U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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THIRTY-SEVENTH MEETING OF THE ADVISORY

COMMITTEE ON BLOOD SAFETY AND AVAILABILITY

(ACBSA)

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FRIDAY,

NOVEMBER 20, 2009

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The Advisory Committee convened, at 8:30 a.m., in the Potomac and Rockville Rooms at the Universities at Shady Grove, located at 9630 Gudelsky Drive, Rockville, Maryland, Arthur W. Bracey, Chair, presiding.

CHAIR PRESENT:

ARTHUR W. BRACEY, M.D.

PUBLIC (VOTING) MEMBERS PRESENT:

JOHN H. ARNOLD, M.D.
ANN MARIE BENZINGER
CHARLES E. HALEY, M.D., M.S.

PETER KOUIDES, M.D.
ILEANA LOPEZ-PLAZA, M.D.
GREGORY J. POMPER, M.D.
RAVINDRA SARODE, M.D.

REPRESENTATIVE (VOTING) MEMBERS PRESENT:

DARRELL J. TRIULZI, M.D., American Association of Blood Banks (AABB)
FREDERICK B. AXELROD, M.D., America's Blood Centers (ABC)

JULIE A. BIRKOFER, Plasma Protein Therapeutics Association (PPTA)

KLAUS NETHER, The Joint Commission

MICHAEL G. ISON, M.D., M.S., United Network for Organ Sharing (UNOS)

LAURENCE CORASH, M.D., Manufacturer

NON-VOTING EX OFFICIO MEMBERS PRESENT:

CAPT MATTHEW J. KUEHNERT, M.D., FACP, U.S. Public Health Service (USPHS), Centers for Disease Control & Prevention (CDC)

ALAN E. WILLIAMS, Ph.D. (filling in for JAY S. EPSTEIN, M.D.), Food and Drug Administration (FDA)

CDR MONIQUE HOLLIS-PERRY, M.D., Department of Defense (DoD)

LCDR LAURA ST. MARTIN, M.D., M.P.H., USPHS, FDA

JIM BOWMAN, M.D., M.S.M, FACS, Health Resources and Services Administration (HRSA)

EXECUTIVE SECRETARY PRESENT:

JERRY A. HOLMBERG, Ph.D.

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Adjourn

1 P-R-O-C-E-E-D-I-N-G-S
2 8:32 a.m.
3 CHAIR BRACEY: (presiding) Good
4 morning and welcome for the second day of our
5 meeting.
6 We have a number of presenters to
7 hear today. We also have a recommendation
8 that we need to set forth.
9 What we will do is change the
10 schedule slightly. We were scheduled for a
11 break at 10:30. In order that our
12 deliberations or discussion following the
13 presentations can be more complete, we are
14 moving the discussion of the presentation of
15 Donna Woods up ahead of that. So, in other
16 words, prior to having the discussion, we will
17 hear the presentation of Dr. Woods at 9:30.
18 So, with that, let's take the roll
19 call.
20 Oh, and we have this nifty limit
21 timer here. In the interest of making sure
22 that the proceedings move at a reasonable

pace, I will signal when we are over the limit because we do have several members that have some need to exit, not too early, but a little bit before 5:00.

DR. HOLMBERG: Thank you, Mr. Chairman.

Before I start with the roll call, just several housekeeping announcements.

If you do need to have a taxi or shuttle at a special time, please make sure that you contact Ms. Renee Wilson, and she will make sure that those arrangements have been made.

Hopefully, all of you received multiple emails during the night. I think that some of the information that had been requested earlier in the day got to you, hopefully, before you got back to your hotel, and it was also beneficial in your deliberation.

Dr. Bracey?

CHAIR BRACEY: Present.

1 DR. HOLMBERG: Dr. Arnold?
2 MEMBER ARNOLD: Present.
3 DR. HOLMBERG: Ms. Benzinger?
4 MEMBER BENZINGER: Present.
5 DR. HOLMBERG: Ms. Finley is
6 absent.
7 Dr. Haley?
8 MEMBER HALEY: Present.
9 DR. HOLMBERG: Dr. James is
10 absent.
11 Dr. Kouides?
12 (No response.)
13 Dr. Lopez?
14 MEMBER LOPEZ-PLAZA: Present.
15 DR. HOLMBERG: Dr. Pierce is
16 absent.
17 Dr. Pomper?
18 MEMBER POMPER: Present.
19 DR. HOLMBERG: Dr. Sarode?
20 MEMBER SARODE: Present.
21 DR. HOLMBERG: Dr. Shander is
22 absent.

1 Ms. Wade is absent.
2 Dr. Yomtovian is absent.
3 Dr. Triulzi?
4 MEMBER TRIULZI: Present.
5 DR. HOLMBERG: Dr. Axelrod?
6 MEMBER AXELROD: Present.
7 DR. HOLMBERG: Ms. Birkofer?
8 MEMBER BIRKOFER: Present.
9 DR. HOLMBERG: Mr. Nether?
10 MEMBER NETHER: Present.
11 DR. HOLMBERG: Dr. Ison?
12 MEMBER ISON: Present.
13 DR. HOLMBERG: And Dr. Corash?
14 MEMBER CORASH: Present.
15 DR. HOLMBERG: Thank you.
16 I think we have the same as we did
17 yesterday. We have 13 voting members present.
18 CHAIR BRACEY: Excellent.
19 For the first presentation today
20 -- yes?
21 DR. HOLMBERG: I do need to read
22 the --

1 CHAIR BRACEY: Okay, sorry.
2 DR. HOLMBERG: As a formality, and
3 also for those that are making presentations,
4 and also anybody that might speak during the
5 open public forum, I do want to read the
6 conflict-of-interest for the record.
7 "The Department of Health and
8 Human Services is convening the November 19th
9 and 20th, 2009, meeting of the Advisory
10 Committee on Blood Safety and Availability
11 under the authority of the Federal Advisory
12 Committee Act (FACA) of 1972. With the
13 exception of the industry representative, all
14 participants of the Committee are special
15 government employees or regular federal
16 employees. Federal employees of various
17 operating divisions of the Department are
18 subject to the federal conflict-of-interest
19 laws and regulations. The federal employees
20 are non-voting members of the Committee.
21 "The Secretary is responsible,
22 under Section 301, 351, 361 of the Public

1 Health Service Act, as amended, and various
2 provisions of the Federal Food, Drug, and
3 Cosmetic Act, for issuing and enforcing
4 regulations concerning the collection,
5 preparation, and distribution of blood, blood
6 products, human tissues, and human organs for
7 issuing and enforcing regulations related to
8 the transmission of communicable diseases and
9 for carrying out research in health fields,
10 including diseases involving in these
11 products.
12 "The Advisory Committee on Blood
13 Safety and Availability shall advise, assist,
14 consult with, and make policy recommendations
15 to the Secretary and the Assistant Secretary
16 for Health regarding these broad
17 responsibilities.
18 "The Department has determined
19 that all members of the Advisory Committee are
20 in compliance with the Federal ethics and
21 conflict-of-interest laws."
22 We would like to remind members

1 and participants that, if there is a personal
2 or financial interest in a topic being
3 discussed, the conflict-of-interest should be
4 disclosed.
5 Thank you.
6 CHAIR BRACEY: Thank you.
7 Our first presentation will be
8 from Dr. Robert Metzger. He will present
9 donor risk assessment and recipient status.
10 Dr. Metzger is the Medical Director of Florida
11 Hospital Transplant Center.
12 Dr. Metzer?
13 DR. METZGER: Thank you, Dr.
14 Bracey.
15 I am also here as the Medical
16 Director of the United Network for Organ
17 Sharing, or UNOS. And just for a little bit
18 more information, I am also the Medical
19 Director of an OPO, TransLife, that covers 10
20 counties in east central Florida, and the
21 Medical Director of a tissue bank in east
22 central Florida. So I have broad experience

1 in transplantation over the past 40 years.
2 I have not been a candidate or
3 recipient on the waiting list, but I am happy
4 to know that you do have such a person on your
5 Committee, which makes this even more
6 important.
7 I am here to look at risk
8 assessment as we use it in terms of developing
9 OPTN policy. Dr. Holmberg specifically asked
10 if we would use our experience that we have
11 had in the past year in looking at this
12 through our donor screening testing for HTLV-I
13 and II. So I have opted to present it in that
14 way.
15 Policy at the OPTN is driven
16 largely by what is on this slide, in that
17 there is an ever-increasing demand,
18 illustrated by the over 100,000 patients
19 currently on the waiting list, with an
20 inadequate supply, with somewhere around 27-
21 28,000 organ transplants per year, about
22 20,000 of those from deceased donors.

1 But this number right here is one
2 that is very disappointing, and that is the
3 8,000 to 9,000 patients on the waiting list
4 who are dying without having the opportunity
5 for that life-saving transplant. So, whenever
6 we address policy, we have to look at
7 balancing patient safety issues versus those
8 of organ availability for the life-saving
9 organs for those patients on the waiting list.
10 Typical policy development works
11 this way: recommendations can come to the
12 OPTN from the OPTN leadership, from national
13 committees, the regions that meet regularly,
14 three or four times a year, or government
15 entities who are in association with the OPTN,
16 such as HRSA, sometimes CDC and CMS.
17 Once the policy is presented, then
18 it is assigned to one of the national
19 committees to discuss and formulate the
20 policy, and research staff is provided to
21 provide the relevant data analysis. The
22 policy, then, is sent out for public comment.

1 Not all policies have to go out for public
2 comment, but those of substantive issues or
3 those affecting allocation must go out for
4 public comment. This is usually a 45-day
5 period, similar to what is done in government
6 policy.
7 Then the national committees must
8 respond to the public comment, and the staff
9 updates the public comment briefing paper.
10 Then the committee presents this to the Board
11 for a vote on the policy.
12 The OPTN tries to develop policy
13 on a consensus basis, not on a dictorial
14 policy. So I would like to develop a
15 consensus within the membership for
16 implementation of policies.
17 Then the Secretary must approve
18 policies that would be enforceable under
19 Social Security, and there aren't very many of
20 those.
21 Well, HTLV-I and II donor testing
22 became an issue this year. OPTN policy

1 mandated prospective screening for HTLV-I and
2 II in 1989, when it wasn't clear that this
3 retrovirus was any different than the HIV
4 virus. Fortunately, that hasn't turned out to
5 be the case.
6 There are currently three FDA-
7 approved screening tests that could be used,
8 the HTLV enzyme immunoassay. However,
9 unfortunately, this is going to be
10 discontinued in the next month. This is the
11 test used by 56 out of the 58 OPOs, and it is
12 a test readily available for single sample
13 testing that we use in the OPOs.
14 There's the Abbott PRISM. That is
15 a high throughput running 160 samples per run,
16 and much more expensive and not readily
17 available, and not timely available on a 24/7
18 basis that we needed it for donor evaluation.
19 And then the bioMerieux, which is
20 FDA-approved, but not available in the United
21 States.
22 In the past, it had been

1 recommended that HTLV-I/II-positive donors not
2 be used for transplantation. However, as the
3 understanding of these viruses evolved, it
4 then was made an option for transplant centers
5 to use these organs at their discretion.
6 However, they were rarely used, and current
7 testing may lead to a significant loss of safe
8 organs.
9 So, at the beginning of the year,
10 we found out that this test was going away.
11 So the OPTN then asked the DTAC, that Dr. Ison
12 will report on, Disease Transmission Advisory
13 Committee, to look at the policy for HTLV and
14 develop any changes that might be needed. A
15 memo went out to the members letting them know
16 that we were doing this because there was
17 considerable angst in the OPO community that
18 they would be out of compliance with OPTN
19 regulations if something weren't done.
20 DTAC then developed an HTLV Donor
21 Screen Advisory Group that was chaired by Dr.
22 Dan Kaul, who is a transplant/infectious

1 doctor at the University of Michigan. It had
2 membership from OPOs, the tissue bank people,
3 transplant surgeons, OPO lab directors, some
4 representatives of commercial laboratories in
5 the country, other infectious disease things,
6 UNOS staff. Then there were also
7 representatives from CDC, HRSA, and the FDA,
8 who were ex officio but consulting with the
9 group.
10 The group was then asked to
11 develop and answer three critical questions:
12 should HTLV testing continue to be required
13 for all donors, and what's the balance between
14 organ loss versus organ safety, to assess the
15 potential impact of not having HTLV serology
16 data available at the time of donation? Will
17 there be a change in outcomes? What are
18 diseases associated with transmission, and how
19 frequently do they occur? And then to advise
20 about alternative testing platforms or
21 approaches to address the loss of the HTLV-I
22 and II testing that is happening this year.

