are -- people are compelled by, you know, various regulations or standards and some not, depending on the participants. And also, it can move to be mandatory in certain respects, but personally, I think that would take a very, very, long time. So I think you have to have something before that to get there.

DR. BRACEY: Let's start -- Dr. Bianco, you had

a comment?

DR. BIANCO: It's -- thank you for letting me give the comment. I think that this system education that Matt placed, that needs to be expanded a little bit, is the feedback. It's not a system that you just want to generate reports that you are fired, or tell everybody, you want to prevent future events if you can, and that’s the ultimate goal that I see for a biovigilance program.

DR. BRACEY: Dr. Kouides.

DR. KOUIDES: Yes, going by this discussion about mandatory reporting, could a recommendation be made to expand on that that we also would recommend perhaps that such mandatory reporting be enforced to the joint commission?

DR. BRACEY: Perhaps we could say -- that’s a point -- point for discussion, and some of the thoughts would be -- would be more generic accrediting agencies.

DR. KOUIDES: I’m just concerned with -- I think there is a consensus there, and I strongly agree about mandatory reporting, but again we have to, I think we are so obligated filling the specifics of that.

DR. BRACEY: Okay, discussion. Mr. Matyas.

MR. MATYAS: Yeah, I -- I mean, what Dr. Kuehnert said is right, and if we're trying, as a goal to get through this --

DR. BRACEY: Yes.

MR. MATYAS: -- first being the linear kind of person, I'd like to see if we could go through each of the questions, because as well, as Dr. Kuehnert said, this really is, goes to number 3, and while we're talking about it, is what we -- well, that is a different version than what we have is what we had had here was --

SPEAKER: This is not the same.

MR. MATYAS: -- specific examples include product traceability, use of centralized air, robust risk communication, again, and putting in mandatory reporting doesn't mean that we're recommending that it must be mandatory reporting but that the scope or rubric of a master strategy would examine mandatory reporting and the like. I think, we don't want to lose it, but I agree with Dr. Kuehnert and what I've learned and heard is, well, make that recommendation and it may or may not go anywhere, that's for others to decide. But I think we need to preserve it as something that should be considered

and thought about as part of the master strategy.

DR. BRACEY: Dr. Roseff.

DR. ROSEFF: I have a question first, may be for Dr. Solomon. Why is blood licensed and tissue registered? You know, what is the difference? How do that -- is there a reason or is it -- and does that have some impact on what we talk about too?

DR. SOLOMON: It's a historical thing that dates back to the early '90s when we didn't regulate tissue prior to then, and then there was the concern about Russian body parts coming into the country from untested donors, and so --

SPEAKER: Thank you.

DR. SOLOMON: I can't sort of defend the decision, I wasn't around then. I think it was a -- an effort to address a problem quickly and not be incredibly burdensome and the normal licensing procedure involved showing safety and efficacy, and it would be -- there were no parameters really to demonstrate efficacy and so efficacy, some people say is sort of implied if you replace a part that's missing in the recipient, or defective with a part from the donor, an equivalent part,

then efficacy is sort of presumed. That's really all the history I know about, and it's just continued that way.

No one has, to my knowledge, suggested that tissue banks be regulated through a licensing procedure. The legal authority that was used to generate the regulations comes from section 361 of the Public Health Service Act, which is focused on prevention of infectious disease, whereas the licensing provisions are in section 351. So I think it would have -- require some sort of a legal juggling or whatever to now, you know, go back or reverse that decision. I haven't heard even a whisper that that's where we want to go, or what the agency is thinking about.

DR. ROSEFF: Because I don't -- not that I love regulation, you know, but I -- but I mean, even from Canada, they said it was when people started getting inspected, people who couldn't meet the requirements started tightening up. And you know, it almost sounds like at least as far as the traceability, and adverse reaction reporting, we have a good system in place for blood. Do we need more teeth to make this happen for tissue, and you know, to say the Joint Commission, so

called, or AABB or AATB can have the teeth, well, its still voluntary. I think people who want to be credited will do what they need to do. But it sounds like, you know, again --

DR. SOLOMON: Perhaps, you don't realize that the tissue banks and eye banks are inspected. We have a field crew that inspects these places to ensure compliance with the rules. The basic difference is, for blood, they have to first submit an application and get approval before they go on the market; for tissues, you can go on the market and the compliance is assessed at the time of inspection. It's not to say that they're less "regulated."

DR. ROSEFF: Right, there are different rules that are in place. What we're hearing is some of the rules may be need to be the same, but again --

DR. BRACEY: There is a question -- comment from Dr. Bloche.

DR. BLOCHE: Yeah, I just had a general one. I apologize, I'm going to have to leave a little after 3:00, so I wanted to offer this overview thought, fully acknowledging that I am, plainly by far the least informed

in this room, with respect to the specifics of much of the industry. First thought, by way of seconding what you had to say, it seemed to me that anything that's proposed as mandatory, or to have at least in a general way, some description of where the books (phonetic) are?

Now, maybe it's specifically the Joint Commission, maybe it's the various accrediting bodies, but plainly, HHS does not have global statutory authority to impose all that. And so something, a lot of you said about how it gets (inaudible) claiming we're not in Canada or Germany, sweeping national --

DR. BRACEY: Right.

SPEAKER: If you put -- Dr. Solomon has --

DR. SOLOMON: Matt, could you clarify from whom to whom is this mandatory reporting? I don't quite understand, from the clinician to whom?

DR. KUEHNERT: I don't know, I'm not the one who suggested mandatory reporting. So I don't -- I don't know what is -- I'm not sure who is --

DR. BRACEY: Well, the mandatory reporting is what we were just discussing, so we really --

DR. KUEHNERT: Right, oh, who --

DR. BRACEY: -- the concept of mandatory reporting.

DR. KUEHNERT: -- if someone wanted to make it mandatory, who would they report to?

DR. BRACEY: Correct.

DR. KUEHNERT: Well, I think that to me, you know, this B, that just got created, it really would fit under F, or what is now probably G. But at the bottom, where it says, there is a gap at the user level, and where I think the gap is, is the clinician thinking of this possibly being related to the allograft and saying I need to report this. Now, who do they report to?

Well, ultimately the healthcare facility, would, in the case of tissues, report to the tissue bank; in the case of organs would report to the OPO, and then it would go to the various regulatory agencies from there. Of course they could just shortcut that and report to MedWatch, I suppose, for blood and tissues. But I'm not -- certainly would not propose a new reporting mechanism but just to strengthen the reporting mechanisms that are already there, but also to facilitate communication of adverse event recognition by having systems like TTSN,

where you share data even before it's spit back out by a regulatory agency, which might take some time.

But it would basically -- I guess, to answer the question, it would be using the reporting mechanisms that exist, but really making sure that they're strengthened. So the clinician, I mean, they’re not going to know who to report to at the tissue -- they don’t even know who the tissue bank is probably, or the OPO. So there's going to have to be a healthcare epidemiologist, quality assurance program, something in the hospital that coordinates the adverse event reporting.

SPEAKER: Okay, can I just finish the -- my earlier --. A kind of global thought I wanted to offer about this question of whether blood gets treated separately from tissues and organs et cetera, versus whether it should all be seen together from a regulatory perspective. The global thought is this, that with respect to vigilance and surveillance, the case seems to me to be powerful for treating this all together, these global information systems. The pyramid is wonderful, it really drives home an important concept. It's astonishing to me that in this country, we’re so kind of fragmented in

this regard. But with respect to the management of risks, with respect to the policies about what to do, once this -- the information comes in; it seems to me, and here I found Dr. Fishman's presentation quite powerfully persuasive.

The problems are so fundamentally different for the different kinds of products. The risk-benefit balances are so different. The dying patient, who needs a liver in 36 hours versus transfusions -- with kidney transplants, somewhere in between, because it seems to me that given the inevitable rigidities that set in, once a regulatory system is set up and people have their compliance officers in the -- kind of following a rigid sort of way.

It seems to me that the case is much weaker, we're combining the risk management of blood, tissues, organs et cetera, its kind of my thought from satellite range as opposed to 30,000 feet or 10,000 feet.

DR. BRACEY: Yeah. So then basically, it sounds to me that really, the questions 1 and 2 are really fairly easy to answer, and the real meat of what we're talking about is within question 3. And we seem to need to decide

finally on this issue of reporting and whether the reporting would be mandatory, compelled, Dr. Pierce.

DR. PIERCE: Well, I think we would be wasting our time if we didn't ask for mandatory reporting, and we have two systems in place, we have MedWatch and we have the CDC that already have mandatory reporting of certain infectious diseases, for instance.

DR. SOLOMON: SPEAKER: No that's not --

DR. BRACEY: Well, Dr. Solomon.

DR. SOLOMON: There's mandatory reporting for the tissue bank or the blood bank or the eye bank but its voluntary reporting for the clinician.

DR. PIERCE: That's right, but I'm -- yes, and so what I'm talking about though is asking for mandatory reporting. But we have systems in place that can already handle that and they need to be beefed up, but they're already there. The systems are there for getting the information out.

DR. BRACEY: Dr. Lopez.

DR. LOPEZ-PLAZA: I think in the long run, I think the mandatory reporting should be there, the ultimate goal, but I think we have to really remember that

if we make something mandatory then we have to be prepared to the always people not complying to that, and you know, going from nothing to all is going to create that kind of problems. So I think that may be perhaps thinking about some kind of pilot project, when we'll learn how the system worked or the biggest efficiencies, how we can make them work better, and then once we had that information, then start thinking on making something mandatory, that’s the -- I mean, the ultimate goal.

DR. BRACEY: Well, one of the things that was discussed and I don’t know if we actually have it included was the idea of making the surveillance, current pilots sustainable, because currently that’s temporary, and we need to seek funding to make that. So perhaps we could enter that as a compromise with a notion that once we make systems sustainable, figure out how to make it work, then the ultimate goal will be to make it mandatory.

SPEAKER: Yeah, that sounds really good.

DR. BRACEY: Dr. Holmberg.

DR. HOLMBERG: But I’m very concerned that if we’re just supporting the TTSN, what are we doing for the blood aspect of it, and as Dr. Bloche mentioned on the

global perspective, I think that we need the vigilance and the surveillance to be linked so that we have the communication to go across all of the biological products.

SPEAKER: Just a comment, any consensus from the committee?

DR. BRACEY: Ms. Finley (phonetic).

MS. FINLEY: Two comments, first of all I think there's been a question raised by my esteemed colleague here about how much authority CDC has to compel this. I don’t know if we need an answer from the general counsel --

DR. BRACEY: None.

MS. FINLEY: We don’t -- they have no authority.

DR. BRACEY: No, authority.

MS. FINLEY: Okay, so may be that’s a place for us to depart from, by, you know -- all right, the second issue I would raise is I see that you’re including some information in here, and I also have a couple of friendly amendments and wordsmithing to the first and second question.

DR. BRACEY: Right, sure.

MS. FINLEY: So I just wanted to make sure

process-wise, we’re going back there, so I raised that issue, and --

DR. BRACEY: No, we will be, in fact, in order -- why don’t we do this. Let's go first to question one, eliminate the easy question. We go to question two, and then the meat will be in three. So question one, I think is pretty straightforward that we all feel -- well, sorry, I don’t want to speak for the committee. Does the committee feel in a unanimous sense that this is the right thing to do?

SPEAKER: Yes.

SPEAKER: Yes.

DR. BRACEY: Okay, now, in terms of the wordsmithing, its -- do we wish to cut down on the verbiage?

SPEAKER: No.

DR. SANDLER: Let's try and get through, you know, we can bog down on wordsmithing.

MS. FINLEY: Okay, but there is an important concept, Dr. Sandler, that I would like to include here. And I don’t want to take up a lot of time, I have four words to add, at the back of that last sentence.

DR. BRACEY: Sure.

MS. FINLEY: So if we're -- are we writing here and then voting, is this up to --

DR. BRACEY: Well, I'd like to just go one by one.

MS. FINLEY: Okay, all right, I just have four words I'd like to add to that.

DR. BRACEY: Okay, well, what's your recommendation?

MS. FINLEY: At the last sentence, "should serve as the foundation of such quality systems with the recognition of the importance of patient safety." I'm uncomfortable with "risk benefit analysis based on the scarcity of tissues. It's a factor; it is not the determining factor. So I just wanted to have that recognized.

DR. BRACEY: Okay, so if -- it's a -- let me -- well, you can read it or do you want me to read it before we vote on it? What's the committee's preference?

SPEAKER: Please read.

MS. FINLEY: -- with a focus on the recognition --

DR. BRACEY: I'll read the last sentence. "Recognizing the difficulty in acquiring some tissues and organs, a careful risk-benefit analysis should serve as the foundation of such quality systems, with the recognition of patient safety." Does that sound fair?

SPEAKER: I guess, not that I disagree with your addition; I don’t know why we need the second sentence?

MS. FINLEY: Okay, then just pull it out, that’s okay with me.

SPEAKER: I mean that -- or the third sentence. Huh?

MS. FINLEY: That’s okay with me.

SPEAKER: I mean, the question is, is there an opportunity to lay out a process for transfusion and transplantation safety for the future? Yes, there's a need to develop processes, that rest of that sentence, while transfusion medicine laboratory processes function at a high level, there's a great need to enhance and further develop quality systems," ending there. I don’t know why we need that.

DR. BRACEY: Well, part of it was the issue that, I guess has been expressed by some of the organ

procurers that the quality systems would begin to interfere with the ability to have access to organs, and we wouldn’t take the benefit-risk into consideration.

SPEAKER: But then that’s -- but shouldn’t that go into -- I don’t know, I’m just being lawyerly, I don’t -- I don’t see how that --

DR. BRACEY: You don’t see added value.

SPEAKER: Yeah, I don’t see what that adds to answering that question.

DR. BRACEY: Okay, Dr. Pierce.

DR. PIERCE: I do think this needs to be general, because there is a big difference between transplanting a patient with a liver who has 24 hours to live and transplanting a patient with a kidney who can live for another five years. So I would just take -- I would take specifics out of this and the documents.

DR. BRACEY: Let's strike it, okay, let's strike it then.

MS. FINLEY: Okay.

DR. BRACEY: Okay, so we'll strike that. So then --

SPEAKER: Do you have a question?

DR. BRACEY: Question, Dr. Bloche?

DR. BLOCHE: Yeah, I just think it's a mistake not to -- it can be elsewhere in the document, I think it’s a mistake not to make reference to risk-benefit -- the risk-benefit perspective, because there's just such a high likelihood that this kind of language can be interpreted in a -- kind of sources-apprentice fashion to promulgate all manner of detailed obligations. Let's treat like things alike, blood is alive and so are organs and tissues, and so let's impose the same obligations.

And I just don’t want to come remotely close to putting the transplant surgeon in a situation where he or she might not be able to save a life because an organ can't be fully tested and vetted in 18 hours. So I just think that risk-benefit language is crucial.

SPEAKER: But doesn’t --

SPEAKER: Wouldn’t that be part of the rubric of a master strategy?

SPEAKER: Yeah.

DR. BRACEY: Well, that’s a good point. We could include it there.

SPEAKER: I mean isn't that a factor, I don’t

know where -- within like the --

DR. BRACEY: It needs to be included, but perhaps not -- okay, okay, all right. Okay, so then --

SPEAKER: -- but it's -- that’s, it should be a factor.

SPEAKER: Yeah.

DR. BRACEY: Okay, so then, yes, there's a need to develop processes to enhance quality improvement in transfusion medicine and transplantation, while transfusion medicine laboratory processes function at a high safety level, there's a great need to enhance and further develop quality systems in tissue banking and transplantation. Dr. Solomon.

DR. SOLOMON: I take issue with the second sentence. It sounds like blood banks are squeaky clean and tissue banks are the dreads of the earth. What evidence is there to show that because --

SPEAKER: Okay.

DR. SOLOMON: -- we don’t have the denominator data. I mean --

SPEAKER: Okay, just the first sentence.

DR. SOLOMON: I think that’s a very insulting

statement.

DR. BRACEY: Okay, so then we'll make it truly brief, and we'll -- I don’t have a problem actually with deleting the second sentence, so you’re fine. Is that okay with the committee?

SPEAKER: Yes.

DR. BRACEY: Okay, all right, so then, yes, there's a great need to develop processes to enhance quality improvement in transfusion medicine and transplantation, very general, okay. Let's move on to -- all in favor, we'll keep it going, motion, all in favor?

SPEAKER: Aye.

DR. BRACEY: Aye, okay, passes. Let's go on to the next piece then. "Is there scientific evidence to support a need for a master strategy?" Here we have "Yes. While the literature is in need of expansion, available infectious disease transmission and error reports substantiate the need for quality improvement. Noting that the risk- benefit profile differs between transfusion, tissue and transplant recipients, all patients treated with these modalities have potential for acquiring life threatening infections if infectious disease screening is

flawed or emerging, unknown agents evolve unchecked over time.

"Non-infectious hazards with potential for implant/transplant failure, through host rejection or graft failure, due to faulty preparation, processing, or testing are also important hazards in this patient population."

SPEAKER: It's just grammar. The second paragraph, using hazards to refer to hazards, may I suggest, that the second hazards, the last -- in the last line, be changed to "factors in this patient population."

DR. BRACEY: Okay. Do we -- is some of this unnecessary?

SPEAKER: I vote to accept it.

SPEAKER: I'm not going to debate that.

DR. BRACEY: Okay, motion, we had a motion, is there a second?

SPEAKER: Yes.

SPEAKER: Second.

DR. BRACEY: All in favor?

SPEAKER: Aye.

DR. BRACEY: Okay, it passes. Now, let's get to the real meat. Dr. Solomon.

DR. SOLOMON: Excuse me, are you supposed to ask for, that the ex-officio members make comments.

DR. BRACEY: Oh, yes.

DR. SOLOMON: I don’t know what that procedure is.

DR. BRACEY: Yeah, you -- yes, you may make a comment, yes.

DR. SOLOMON: Okay, for the second question, I would answer no, there isn't scientific evidence to support a need. I think we need first to do the gap analysis, which is occurring now and then analyze that and see where -- if there are gaps and where there are, I don’t think its ipso facto that there is scientific evidence to support a need.

DR. BRACEY: A need for hemovigilance -- biovigilance? What does the committee -- Dr. Roseff?

DR. ROSEFF: I think I agree with that. You know, may be the question is almost wrong. You know, we’re answering a question, we know that we have a lack of scientific evidence in a lot of the things that we’re

dealing with. So is there scientific evidence, may be it's not necessary currently, you know, we have -- we have understanding, we have anecdote, we have reports and that should lead to supporting a structure to get more scientific evidence again, because we have different tissue we're looking at, different risk factors, so I think that's a good point that we don't have adequate scientific evidence but that -- that's not the question almost at this point to us, that we need to do something, we need to have a master strategy while we're looking for scientific evidence, based on what we see is happening.