1 So the work group then met in
2 March and April to develop a response to this
3 that, then, the Chair presented to the DTAC,
4 first, at a live meeting on May 6th and then
5 in a follow-up teleconference, and presented
6 some of the following data:
7 They analyzed HTLV-associated
8 disease. This virus is endemic in the
9 Caribbean and parts of Africa, Asia,
10 Australia, and New Zealand. In a large amount
11 of patients who have this virus it is
12 asymptomatic, but in about 3 to 6 percent
13 there is associated disease. About 80 percent
14 of those individuals have an adult T cell
15 leukemia/lymphoma, and the other 20 percent,
16 the HTLV-related myelopathy or tropical
17 spastic paraparesis. For the large part, it
18 remains asymptomatic.
19 The testing does not distinguish
20 between HTLV-I and II, and the HTLV-II,
21 actually, is more common and endemic in the
22 American Indian population and is more common

1 in IV drug users, but it is not clear whether
2 there is any significant disease associated
3 with it.
4 So we did have some data, the
5 prevalence of test-positive potential donors.
6 There were seven OPO labs who did HTLV
7 screening and found the screen positive in 150
8 of little over 14,000 potential donors, for a
9 prevalence of a little over 1 percent.
10 Three labs, with 11,000 potential
11 donors, did subsequent confirmatory testing
12 and found 56 of the 11,000, for 0.5 percent of
13 that population. Then one lab went on to do
14 confirmatory testing between I and II, and
15 there was one positive donor out of a little
16 over 3400, although not all of these were
17 tested, for a prevalence of 0.3 percent in
18 this donor population.
19 So we then looked at the UNOS
20 database, and since 1999, there had been 162
21 organs transplanted from HTLV-I and II-
22 positive donors. In reviewing the data, there

1 were no transmissions of malignancy. However,
2 there wasn't any data on neurologic disease.
3 And when you looked at these
4 donors, the average number of organs
5 transplanted per donor in the United States is
6 around three organs per donor, and for the
7 HTLV-positive donors it was only one. So that
8 even though some of these were used, most of
9 the organs were not used in these donors.
10 So, if you look at 8,000 donors we
11 have per year, then doing this screening test,
12 you would find about 83 positive screening
13 tests, and you wouldn't know whether these
14 were false-positive or HTLV-I or II. And of
15 these, you might get two confirmatory positive
16 tests for HTLV-I.
17 If you look at the estimated
18 number of organs lost, this would be 45 to 65
19 donors, or 135 to 195 organs lost per year
20 from false-positive screen or HTLV-II
21 infection, and another 32 organs not used from
22 16 recovered donors, for a total of somewhere

1 around 160 to 230 organs that would be lost
2 that were safe organs, throwing out donors who
3 tested positive with the screen test.
4 There is one fairly well-
5 documented transmission in Spain in 2003,
6 where one donor transmitted disease to three
7 recipients that developed over the following
8 two years the HTLV-I myelopathy. There are a
9 few other published articles and data on 177
10 recipients, and only four had documented
11 HTLV-I myelopathy and none with associated
12 disease. But there is a relative lack of data
13 on this.
14 So the options then available that
15 the group presented was to use the Abbott
16 PRISM assay, but this was rapidly ruled out
17 because the test system is optimized for a
18 high volume. There weren't labs available at
19 all OPOs that would do this on a 24/7 basis
20 with a six- to ten-hour turnaround time that
21 we need in order to run the match runs. So
22 this didn't seem likely.

1 The research-use-only assays are
2 not allowed for clinical use. So that wasn't
3 an option.
4 The PRISM is also quite expensive.
5 As you can see, the platform costs $850,000,
6 and using the reagents which are set up to run
7 160 tests, it is quite expensive. And an OPO
8 doing 100 to 200 donors a year, obviously,
9 couldn't afford that.
10 So the other possibility was to do
11 retrospective testing. This would allow for
12 labs, for the OPOs, to send samples to labs to
13 get testing retrospectively. The results,
14 then, could be communicated to transplant
15 centers and subsequently to the recipients,
16 and allowed for centers to monitor the
17 recipients with positive results.
18 And the benefits would be
19 continued screening and informing patients and
20 monitoring them perhaps more closely for
21 disease, although our transplant recipients
22 tend to get monitored fairly closely anyway.

1 There are a lot of challenges with
2 this. Not the most important, but there are
3 significant problems with collecting and
4 storing appropriate samples for primary and
5 confirmatory testing, for determining which
6 donors have HTLV-I versus HTLV-II infections.
7 So it would be optimal to do confirmatory
8 testing, and all confirmatory tests are
9 research-use-only assays, even the one used by
10 the CDC, I am told.
11 So informing patients of results
12 is also of concern at the transplant center
13 because the natural history of HTLV infections
14 is not clearly known in this setting, and
15 there is no proven therapy for these HTLV-I's.
16 So, if you tell a potential recipient that
17 you've got this virus, we don't know what is
18 going to happen, and they go to bed every
19 night worrying about it, it is also of some
20 concern to the transplant centers.
21 And there are legal ramifications
22 of disease associated with infection,

1 transmission, and the resources are not
2 available right now for collecting and
3 analyzing the data.
4 So the other option, then, is to
5 discontinue HTLV donor screening. There was
6 significant support for discontinuing
7 screening of all donors based on the presented
8 data by the group.
9 The low incidence in the donor
10 pool, the assay can't differentiate between
11 the two, the significant false-positive rate,
12 loss of donors, and few documented clinically-
13 meaningful transmissions, and there's
14 significant concerns, though, that the quality
15 of the available data is limited. Few labs
16 have done confirmatory testing, and there may
17 be variability in the incidents. The risk
18 factors of donors with HTLV-I infection
19 haven't been defined, and is the low incidence
20 of disease transmissions secondary to lack of
21 screening of recipients or recognition of
22 disease, and how many screened positive donors

1 had HTLV-I to transmit? So the impact of not
2 testing is also unclear.
3 So the DTAC presented this to the
4 OPTN/UNOS Board of Directors in June of this
5 year. The Board, after a very long
6 discussion, much longer than anybody
7 anticipated, and I'm sure Dr. Ison didn't
8 anticipate that long period in front of the
9 Board, resolved that the OPTN discontinue the
10 requirement of prospective HTLV testing for
11 deceased donors, effective pending notice to
12 the members.
13 And then, it further resolved that
14 retrospective testing with confirmation shall
15 be performed in all deceased donors and
16 implementation should be delayed to permit a
17 minimum 45-day public comment period and
18 review by the Executive Committee, and there
19 shall be a two-year window for retrospective
20 testing.
21 This resolution kind of confused
22 things down the road, in my opinion. It did

1 say that the Executive Committee was going to
2 make the final decision. This was because the
3 Board didn't meet, and it only meets twice a
4 year, and it wasn't going to meet again in
5 time to have a policy that would go into
6 effect and keep the OPOs compliant by the end
7 of the year.
8 The DTAC also recommended, then,
9 after this, that retrospective testing was the
10 way they would like to see it go with the
11 accumulation of data to look at this. So what
12 went out as a policy proposal -- and this is
13 always kind of confusing, too; it goes out
14 into the public policy into the regions, and
15 they just strike out the HTLV-I and II and
16 then the policy on retrospective testing.
17 And this went out to public
18 comment through August and September of 2009,
19 as you can see on the slide. The public
20 comment, although a little bit confusing, was
21 pretty unanimous in the regions and the
22 committees in the concern that this is

1 research study and not under the purview of
2 the OPTN, that we aren't funded for this; the
3 policy would cause unnecessary anxiety in
4 recipients, and it would waste good organs
5 with false-positive or HTLV-II-positive tests.
6 That it would increase deaths on the waitlist,
7 and that a two-year study would encounter only
8 two to four true positive HTLV-I donors, and
9 if the tests really weren't currently
10 required, we probably wouldn't even be
11 considering adding this test to our repertoire
12 at this point in time.
13 So the DTAC, then, presented the
14 results of the public comment to the Executive
15 Committee on December 23rd of this year (sic),
16 and the Executive Committee then voted to
17 eliminate HTLV testing and to not to do
18 retrospective testing in the future.
19 In conclusion, then, the policy
20 change does conform to our efforts to follow
21 the OPTN final rule, in that ultimately it was
22 based on sound medical judgment; it seeked to

1 achieve the best use of donated organs. It
2 was designed to avoid wasting of organs, to
3 avoid futile transplants, to promote patient
4 access to transplantation, to promote the
5 efficient management of organ replacement, and
6 to consider patient safety issues.
7 And thank you, and I will take any
8 questions.
9 CHAIR BRACEY: Thank you.
10 We will open up for Committee
11 comments or questions.
12 Dr. Trilulzi?
13 MEMBER TRIULZI: Thank you, Dr.
14 Metzger.
15 Just a clarification question:
16 the 1 percent prevalence that was reported, is
17 that in organ donors whose history screen was
18 completely negative? Or did that include all
19 comers?
20 DR. METZGER: That included all
21 comers as potential donors. So there wasn't
22 any exclusionary criteria, except the general

1 exclusionary criteria.

2 MEMBER TRIULZI: So I guess what I

3 am getting at is you may have an IV drug user

4 in whom you use organs. Is that included in

5 that prevalence rate?

6 DR. METZGER: It would have been,

7 yes. It would have been any potential donor.

8 MEMBER TRIULZI: So, if you looked

9 at the positives that you had, the small

10 number, could they have been excluded through

11 donor screening as opposed to testing? And if

12 you did have a donor who had a history of IV

13 drug use, you still wouldn't test such a

14 donor, or a donor who came from endemic area?

15 DR. METZGER: I think, for a

16 number of the tests, Dr. Triulzi, we would

17 probably do some donor profiling. I know I

18 come from Florida. So we are in an area that

19 has a fair population from the Caribbean. So

20 we are looking at doing some type of testing

21 on profile patients, as we do with Chagas.

22 MEMBER TRIULZI: Yes, so selected

1 testing?

2 DR. METZGER: On those tests, on

3 the OPOs that reported there, it is hard to

4 know. We don't necessarily rule out IV drug

5 use in a donor. So those patients could be

6 used for life-saving transplants, especially

7 for heart, liver, and lung transplants.

8 MEMBER TRIULZI: Because this

9 statement that because it is low prevalence in

10 the organ donors as a blanket statement is

11 probably not the same, it won't be the same if

12 you look at IV drug users --

13 DR. METZGER: Right.

14 MEMBER TRIULZI: -- or donors from

15 endemic areas. So a variation may be that, if

16 there is a risk factor for HTLV identified,

17 then you would want to test that.

18 DR. METZGER: And I think that

19 that is one of the studies I think that we

20 would like to perhaps get some resources for.

21 There are a couple of areas in the country

22 where there might be a higher prevalence of

1 this, ours being one of them. And I am
2 thinking of putting together -- there are four
3 OPOs in Florida. Hopefully, with Dr. Ison's
4 help and some resources from somewhere, to get
5 the four OPOs to do a study on testing in our
6 donor population in Florida.
7 CHAIR BRACEY: We have a question
8 from Dr. Williams, but may I ask a question of
9 Dr. Williams?
10 One of the issues that was
11 addressed was the availability of assays that
12 are research-use-only. There are some
13 diagnostic tests that are used and labeled as
14 such. In other words, because the assay is
15 labeled "research-use-only" doesn't mean that
16 it is a meaningless assay.
17 But would you comment on that?
18 MEMBER WILLIAMS: Yes, on that
19 particular question, I think, you know, the
20 answer is to discuss the situation with the
21 agency because I think in all cases the agency
22 will want to do the right thing as far as

1 available tests. So I think there are no
2 hard-and-fast rules that would necessarily
3 govern that in the shortage of an available
4 test.
5 My question is related, and that
6 is, and we probably all know the answer, but
7 would this screening policy have come under
8 review at all, had the availability of the
9 tests been a real problem? In other words, is
10 this a situation where lack of a suitable
11 screening test has, in fact, changed the
12 standard for donor screening?
13 DR. METZGER: I think I would have
14 to answer that in the affirmative at this
15 point in time because that is what brought it
16 to the forefront.
17 And also, for another reason, in
18 that whenever we have to change our IT
19 processes at the OPTN, especially related to
20 allocation, it is very expensive. So we don't
21 do it unless we really have to.
22 So I think it did come to the

1 forefront because the test is going away.
2 CHAIR BRACEY: Question from Dr.
3 Holmberg?
4 DR. HOLMBERG: Yes, thank you very
5 much. I appreciate you using this as a case
6 example of your process.
7 Yesterday, when we were discussing
8 the gap, the white paper and the gaps, one of
9 the gaps that was identified by the organ
10 people within HRSA was that there is no sample
11 retention.
12 Is there any plan to make sure
13 that there are samples on the deceased donor
14 that could be reviewed later, if something
15 happened in the recipient?
16 DR. METZGER: It is kind of
17 standard policy for OPOs to keep samples
18 around for seven years. So, actually, we do
19 have samples on most of our donors.
20 Unfortunately, we don't always have adequate
21 samples because, when that donor hits the ER,
22 everybody is fighting for the blood sample,

1 the ME, us, and sometimes there just isn't
2 enough sample left on a specific donor to
3 save. But we do keep samples in our OPO for
4 seven years. So there are samples of the
5 donors.
6 From the recipient's standpoint,
7 that is not as likely. There may be samples
8 of recipients at transplant centers, but not
9 necessarily.
10 DR. HOLMBERG: But this is not a
11 policy of the OPTN?
12 DR. METZGER: Correct, it is not
13 an OPTN policy.
14 DR. HOLMBERG: Okay, and the other
15 thing is that, now that the OPTN has made this
16 change, and I know that we are going to be
17 having some more discussion on informed
18 consent, but is this now part of the informed
19 consent process?
20 DR. METZGER: We don't dictate
21 specifically what has to be in the informed
22 consent at the transplant center. We do have

1 broad policies that say that the individual
2 has to be informed of the Public Health
3 Service/CDC risk and should be informed of
4 other increased risk, and should be informed
5 specifically of what that Public Health
6 Service increased risk is at the time that the
7 organ is offered to the recipient.
8 Transplant centers usually will
9 approach that in two ways. When they do the
10 initial evaluation of the recipient, they will
11 discuss with them the broad spectrum of organ
12 donors and organs that might become available
13 to them. Then a second informed consent is
14 usually obtained and asked for at the time of
15 the donation with the specifics of that
16 specific organ.
17 At the Board meeting in this past
18 week, this was reiterated by the Executive
19 Committee, that the transplant center should
20 specifically identify to the recipient what
21 the high-risk factors are.
22 Regarding Dr. Williams -- or the

1 other thing that would be nice to see would be
2 an easy-to-run test that confirms HTLV-I. So
3 it would be nice if the industry could proceed
4 with developing a test such as that in the
5 future that would be available in a timely
6 manner for OPOs to use.
7 CHAIR BRACEY: Additional
8 comments? Dr. Ison?
9 MEMBER ISON: So just a
10 clarification about the research-use-only
11 assays: so that was something that, actually,
12 we did engage FDA in a discussion and,
13 basically, it was suggested that it may not be
14 a legal option to use that.
15 Further, when we approached the
16 different research-use-only companies, there
17 were several of the larger testing labs that
18 actually were willing to run the RUO test in
19 parallel with the approved test, to see what
20 the test characteristics. And one of those
21 RUO companies refused to send those to the lab
22 for research because they realized that it

1 would potentially lead to this unintended use
2 of the RUO for that indication.
3 And then, I think the other thing
4 that really this highlights is, as the Chair
5 of the Committee, we felt relatively strongly
6 that retrospective testing was an important
7 thing to do because, if you look at the
8 transplant community's approach to date, it
9 has been relatively risk-averse for this
10 pathogen, as evidenced by the very low
11 utilization. It is estimated that about 10
12 percent of the HTLV-I/II-positive organs are
13 used by the transplant community currently
14 with the testing in place.
15 I think part of that was
16 education. When we educated the community,
17 literally, every regional meeting where we
18 presented this, everyone's kind of lightbulb
19 went on, saying that maybe there is a lesser
20 risk in certain patients, so that it might be
21 okay to use this.
22 But the thought process behind the

1 retrospective testing is we actually don't
2 have good answers to know what are the markers
3 that may be also positive in patients with
4 HTLV-I testing. What is the relative risk in
5 IV drug abusers, certain populations? And
6 particularly because in the United States we
7 have mixed populations, we have people that
8 are half-Japanese/half-American, is that risk
9 passed on? What is the degree of that risk?
10 So, really, the goal of that
11 retrospective testing was to get this
12 information. Personally, I don't think it was
13 a research project. It was a change in the
14 community standard, but I think the transplant
15 community felt that it was a research project.
16 The Committee actually had, DTAC,
17 actually, in its final deliberations looking
18 at the public comment, the feedback that we
19 had gotten, really came on the stance that the
20 reality is, if we knew that this was something
21 that was fundable as a research project and
22 there was actually a mechanism to do that,

1 that would have been our preference.