SPEAKER: I think you can accomplish that by actually answering the question without answering the question by not putting a yes or no. It's -- while the literature is in need of expansion?

DR. BRACEY: Yeah, that's a good point. Dr. Bloche or Ms. -- Dr. Bloche.

DR. BLOCHE: I agree with what Dr. Roseff just said, may be a way to wordsmith this is just ask does our current understanding of the problem support -- support a need for a master strategy?

DR. BRACEY: The only problem is that these are

questions that we've received and --

SPEAKER: It's not really -- the irony is if there were, you know, clear cut scientific evidence, -- you lest (phonetic) have a need for a strategy, so -- I basically agree that the question is --

DR. BRACEY: Ms. Finley.

MS. FINLEY: I work my way through colleges, I proofread throughout the day, let me see if I can help you. While scientific evidence is lacking or is not available, and needs to be -- is not fully mature, needs to be collected, available infectious disease transmission and error reports substantiate the need for quality improvement, does that satisfy everybody?

DR. BRACEY: That sounds good to me.

SPEAKER: Omit the 's'.

DR. BRACEY: Omit the 's', yeah, right, okay, so we'll omit the 's', okay. Okay, so while the available scientific -- let's go back over that again, "While the available scientific literature is lacking," is that right?

MS. FINLEY: No, what did you see, what was your word?

SPEAKER: Maturing.

MS. FINLEY: Is maturing.

DR. BRACEY: Okay, "While the available scientific literature is maturing" --

MS. FINLEY: -- available infectious --

DR. BRACEY: -- yeah, available infectious --

MS. FINLEY: -- infectious disease transmission, or you could say is still maturing, indicating it is a process, in the middle of a process.

DR. BRACEY: Okay, "still," still hold on.

MS. FINLEY: Still.

DR. BRACEY: Okay, substantiate the need for quality improvement.

SPEAKER: Should the first "available" be removed?

MS. FINLEY: I’m sorry.

SPEAKER: Should the first "available" be removed, you have "available" twice.

DR. BRACEY: Yeah, it's a good point, right.

MS. FINLEY: Yeah.

SPEAKER: Mr. Chairman, to be responsive, we should change "literature" to "evidence."

DR. BRACEY: Yes, that’s a very good --

SPEAKER: It's not responsive the way it --

DR. BRACEY: So "scientific evidence," okay. So "While scientific" -- just put, "While scientific evidence is still maturing, available infectious disease transmission and error reports substantiate the need for quality improvement. Noting the benefit-risk profile difference between transfusion, tissue, and transplant recipients, all patients treated with these modalities have potential for acquiring life threatening infections, if infectious disease screening is flawed or emerging, unknown diseases evolve unchecked over time."

SPEAKER: Have we answered yet the question whether or not there's a need for a master -- I mean, we’re saying there's a need, but is there a need for a master strategy?

DR. BRACEY: Well, here they're just asking, is there evidence, scientific evidence.

SPEAKER: Okay.

DR. BRACEY: So we’re sort of skirting the issue.

SPEAKER: Okay, I mean, if you want to put that

in.

DR. BRACEY: And then in the second piece, "Non-infectious hazards with potential for implant/transplant failure through host-rejection or graft failure, due to faulty preparation processing or testing are also important factors in this patient population."

SPEAKER: What about the errors?

DR. BRACEY: We've got it -- oh yeah, well, we will say faulty -- yeah, so you want to include "errors"? What do you think?

DR. SOLOMON: I think we should delete that part due to, because until we -- there could be other factors that they're due to, not just these. It could be due to something in the recipient for instance.

DR. BRACEY: So you’re saying just -- just say that "Non-infectious hazards with potential for implant failure" -- "implant/transplant failure through host rejection or graft failure are also important factors," yeah. We could -- Dr. Sandler.

DR. SANDLER: Yeah, again to be responsive, if we can go back to the first sentence and try and make that first -- the first sentence in the answer to two, can we

roll up -- yeah. So they're asking us, "Is there scientific evidence to support a need for master strategy?" And to answer the question, it seems, while scientific evidence is maturing, available infectious diseases, transmission, error reports, substantiate the need for a master strategy. Why introduce quality improvement, I mean, he's asking if you want a master strategy, you just tell him, "Yeah."

DR. BRACEY: Excellent, yeah, okay. Ms. Benzinger.

MS. BENZINGER: Yes, I was -- wanted to make that point too, but I wanted to put in there, "safety" should be in there versus "quality improvement," that's what your master strategy is here for, it's to improve the safety.

SPEAKER: Master strategy for safety.

DR. BRACEY: Masters strategy for safety, yeah, excellent, okay. So -- Dr. Pierce.

DR. PIERCE: I don't really know what "Scientific evidence is still maturing," I don't know what that means? You know, what does that mean?

DR. BRACEY: Well, I mean, we take it to mean

that the data are still coming, they’re coming forth.

DR. PEIRCE: Well, so how many cases of transmission of an infectious disease, because of a lack of a system being in place do you need in order to have a mature scientific strategy?

DR. BRACEY: True, good question. How about, "While scientific evidence is --

SPEAKER: Still accruing?

DR. PIERCE: Well, it's not -- it's always going to be accruing.

DR. BRACEY: Yeah.

DR. PIERCE: Scientific evidence is scientific evidence.

DR. BRACEY: How about is limited, how about is limited.

DR. PIERCE: We have New England Journal papers, we have newspaper articles that have been supplied.

DR. BRACEY: Right.

DR. PIERCE: I think the scientific evidence is out there that these organs can transmit diseases, and there are a whole variety of reasons why that may be the case. In some cases, there might be nothing that can be

done about that. In other cases, there are improvements that can be made in the procurement and testing of these organs and tissues that would have an effect.

DR. BRACEY: So if we said, "While scientific evidence" --

MS. FINLEY: Is incomplete?

DR. BRACEY: -- "regarding infectious disease transmission and error reports substantiates" -- that's -- okay, wait a minute, "While scientific evidence is incomplete" --

MS. FINLEY: Is necessary?

SPEAKER: Seems complete enough to me.

DR. BRACEY: That's the question, that's the question.

DR. LOPEZ-PLAZA: Are we talking about something being incomplete or something evolving to the point that as we know more, we're adapting what we do.

DR. BRACEY: Well, the question is how much evidence do you need to take action, I mean, that seems to be what the question --

MS. FINLEY: Could we just --

SPEAKER: If you have somebody that marks down

HIV -ve, when they should have marked down HIV +ve, how much more scientific evidence do you need to say that there's something wrong with the system?

DR. BRACEY: Okay, how about this? "While scientific evidence is limited, available infectious disease transmission and error reports substantiate the need for master strategy for safety." We just say that it's limited, and that --

SPEAKER: I would say surveillance evidence is limited because we don’t have all the surveillance systems in place.

DR. BRACEY: Okay.

SPEAKER: We know that infectious diseases can be transmitted via organs and tissues.

DR. BRACEY: Okay, so "While surveillance evidence is limited" --

SPEAKER: Because we don’t have surveillance systems.

DR. BRACEY: -- "available infectious disease transmission and error reports substantiate the need for a master strategy for safety. Is that acceptable to the group?

MS. FINLEY: Yes, it's very acceptable.

DR. BRACEY: "Noting that the benefit risk profile differs for transfusion, tissue, and transplant recipients, all patients treated with these modalities have potential for acquitting life threatening infections if infectious disease screening is flawed or emerging unknown diseases evolve"--

SPEAKER: Or error --

MS. FINLEY: Or if you get -- if you have errors, and just get rid of that last paragraph.

DR. BRACEY: Cut it --

MS. FINLEY: I would just -- if you -- what that’s basically saying is --

DR. BRACEY: Yeah, yeah, right, right.

MS. FINLEY: -- is the errors are --

DR. BRACEY: Okay, good point, so scratch that last paragraph.

SPEAKER: Mr. Chairman.

DR. BRACEY: Oh, yes.

DR. SANDLER: Can I make an edit on the first sentence, "While surveillance evidence is limited, reports of infectious disease transmission and errors

substantiate" --

DR. BRACEY: Very good, reports of infectious disease transmission and error --

DR. SANDLER: -- and errors substantiate. Reports of transmission and errors is the operative thought.

DR. BRACEY: Right, right. Okay, it looks like a good statement created with some words missing. Is the committee ready to vote on this statement now?

MS. FINLEY: Yes.

SPEAKER: I move.

DR. BRACEY: Second?

SPEAKER: Second.

DR. BRACEY: All in favor?

SPEAKER: Aye.

DR. BRACEY: Aye, it passes. Okay, now lets get to the meat, let's get to the meat of the topic here, and that is number three. Okay, "What should the scope(rubric) of the" -- "What should be the scope(rubric) of a master strategy?" So here we have, "Recipient outcome surveillance (Biovigilance System). (a) Identify all donors with common identification numbers, linked to

biological products that are uniquely identified. (b) Compelled data reporting through appropriate mechanism, i.e., regulation requirement, license requirement, joint commission," well, there's some alphabets in here. We could do an e.g. But the question is, do you feel -- the idea is that it wouldn't be mandatory but it would be compelled. Ms. Finley?

MS. FINLEY: I would just add on (b) from -- to the public health authority and to patient recipients.

DR. BRACEY: Okay, so to the public health authority --

MS. FINLEY: And to patient recipients.

DR. BRACEY: -- and patient recipients, do we need to specify CDC?

MS. FINLEY: I -- no, I don't think we do, because I think it varies, and sometimes it's up to -- yeah.

SPEAKER: And to patients --

MS. FINLEY: And to donor recipients.