2 Because the main pushback that

3 people were giving was related to, what do you

4 do with the information when you have a

5 positive test? Because the policy with the

6 retrospective testing would have required

7 determining whether it was HTLV-I versus

8 HTLV-II, which would have potentially informed

9 that degree of informed consent for the

10 recipient.

11 But, really, there is no standard

12 as to whether you need to monitor viral loads.

13 There is no therapy for these patients. And

14 really, it would be waiting for some disease

15 to develop in that individual.

16 So, if it were done in a research

17 project, there are actually ways that you

18 could actually design the study such that

19 information could be disclosed in a more

20 controlled way, and patients upfront would

21 recognize that they were part of that study.

22 But it was felt, since there is

1 not a mechanism currently to fund such
2 research, we couldn't recommend that since it
3 really wasn't a viable option at this point.
4 CHAIR BRACEY: Dr. Holmberg?
5 DR. HOLMBERG: Just another
6 question that really refers to the
7 presentation from Mr. Graham yesterday, since
8 you do represent the UNOS.
9 We heard that there was a
10 scientific research arm under contract with
11 the OPTN. Was there any thought of expanding
12 some of the capabilities of this research arm
13 to collect data?
14 It sounds like the data that are
15 collected are primarily availability, matching
16 the availability aspects and not the safety
17 aspects.
18 DR. METZGER: The research arm
19 that you talked about, Scientific Registry for
20 Transplant Recipients, is a separate contract
21 under HRSA, not under the OPTN. They are two
22 separate contracts.

1 UNOS used to have the contract for
2 the scientific research, but it was given to
3 another organization, which is now Arbor
4 Research.
5 Data collection in the OPTN is a
6 sore point. Actually, five years ago, the
7 Societies, the American Society of Transplant
8 Surgeons, the American Society of
9 Transplantation, very vocally and
10 energetically objected to all of the data
11 elements and went through all the data
12 elements that we collect in the OPTN very
13 scrupulously, and presented to us the high
14 cost of all the data elements that we collect.
15 We actually removed a lot of unnecessary
16 elements.
17 So, whenever we are asked to
18 collect more data, it becomes a broad
19 transplant-wide issue that the Societies ask
20 us very vehemently to justify. So whether we
21 will be able to collect this data will depend
22 on the resources that we have available. I

1 think, as you were told yesterday, the budget
2 for the OPTN comes primarily from the
3 registration fees of the recipients and not
4 from funding from the federal government.
5 That amount has been held at about $2 million.
6 It may increase to $3 million in the coming
7 year, hopefully, and maybe a little bit more
8 in the future. But, right now, it is not
9 available.
10 CHAIR BRACEY: Dr. Triulzi?
11 MEMBER TRIULZI: I would say that
12 I am personally uncomfortable with the
13 response to not having an approved assay being
14 to drop the test.
15 Michael mentioned that the
16 alternative assays which are not FDA-licensed
17 for that application, but are for research-
18 only has, quote, "legal" -- you said the word
19 "legal" -- issues. Is there a process for
20 variance that the FDA recognizes that there's
21 a clinical need? And has that been pursued as
22 an alternative to dropping the test?

1 I mean I think, when we are going
2 to be using IV drug users as organ donors or
3 people from endemic areas and not to do the
4 test, that doesn't seem like an appropriate
5 response to me.
6 DR. METZGER: Well, I understand
7 your concern. The test isn't available on a
8 timely basis right now. We were told that
9 these research-use-only tests that are
10 available can't be used clinically by
11 regulation. So the laboratories are unwilling
12 to allow this to happen. I don't know whether
13 there's any way around this at all at this
14 point in time and whether those laboratories
15 would be able to supply the necessary process
16 to the 58 OPOs that require it.
17 CHAIR BRACEY: Dr. Williams?
18 MEMBER WILLIAMS: As far as
19 timing, has the screening now stopped or --
20 DR. METZGER: The screening we
21 will probably see sometime towards the end of
22 the year; that is when Abbott is retiring the

1 platform and the providing of reagents for the
2 test. Some of the OPOs have tried to stock up
3 on the reagents.
4 But, also, you know, in looking at
5 it in this analysis, we are throwing out a lot
6 of good organs based on this screening test.
7 So people are dying in excess of those that
8 would be impacted. That is one the things
9 that it is important to consider when you are
10 a candidate on that waitlist, and it is one of
11 the things that has to be decided by that
12 transplant surgeon at three o'clock in the
13 morning when he gets the call on a specific
14 donor.
15 CHAIR BRACEY: Mr. Brubaker, a
16 comment?
17 MR. BRUBAKER: Yes, if I could
18 make a comment. There's an AOPO standard that
19 requires that, if any archived sample remains
20 from a donor whose organs were successfully
21 transplanted, that you must, you shall, retain
22 serum or plasma sample or some other tissue

1 type for 10 years.

2 I know that was created -- we have

3 a very similar standard in AATB standards for

4 tissue donors. Those two standards were

5 created at the same time back in the early

6 1990s, after the first HIV case was realized,

7 and there was no sample that was retained, and

8 only tissue was tested to determine that that

9 donor was, you know, five years later when it

10 was realized, was actually HIV-positive.

11 So I know not every OPO is

12 accredited by AOPO, but most of them are, and

13 there is that standard. And, of course, then,

14 there's the mirrored one with AATB as well.

15 CHAIR BRACEY: To stay on time,

16 maybe we will have the last question, kindly,

17 from Dr. Kuehnert.

18 MEMBER KUEHNERT: I just thank you

19 for the presentation. I just want to ask Dr.

20 Metzger about -- maybe I missed the slide, but

21 how many people are dying because HTLV is

22 being tested for? Has that analysis been

1 done?

2 DR. METZGER: Only that we would

3 expect that there are probably somewhere

4 around 160 to 200-some organs that are

5 discarded that are probably safe.

6 MEMBER KUEHNERT: So how does that

7 translate to a death? Because this statement

8 is made often, that people are dying. Then

9 the data are that the organs are discarded.

10 So I am just wondering, is there a

11 conversion factor of organs discarded to

12 deaths?

13 DR. METZGER: No, not that I am

14 aware of, although one could anticipate that

15 usually 40 percent of the organs recovered are

16 those of the life-saving organs. So you could

17 extrapolate it that way.

18 MEMBER ISON: I think to kind of

19 go along those lines, if you go back to that

20 one slide that showed which organs are being

21 used, actually, hearts and lungs, for which

22 the link between death on the waiting list is

1 highest, actually had the lowest utilization
2 of those organs.
3 CHAIR BRACEY: We need to move on,
4 then, to the next speaker.
5 Thank you, Dr. Metzger.
6 The next speaker is Dr. Scott
7 Halpern. Dr. Halpern is from the Division of
8 Pulmonary and Critical Care Medicine at the
9 Center of Epidemiology and Biostatistics at
10 the University of Pennsylvania Medical School.
11 He will present on balancing the availability
12 with risk, how to keep organs and tissues safe
13 and recipients aware.
14 Dr. Halpern?
15 DR. HALPERN: Okay. I would like
16 to thank Dr. Holmberg and the rest of the
17 Committee for inviting me to participate
18 today.
19 When I am not taking care of
20 patients and donors in the ICU, I spend a lot
21 of my time thinking about conceptual
22 frameworks for considering tensions that

1 underlie tradeoffs that often have to be made
2 between the interests of individuals and the
3 interests of groups. Also, I do some
4 empirical work in the area.
5 My goal today is to try to provide
6 a conceptual framework for how we can think
7 about the organ supply risk as an element of
8 benefit, and what that conceptualization and
9 the principles that follow from it mean for
10 what we ought to be doing about informed
11 consent for recipients.
12 Here's my disclosure slide.
13 And I would like to make four
14 central points, the last of which isn't
15 showing up, but that is okay.
16 The first central point that I
17 would like to make today is that scarcity of
18 public goods, such as organs, leads
19 inescapably to what Guido Calabresi, a former
20 Dean of Yale Law School, described as "tragic
21 choices" in a book by the same title in 1977.
22 I will describe a little more what I mean by

1 these tragic choices and why they are tragic.
2 But the core element is,
3 inevitably, some people will be harmed in our
4 effort to promote the greater good. These
5 choices, because of their tragic nature, need
6 to have four properties in the ways in which
7 that they are made.
8 They need to be made
9 transparently, equitably, efficiently, and
10 accountably. And I will describe in a bit
11 more detail what I mean by each of these four
12 elements.
13 I would like to make the further
14 point that considerations of risks and
15 benefits to all recipients are inextricably
16 linked and inherently uncertain, and that
17 because of all of these three foregoing
18 points, a nationally-standardized process of
19 prospective consent best promotes patient
20 autonomy without unduly sacrificing safety.
21 So it is due to the scarcity in
22 the organ supplies, I think Dr. Metzger made

1 very clear in his prior presentation, that we
2 don't bar donors with non-standard risk
3 profiles from contributing to the organ supply
4 in the same way that we do bar them from, in
5 general, contributing to the blood supply. It
6 is because scarcity is a far more salient
7 feature of the organ supply than in the blood
8 supply, at least presently.
9 Indeed, over the years, we have
10 noticed that we have allowed increasingly more
11 donors with non-standard risk profiles, both
12 those formerly called CDC high risk or
13 increased risk for harboring transmittable
14 infections, expanded criteria donors, and
15 donors after circulatory determination of
16 death.
17 These are data from our local OPO
18 in Region II, where we now have roughly half
19 of our organs coming from a, quote/unquote,
20 "non-standard donor".
21 And it is given such scarcity that
22 we need to make choices than inevitably pit

1 the interests of the individual organ
2 recipient against the interests of all
3 potential organ recipients. These are
4 difficult or tragic choices, indeed.
5 And if we are going to do this,
6 these are the four principles that I think we
7 need to adhere to.
8 So the first is transparency. We
9 need to make these decisions transparently
10 because they inevitably impact on the well-
11 being of the patients we are trying to help.
12 So, if we do it covertly, we are not allowing
13 them their proper right to deliberate on the
14 mechanisms by which we make these principles.
15 Indeed, it is not simply this
16 normative propriety, but actually being
17 transparent, there's a fair bit of evidence,
18 would also promote the goals we are trying to
19 accommodate. So we learned in the 2004 flu
20 pandemic in the United States, and the UK has
21 learned over the years with the adoption of
22 the National Institute for Clinical

1 Excellence, that when the need to make tough
2 choices is made clear to people, they tend to
3 go along with it and tend to accept it. But
4 when those choices are made covertly, that is
5 when a lot of pushback occurs.
6 The second principle is
7 efficiency. This should be pretty
8 straightforward for most of the members of
9 this audience. The basic gist here is that
10 the way we allocate our organs ought to
11 minimize waste, minimize delays to the extent
12 possible.
13 Third is equity, which is that, in
14 the pursuit of allocating organs, we ought not
15 create discriminatory systems that prevent
16 certain patient groups that have morally
17 similar claims on resources from accessing
18 those resources less frequently than other
19 patient groups with morally similar claims.
20 And then finally is
21 accountability. That the decisions we make to
22 allocate these resources ought to be done in

1 ways that, when it becomes evident that we are
2 not achieving the goals that they were set out
3 to achieve, there are processes in place,
4 mechanisms, for adjudication.
5 So, given these principles, a key
6 and often overlooked element of transparency
7 of organ transplantation is the need to be
8 crystal clear about what our overall goals
9 are. I think these goals reflect, but are not
10 identical to, the goals or the spirit at least
11 of the final rule.
12 So the first goal we might
13 entertain is that we want to maximize the
14 number of lives saved.
15 The second is that we want to
16 maximize the number of life-years gained or,
17 even better, quality-adjusted life-years
18 gained.
19 And the third is that, as we are
20 pursuing both goals one and two, we want to
21 avoid inequities based on morally-irrelevant
22 patient characteristics. Gender, race,

1 morally-irrelevant characteristics. We are
2 not talking about survival probabilities here.
3 Okay?
4 So, as long as decisions are made
5 transparently and with patients' consent, you
6 might imagine two policies that look something
7 like this. So policy one uses only standard
8 organs. And let's say, for argument's sake,
9 that this policy would save 7,000 lives
10 annually and would add 70,000 quality-adjusted
11 life-years to waitlisted patients.
12 Policy two uses organs of low, but
13 variable risk and, thus, saves more lives,
14 10,000, and adds 85,000 quality-adjusted life-
15 years to waitlisted patients.
16 Note that acknowledging that some
17 patients, particularly those that tend to be
18 near the tops of their respective waiting
19 lists, will not derive the exact same benefit
20 as they would have if only standard organs
21 were used.
22 That is why the 10,000 might only

1 yield, say, 85,000 quality-adjusted life-years
2 or, roughly, 8.5 per life saved, as opposed to
3 10 per life saved in the first scenario.
4 These are hypothetical numbers,
5 but I think they relate to a central point
6 that I would like to leave you with today:
7 that policy two has to be preferred. I don't
8 know that there is a morally-justifiable way
9 around that.
10 That because it is a dominant
11 strategy in terms of both the number of lives
12 saved and it is a dominant strategy in terms
13 of the number of quality-adjusted life-years
14 gained, it is to be the preferred strategy,
15 even though there are certain individuals that
16 may not fare quite as well.
17 Okay. We also need to be
18 transparent in how we characterize the organ
19 supply. So the organ supply, in my view, is
20 not a market of intermittently-available goods
21 from which eligible recipients at the top of
22 the list might make selections to promote

1 their well-being.

2 The organ supply is a singular

3 public good that we ought to be distributing

4 so as to maximize public health. It is a good

5 that we take from members of the public and

6 that we use to promote public health.

7 Public health ethics, not

8 individual patient ethics, are the moral

9 underpinning of organ allocation. This

10 doesn't meant that we should ignore informed

11 consent, but the way we are going to

12 adjudicate appropriate informed consent ought

13 to stem from this general conceptualization.

14 So what I thought I would do is

15 walk you through a research program that we

16 just completed at Penn that doesn't relate to

17 safety per se, but, actually, I think gets

18 nicely at the saliency of the intrinsic

19 tradeoffs between benefit for the individual

20 and benefit for the group, and actually tries

21 to get at a point that I think Dr. Kuehnert

22 brought up in his question earlier about how

1 we get at linking or knowing what the effects
2 of a decision at an allocation level or at a
3 testing level relate or link to numbers of
4 deaths on the waiting list, and how we can go
5 about quantifying this. This is a general
6 methodology that I think might be useful for
7 thinking about going forward.
8 So, again, this isn't a safety
9 question. This is sort of a pure efficacy
10 question.
11 All right. So what I am showing
12 you here is two different ways of risk-
13 adjusting, adjusting for confounders for the
14 central dilemma of what we ought to be doing
15 for patients with end-stage COPD who are on
16 the lung transplant waiting list.
17 For a lot of years, we didn't know
18 what the right strategy was, whether we should
19 give them a single lung transplant or a double
20 lung transplant. There are a lot of
21 biologically-driven reasons to favor both and
22 some anecdotally experiences suggesting that

1 double lung transplants did better than single
2 for this patient population.
3 And as you can see, regardless of
4 the methodology used for risk adjustment and
5 confounder adjustment, you would rather be on
6 the blue curve than the red curve. So the
7 blue curve are people who got bilateral lung
8 transplants, and the red curve are people who
9 got single lung transplants. And that
10 regardless of method of adjustment, for the
11 individual, providing two lungs promotes
12 better survival over at least 10 years of
13 followup than does providing one lung. So
14 we're done, right?
15 Well, of course it is not quite
16 that easy because the decision to provide two
17 lungs to a given COPD patient under conditions
18 of scarcity inevitably and inescapably means
19 that there will be fewer lungs available for
20 those on the waiting list.
21 So how can we get about
22 adjudicating this decision from society's

1 perspective?

2 So this is a general schema. I am

3 not going to walk you through this slide. But

4 it is a schema of the Markov model decision

5 process we set up that essentially compares an

6 allocation strategy of double lung transplants

7 for all COPD patients versus single lung

8 transplants for all COPD patients. This is

9 actually one-sixteenth of the Markov model.

10 You can get a flavor for how complex this is.

11 But much more salient for this

12 purpose is to walk you through what some of

13 the inputs are, the processes that you would

14 need to consider to get at the right answer.

15 So we varied the magnitude of the

16 survival advantage for double versus single

17 lung transplant, using as the base case the

18 estimates from that Lancet paper that I showed

19 you a couple of slides earlier.

20 We varied the daily probability of

21 donors becoming available, in recognition that

22 in geographically-heterogenous regions across

1 the country that number is going to vary quite
2 substantially, actually. We wanted our model
3 to be sensitive to those innate and underlying
4 variations across the country.
5 We varied the characteristics of
6 the, quote, "next" patients list. These are
7 to accommodate the fact that the level of
8 illness of the next people on the list is
9 going to impact the propriety of the decision
10 to give two lungs to the first person on the
11 list.
12 Then, finally, we looked at the
13 level of competition, which is not the
14 severity of illness of those on the list, but
15 the number of people on the list. We did that
16 based on an earlier study that we completed
17 that was just published earlier this year
18 showing that across the country, across the 11
19 regions, you can see that when we stratify
20 people by blood group, that certain parts of
21 the country have far greater numbers of people
22 on the list in the average day. This is from

1 2005 through 2008.

2 So you can see that, for example,

3 in the Southwest, if you are blood type O, on

4 the average day there are more than 45 people

5 competing for the same organ as you; whereas,

6 if you are a blood type A/B, it doesn't really

7 matter where you live, there's not a whole lot

8 of competition.

9 So these differences regionally in

10 the level competition have important

11 implications for what the right answer of this

12 full-model output is going to be. These are

13 the types of variations that I think safety

14 analyses also might accommodate.

15 So, just to walk you through

16 quickly the results of our analysis, using

17 base assumptions and a thousand simulated

18 patients, single lung transplant was favored

19 universally, so long as the goal was to

20 maximize the number of transplants, now the

21 corollary to that, of course, being minimizing

22 the number of waitlist deaths.

1 Double lung transplant, by
2 contrast, was favored if the goal was to
3 maximize total life-years gain. Now the exact
4 numbers here are artifacts of the number of
5 patients who choose to run through the
6 analyses. What is relevant is the relative
7 increases on both matrixes for both
8 strategies.
9 So here we seem to have a
10 conflict. One approach favors one goal; the
11 other approach favors the other goal.
12 But when we subject these results
13 to sensitivity analyses where we vary all the
14 assumptions that I told you about earlier,
15 single lung transplant was always favored for
16 maximizing transplants, regardless of the
17 values of the model inputs and actually became
18 increasingly favored for maximizing life-years
19 gains, the second outcome I mentioned. As
20 donor availability fell, waitlisted patients,
21 daily probabilities of death rose as regional
22 competition increased in those red areas of

1 the map I showed you and as the magnitude of
2 the survival advantage fell.
3 So these are the types of
4 considerations that were relevant to this
5 policy decision and led to some general
6 conclusions that the specific goals of
7 resource allocation, whether it is total
8 numbers of life-years gained versus the total
9 number of lives saved, influenced what the
10 right decision is, but that, in general,
11 transplant physicians should consider their
12 current regional circumstances in deciding
13 whether to allocate one or two lungs.
14 This is a paper some of you may be
15 more familiar with by Dr. Schweitzer where
16 they basically used identical methods to
17 compare policy for dialysis patients, whether
18 we should discard organs from donors who met
19 traditional CDC criteria for increased risk
20 versus transplant all of these. This is their
21 Markov model. I won't walk you through this
22 one, either.

1 But what I will say is that what
2 they found in this case is that the interest
3 of society actually overlapped with the
4 interest of individuals under some of their
5 assumptions, not all. The rationale there was
6 that, to the extent that we discard those
7 organs, people on dialysis are on dialysis for
8 longer and, thus, more susceptible to
9 developing hepatitis C through their dialysis.
10 Again, sensitivity analyses are
11 essential there, but it is another example of
12 what I think is a very viable approach to get
13 at some of these questions that we are all
14 struggling with.
15 So what does this all mean for
16 informed consent? Well, I think the first
17 thing is we need a standardized process. We
18 can't have the variability that Dr. Metzger
19 mentioned, and it is a national problem right
20 now.
21 I know before the Chicago case,
22 about two years ago now, we did a survey of

1 our donor service area and found inordinate
2 variability in policies across transplant
3 centers and, indeed, across programs within
4 our own center. We have five transplant
5 programs at Penn. None of the five use the
6 same process for informing their patients of
7 donor characteristics.
8 This is a problem. This is a
9 problem because the way in which we go about
10 informed consent has inevitable consequences
11 for an individual's odds of receiving non-
12 standard organs, and that is inequitable.
13 As just another example, one thing
14 that UNOS had mandated, even before the
15 Chicago case, was that for those on the kidney
16 transplant waiting list, people should make a
17 decision prospectively, at the time of
18 listing, about whether they want to take ECD,
19 expanded criteria donors, or not.
20 But what they found was that the
21 range of people saying that they would take
22 ECD kidneys across donor service areas ranged

1 from 2 percent to 95 percent. Now America is
2 a pretty heterogenous place. We have a lot of
3 different values, but do we really believe
4 that there is that much regional variability
5 in the way people make decisions? Or is it
6 that it is more likely an artifact of
7 differences in the way we are going about
8 doing consent?
9 So the second implication: if we
10 can agree that we need standardization, then
11 we are still left with a problem of how to go
12 about doing it. I think there's two basic
13 models. I am going to walk you through the
14 model that UNOS, with incredibly good
15 intentions, has promoted. I am going to go
16 through what I think are a few flaws in this
17 model.
18 So the model, essentially, is what
19 we can call organ-specific consent, which is
20 the idea that at the time that an organ
21 becomes available, we are going to go through
22 the unique characteristics of the donor from

1 which that organ came and discuss it with the
2 patient, and try to get at an answer about
3 whether the patient wants to accept or reject
4 that specific organ.
5 So the first and biggest problem,
6 by far the biggest problem, is this is not
7 informed consent at all. This doesn't
8 resemble any of the formal goals of an
9 informed consent process, both from a legal
10 perspective, where the standard is disclosure
11 -- this may be disclosure, but disclosure
12 requires understanding. In the heat of the
13 moment, it is very hard to imagine that good
14 understanding could take place over what the
15 exact risks are.
16 And it certainly doesn't heed the
17 goals of informed consent from an ethical
18 perspective, where the goal isn't simply
19 disclosure, but it is actually promotion of
20 autonomy. So how is an individual in the heat
21 of the moment -- an organ has just been
22 offered; there's all sorts of risks flying at

1 you, and your goal, it is 2:00 in the morning,
2 not even getting at the increasingly common
3 dilemma where a patient's illness, by the time
4 they have gotten to the head of the list, is
5 so severe that they are incapable, medically
6 incapable, of making good decisions.
7 My colleague George Loewenstein at
8 Carnegie Mellon has done a wealth of
9 incredibly thoughtful work in the psychology
10 literature showing that the decisions we make
11 in these heated circumstances have no
12 correspondence whatsoever to our underlying
13 values and preferences. And if they don't,
14 then it is very hard to argue that decisions
15 made at the time that a specific organ is
16 offered do anything whatsoever to promote our
17 individual autonomy.
18 The second problem with organ-
19 specific consent is that there are some
20 potential inefficiencies. So, for example,
21 the time it takes to deliberate how we go
22 about whether the individual patient wants

1 that organ or not, that is a delay while the
2 organ is becoming ischemic, and that might
3 defray our ability to use more standard
4 criteria for matching, height in the case of
5 lungs, HLA matching in the case of kidneys --
6 you understand the point -- blood group, of
7 course. I don't think this concern is nearly
8 as powerful as the former, but it is relevant.
9 Then, finally, there's substantial
10 potential for undue social biases to influence
11 organ allocation. This is particularly true
12 in the case where we are talking about risks
13 for HIV, which is historically stigmatized.
14 It enables for people's underlying social
15 biases to influence their decisions to accept
16 or reject an organ that aren't based on
17 medical risks, but rather more nebulous
18 aversions to the types of people from which
19 these organs come.
20 At least from my perspective, in
21 the allocation of a social or public good,
22 allowing for such nebulous aversions, it ought

1 not be part of what we are doing.
2 So what is the alternative? Can
3 we do better? I think we can. So these are
4 the core elements of the model we put forth
5 that we call prospective consent.
6 The first element is that we start
7 with a thorough shared decisionmaking process
8 at the time that patients are listed for
9 whichever organ it is or whichever list that
10 they are going to go on. This allows for
11 accommodation of truly different values and
12 priorities among patients.
13 Imagine two 50-year-old gentlemen
14 on the kidney waiting list. One of them might
15 have had polycystic kidney disease, goes to
16 dialysis three times a week, but has been
17 doing rather well with this, plays with his
18 kids, maintains his work, no real side effects
19 from the dialysis.
20 His decision to accept or reject
21 non-standard organs is going to be very
22 different from his colleague on the waiting

1 list, another 50-year-old who has uncontrolled
2 hypertension, refractory diabetes, severe
3 cramping every time he gets to the dialysis
4 clinic, has already had an amputation, all the
5 consequences that you would hope to avoid.
6 The first patient might very
7 reasonably and logically say, "I would prefer
8 to hold out and wait for a perfect organ." A
9 perfect organ. The second patient might feel,
10 and rationally so, very differently. "I want
11 to cast my net more broadly to allow me the
12 best chance of getting off this dreaded
13 dialysis." We ought to be getting at the
14 simultaneous risks of accepting a non-standard
15 organ and risks of remaining on the waiting
16 list when we have these conversations upfront.
17 Second, patients should then make
18 a choice between accepting or rejecting these
19 non-standard organs. Now this is a point of
20 considerable controversy. When we initially
21 proposed this model, we framed it as a choice
22 between accepting only standard organs or

1 accepting all organs, a dichotomous choice.
2 I will say that my thinking on
3 this issue has evolved over time. Although
4 the rationale for doing it this way was so as
5 to mitigate the potential for these nebulous
6 aversions to historically discriminated-
7 against groups from playing into these
8 decisions, I do now appreciate that there may
9 be benefits to a finer degree of granularity
10 in this choice because the risks associated
11 with donors with, for example, CDC historic
12 criteria for infectious diseases are very
13 different, orders of magnitude smaller, than
14 the risks associated with, for example,
15 expanded criteria or DCD donors. So that, I
16 think, is maybe a point that we could discuss
17 later, what the appropriate approach there is.
18 Third, patients should declare
19 whether their decision would change if their
20 clinical status changed and they lost their
21 decisional capacity. They should declare this
22 upfront, much like an advance directive is.