SPEAKER: And I'm not sure it should be data reporting, I don't -- I think data is a little bit broad.

DR. BRACEY: Just say, "Compelled reporting."

SPEAKER: Adverse outcomes.

SPEAKER: Adverse event reporting or adverse outcome reporting.

DR. BRACEY: Okay, it's "Compel --

SPEAKER: And that would have --

DR. BRACEY: -- adverse event reporting.

MS. FINLEY: Does that include errors?

SPEAKER: Yes.

DR. BRACEY: So, "Compel adverse event reporting through appropriate mechanism" -- that doesn’t.

SPEAKER: And I thought I heard -- may be I was reading into what you were saying Henry, but I guess what I thought was you were saying was to jump from right that mechanism to the public health authority, is that --

MS. FINLEY: You know, if -- yeah, I don’t have a problem with -- I mean, that’s wasn’t what I was suggesting but may be taking some of the words out would enable us to --

DR. BRACEY: Yeah, focus more.

MS. FINLEY: -- get rid of that alphabets, so --

DR. BRACEY: Right.

MS. FINLEY: And I want to be careful here that

we’re not compelling the department to do too much. You know, we want to give more, put more flesh on the bones here, but ultimately, that’s the agency's responsibility.

DR. BRACEY: Right.

SPEAKER: I think what I’m hearing from a lot of individuals is that may be there might be years before rule-making could take place. And I think what I heard from the committee and the discussions today were that there were standards and accreditations that could be the steps.

DR. BRACEY: Right, so if we say, "Compel adverse event reporting through the appropriate mechanism from hospital based" -- we don’t need a capital on that, based safety personnel, I don’t know if we need to -- do we need to specify bio-safety?

MS. FINLEY: I don’t think so.

MS. LOPEZ-PLAZA: I have a comment on that. I mean, I -- and this is personal. In the hospital, like in the blood bank, we are kind of the persons responsible for a lot of these things, that we’re held accountable for, but still -- so I mean, but there's not -- is the safety office just ours, like from the blood point of view. So I

think that there should be some hospital based reporting mechanism or surveillance mechanism that then reports to the biovigilance team, and I don’t -- I would not put anyone specific in my -- I don’t think it's for safety personnel, because I’m not a safety personnel, but I’m responsible to what I release from the -- from my site.

DR. BRACEY: So you're saying from a hospital based safety system?

MS. LOPEZ-PLAZA: No, from the hospital based surveillance system. (inaudible) been reporting, the thing is that it could be different people, not a safety officer.

DR. BRACEY: Okay.

MS. FINLEY: What about responsible -- hospital based responsible personnel or --

DR. BRACEY: From --

SPEAKER: Let me make it even simpler, why don’t you take out the front, "Compel adverse event reporting to the public health authority and to donor recipients."

SPEAKER: That’s it, yeah, that’s -- yeah, because we’re being very prescriptive by saying hospital based.

SPEAKER: Right, I mean --

DR. SOLOMON: Haven't you left out the tissue bank, eye bank and blood center there.

SPEAKER: That’s why take in that -- the hospital.

SPEAKER: To the public health authority -- well, if we report it to the public health authority and the system works in the public health authority, would notify the tissue bank.

DR. SOLOMON: No, then you've lost time. You’re still missing a link, I think, remember that depending on what you’re doing you have the recipient, you have the physician that is taking care of the recipient, you have the person that distributes their whatever in the hospital --

SPEAKER: Okay,

DR. SOLOMON: And then you have the agency that provided that to the hospital.

DR. BRACEY: Okay, so what if you say, "Compel adverse event reporting through appropriate mechanism to include tissue bank, public health authority, donor, physicians. And that way you get all the people that you

think are important.

DR. LOPEZ-PLAZA: We are still missing the initial part, I mean, again, the biggest problem is, you know, coming from the recipient of, and I think that you have to specify that -- I prepared mechanism that will include from -- from collection to distribution to, you know, till the end, I don’t know, I mean, you have to address that because that’s where you're going to have a lot of problems with compliance.

MS. FINLEY: And should we compel that centralized mechanism in the facility too, because that’s -- its' -- you know, we know in blood who does it, who does the reporting, we don’t know in the hospital or any facility, so --

DR. BRACEY: Okay.

DR. LOPEZ-PLAZA: And you may have hospitals that decide to keep the differencing separated but still have a central reporting system, and with two or three different accountable persons.

DR. BRACEY: What if -- instead of being so prescriptive, you say, "Compel adversary report" -- "Compel adverse event reporting to ensure" --

MS. LOPEZ-PLAZA: From collection to donor receipt.

SPEAKER: Yeah, yeah.

SPEAKER: Yes, exactly, that --

SPEAKER: From hospital to supplier.

SPEAKER: Right.

DR. BRACEY: So a process -- "Compel a process of adverse event reporting from the facility to -- from the healthcare facility to the vendor, Dr. Sandler.

DR. SANDLER: I was thinking that this is an opportunity to specify that we want to compel a process of reporting adverse events for tissue, organ, and blood collection and therapy at all stages to the agency. I mean, do we want to be specific and make sure that we're covering the waterfront so to speak.

MS. FINLEY: We might also want to include the word "processing" in there.

DR. SANDLER: It wasn't cellular therapy. I think we've got three things. I think we've got tissue, organs, and blood, if I'm not mistaken. Those are the three things we're addressing, is that correct?

DR. BRACEY: Yes, those are the three --

DR. SANDLER: Yeah, and I'd say therapy.

DR. BRACEY: Comment, Dr. Whitaker, sorry.

DR. WHITAKER: I'm not a lawyer but -- I'm not a lawyer but I think that if every adverse event gets reported to the donor recipient, or to the recipient of the tissue, organ, or blood therapy, the hospitals are going to have issue with that.

DR. SANDLER: I'm the hospital representative and the word "compel a process," satisfies my need to have some editing thing. In other words, it doesn't say compel adverse reporting, it says compel a process, and by saying process, I think that that makes it possible to flush it out so it's not an annoyance.

SPEAKER: Or you could put as appropriate at the end.

SPEAKER: Or as appropriate.

SPEAKER: Okay.

SPEAKER: As appropriate.

DR. SOLOMON: I think we should include cells, the reproductive --

DR. BRACEY: Okay, so -- okay, we have a motion for cells.

SPEAKER: So moved.

DR. SOLOMON: And the thing is why wouldn’t you want some investigation before you go and tell the recipient?

SPEAKER: Well, no, we’re having a process.

MS. FINLEY: It's a process, we’re not saying there's no investigation.

SPEAKER: No saying we’re just going to go and report, we’re going to have a process.

SPEAKER: Just like there is with blood.

DR. BRACEY: So compel a process of adverse event reporting for tissue, organ, cellular and blood therapy through appropriate mechanisms to designated public health authority or authorities?

SPEAKER: -- ties.

DR. BRACEY: -- authorities, and to donor recipients as appropriate. Yes.

SPEAKER: (Off mic).

DR. BRACEY: Okay.

SPEAKER: Do we need donor? Take it out? And then why is the eye separate from organ?

DR. BRACEY: That was -- is the eye truly

separate from other organs?

SPEAKER: No, move to the mic please..

SPEAKER: (Off mic).

DR. BRACEY: Well if we -- what we could do, we could basically define -- make a definition, include eye under the definition of organs.

SPEAKER: No, eye tissue is not organ, it's a tissue.

SPEAKER: Well, it's a tissue -- so it's included under tissue then.

SPEAKER: By definition, we’re dealing with tissues and organs.

SPEAKER: Yeah, true, true, with yeah, quite right, yeah. so let's leave it like that, tissues and organs, because that’s what we've been given the authority to address, (inaudible).

SPEAKER: I'd like to have a clarified what -- the adding of "as appropriate to the recipients." Because there you’re walking a line of, you can interpret that anyway you like. It's not appropriate to scare them because -- oh, because this other person who received a kidney came down with CJD.

DR. BRACEY: Right, but what we're saying --

SPEAKER: We don't want to alarm a patient, so that's what I'm saying, as appropriate is too big of a loophole for me.

DR. BRACEY: When we do adverse event reporting, we don't report only events that are associated with injury, we report all deviations. Some deviations are so minor, yes, they can lead to multiple deviations into a final event, but there's no reason to report the most minor deviation to the recipient.

SPEAKER: But to Anne Marie's point then though, and then isn't that part of the process. We've said on various other things, we don't have to get into that levels as of --

SPEAKER: Yeah, we don't need "as appropriate" because we're compelling a process.

SPEAKER: That's right, and the process will take care of appropriateness.

SPEAKER: Responsibility is the agency's too.

SPEAKER: But Dr. Bracey, I think that one of the things that we may have overlooked here, is that I think we got carried away with tissues, and we think that

maybe the donor has already deceased, and I think that we’re trying to capture all of this, and I think that we've just gone to the recipient, we haven’t gone to the donor side. You know, may be something might be evident through the surveillance process that is needed to be communicated to the donor.

MS. FINLEY: Well, actually that’s a good point, because if the donor has an infectious disease and they have a family member with whom they've been intimate, then that might be important. So I would say, and to recipients and donors.

DR. BRACEY: That’s a good point, yeah, recipients and donors, because it could also be a living donor.

MS. FINLEY: Yeah, that’s -- yeah, you’re very right.

DR. BRACEY: Okay. Can we go back up to the beginning -- not, not -- of three. "So what should be the scope(rubric) of the master strategy? One, recipient outcome surveillance, identify all donors through common identifiers, compel a process of that adverse event reporting for tissue, organ, and blood therapy through

appropriate mechanisms to designated public health authority to recipients and donors; (c) trace all biologic products to the clinical user and recipient; (d) recognize transmissible events resulting in adverse outcome including, infectious agents, malignancy, toxins; (e) build communication network to share data from users and to disseminate data to users. That sounds --

DR. BRACEY: Yeah, that’s redundant, isn't it?