1 This is a way of promoting their autonomy.
2 Fourth, patients should be allowed
3 to revisit this decision at any time. Nothing
4 in this policy bars them from saying, "You
5 know what, Doc? I've been thinking more about
6 this, and actually, now dialysis has become
7 real burdensome to me. Now I want non-
8 standard organs." Or the very opposite.
9 Fifth, transplant physicians
10 should retain discretion to use their judgment
11 in tough cases. Okay? I don't think any of
12 us want our doctors to forego any
13 decisionmaking in the heat of the moment when
14 there are tough calls that have to be made
15 between a patient who is rapidly dying and the
16 only organ that becomes available is a
17 considerably high-risk organ. We want our
18 physicians to be involved in those decisions.
19 We want them to be able to discuss them openly
20 with patients, even at that time. We just
21 don't want to require them to do so.
22 We don't want that to be the

1 standard, such that failure to do so carries
2 potential consequences for the clinicians,
3 when that failure would not necessarily be a
4 failure of autonomy.
5 Almost there. All right.
6 So what are some of the benefits?
7 I think this enables truly informed consent.
8 I hope I have made that point clear because I
9 think this is the most important point of what
10 I am trying to convey to you.
11 It promotes some augmented
12 efficiency in organ distribution. It is
13 flexible to inevitable changes in definitions
14 of what it really means to be a standard
15 organ. When Chagas disease or HTLV-I or
16 something else that we haven't even
17 anticipated yet comes into the picture, we can
18 accommodate that neatly into a group without
19 providing false assurances regarding some
20 certainty that we have about exactly what
21 those risks are.
22 The dichotomous choice that I had

1 initially proposed would also limit the
2 influences of social biases in allocating the
3 public good, although, again, I am now
4 increasingly sensitive to the possibility that
5 a more granular, a trichotomous or four-level
6 choice may, in fact, be more in the patient's
7 interest than the initial way we framed it.
8 So, just to review the central
9 points I made, I have tried to impart to you
10 that scarcity of public goods leads
11 inescapably to really tough decisions, and
12 that, in making these decisions, we ought to
13 have at the forefront of our minds goals of
14 transparency, equity, efficiency, and
15 accountability; that we can't consider risk
16 separately from benefit. Risk is not a
17 morally -- in and of itself, risk is not
18 morally important. It is only important to
19 the extent that it promotes the number of
20 quality-adjusted life-years again, and that a
21 nationally-standardized process or perspective
22 of consent may best accommodate these goals.

1 I will stop there.
2 CHAIR BRACEY: Thank you.
3 Dr. Williams?
4 MEMBER WILLIAMS: Yes. Thank you
5 very much, Scott.
6 The question is, has the adequacy
7 of informed consent in an ECD situation been
8 tested in the courts?
9 DR. HALPERN: Not that I am aware
10 of. If someone knows otherwise, please raise
11 your hand.
12 I don't know that the ECD model
13 has been generalized, let alone tested in a
14 legal situation. It always struck me as odd
15 that the original policy was to make kidney
16 transplant recipients make a decision upfront
17 about accepting ECD organs or not, but all the
18 other categories of increased-risk organs, if
19 you will, there was no policy about that.
20 Obviously, that policy hasn't been adhered to
21 very consistently.
22 CHAIR BRACEY: Dr. Ison?

1 MEMBER ISON: A couple of
2 clarifications and points. This audience may
3 not fully understand what you mean by non-
4 standard organs because, in my opinion, the
5 chunk of 54 percent is definitely a very
6 different group.
7 So if you could define what you
8 mean by non-standard risks specifically for
9 the Committee, I think it would be very
10 helpful.
11 DR. HALPERN: Sure. So the way we
12 initially conceptualized it was that we
13 actually don't know all the risks. When
14 evaluating a donor's risk profile, we can
15 identify things that we know lead to higher
16 risk and we can acknowledge that there may be
17 some things that we just don't know connote
18 higher risk.
19 So a standard organ would be an
20 organ from a donor without any known factor
21 that increases the donor's risk profile, and
22 a non-standard organ would be anything else.

1 This is the dichotomous choice that we
2 initially promoted.
3 So that would include,
4 quote/unquote, "non-standard features" like
5 donation after circulatory determination of
6 death, which I think the literature is now
7 pretty clear on, at least in the case of
8 livers. They do much worse than from
9 neurologic determination of death.
10 It would include expanded criteria
11 donors. It would include donors who harbor or
12 who have behaviors that make them more likely
13 to be harboring infectious risks.
14 So that is the way I was using the
15 term. I could not agree more that this is a
16 heterogeneous group, to say the least.
17 MEMBER ISON: Then two kind of
18 follow-on questions with that. This is one
19 perspective of the consenting process. I
20 think what it doesn't take into account, and
21 I wonder what your thoughts on this are, are
22 that there are changes over time. If you look

1 at a kidney donor, they are listed, on
2 average, five years before they're
3 transplanted. A lot can happen.
4 Unfortunately, their day-to-day
5 care isn't with the transplant center. It is
6 with an external nephrologist, typically. So
7 the challenge is that we have no impact
8 necessarily on that nephrologist.
9 Likewise, the current paradigm for
10 consenting patients is they actually get two
11 consents. They get information and consenting
12 at the time of listing, and then additional
13 consenting at the time of organ offer. Many,
14 myself included, think that there's actually
15 clear benefit in that. There is risk with
16 regard to social stigmatization and whatnot.
17 But the second part of the
18 question is, do you think that that can be
19 overcome with better informing as part of the
20 informed consent? And as a corollary of that,
21 is there enough data or is research needed to
22 understand what the gaps are from a

1 clinician's knowledge and consenting process
2 and from a patient's perspective,
3 understanding and recognizing what the true
4 risk is from that particular organ?
5 DR. HALPERN: A lot of great
6 points raised. I will try to address them in
7 turn.
8 So I think the first question, if
9 I understand it properly, is, what are the
10 relative merits, or lack thereof, of a dual-
11 consent process, one that occurs not just
12 upfront at the time of listing, as we are
13 advocating, but also, and if I understand it
14 correctly, mandatorily again at the time that
15 a specific organ becomes available.
16 Fundamentally, I don't think
17 there's anything wrong with that, but I am
18 concerned about standardizing that policy for
19 two reasons. One is it allows for a lot of
20 consternation and concern and uncertainty if
21 the decisions that a patient made at those two
22 time points differ. How do we adjudicate that

1 process?

2 What I would say is that the

3 decision made upfront -- and this is

4 recognizing that we know from the decision

5 psychology literature that decisions that

6 patients make at one point in time don't

7 perfectly predict their values and preferences

8 later.

9 But in this case, the ways in

10 which the consent discussion would go in the

11 heat of the moment I think are far more

12 powerful not deterrence, but barriers to any

13 effort to promote that patient's autonomy than

14 the potential imperfect prediction of a

15 decision made in the forefront.

16 So I am just not sure how we would

17 adjudicate that situation if differences

18 arose. It is for that reason that I would

19 advocate not requiring the second consent, but

20 certainly not barring it, either.

21 I have to admit now I am

22 forgetting the second element.

1 MEMBER ISON: So the second
2 element deals with, do we know? So, for
3 example, you say they can't make that decision
4 in the heat of the moment. Do we know what
5 they are thinking? Do we know what the
6 clinicians are saying? And is it really not
7 that we shouldn't do it, but maybe we should
8 do it better?
9 DR. HALPERN: Yes. So the honest
10 answer is, no, we don't know. The corollaries
11 to that answer are that it is very tough work
12 to do. It is not impossible.
13 So what we do know is that people
14 in similarly tense situations, whether good or
15 bad, people who just won the lottery or people
16 who just got saved from an airplane crash, the
17 decisions they make in those heightened, tense
18 circumstances, careful interviews with people
19 in those circumstances reveal that their
20 thought processes don't really correspond, in
21 retrospect, to what they really wanted to be
22 saying.

1 Do we know it in the case of organ
2 donation? No. Could we study it? Yes, I
3 suppose we could. It would be a tough task,
4 but not an impossible one at all.
5 I am not sure I would wait for
6 that information to put forth a standardized
7 policy. I think one thing I would like to
8 leave you with is that we need a standardized
9 policy, one way or another, even if we can't
10 agree on exactly the elements of that policy.
11 MEMBER ISON: Although I would
12 point out we do have a standardized policy
13 with CMS regulations and UNOS Policy 4.1.
14 DR. HALPERN: I guess I mean one
15 that is adhered to in a standardized fashion.
16 CHAIR BRACEY: Dr. Triulzi, and
17 then we will probably have to wrap up the
18 questions there.
19 MEMBER TRIULZI: Yes, thank you
20 for a very interesting, well-done
21 presentation.
22 Can you comment about, you use the

1 term a "morally-relevant factor", about a
2 first versus a second or a subsequent
3 transplant? Also, in the Markov models, let's
4 take the double versus single lung. If you
5 have the opportunity to get a second lung
6 transplant, another lung later, it could put
7 you back onto the survival curve of the double
8 lung transplant. Is that accounted for in the
9 model? In other words, the ability to get a
10 second transplant later?
11 DR. HALPERN: So the morally-
12 relevant factors is always one that I find to
13 be interesting. It is something we talk about
14 in my lectures to the medical students
15 regularly.
16 So it is not exactly clear what
17 that is because we live in a pluralistic
18 society. Then we may have different values.
19 But I think there are some things
20 that reasonable people could agree upon ought
21 not be factors on which we allocate organs.
22 I think sex or gender would meet that

1 standard. I think race would meet that
2 standard.
3 I think all reasonable people
4 would agree that potential to benefit would be
5 a standard on which we ought to be basing, at
6 least to some extent, allocation decisions.
7 So those are the two poles.
8 In between those poles, there's
9 lots of things. There are things like, was
10 the patient responsible for causing their
11 illness, the alcoholic cirrhotic or the
12 smoking COPD patient? Reasonable people might
13 disagree about the moral appropriateness of
14 that criterion. Reasonable people might agree
15 about whether people should get a second
16 chance after a first transplant failed.
17 I do think that what drives that
18 decision is more a sense of ownership of that
19 patient among the transplant team, more so
20 than some moral rankling with the
21 appropriateness or lack of appropriateness of
22 that allocation strategy.

1 I think reasonable people would
2 disagree on the appropriateness of age as a
3 rationing criteria. Okay? There are lots of
4 arguments that suggest that it is a very good
5 rationing criterion, but it is a very
6 topically-sensitive one, as you know, in
7 recent debates about healthcare reform.
8 As to whether we accounted for it
9 in our model, we did build in -- it is such a
10 small proportion of the lung transplant
11 population, that we did build it in. I didn't
12 put it on the slide because it had no
13 meaningful effects on the estimates.
14 CHAIR BRACEY: Dr. Sarode?
15 MEMBER SARODE: Scott, excellent
16 presentation.
17 You focus almost the whole talk on
18 consent for organs. What are your thoughts on
19 tissues?
20 DR. HALPERN: Yes, it is a good
21 appreciation of a narrowness of my
22 perspective. And I apologize for that.

1 I think the core principles are
2 the core principles. I don't think the type
3 of resource that we are allocating -- you
4 know, I think about allocating ICU beds for a
5 living. I think the same core principles
6 ought to go in these morally-relevant and
7 morally-irrelevant differences between patient
8 groups. I think they are the same criteria
9 for allocating any type of resource that
10 simply doesn't exist in adequate supply.
11 I do appreciate that scarcity in
12 the tissue world may not be as salient a
13 feature as scarcity in the organ world. For
14 that reason, the pendulum itself, if you will,
15 may shift more towards a protective standpoint
16 that accommodates risk reduction because the
17 overall consequences from a societal
18 perspective of shifting the pendulum in
19 conditions of lower scarcity are more
20 absorbable, if you will.
21 So I don't think the principles
22 differ, but the way those principles play out

1 in allocating a less scarce resource might
2 differ. So the conclusions may differ, even
3 though we are using the same logic to get at
4 those conclusions.
5 CHAIR BRACEY: Thank you, Dr.
6 Halpern, for a very excellent presentation and
7 great discussion.
8 Our next speaker, and we are going
9 a little bit out of the plan, but we thought
10 it would be good, again, to hear Dr. Woods'
11 presentation before we begin to discuss these
12 issues.
13 So Dr. Woods is from the Institute
14 for Healthcare Studies at the Feinberg School
15 of Medicine, Graduate School of Northwestern
16 University. She will present an overview of
17 the unique issues related to safety in organ
18 transplantation.
19 DR. WOODS: I am really delighted
20 to be here today, and to be invited here to
21 talk to you about patient safety, which is my
22 area of focus and passion.

1 I guess I would really like to
2 applaud you for expanding your view on what
3 safety is into the solid organ transplantation
4 arena.
5 I am here, as you said, from
6 Northwestern. I am going to share with you
7 some of the unique issues related to the
8 safety of organ transplantation.
9 Now patient safety is a relatively
10 new field and was somewhat kicked off,
11 although there were some studies prior to
12 that, was really kicked off as a major field
13 at the publication of the Institute of
14 Medicine reports that estimated between 48,000
15 and 96,000 deaths attributable to preventable
16 adverse events each year in the United States.
17 We now know that that is a very
18 conservative estimate. We have information
19 from the CDC that just infections alone may be
20 in that range. The Institute for Healthcare
21 Studies reports that they reduced deaths by
22 120,000 in a year and two months, and I don't

1 think that anybody who has an affiliation with
2 any institution can say that they have been
3 eliminated. So these rates were initially
4 assessed to be around the fifth leading cause
5 of death, greater than the number of deaths
6 from all unintentional accidents and diabetes,
7 with significant cost.
8 But these reports did more than
9 just present the epidemiology. They presented
10 a paradigm shift for us to think about these
11 events in a different way. Whereas, it had
12 been thought that there were just bad apples,
13 bad events, bad institutions, there was now an
14 understanding, because of the magnitude of
15 this problem, that this is a systemic problem,
16 that we have to really think about, how do we
17 design our healthcare system to be more safe?
18 So here is medical errors
19 represented in line with other major leading
20 causes of death. That is not where we want
21 it, and transplantation is in there. It is
22 not representing all of it, but it is in

1 there.

2 Then this is a slide that compares

3 the safety of healthcare with other high-risk

4 industries. Because what we do in healthcare

5 is high-risk. It is life-saving, but it

6 applies high-risk methodologies.

7 So, on your right, you see this

8 ultra-safe category where you have nuclear

9 power, European railroads, and fortunately for

10 those of us who had to travel here by air,

11 scheduled airlines. These are fields, these

12 are industries that can't afford an event.

13 They believe they need to do all their work

14 prospectively. They have got to figure out

15 what kinds of events could happen and avoid

16 them before they ever do.

17 So, in nuclear power, they have

18 estimations of problems that might occur in

19 1,000 years. That is a model to think about

20 in terms of the way we operate in healthcare.

21 Then, if you look at the righthand

22 column -- so what this is showing is, on the

1 side, it is total lives lost per year, and
2 across the bottom, the number of encounters
3 for each fatality.
4 Healthcare, while it has a greater
5 volume than bungee jumping, is in the same
6 category of risk. I don't think that we want
7 to see it that way.
8 So I see safety, patient safety,
9 as a systemic problem, much like marbles on a
10 stairs. There are marbles everywhere.
11 What we have done in healthcare is
12 teach people to be very effective at
13 navigating around these marbles whenever they
14 need to traverse the stairs. And an
15 alternative approach is to identify and
16 eliminate these risks for great systemic
17 safety.
18 Organ transplantation is a
19 surgical procedure. It involves a surgical
20 procedure. And again, I want to comment that
21 I am delighted that you are thinking about
22 organ transplantation somewhat differently

1 from blood because I think that they have
2 somewhat essentially different processes.
3 While medications are delivered as
4 part of a transplantation protocol, blood
5 safety is more akin, more comparable to a
6 medication safety or medication process and
7 applies the practices of medication safety to
8 address its risks.
9 Transplantation, while, as I said,
10 it includes those, is a surgical procedure and
11 must think about, in order to really achieve
12 safety, it must be thought about as a surgical
13 procedure and apply those principles to those
14 types of processes.
15 And as we see here, from those
16 initial studies, nearly half were surgical in
17 nature, from both the medical practice study
18 and the Colorado and Utah medical practice
19 study. You want to know why these studies
20 continue to be quoted. Well, they were a part
21 of a very important IOM report, but they also
22 represent population-based assessments of

1 safety. And there are very few of those. It
2 is hard to get a denominator. So I want to
3 sort of highlight for you that that could be
4 an opportunity for learning, for organ
5 transplantation as well.
6 Here are a couple of relatively-
7 recent articles demonstrating different kinds
8 of methodologies that can be applied in safety
9 for learning about risk. So Christian, et
10 al., did extensive observations within the OR
11 suite of nine long, complex general surgery
12 cases. They found 88 instances of lost
13 information; 86 percent had significant impact
14 on the progression of the case, the
15 uncertainty of the team members, and increased
16 risk to the patient. Five of these events led
17 to measurable changes in patient status.
18 Zingg, et al., looked at 139
19 critical incident reports. Thirty-six of
20 these led to death or permanent disability.
21 So this is a risky area.
22 Mazzocco and colleagues, in 2009,

1 report that complications and death following
2 surgery are more likely when surgical team
3 members do not exhibit team behavior. So
4 there's not good communication. There is not
5 a good culture where issues that could cause
6 harm to the patient could be raised and
7 addressed.
8 Just to broaden your thinking for
9 a moment about examples of types of issues
10 that can be related to a surgery, there are
11 infections; medication issues; specimen
12 labeling and handling; correct side, site,
13 procedure, patient; teamwork and
14 communication; diagnostic/technical aspects of
15 the procedure performance itself, and patient
16 handoffs. It is just, you know, a little bit
17 of a menu to begin your thinking about where
18 some of the problems can exist.
19 And how complex these can be. So
20 this diagram, you don't need to read the
21 words. It is really kind of pictorial in
22 nature. This is a diagram of the preparation

1 for a surgery to address correct patient,
2 procedure, site, and side. What you see in
3 blue there is the universe protocol. What you
4 see in red is the WHO checklist.
5 And interestingly enough, they
6 don't overlap. If you only do the universal
7 protocol, which is our standard here in the
8 United States, you are not doing those things
9 that are related to preventing these rare, but
10 significant wrong patient, wrong side, wrong
11 site, procedure occurrences which can occur in
12 organ transplantation. If you only apply the
13 WHO, you also do not address many of the
14 significant risks that have been identified as
15 part of that process, the fail point in the
16 process of identifying the correct patient
17 side, site, and procedure.
18 So, focusing down a little bit
19 onto organ transplantation safety, safety
20 issues are demonstrated to exist. Many high-
21 profile, high-harm events have occurred that
22 people are very familiar with. However,

1 there's very limited systematic investigation
2 of safety issues. There's investigation of
3 each case as it comes down, big-profile issue,
4 but there's not a good sense of systematic
5 investigation.
6 I am going to go back to this
7 previous slide for just a minute. What is
8 green on the bottom is the result of the
9 Pennsylvania Authority on Patient Safety
10 mandated all wrong site, wrong procedure --
11 they had a list of events that must be
12 reported to their system, and they have a very
13 hard stick-and-carrot policy. So they have
14 substantial cooperation.
15 So they had over 400 wrong site,
16 wrong side, wrong procedure, wrong patient
17 cases that they drilled down into and found
18 that there were 48 fail points. While
19 institutions were having an event, doing their
20 root-cause analysis, plugging the holes in
21 their root-cause analyses, they were are
22 shocked to find that they had another event.

1 What was the different fail point?
2 They were able to analyze across
3 all of these different institutions the
4 critical fail points that all had to be
5 plugged in order to have a completely-reliable
6 process.
7 So there's a need for systemic
8 investigation of safety issues, and safety
9 improvement can impact outcomes. It can
10 impact it for recipients and for living donor
11 safety.
12 Now this is an example of a
13 probabilistic risk assessment. I don't know
14 if you know what that term is. It is a
15 sophisticated analysis methodology that comes
16 from nuclear power that analyzed before and
17 after the Duke event for the ABO incompatible
18 thoracic organ transplantation. You know,
19 that is not very common. That is pretty rare,
20 but it occurred.
21 But they were able to demonstrate
22 that, by adding open offer processes, added to

1 the ABO compatibility cross-tracking data,
2 putting that into the UNOS system reduced the
3 risk substantially.
4 Then ABO compatibility testing,
5 making that the same for the open offer
6 process as for the match list directive
7 process further reduced the risk, again,
8 trying to prospectively identify where the
9 risk exists and not waiting for one of these
10 terrible events to happen, but being able to,
11 then, prevent it or make it much less likely
12 to occur.
13 So I want to share with you a
14 little bit about our Transplantation Safety
15 Outcomes Group, which is part of the
16 Northwestern University Transplantation
17 Outcomes Research Collaborative. That is a
18 lot of words. I don't know if it parsed for
19 you.
20 But we have a group that is
21 focused on safety, and it is transplantation
22 surgeons, ID administrators with health

1 services, patient safety researchers, to look
2 at how to think about identifying and
3 addressing the risks in organ transplantation.
4 So we map the process, understand
5 the nature of the problems that occur, and
6 intend to estimate the rates. We have
7 conducted a failure modes effects analysis for
8 the transplantation process pre-procedure,
9 procedure, post-procedure, and then drilled
10 down on specific aspects of it. We have
11 conducted a critical incident analysis.
12 We are in the process of
13 developing that right now, where a number of
14 people read the critical incidents that have
15 been reported by clinicians and code them by
16 the type of event that they are, and then,
17 again, dig down into them.
18 Then we have an active
19 surveillance process that we intend to produce
20 rates with, using a safety debriefing for each
21 -- right now, we are applying it to living
22 donor surgeries, living donor liver

1 transplantation surgeries. We also have
2 conducted it on a number of deceased donor
3 liver transplantations and a chart review.
4 I am going to share with you a
5 little bit of what we have. It is very
6 preliminary results, but I think you will see,
7 from these results, the benefit that we can
8 have from it.
9 This is the description of the
10 process of the failure modes effects analysis.
11 We define the topic, assemble a team of all
12 those involved in the process, graphically
13 describe it, conduct an analysis which is
14 really looking at the frequency of fail points
15 and their consequences if they occur. Then
16 you identify actions and outcome measures.
17 This is a small segment of the
18 donor selection process of the living donor
19 and the deceased donor. The living donor is
20 on the right -- on the left, sorry. The
21 deceased donor is on the right.
22 This is a mapping of that process.

1 This is an example of the risk results from
2 that process. If you look at the columns
3 there, you can see that results delayed right
4 there, results delayed. It is about 1 in 10
5 cases.
6 Here we have inadequate or
7 inaccurate physical done for a deceased donor
8 or inadequate history available. It is fairly
9 frequent and leads to fairly significant
10 impact when information is lost. So we assess
11 and can prioritize the areas for focus through
12 this process.
13 So, for the active surveillance,
14 the safety debriefing, we are interested in
15 trying to get a case-based assessment, where
16 there is an enumerator and a denominator. And
17 denominators are really the hard part in
18 safety assessment.
19 We are looking at both events, bad
20 things that happen, that really happen, and
21 near-misses, problems that occurred that were
22 caught by somebody, that there was an

1 intervention such that they didn't affect the
2 patient and the patient's outcome.
3 And we are interested in multiple
4 perspectives because in any transplantation
5 there can be 20 or more people involved, and
6 they all have a different piece of the puzzle.
7 We had relatively open-ended
8 questions with some probes around
9 unanticipated safety-related problems, things
10 that made the transplantation more difficult.
11 Often the things that were difficult were
12 problems in the processes that could have led
13 to other kinds of problems, adverse events,
14 near-misses.
15 Participants in the surgery were
16 asked to complete these at the end of each
17 surgery within 48 hours. We have now data for
18 13 LDLT surgeries. We have 68 surveys from
19 these different surgeries. And the
20 distribution of the kinds of problems that we
21 are seeing, teamwork and communication are
22 clearly important issues. IT equipment issues

1 and staffing are all reported.

2 I am giving you a little bit of a

3 sense of what kinds of things people were

4 talking about. These are not the kinds of

5 things you will get from a chart review. So

6 we will have a chart review as well to look

7 for things that do get documented, but we are

8 also looking for the things that don't get

9 documented, to understand where the reservoir

10 of risk is in these processes.

11 "I was not present during the

12 official timeout, as I was also performing my

13 duties for a cadaveric liver/kidney

14 transplantation."

15 Unclear communication between

16 surgeon and circulating nurses regarding

17 obtaining blood vessels from a blood bank and

18 the need to set up a bench table.

19 For IT equipment issues, these are

20 just examples. We have many more, as I just

21 said.

22 Power supply for anesthesia

1 machine shortcircuited. Problems with
2 equipment and materials necessary to profuse
3 the liver graft not available on time. Packs
4 not available on OR monitor; unable to
5 visualize donor anatomy.
6 For staffing, primary donor
7 surgeons had been up all night doing surgery.
8 OR staff thought we were not doing or
9 postponing the LDLT because we did a DDLT
10 until 9:00 a.m. that day.
11 So this gives us the multiple
12 holes that could align with -- you know, it is
13 very hard sometimes to see how those holes
14 could align prospectively. This analysis
15 gives us the data that can help us to map
16 those kinds of problems.
17 So, to sort of conclude with some
18 methods for you to think about in terms of how
19 to approach safety assessment, there are
20 methodologies like root-causes analyses.
21 These are qualitative methods. Failure mode
22 effects analyses can be qualitative or

1 quantitative in aspects. Probabilistic risk
2 assessment has also qualitative and
3 quantitative versions and aspects.
4 Surveillance, event reporting, and by event
5 reporting I mean specific events. You must
6 report bloodstream infection. You must report
7 a wrong side surgery, you know, that kind of
8 thing. You must report certain kinds of
9 medication errors.
10 Near-miss reporting, as I
11 mentioned, captures the things that are going
12 on in the interstices that we just luckily,
13 there by the grace of God, didn't have
14 anything happen, but you catch and you learn
15 about them, so that you don't end up having
16 that occur for the next patient.
17 Then active safety surveillance
18 where you ask people proximate to the context
19 in which they have provided a particular kind
20 of care about the things that happened, so
21 that you can collect, again, more rich data
22 about the processes.