SPEAKER: Just why not drop that "Share data."

DR. BRACEY: Yeah, let's drop "Share data."

SPEAKER: (inaudible) data. I would --

DR. BRACEY: To disseminate data, to use it.

SPEAKER: Okay.

SPEAKER: Can we go back up a little bit?

DR. BRACEY: Okay, go back up a little bit.

SPEAKER: And higher -- on (c) can we go -- can we again use "recipient and donor," trace all, because the trace has to be backwards and forwards.

DR. BRACEY: Yeah, that’s a good point.

MS. FINLEY: Okay.

DR. BRACEY: Build communication network to -- okay, so, trace all biologic products, clinical user, and

-- to the clinical user, recipient, and donor.

SPEAKER: Okay.

MS. FINLEY: Under (d), you just want to increase outcome to outcomes to be consistent with the --

DR. BRACEY: Yeah, right. So you can scratch that and under (c), in other words "Clinical user, recipient, and donor," what -- you get rid of one of the -- that's first hand. Okay. Moving down to (f), "Allow efficient" --

SPEAKER: I'm sorry, can you -- when you do (f), can you still have (b) up there? Or (c), I'm sorry, (c).

DR. BRACEY: "Trace all biologic products to the clinical user, recipient and donor."

SPEAKER: Yeah, what's the difference between that and "Allow efficient trace forward and trace back"?

SPEAKER: I think it's the same.

DR. BRACEY: That's the same thing.

SPEAKER: And then on "(g) given large gaps at the user level, we need healthcare based programs to coordinate adverse event recording," isn't that (a) or (b), (b).

MS. FINLEY: Yeah, I think we can do without

those two.

DR. BRACEY: Okay.

SPEAKER: I do like the -- looking at the word "efficient" though, I think we do need to address and -- up, I guess, to go up, tracing that it needs to be a timely tracing, you know, it's not --

DR. BRACEY: Okay.

SPEAKER: Yeah, I like that.

DR. BRACEY: Efficient.

SPEAKER: Could we specifically state "timely" because that has been a varied source effect on the Hepatitis C issue --

DR. BRACEY: Efficient and timely

SPEAKER: Yes.

SPEAKER: Timely and --

SPEAKER: Timely and efficiently trace.

DR. BRACEY: Okay. So then we move down to the next level. Well, okay -- okay, "There is a need for new approaches to emerging infectious disease monitoring, including informatic tools and evidence-based research."

SPEAKER: Well, but that doesn’t answer the question.

DR. BRACEY: That doesn’t answer the question.

SPEAKER: I think that we started at one, saying "Recipient outcome surveillance," and I think what we really want to do is --

DR. BRACEY: Would we develop informatic tools --

SPEAKER: I think that might be better.

DR. BRACEY: -- to aid surveillance.

SPEAKER: Would informatic include --

SPEAKER: Yeah, but may be start the sentence there, there is a need --

DR. BRACEY: Yeah, start the sentence, yeah, so you go back -- delete all the way to "develop."

SPEAKER: Do what?

DR. BRACEY: Just delete all the way to develop.

SPEAKER: No, the other way.

SPEAKER: Delete that or delete from there?

SPEAKER: No, no.

SPEAKER: No, before "develop."

DR. BRACEY: Okay, delete. So "develop informatic tools and evidence based research to" -- what’s the wording, to aid surveillance or --

SPEAKER: To support.

SPEAKER: To support.

SPEAKER: To support surveillance and evidence based research.

SPEAKER: Yes

SPEAKER: All right.

SPEAKER: Well, support surveillance process improvement too.

SPEAKER: Say that again.

SPEAKER: And research, I don’t even know if you need the words "evidence based."

SPEAKER: It's --

DR. BRACEY: That’s kind of a good buzz word.

SPEAKER: -- buzz word now-a-days.

SPEAKER: Well, I know, but the issue here is that we don’t have a lot of evidence on a lot of these emerging pathogens, so --

SPEAKER: But I would -- I'd like to say, I would like to throw out to the committee that may be to support surveillance, process improvement and evidence based research.

SPEAKER: Yeah, it's good point. Okay, all

right, so o -- should it be to or develop. Just develop informatics, okay.

SPEAKER: Right.

Then number three.

SPEAKER: (inaudible) include other strategic plan elements such as --

SPEAKER: Right.

DR. BRACEY: Include --

SPEAKER: You rather like lower case P there, including other strategic plan elements such as --

SPEAKER: And is that where we get into risk-benefit.?

DR. BRACEY: You’re right, we need to get into there.

SPEAKER: Okay, I don’t know that we need the words, which can be developed at subsequent meetings. It's really the department's call there.

SPEAKER: Yeah.

SPEAKER: Commonality.

DR. BRACEY: Now, we need risk benefits. That’s -- as in number four.

SPEAKER: It's up to you guys.

DR. BRACEY: Let's go back, let's go back.

SPEAKER: I mean, because I think the areas of commonality.

SPEAKER: That’s risk-benefit is common to all of them.

SPEAKER: That has to be considered in commonality.

DR. BRACEY: Can we go to the top of three then. So we’re talking about the scope -- "Scope of recipient outcome surveillance: Identify all donors using common identification numbers linked to biological products that are uniquely identified to compel a process of adverse event reporting for tissue, organ, and blood therapy through appropriate mechanisms to designated public health authorities and to recipients and donors; timely and efficiently trace all biologic products to the clinical user, recipient, and donor; recognize transmissible events resulting in adverse outcomes including the three sub-bullets - build communication network to disseminate data to users. Two, develop informatic tools to support surveillance process improvement and evidence based research. Three, include other strategic plan

developments such as donor recruitment, donor screening, research coordination, emergency preparedness," and then we still have an adverse --

SPEAKER: Well, I guess my question is wouldn’t it be the first thing that as part of the strategy, the risk benefit analysis is -- conducted risk-benefit analysis on various areas, and then -- because that overrides, does it not.

DR. BRACEY: Yeah, okay.

MS. FINLEY: Well, except we don’t have evidence for a lot of the risks here, and what I want to stay away from is the same kind of risk benefits, because we didn’t have the information that led us to this committee and where we were in the '90s. So there's a great deal of sensitivity over that concept in this community. So I think may be you could flush that out a little bit, so that we are clear about what you’re referring to, development of evidence in this area.

SPEAKER: May be go back to one and say, add to one saying, "enough evidence to support," where we say -- where is it?

SPEAKER: Go to number one or --

SPEAKER: I would do that as a --

SPEAKER: Okay, never mind.

DR. BRACEY: Well, I mean, really, this is the scope of what the plan is.

MS. FINLEY: I think it looks good now.

DR. BRACEY: I mean, I don’t think we’re missing anything.

SPEAKER: Looking at kind of risk benefit analysis, because as you --

MS. FINLEY: Exactly, but it's the way that its worded, that -- historically, that has some concerns. I beg your pardon.

DR. BRACEY: Right, but we left it unsaid.

SPEAKER: We didn’t -- we didn’t put it in there.

DR. BRACEY: We didn’t put it in.

MS. FINLEY: We didn’t put mandatory in?

SPEAKER: So should we put it under 1(b), compel process of mandatory events.

MS. FINLEY: Yeah, I'd like that. Mandatory adverse event.

DR. BRACEY: Well, what we were thinking of is

we didn’t have -- really have any enforcement capability.

MS. FINLEY: Well, except that its really the department's call as to whether they want to do that. I mean, there are ways that they can compel --

SPEAKER: You mentioned through joint commission, but you’re right, that’s not in our scope to propose that I guess, or do you want to propose.

SPEAKER: Can we propose it, I mean --

SPEAKER: We could propose it, yes?

SPEAKER: I mean, it can be proposed to be examined, I mean, that’s what we’re doing.

MS. FINLEY: Right, that’s my point.

SPEAKER: We -- we have -- I mean, not trying to minimize, but we’re making proposal to be examined.

SPEAKER: But remember that the point we have in here is that you’re making something mandatory, you have to have the capability of investigating each one of them. And I think right now it's more important to capture the things than to worry about making mandatory.

MS. FINLEY: Well, I think the concept of mandatory versus voluntary is a concept that we should -- we've been asked to comment on. It's not our

responsibility to find a way to enforce this. That's Dr. Agwunobi's.

Ours is to make recommendations only. He's asked us to comment on this; the issue of mandatory versus voluntary is on the table. If we want to be silent about it, that's fine, but we need to make –-

SPEAKER: Right.

SPEAKER: –- a decision.

SPEAKER: Now, what is the Committee's sense in terms of a "mandatory," versus a "voluntary," –-

SPEAKER: I think I'd like it to see it say. "Recommend a process of mandatory, adverse event-reporting."

SPEAKER: I think that's fine.

DR. BRACEY: Are there any "nays"? Motion?

SPEAKER: Motion.

DR. BRACEY: Second?

SPEAKER: Second.

DR. BRACEY: All in favor?

SPEAKERS: Aye.

DR. BRACEY: So, Okay, all right. So to compel a process of mandatory –-

SPEAKER: Recommend –-

SPEAKER: Recommend a process.

DR. LOPEZ-PLAZA: Of “Mandatory adverse event reporting,” to the Department –-

SPEAKER: Yeah.

SPEAKER: Okay.