1 Chart review is still an effective
2 method. There are many things that can be
3 found in a chart, and we are developing an
4 organ transplantation-specific chart review
5 tool that is actually in the process of being
6 validated right now.
7 Additional things to think about
8 measures of effective organ transplantation.
9 You know, walking down the road that folks
10 around diabetes and heart failure walked down
11 about a decade and a half ago, you know,
12 figuring out what are the frequent clinical
13 contexts that you want to observe, potentially
14 where there is significant harm in the
15 outcomes. What are the clinical and process
16 indicators for the relevant positive outcomes,
17 so that process measures like A1C, the level
18 of A1C; it took like three years for people to
19 figure out that that is something that they
20 thought was an important marker of how the
21 care is being delivered to a diabetic patient.
22 It is not an easy, rolling-off-the-log

1 activity, but I think it is one that I would
2 recommend that you consider.
3 Then there is observation,
4 actually going to an aspect of care and
5 observing the process, which can be
6 particularly important if you are going to
7 make a change and redesign the process to
8 ensure that you haven't added new or different
9 risks into the process, which many of you who
10 may have suffered through the implementation
11 of a medical EMR may be quite aware of.
12 I wanted to share with you the
13 members of our Transplantation Safety Outcomes
14 Group in our NUTORC collaborative.
15 If you have any questions, I am
16 happy to answer them.
17 CHAIR BRACEY: Thank you.
18 I think that, in the interest of
19 time, maybe we will take one or two questions,
20 but I would like to limit the discussion.
21 Dr. Kuehnert and then Dr. Ison.
22 MEMBER KUEHNERT: Thank you. That

1 was a really nice talk.

2 It strikes me that what you are

3 trying to do is very similar to what we have

4 done in the infection control arena, of

5 course, with patient safety, and also with

6 hemovigilance in blood safety in piloting and

7 now implementation of the hemovigilance module

8 of the National Healthcare Safety Network.

9 I was wondering, as you brought

10 this into the patient safety arena, the idea

11 of organ safety, whether there has been

12 pushback from some clinicians at your

13 institution, or otherwise nationally, in terms

14 of concerns about somehow impacting

15 availability because you implement safety

16 systems.

17 I am just wondering if you are

18 running into that sort of issue and how you

19 overcome that by emphasizing that organ

20 transplant is part of healthcare, and rather

21 than being an experiment, it actually is a

22 healthcare procedure on the same continuum as

1 any other healthcare procedure.

2 DR. WOODS: Well, within our

3 institution, we have great leadership from

4 Mike Abecassis, Dr. Michael Abecassis, who has

5 encouraged everyone to participate actively in

6 this process, and the way that we collect data

7 doesn't sort of reflect back this nurse or

8 that doctor did this thing, but we are trying,

9 again, to study the systems.

10 I think where we have run into

11 some trouble is a little bit of confusion

12 about what does safety mean. Because a lot of

13 organ transplantation surgeons think about

14 safety as like safety efficacy. Is it a safe

15 way to go to do a living donor or a hand-

16 assist laparoscopic procedure, or that kind of

17 thing?

18 So they are thinking, because it

19 is the cutting-edge thing that you are talking

20 about, so there is often a conversation that

21 has to happen to, "Oh, no. Oh, that? Uh-huh.

22 Well, why do we have to worry about that?"

1 "Oh, okay, well, now I get it."
2 So it is kind of new for folks to
3 think about, but once they think about it, we
4 have found that pretty much everyone we have
5 talked to has been quite interested.
6 We are participating in this A2ALL
7 Consortium. They just established a Safety
8 Committee, basically, through that
9 conversation process. "Oh, yeah, now I get
10 it."
11 MEMBER KUEHNERT: Well, I think if
12 you somehow could export that discussion
13 nationally, it would be very helpful. As much
14 as the Committee could help with that, in
15 making organ safety as a laudable concept that
16 we need to achieve while being respectful of
17 availability, that would be very helpful for
18 the national effort overall.
19 DR. WOODS: I think availability,
20 actually, puts an underline, you know,
21 underscore under it because this is a very
22 precious resource. You don't want to, one,

1 hurt a living donor. You don't want to,
2 through some mishap that you could have, if
3 you had studied it, realized the cause of
4 trouble that led to graft loss or other
5 unintended outcomes.
6 CHAIR BRACEY: Dr. Ison, you had a
7 question or comment?
8 MEMBER ISON: Well, that leads to
9 what I was going to ask, which is kind of
10 linked questions.
11 No. 1, as a disclosure, I am part
12 of this group, of course. This was shown.
13 DR. WOODS: He's up there, yes.
14 MEMBER ISON: But the issue is you
15 have shown what we are doing at our level.
16 What do you think can be done looking at
17 national systems?
18 And No. 2, would you mind
19 commenting on if there's funding for this type
20 of research?
21 DR. WOODS: Right. Just in case
22 somebody asked me, some recommendations. I

1 think there ought to be targeted research as
2 a start, you know, comparable to something
3 that was done by the IOM, where you are
4 actually getting a rate-based understanding of
5 what some of the high-profile, not just the
6 high-profile, the key priority risks are.
7 Then do some drilling down into those to
8 understand the nature of them, what is
9 contributing to them.
10 I think that you have a decision
11 before you around mandatory reporting of
12 specific events. And I do think that it is a
13 good idea to identify what events you want to
14 have collected, which you could learn from
15 targeted research.
16 But near-miss reporting or getting
17 access to some aspect of near-miss reporting
18 to really guide your thinking has been shown
19 to be extremely helpful in the aviation
20 industry. They have parallel processes, where
21 big events are required to be reported, and
22 then they also have a near-miss reporting

1 system where they get a lot of the things that
2 could be contributing to those big things. So
3 they can learn about them and maybe even fix
4 them before the big thing happens.
5 Then considering transplantation
6 safety measure development, because we now
7 know a lot about the quality and safety of
8 healthcare because there were measures.
9 MEMBER ISON: Just as a point, I
10 didn't know she had that slide. This wasn't
11 a setup question.
12 (Laughter.)
13 DR. WOODS: Okay. So those would
14 be some thoughts that you might consider to
15 inform your processes going forward.
16 MEMBER ISON: And then funding, is
17 there funding for this currently?
18 DR. WOODS: There is not currently
19 funding available. AHRQ has been charged
20 largely with safety, but has not really had
21 transplantation safety on its radar screen.
22 I know HRSA is charged with a lot

1 of oversight around transplantation, and I
2 don't believe organ transplantation safety is
3 on -- it is on the screen; it is just sort of
4 coming up right now.
5 Mike Ison is going to talk about
6 what UNOS has been doing to begin to collect
7 data like this. I think it is fairly
8 provocative, and I think you will find that
9 pretty interesting.
10 CHAIR BRACEY: Thank you.
11 I think we need to take a break
12 now. Let's reconvene in 15 minutes. That
13 would be 20 minutes to the hour.
14 (Whereupon, the foregoing matter
15 went off the record at 10:26 a.m. and went
16 back on the record at 10:41 a.m.)
17 CHAIR BRACEY: Our next item will
18 be to hear on safety from the patient's view.
19 We have as our first speaker Pam Alesescu, and
20 I believe that we have her on phone. Is that
21 correct?
22 Hello.

1 DR. HOLMBERG: We are getting her
2 up right now.
3 CHAIR BRACEY: Oh, okay.
4 DR. HOLMBERG: She is standing by.
5 CHAIR BRACEY: Okay. And there is
6 a printout of her report to us. You all have
7 a handout.
8 DR. HOLMBERG: Okay. Pam, are you
9 there?
10 MS. ALESESCU: Yes, I am.
11 DR. HOLMBERG: Okay. You are
12 live, and I am trying to get your slides up
13 right now.
14 MS. ALESESCU: Okay.
15 CHAIR BRACEY: Good morning. How
16 are you?
17 MS. ALESESCU: I am fine, thank
18 you.
19 Good morning. My name is Pam
20 Alesescu. I am located here in Morro Bay,
21 California, on the central coast, halfway
22 between San Francisco and Los Angeles.

1 First, I would like to commend the
2 willingness of the Advisory Committee on Blood
3 Safety and Availability to consider the
4 patient perspective and experience of
5 receiving tissue for transplantation, and the
6 subsequent outcomes of such procedures, while
7 working towards a reasonable balance between
8 safety and risk analysis. So I thank you.
9 In 2001, my husband, Ken Alesescu,
10 and father of our two sons, 11 and 14,
11 underwent aortic valve replacement with an
12 aortic valve allograft. Subsequently, Ken
13 developed Candida tropicalis septicemia, which
14 resulted in fungal vegetation developing on
15 the allograft and then becoming dislodged and
16 traveling to the brain, which resulted in a
17 right-sided hemorrhagic stroke, leaving him
18 with complete paralysis on the entire left
19 side of his body.
20 It was at this time it was
21 determined that the aortic valve allograft was
22 the locus for his Candida tropicalis

1 septicemia.

2 He then underwent six weeks of IV

3 amphotericin treatment. Unfortunately, the

4 amphotericin treatment was unable to

5 completely eradicate the infection, and the

6 fungus continued to spread slowly to his

7 spine, destroying the vertebrae in both his

8 lumbar and cervical spine, which resulted in

9 cervical and lumbar spine reconstruction.

10 Ken, once again, had to enter

11 another six weeks of IV amphotericin

12 treatment. In between spinal surgeries, Ken

13 underwent his second aortic valve replacement,

14 replacing the first aortic valve, which was

15 destroyed from the fungal contamination, with

16 another aortic valve allograft.

17 Unfortunately, that valve also

18 developed an infection, and over time was

19 destroyed, this time from a bacteria called

20 Enterococcus faecalis, and Ken, once again,

21 became septic.

22 At this point, he underwent months

1 of IV vancomycin therapy, waiting to become a
2 stronger candidate for a third valve
3 replacement.
4 It was during this time Ken
5 developed a seizure disorder and hydrocephalus
6 from the continuing infection process.
7 During the waiting process, Ken
8 underwent cerebral shunt surgery, in an effort
9 to reduce the pressure on his brain, which
10 also made him a better surgical candidate for
11 a third valve replacement.
12 Ultimately, Ken underwent a third
13 valve replacement within 14 months with a
14 porcine aortic valve and a prescription of
15 lifetime Diflucan therapy.
16 Over the next three years, Ken
17 remained bedridden and found himself in and
18 out of the hospital from progressive
19 complications resulting from the continuing
20 and reoccurring fungal infection. In the end,
21 Candida tropicalis reappeared, and this time
22 had entered into his brain.

1 Once again, another six weeks of
2 IV amphotericin was administered, but
3 ultimately deemed futile. Ken was now
4 starting to experience kidney problems, and
5 his veins started to collapse after repeated
6 and prolonged IV therapy.
7 Doctors deemed treatment as
8 unsuccessful and an effort in futility. At
9 this point, Ken's condition continued to
10 deteriorate. He lost bowel and bladder
11 function. He had difficulty with swallowing.
12 He was losing and began to have difficulty
13 with his speech.
14 Sadly, it was at this time he
15 entered hospice care. Within two months, he
16 died quietly at home with his family
17 surrounding him.
18 It was determined through an FDA
19 investigation that this particular tissue
20 processor involved in Ken's case made the
21 decision to cut corners on accepted
22 procedures. Such procedures, if utilized,

1 would have increased patient safety for
2 receiving tissue. What was particularly
3 disheartening in this instance was the tissues
4 processor's actions remained within FDA
5 regulations and guidelines.
6 There have been other documented
7 cases of tissues linked to inefficient
8 processing and not using validated aseptic
9 techniques, which resulted in patients
10 becoming septic dating back to the late 1990s.
11 I must also add that, while such
12 actions were very serious, this problem was
13 also compounded by a lack of surveillance and
14 a lack of reporting of adverse events
15 associated with tissue allografts to
16 appropriate agencies.
17 Because of the lack of
18 surveillance and reporting of adverse events,
19 initially, physicians and hospitals neglected
20 to seriously consider allograft-associated
21 infections as the cause of my husband's
22 progressive symptoms.