DR. LOPEZ-PLAZA: Or “Mandatory process for –-

SPEAKER: There you go, of course.

DR. LOPEZ-PLAZA: “Recommend a process for –-

SPEAKER: –- process for.

SPEAKER: “4.”

SPEAKER: All right.

DR. LOPEZ-PLAZA: It would be “Recommend a mandatory process for adverse event reporting.”

SPEAKER: Okay.

SPEAKER: Excuse me, do you want the Assistant Secretary to -- are you asking the Assistant Secretary to recommend a process, or are you asking the Secretary to create or establish a process?

SPEAKER: Yeah, that’s a good point.

SPEAKER: I think that’s to recommend the above.

SPEAKER: The “recommend” –-

SPEAKER: Are we recommending this task.

SPEAKER: We're recommending it.

SPEAKER: Right.

SPEAKER: My amendment was for "Mandatory Adverse Event Reporting," not a "Mandatory Process."

SPEAKER: That's right.

SPEAKER: "Recommend a process for mandatory adverse" –- that's what we voted on.

SPEAKER: Recommend a process, okay.

SPEAKER: (inaudible) okay.

SPEAKER: No, but the issues we recommend –-

SPEAKER: Yeah, this is the master strategy, right –- you don't, we're all –-

SPEAKER: Everything here is a recommendation.

DR. BRACEY: Yeah, just start with, "A process."

SPEAKER: A process.

SPEAKER: No.

SPEAKER: No, stop it.

(Laughter)

SPEAKER: We'll be here all night.

DR. BRACEY: Okay, let's –- can we go back to the top then? Okay. So what should the scope be? "The

scope would be to identify this then a process for mandatory adverse," yeah, "event reporting of tissue, for tissue, organs, and blood therapy through appropriate mechanisms to designated public health authorities, and to recipients and donors."

SPEAKER: Yeah.

SPEAKER: Not "meriting," and donors?

SPEAKER: Ms. Benzinger.

MS. BENZINGER: I would suggest that you also included down here at the bottom of it, an education of your –- that was one thing that we had back here, was, getting the surgeons and everybody on the same track –-

SPEAKER: Okay.

MS. BENZINGER: So if you're going to –- is an "education" a continuing education process?

SPEAKER: Isn't that part of "E" –-

SPEAKER: Wouldn't that be a part of –-

SPEAKER: –- "Communication"?

SPEAKER: Yeah, actually in a broader sense, yeah, because communication would incorporate education. Could.

MS. BENZINGER: Could, but doesn't. If we're

going to, if we were looking for a master strategy, that strategy should include that the hospital personnel know that there is a mandatory continued education for these people to keep them up-to-date on what is required.

SPEAKER: Actually for most Federal agencies within the Department of HHS, if they issue a regulation or anything that becomes mandatory, they are almost always going to implement an educational guidance and process with that.

SPEAKER: So why don't we say, instead of, "Mandatory," "implement a continuing education process."?

SPEAKER: If I could just make a suggestion –- if we went up to "E" and just put, "Build communication and education." If you want to say "continuing education," that's fine, but that is the, that is one of the roles of some of the organizations that testified --

SPEAKER: Yeah, okay.

SPEAKER: –- and that's what they're really very good at.

SPEAKER: So it will be "communication and education."

SPEAKER: On number?

SPEAKER: That's "E."

SPEAKER: Under "E."

SPEAKER: No, on top.

SPEAKER: 1-E.

SPEAKER: 1-E.

SPEAKER: What's this, "Build communication ––

SPEAKER: Top of the screen ––

SPEAKER: "Network and educational."

SPEAKER: "Communication and education network."

SPEAKER: Do you want to say, "support," since we recognize that they're already there, next to that "build"?

SPEAKER: Well, we don't think there's a communication network there.

SPEAKER: Yeah. It was just ––

SPEAKER: And if you want to use, "and support an educational network," that's fine with me.

SPEAKER: Okay.

SPEAKER: I'm still concerned about the "mandatory process," because something happened when we wrote the words and I had to run out the ––

SPEAKER: You want to go back?

SPEAKER: Yes, please.

SPEAKER: Can we go back? Okay.

SPEAKER: I thought we were trying to have "mandatory reporting of an adverse event process," okay. In other words, the process is within the facility. And such as Dr. Sandler said, if you tell me the process, then it gives me the opportunity to edit what I don't need to say. I think we've changed the meaning here.

SPEAKER: Okay. In what sense, I mean we want "adverse event reporting," all the way down to the "donors of appropriate," so --

SPEAKER: I think we want a mandatory process, a mandatory reporting of a continuing education process.

SPEAKER: If I could just make a suggestion. If we went up to E and just put "build communication and education," if you want to say "continuing education," that's fine. But that is one of the roles of some of the organizations that testified.

SPEAKER: Yeah, okay.

SPEAKER: And that's what they're really very good at. So --

SPEAKER: So it would be "communication and

education”.

SPEAKER: I don’t know what --

SPEAKER: That’s E.

SPEAKER: Under E.

SPEAKER: E. No, on the top.

SPEAKER: 1E.

SPEAKER: 1E.

SPEAKER: Where it says “build communication” --

SPEAKER: Top of the screen.

SPEAKER: Oh.

SPEAKER: “Network and educational” --

SPEAKER: “Communication and education network”.

SPEAKER: Do we want to say “support” since we recognize that they’re already there, instead of “build”?

SPEAKER: Well, we don’t think there is a communication network there.

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SPEAKER: Okay, in what sense? I mean we want adverse event reporting all the way down to the donors, if appropriate. So --

SPEAKER: I think we want a mandatory process, a mandatory reporting of a -- help me out here.

SPEAKER: You’re saying a mandatory adverse event reporting process?

SPEAKER: I tell you --

SPEAKER: System.

SPEAKER: -- why don’t you start with “mandatory” and that’s the end of it. Mandatory adverse reporting -- event reporting for tissue and, you know, I --

SPEAKER: Yeah, right. Yeah, right.

SPEAKER: So if you just start it --

SPEAKER: -- process to do it. I mean --

SPEAKER: Add “mandatory adverse event reporting,” would that solve it?

SPEAKER: Say that again.

SPEAKER: Just start -- write where it is right now.

SPEAKER: “Mandatory,” yeah, right there.

SPEAKER: Yeah.

SPEAKER: Okay.

SPEAKER: So that’s “mandatory adverse event reporting for tissue, organ, and blood” --

SPEAKER: And then you’ll develop your own process to be able to comply with that.

SPEAKER: There still has to be a process there. I mean I don’t -- I think that what you’re trying -- you’re doing there is that any -- we’re going to have to scope our --

SPEAKER: “Process”.

SPEAKER: -- adverse event.

SPEAKER: Thank you. You read my mind.

SPEAKER: Okay, so “mandatory events reporting

process” --

SPEAKER: Fine.

SPEAKER: -- does that -- okay.

SPEAKER: Okay.

SPEAKER: All right.

SPEAKER: Something was rich.

SPEAKER: Okay.

SPEAKER: That --

SPEAKER: All right, let’s take it from the top then.

SPEAKER: Again?

SPEAKER: No, so --

(Laughter)

SPEAKER: -- outcome surveillance. We have the identification piece. We have the mandatory adverse event reporting, timely and efficient tracing. Next.

SPEAKER: Hold on.

SPEAKER: Yeah, we’re settled on “recognized transmissible,” and then, “E, build communication networks, develop informatic tools, include other strategic plans”. Yeah.

SPEAKER: And number 3. You said “include other

strategic plans as elements as needed, such as” because you’re going to be able to add or subtract from that. I mean right now you’re identifying those four areas, but there might be other areas that you want too.

SPEAKER: That’s a good point. Okay, all right. Is --

SPEAKER: I move to approve.

SPEAKER: Is there a motion?

SPEAKER: Yeah.

SPEAKER: There’s a motion. A second? Okay, all in favor?

SPEAKERS: Aye.

SPEAKER: Against? All right, it passes. Let’s go on now to the next level.

SPEAKER: Hold that thought.

SPEAKER: The next question is what are the, oh, yeah, areas of commonality with blood products, progenitive cells, bone marrow, tissue, and organs. This was pretty much something that was fairly non-controversial.

SPEAKER: Motion to accept.

SPEAKER: Second?

SPEAKER: Second.

SPEAKER: Yes.

SPEAKER: I also -- this is where I just say we've answered the question and I agree with that and will support that. But I also think the unstated is what also needs to be evaluated are what the differences are.

SPEAKER: Good point. Here --

SPEAKER: I know that's the question and we can --

SPEAKER: So here's to what risk-benefit analysis, you know --

SPEAKER: Okay.

SPEAKER: Well, I'm not sure. I just --

SPEAKER: -- that term, okay.

SPEAKER: Can't change the question.

SPEAKER: No, you can't change the question.

SPEAKER: Sorry.

SPEAKER: No. What I'm just saying is at the end --

SPEAKER: No, I think you can change the question. You can add that -- those two words.

SPEAKER: Well --

SPEAKER: Well, but I don’t think we have time or we’ve heard about the commonality.

SPEAKER: So then as you go down --

SPEAKER: And then really at the end it’s -- but we also need to evaluate --

SPEAKER: No, just make a statement at the end that there are differences, recognize differences.

SPEAKER: -- in addition to these areas in common, we also need to evaluate the differences.

SPEAKER: The differences, okay. That’s fair. So in addition to these commonalities, we need to evaluate the differences, okay. Okay, all right, so moving --

SPEAKER: We need -- there is a need. The --

SPEAKER: Oh, yeah, comment from the floor. Sorry.

SPEAKER: Allie (off mic) of AABB. What is 11J, “surveillance of product quality”? What is that?

SPEAKER: It looks like (off mic).

SPEAKER: To assess whether or not there’s good manufacturing -- yeah, (inaudible).

SPEAKER: Practices.

SPEAKER: Practices.

SPEAKER: Practices.

SPEAKER: Practices?

SPEAKER: Yeah.

SPEAKER: GMP, sort of --

SPEAKER: GMP.

SPEAKER: Why can’t you just say “GMP” versus “surveillance of product quality”?

SPEAKER: Yeah, just put “GMP,” right.

SPEAKER: And get rid of --

SPEAKER: No, get rid of “surveillance”.

SPEAKER: Just “GMP”.

SPEAKER: Just -- what is that?

SPEAKER: Good Manufacturing Practices.

SPEAKER: I think that was the question you had.

SPEAKER: Could we put “GMP/GTP”?

SPEAKER: Absolutely.

SPEAKER: Yeah, that’s right.

SPEAKER: -- isn’t there a different one for --

SPEAKER: Yeah, right.

SPEAKER: GTP?

SPEAKER: Right.

SPEAKER: Good Tissue --

SPEAKERS: Good Tissue Practices.

SPEAKER: Good Tissue Practices. All right, okay, so --

SPEAKER: With that then I will -- I move that this be approved.

SPEAKER: Is there a second?

SPEAKER: Second.

SPEAKER: All in favor?

SPEAKERS: Aye.

SPEAKER: Opposed? All right, it passes. Let's move on to the next one then.

SPEAKER: Number 5, how best should this be done with the stakeholders? How do we begin? So we talked about "develop a forum for" -- you know, that's, you know, for development. How about "develop a forum for evaluation of common priorities"?

SPEAKER: Okay.

SPEAKER: "Deliberating"?

SPEAKER: Or "deliberating," yeah.

SPEAKER: May I suggest removing the "evidence-based decision making"? We don't have evidence. We've already said that in the first section.

SPEAKER: On the -- okay.

SPEAKER: And that is a term of some weight here.

SPEAKER: -- “Common priorities”.

SPEAKER: “For deliberation of common priorities”?

SPEAKER: Priorities.

SPEAKER: So would --

SPEAKER: And just take out “using evidence-based decision making”. If we don’t have the evidence, we can’t base decisions on it. And for a lot of these things, we don’t have it.

SPEAKER: And I guess -- that last sentence about the overlap, is that necessary?

SPEAKER: No.

SPEAKER: Not necessary.

SPEAKER: I’d also change the word “recipient” to “consumers”. It’s the more appropriate term.

SPEAKER: Okay, then scratch the last two sentences.

SPEAKER: The --

SPEAKER: Oh, (inaudible).

SPEAKER: If we have HRSA, the comparable thing would be FDA or at least CBER.

SPEAKER: Yeah.

SPEAKER: Oh, we were going to scratch the reference to all of the specifics. Is that fair?

SPEAKER: Yeah.

SPEAKER: Do you want to say “considerable regulatory overlap”?

SPEAKER: Well, the --

SPEAKER: Well, and this was -- before we answer that, if I can say forums are great, but there’s got to be somebody who’s ultimately responsible and takes charge.

SPEAKER: I’ll do that.

SPEAKER: How about “HHS should convene a forum”?

SPEAKER: Oh.

SPEAKER: “HHS should convene a forum”?

SPEAKER: How about this? So “HHS should convene a forum”.

SPEAKER: -- want me to scratch that?

SPEAKER: Scratch that.

SPEAKER: You want those two sentences to --

SPEAKER: Yes.

SPEAKER: Yeah, go ahead.

SPEAKER: -- and then just put “HHS” at the top.

SPEAKER: Just take out “develop”.

SPEAKER: Yeah, “HHS should convene a forum for deliberating common priorities”.

SPEAKER: “And streamlining regulatory overlap”?

SPEAKER: No, they’re ultimately responsible. Let them sort that out.

SPEAKER: And then we’ll just have “stakeholders” there.

SPEAKER: Okay --

SPEAKER: Yeah, Mr. DUBLIN.

MR. DUBLIN: Just a slight suggestion. I agree (off mic) Finley switching to consumers. But we’ve always used consumer/end users because there has been -- sometimes consumers are seen as medical people. So if we say consumer/end users --

SPEAKER: Yeah.

SPEAKER: -- you know, I was putting it in there arm.

SPEAKER: If that’s okay.

SPEAKER: That’s okay with me. Committee?

SPEAKER: Good.

SPEAKER: That’s fine.

SPEAKER: Okay, “end users”.

SPEAKER: Thank you, Mr. Chairman.

SPEAKER: Actually, I think earlier in the document we do say “recipients”.

SPEAKER: Recipients and donors.

SPEAKER: Yeah.

SPEAKER: Okay, but --

SPEAKER: Our --

SPEAKER: Marie changed it to “consumers”.

SPEAKER: I think consumers -- it’s not just recipients because there are consumers who are ultimately going to receive this as recipients, but they are not going to have received it at that point.

SPEAKER: That would also incorporate the hospitals as well.

SPEAKER: Right, and hospitals’ organ --

SPEAKER: And if you add “end users”, you’re certainly getting who puts it in their arm.

SPEAKER: Right, okay.

SPEAKER: Okay.

SPEAKER: All right, “HHS should convene a forum for” -- yeah, “for deliberating common priorities.

Stakeholders should include regulators, accrediting agencies, manufacturers, clinicians, consumers, and end users." Sound fair?

SPEAKER: Yeah.

SPEAKER: Now these efforts need to be public-private partnerships with transparent collaboration and data sharing. But the task of biovigilance is inherently a public health mission and government-based origin. That doesn't sound right. And structure of the system should reflect that premise.

SPEAKER: I think those two senses are diametrically opposed. It's mandating public-private partnerships which I do not think is the responsibility and authority of this committee. We can say we're cognizant of existing public-private efforts. But we cannot mandate that the department use them as opposed to, you know, rulemaking or anything else. That's really a decision for Dr. Agwunobi and the secretary.

SPEAKER: But isn't that all captured within the second clause of the first paragraph?

SPEAKER: Oh, right.

SPEAKER: No, I think the first statement, these

efforts need to be is mandatory. And that's --

SPEAKER: No, what I'm saying is I don't know if we need the second paragraph.

SPEAKER: Yeah, I agree --

SPEAKER: Because we have -- the stakeholders should include, and it says, consumers, end users, clinicians, manufacturers.

SPEAKER: Yeah, that's fine with me.

SPEAKER: Yeah, that's fine.

SPEAKER: (Off mic.)

SPEAKER: Yeah, because the two are diametrically opposed. That is true.

SPEAKER: Well, regulators are public health agencies.

SPEAKER: No, I was talking about in the bottom one says public -- the government does it all and the other says you need to have the private side.

SPEAKER: No, but what Ann Marie is saying --

SPEAKER: No --

SPEAKER: Let's get rid of that.

SPEAKER: Yeah.

SPEAKER: Get rid of the bottom paragraph?

SPEAKER: Get rid of it.

SPEAKER: Right, but what also I thought I heard Ann Marie say is that maybe with public health agencies, we don't need the regulators.

SPEAKER: Yeah, I mean I'm not going to, you know --

SPEAKER: Yeah, you're right, yeah.

SPEAKER: -- go to town on that one. But I thought it was redundant.

SPEAKER: A little more positive turn.

SPEAKER: Right.

SPEAKER: Okay, "HHS should convene a forum for deliberating common priorities. Stakeholders should include public health agencies, accrediting agencies, manufacturers, clinicians, consumers, and end users."

SPEAKER: Is there a need for HHS to take ownership of the issue or is that implicit?

SPEAKER: I think they're --

SPEAKER: Or you could say "convene and direct".

SPEAKER: Well, I mean "convene", I think that that's fine. But I guess the question is -- it's obviously within statutory purview, but are we meaning to say to the

secretary that the department needs to take ownership of this?

SPEAKER: Well, but then we can’t --

SPEAKER: Because all we’ve said is that the secretary just needs to get a group of people to talk.

SPEAKER: Yes, I --

SPEAKER: Yeah, but I guess the only thing I’m thinking is we become a bit prescriptive. Why not leave it up to the government to decide what works best?

SPEAKER: No, but I think what we’re trying to say is that the secretary needs to take ownership of deciding by convening.

SPEAKER: So it’s not a private sector --

SPEAKER: No, it’s -- but it’s -- it should be having private and just the same stakeholders, but that the secretary is -- needs to take ownership of this issue and not just get people together. We’re the ones who are kind of convening and doing that.

SPEAKER: I sense that Dr. Sandler is going to get us out of this.

DR. SANDLER: Well, I think that this is the whole center of what we’re doing here, this point that someone’s

got to take charge. And I think we're saying it should be the office of the assistant secretary. And where I find that belonging is not buried down in Question 6, but if I understand the document that was distributed, I'm holding it up here, Art.

DR. BRACEY: Yes.

DR. SANDLER: This is our document. Is that right?

DR. BRACEY: That's right.

DR. SANDLER: Okay, then the third paragraph, I'll read how weak it is. "Formation of an HHS and PHS biovigilance task force would be an important step for identification of vigilance data." It should participate. There's no teeth in there. And it seems to me we want to say something like that this committee recommends the formation as an important step and so on and so forth. And then at that point, we could put in the point that's being made which is the secretary should take charge or whatever language we want to use. It seems to me that that paragraph is where we want to make the point that's being made, not bury it.

DR. BRACEY: Yeah, but the -- but we want -- this

is --

DR. SANDLER: The preamble, is that correct?

DR. BRACEY: This is a done deal.

SPEAKER: Okay, but --

DR. SANDLER: It's a done deal?

DR. BRACEY: Yeah, this is from '06.

DR. SANDLER: Oh, this is from '06.

DR. BRACEY: Yeah, this --

SPEAKER: And this one has '06 as a basis.

DR. SANDLER: Okay, that's what my question was, okay.

SPEAKER: Okay. Can I make one other suggestion? It was -- you just inserted ACBSA (phonetic), we are not taking charge of this forum, it's the secretary.

DR. SANDLER: Yeah, that was my intent.

SPEAKER: Right, no, but that was just inserted. We did not agree on that.

DR. BRACEY: "The HHS should convene a forum for deliberating common priorities. Stakeholders should include" -- so the issue is whether we should state explicitly the direction.

SPEAKER: Right.

SPEAKER: What about the FACA rules?

DR. BRACEY: It needs to be stronger. I'm hearing the committee members, Ms. Benzinger, Dr. Pierce. "Should convene and" --

SPEAKER: I don't like the word --

SPEAKER: I'm actually --

SPEAKER: -- we know it's a priority.

SPEAKER: I'm fine with the way that is.

DR. BRACEY: The way this is?

SPEAKER: Yeah. If I could take the liberty, I need to go, but for number 6, I think there should be some level of accountability. So in terms of resources needed, I think it's not just funding, but it's designated individuals or departments.

DR. BRACEY: Okay.

SPEAKER: How about this? How about "HHS should be responsible for developing and implementing a master strategy and shall convene a forum."?

SPEAKER: Okay, that's fine.

DR. BRACEY: Okay.

SPEAKER: That sounds good.

DR. BRACEY: Okay.

SPEAKER: And then could we strike out the "deliberating common priorities"? I mean we know this is a priority.

DR. BRACEY: Yeah, we can -- yeah, right, because -- yeah, right.

SPEAKER: Yeah, "a forum for stakeholders". That's fine.

DR. BRACEY: Right, okay.

SPEAKER: "Responsible for implementing the strategic" --

SPEAKER: "Implementing the master strategy".

SPEAKER: "A master strategy".

DR. BRACEY: "And convening a forum for deliberating" --

SPEAKER: No, no.

DR. BRACEY: No, no, we got rid of that.

SPEAKER: "And convening a forum of stakeholders" --

DR. BRACEY: "To include".

SPEAKER: -- "to include" --

SPEAKER: A forum what?

SPEAKER: "Of stakeholders".

SPEAKER: “For stakeholders”.

SPEAKER: “Of” and then go to “stakeholders”.

DR. BRACEY: So this is fine with you, Dr. Pierce?

DR. PIERCE: Except for the point number 6.

SPEAKER: “To include”.

DR. BRACEY: So point number 6, you’re looking for --

SPEAKER: I think there needs to be some level of designation of personnel. It’s not just a question of costs, it’s increased appropriations. It is that agencies need to develop plans for specific departments to have responsibility for this. For instance, at the CDC, there is already surveillance mechanisms in place. Those are the ones that need to be amplified.

DR. BRACEY: Okay.

SPEAKER: What -- and that fallout from number 5, HHS does implement a master strategy.

DR. BRACEY: That -- right.

SPEAKER: I mean that --

DR. BRACEY: Because the master strategy would include having the resources to get it right.

SPEAKER: Yeah.

SPEAKER: I mean --

SPEAKER: Yeah.

SPEAKER: Yeah.

SPEAKER: That would be incumbent upon the department to identify responsible agencies, parties, funding, the whole nine yards.

DR. BRACEY: Right, and so then we could just say “increase appropriations, if needed”.

SPEAKER: Okay -- no, I’m sorry. You cannot use the word “appropriations”. That’s a very specific legislative term.

DR. BRACEY: Right.

SPEAKER: You can say “seek increased resources”, what we are recommending as a committee to the secretary. Appropriations come from the Congress.

DR. BRACEY: Okay.

SPEAKER: We can direct the secretary to seek appropriate funding for -- to accomplish the master strategy and the stakeholders’ meeting. But we don’t have the authority to compel the Congress to do that, even if we’re right.

SPEAKER: And to the point, and I don’t mean to be

derogatory towards the secretary, I think it's an unfair question. I don't think in two days -- we know what resources --

SPEAKER: Oh, we --

SPEAKER: -- completely mean and what are the estimated costs. I mean --

DR. BRACEY: Oh, I have no idea.

SPEAKER: Exactly. So -- I mean that's kind of the answer. We have no idea. That we need to figure out.

SPEAKER: But could we say up there "implementing a master strategy with appropriate resources"?

DR. BRACEY: And then leave it at that.

SPEAKER: Right.

DR. BRACEY: And then "see number 5".

SPEAKER: Right.

SPEAKER: Yes.

SPEAKER: Yeah.

SPEAKER: But with appropriate resources, period.

SPEAKER: And then start, you know, the convening of a forum -- maybe another sentence.

SPEAKER: No, I think you were saying "with appropriate resources" goes after the word "strategy" in the

second line.

SPEAKER: Right.

SPEAKER: What is appropriate --

SPEAKER: -- is appropriate resources.

SPEAKER: Right.

SPEAKER: “HHS should also convene a forum”.

SPEAKER: Period.

DR. BRACEY: “Should convene a forum for” -- “of stakeholders”. Yeah.

SPEAKER: I hate to bring this up this late in the day. But the way that that reads, it looks as though we should convene the master strategy, then hold the stakeholders’ conference. May I suggest that we just take the stakeholders’ conference sentence and put it in front of “HHS should be responsible for implementing a master strategy with appropriate resources.” And if you want to link the two, you could say, “with appropriate resources based on input from the stakeholders’ conference.”

DR. BRACEY: “Based on input” --

SPEAKER: “From the stakeholders’ conference.”

SPEAKER: Or just “from stakeholders”.

SPEAKER: Okay, that’s fine.

DR. BRACEY: Yeah, “from stakeholders”. Dr. (inaudible).

SPEAKER: Could I suggest we have the word “additional” someplace because what sometimes happens is resources are taken from an existing area and moved into this effort.

SPEAKER: New money.

SPEAKER: The Peter-Paul principle.

SPEAKER: Okay, you’re putting that sentence back, right? You’re going to put it in front, right, the stakeholders’ one?

SPEAKER: You want that whole sentence in front --

SPEAKER: Yeah, we want it -- save that.

SPEAKER: Oops.

SPEAKER: Go to Edit.

SPEAKER: The only problem is --

DR. BRACEY: “Stakeholders” encompasses everybody.

SPEAKER: The only --

SPEAKER: Right, but we asked for a stakeholders’ conference.

DR. BRACEY: Okay.

SPEAKER: And we didn’t take that out. I’m just

saying that --

DR. BRACEY: Just to identify who the stakeholders --

SPEAKER: That should really -- because we said what should be done with the stakeholders. We have to answer that question first. Put the second sentence that you're restoring first and then put "HHS should be responsible", you know, second.

SPEAKER: Yeah, that's --

SPEAKER: Right there, yeah.

SPEAKER: Yeah, and then you've linked the two with that additional phrase you just included.

DR. BRACEY: All right, so move the sentence?

SPEAKER: Yeah, just move the second sentence to be first.

DR. BRACEY: Just switch the order. All right, so "HHS should convene a forum of stakeholders to include public health agencies, accrediting agencies, manufacturers, clinicians, consumers, end users. HHS should be responsible for implementing a master strategy with appropriate resources based on input from stakeholders."

SPEAKER: Good.

SPEAKER: Wasn’t there an additional --

SPEAKER: No, but you were saying --

DR. BRACEY: Additional.

SPEAKER: Well, what we’re saying as a suggestion that it’s really HHS should be asking for additional resources. The only way to do that is to go through the appropriations process.

SPEAKER: Right, but the secretary has to ask for that.

SPEAKER: Right.

SPEAKER: So we can’t -- I mean what we’ve done is make the recommendation appropriate to what our authority is here. We can’t mandate that appropriations come from the Congress.

DR. BRACEY: Yeah, so what -- we just get rid of “additional” then. Does -- I mean does that really --

SPEAKER: No, I mean I think we -- I could live with --

SPEAKER: I mean I understand the folks who are within the agency wanting that. I completely understand and agree. But unless we are going to say that HHS, during the budgetary process, must ask for more resources on this, it’s

meaningless.

SPEAKER: I don’t think we can build the case on that at this point.

DR. BRACEY: Right. Okay, so is there a motion?

SPEAKER: Yeah --

SPEAKER: I move.

DR. BRACEY: Second --

SPEAKER: Second.

DR. BRACEY: Okay, all in favor then?

SPEAKERS: Aye.

DR. BRACEY: Nay? No nays. Now under number 6, should we just simply say “defer to number 5”?

SPEAKER: Yes.

SPEAKER: Yes.

SPEAKER: Yes.

DR. BRACEY: Yeah.

SPEAKER: So moved.

DR. BRACEY: Okay, second?

(Laughter)

DR. BRACEY: All right. No, defer or refer. People, which one, refer or defer?

SPEAKER: We can’t --

SPEAKER: See.

DR. BRACEY: See.

SPEAKER: See number 5.

SPEAKER: See number 5.

SPEAKER: We do have a quorum, I take it.

SPEAKER: We had a -- we really can’t vote on number 6.

SPEAKER: We had all the way through number 5. But we had number 5. Okay.

(Whereupon, the PROCEEDINGS, were adjourned)

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