1 As I learned more about the tissue
2 industry, I was surprised at the lack of
3 information surgeons and hospitals had in
4 regard to the processing of tissue and the
5 possibility of allograft-associated infections
6 as being a possible producer of septicemia.
7 It became clear to me that
8 information between tissue processors, health
9 agencies, and surgeons was inefficient, and
10 surgeons had the understanding that the tissue
11 they were using was a sterile product and
12 would never consider the tissue as the culprit
13 in an allograft-associated infection.
14 According to multiple articles
15 printed in various medical periodicals, they
16 claimed that FDA regulations do not require
17 companies processing heart valve allografts to
18 specify details of their disinfection process
19 used, fighting proprietary processes.
20 I understand that additional
21 measures could be taken, such as the
22 standardization and validation of the

1 disinfection process to enable the ability to
2 identify such organisms which cannot be
3 eradicated under present processing, would
4 indicate the allograft should be discarded.
5 It would also be prudent for
6 tissue processors to work towards the
7 development of a validative process which can
8 eradicate the most common and prevalent
9 harmful organisms, in an effort to be able to
10 utilize most tissues safely.
11 From the patient perspective, I
12 realize trying to achieve 100 percent safety
13 within blood, organ, cells, and tissue is
14 unrealistic. I also realize it is probably
15 next to impossible to treat and evaluate
16 human-derived resources for every type of
17 fungal, bacterial, or viral contamination, and
18 that doing so can become cumbersome and
19 costly.
20 It seems much more reasonable to
21 try to achieve a reasonable balance between
22 risk assessment and cost-effectiveness. I

1 also believe it is incredibly important for
2 further education and evaluation of human-
3 derived resources to become disseminated to
4 the physicians and, in turn, to the patients,
5 so that they can make an informed decision
6 about their treatment options.
7 As a patient, I have concerns
8 regarding further testing and additional
9 regulations to be implemented, if they are not
10 going to be evaluated and enforced by
11 appropriate agencies. I also understand,
12 currently, there is not enough resources to
13 retain additional agents to inspect and
14 enforce regulations and testing which is
15 already available.
16 My question now becomes, why add
17 more policies and procedures if you do not
18 have the resources to enforce statutes that
19 are already on the books?
20 My husband and a number of other
21 families paid huge prices for the decision
22 made by some tissue processors and the lack of

1 enforced FDA guidelines, processes, and
2 procedures and surveillance.
3 I would ask that you try to not to
4 define every event or procedure, but I would
5 ask that the agencies involved could determine
6 and set clear, best-documented practices,
7 techniques, standards, and procedures for the
8 handling of tissue in the most proficient and
9 efficient way to ensure the best possible
10 outcome for patients, and that an appropriate
11 risk/benefit analysis be examined and clearly
12 explained to the patient.
13 Also, enforce culpability of
14 tissue processors if adverse events do occur,
15 and if determined through a thorough
16 investigation that appropriate procedures were
17 not followed, and that the generally-accepted
18 standards were not conducted, that appropriate
19 action would be taken to ensure such adverse
20 events do not occur again.
21 I greatly respect those donors and
22 their families who so graciously and

1 unselfishly give the gift of life to others
2 through blood, tissue, and organ donation. We
3 owe it to donors' families and to the patients
4 who receive these precious gifts to handle
5 such contributions in such a manner that the
6 goal is to ensure the safest and best possible
7 outcome is achieved, and that patient safety
8 is always in the forefront.
9 Again, I would like to take this
10 time to commend all of you in your willingness
11 to work toward a goal of achieving the best
12 possible outcomes for the patients through
13 blood, tissue, and organ donations. I really
14 appreciate you taking out this time and
15 allowing me to speak today. Thank you.
16 CHAIR BRACEY: Thank you. Those
17 are very important comments.
18 Questions or comments from the
19 Committee?
20 (No response.)
21 If not -- just a second. Dr.
22 Kuehnert?

1 MEMBER KUEHNERT: Hi. I just
2 wanted to thank you, Ms. Alesescu, for your
3 comments. They are very important, and we
4 appreciate you giving the patient perspective.
5 MS. ALESESCU: Okay. Thank you.
6 MEMBER KUEHNERT: I wanted to ask
7 you, through all of this, you know, we have
8 discussed things, and you have brought
9 important issues to my attention personally.
10 We, through any surveillance
11 mechanism, did not hear about this case. I
12 was just wondering what your interactions were
13 with public health through this whole
14 experience that you and your husband had.
15 MS. ALESESCU: I was in contact --
16 I did have experiences with, I spoke with Dr.
17 Kaner from the CDC during the time. I had
18 reported it to FDA here in California, and
19 they didn't seem very interested. I did
20 report it to the Health and Human Services
21 here in California, and they also did not seem
22 very interested. Then I spoke a couple of

1 times to FDA down in Atlanta and didn't get a
2 whole lot of information.
3 Other than that, that is pretty
4 much all of the interaction I had with public
5 agencies at the time.
6 MEMBER KUEHNERT: Thank you. I
7 want to let you know that we are working very
8 hard to work with state and local health
9 departments to be aware of these risks, so
10 they can be more responsive in the future.
11 MS. ALESESCU: Okay. I really,
12 really appreciate it. Thank you so much.
13 CHAIR BRACEY: Oh, yes, Dr. St.
14 Martin?
15 MEMBER ST. MARTIN: Hi. Thank you
16 for sharing your story with us.
17 I did want to comment, at least to
18 clarify to the Committee that the current
19 tissue rules became effective May 25th of
20 2005, and acknowledge that the tissue rules
21 prior to that were very limited in scope.
22 There was no requirement for adverse reaction

1 reporting, and there were no good tissue
2 practice regulations in place.
3 I am not entirely certain at the
4 time of your husband's implant whether heart
5 valves were regulated as a tissue or a device.
6 MS. ALESESCU: At the time, they
7 were regulated as a device, as I understand
8 it, because it was in 2001 that he had the
9 implant.
10 MEMBER ST. MARTIN: But we are
11 certainly concerned with these types of safety
12 concerns. We are making strides to improve
13 the safety of tissues. We do now have adverse
14 reaction reporting, and heart valves now are
15 subject to the adverse reaction reporting
16 requirements under the current tissues rules,
17 as well as the good tissue practices, which
18 would ensure that the manufacturing is done in
19 a way that would avoid transmission of
20 communicable diseases and avoid contamination
21 of products.
22 So thank you for sharing.

1 MS. ALESESCU: I mean I absolutely
2 support tissue donation and organ donation.
3 Overall, I think it is a wonderful modality
4 for helping patients, and I would just like to
5 see -- I have been in contact with several
6 families that have experienced similar
7 situations to my husband's, who also lost
8 family members through tissue contamination.
9 I really greatly thank you so
10 much, all of you, who care enough to try to
11 get all this resolved. I am sure that things
12 are going to become a lot better and probably
13 already are. So thank you very much.
14 CHAIR BRACEY: Thank you.
15 So is there an additional
16 question?
17 (No response.)
18 Okay. Thank you again very much.
19 MS. ALESESCU: Okay. Thank you.
20 Bye-bye.
21 CHAIR BRACEY: Our next presenter
22 on safety from the patient's view is Donna

1 Leubke.

2 She's here?

3 MS. LEUBKE: I don't have

4 PowerPoint slides today for you.

5 Dr. Holmberg, members of the

6 Advisory Committee, I am Donna Leubke, a nurse

7 practitioner from Metro Health Medical Center

8 in Cleveland, Ohio.

9 Fifteen years ago, I donated a

10 kidney to my sister, and several years later

11 she had a life-saving liver transplant.

12 In 2006, I completed a three-year

13 term on the OPTN and UNOS Board of Directors,

14 and currently am on the Board of Directors of

15 LifeBanc, the organ procurement organization

16 serving northeast Ohio.

17 For seven years, I have also been

18 part of the Living Organ Donor Advocate

19 Program, which is a group of living donors who

20 are actively pursuing safety for living donors

21 in the United States.

22 Today I would like to thank you

1 for the opportunity to present a most
2 interesting case of acute hepatitis C
3 transmission in a kidney transplant recipient.
4 The case involves a 44-year-old woman who was
5 diagnosed with end-stage renal disease due to
6 membranous nephropathy. While on dialysis,
7 she was stable, cared for her family, and
8 worked a job outside of the home.
9 As her kidneys were failing, she
10 was not referred for transplant evaluation.
11 On her own, she sought out local transplant
12 programs and was subsequently placed on the
13 National Diseased Donor waitlist for a kidney
14 transplant. She was listed not only at one
15 transplant center, but opted to multiple
16 lists.
17 Early one morning, the phone
18 rings. The transplant coordinator at hospital
19 No. 2 tells her to come in for a perfectly-
20 matched 19-year-old kidney. The kidney is as
21 good as an identical twin, and she is ahead of
22 thousands on the list. This is what she was

1 told.

2 The transplant is completed. She

3 returned home. Followup of her kidney

4 function was coordinated with the local

5 nephrologist. Over the months following

6 donation, he notices an elevation in her liver

7 enzymes. Thinking the abnormal lab work was

8 related to immunosuppression medication, he

9 called the transplant program for dose

10 adjustment orders. Then, for some reason, he

11 ordered a hepatitis panel. It came back

12 positive.

13 This case took place on September

14 19th, 2004. Who knew about the hepatitis C,

15 what did they know, and what was their

16 responsibility?

17 The nephrologist knew. He drew

18 the studies and he ordered the tests and

19 reviewed the results. The transplant surgeon

20 knew. The transplant coordinator knew. The

21 social worker, the hospital administration,

22 laboratory personnel, UNOS personnel, OPO

1 personnel, FDA personnel, and the State End-
2 Stage Renal Disease Network Community Services
3 Coordinator, because these were all the many
4 people that this woman had either spoken with
5 or personally met with.
6 The lab reported the acute panel
7 to the local health department. However,
8 their personnel did not follow up because of
9 the lack of a physician report.
10 Two months ago, I received a phone
11 call at my office. Then three boxes of
12 medical records were delivered to my home, and
13 I knew.
14 I reported this case of acute
15 hepatitis C to the State Department of Health,
16 to the Centers for Disease Control, and to
17 HRSA's Division of Transplantation.
18 Imagine the psychosocial
19 implications of having a hepatitis C diagnosis
20 associated with transplant. Imagine the
21 failures, the disappointments, due to the lack
22 of response to her many concerns. She wanted

1 answers. She wanted the truth.

2 Now a new burden of disease and

3 apprehension about the very medical community

4 that she needed to trust. Imagine the

5 profound sense of betrayal by those she needed

6 to trust, not only the medical community, but

7 the agencies and organizations charged with

8 public safety.

9 In a bold move to take control of

10 her life, last month she fired her

11 nephrologist. He never reported the case. He

12 stood silently and watched the toll this has

13 taken on her and her family. He did not

14 bother to call anyone. He did not bother to

15 advocate for her.

16 Think of her husband, not only

17 their intimate relationship, but their day-to-

18 day. He trusted this transplant surgeon with

19 his wife.

20 Think of their sons and imagine

21 parenting through these five difficult years.

22 What about her life expectancy? Is it now

1 shortened?

2 She was told she could not be

3 treated for the hepatitis C or she would lose

4 the kidney. And she is also at an increased

5 risk of liver cancer due to the hepatitis

6 combined with her immunosuppression. If she

7 dies of hepatitis, was the transplant a

8 success?

9 What was known about the donor?

10 He was a young man who sustained a closed head

11 injury. He had a blood-clotting disorder.

12 There was limited social history. Many of us

13 don't live with nuclear families where you are

14 going to get a detailed social history. That

15 is just a fact of life. He did not live with

16 his parents.

17 Consent was given by his mother.

18 He presented to the emergency room actually

19 sort of in dire straits, and over the period

20 of the time from presentation to organ

21 recovery, he received packed red blood cells,

22 fresh frozen plasma, cryoprecipitate, along

1 with 12 liters of IV fluid. The hepatitis
2 panel was drawn after the transfusions, and
3 the hepatitis antibody test was noted as
4 negative.
5 So, from the time he presented to
6 the emergency department to recovery was about
7 40 hours. And from clamp time to her
8 transplant was almost 24 hours.
9 Another question: why did it take
10 so long to place this kidney? This was he
11 suffered a cardiac arrest in the time he was
12 in the operating room and CPower was
13 initiated. He was documented as a NHBD, or an
14 non-heart-beating donor.
15 She was led to believe this was a
16 perfectly-matched standard criteria deceased
17 donor kidney. She was not told that it met
18 criteria to be classified as an expanded
19 criteria donor of kidney.
20 No doubt, if she had been fully
21 informed only hours earlier a surgeon at
22 hospital No. 1 had declined this kidney for

1 her due to poor quality, she would have
2 refused it at hospital two. So multiple
3 listing did not advantage this woman.
4 Hospital No. 2 was the fourth
5 nationally listed, and that is, there is some
6 documentation in the handout that I gave on
7 the UNOS forms that she obtained.
8 So what about the OPO and the
9 surgeon? Are there some times that we make
10 decisions with incomplete data? Is sometimes
11 data inaccurate, misrepresented, or
12 misleading? Was there really a crisis going
13 on?
14 We hear it every day. The
15 deepening crisis, the widening gap between
16 supply and demand. Are there really 104,000
17 suitable candidates for transplantation on the
18 national waitlist? Are there really 82,000
19 people waiting for a kidney offer today? Was
20 there pressure to meet that 75 percent
21 conversion rate and get those 3.75 organs per
22 donor? Was there pressure for the surgeon at

1 hospital No. 2 to go to transplant with that
2 kidney for this woman? What could have and
3 should have been done differently?
4 This was and is someone's life.
5 She deserved better. She deserved a system
6 that helps its workers value the truth and
7 respond to existing rules in a truthful
8 manner. All she wanted was a kidney
9 transplant.
10 Thank you.
11 CHAIR BRACEY: Thank you, again,
12 for that important insight.
13 MS. LEUBKE: Any questions?
14 CHAIR BRACEY: Questions or
15 comments from the Committee? Dr. Sarode?
16 MEMBER SARODE: Thank you for
17 presenting that case.
18 Do you know what happened to some
19 of the other organs from that donor?
20 MS. LEUBKE: That I don't know.
21 That would be up to the federal agencies that
22 I spoke with, what they have been able to

1 track. I don't know.

2 MEMBER KUEHNERT: Since this event

3 has been brought to our attention, we are

4 investigating it, and the results are pending,

5 but we are actively investigating this

6 situation.

7 CHAIR BRACEY: Dr. Holmberg?

8 DR. HOLMBERG: Yes, thank you.

9 You mentioned that the other

10 hospital had refused the donor. How aware are

11 transplantation centers to information

12 concerning the other facilities that have

13 denied or rejected the donation?

14 MS. LEUBKE: What I can answer

15 from what she had sent me to review is, when

16 someone multiple lists, they are listed under

17 their Social Security number and a

18 registration number. So she was listed -- she

19 had two different registrations in the UNOS

20 system. So she was basically two different-

21 looking people. So there was no link between

22 her being the same patient at hospital No. 1

1 and hospital No. 4. And I have those papers.
2 CHAIR BRACEY: Dr. Bowman?
3 MEMBER BOWMAN: Yes, Dr. Holmberg,
4 I think what you are asking is, when a kidney
5 or an organ is offered to a particular
6 transplant center, I think you are asking, are
7 they aware of how many other transplant
8 centers have already had an offer for that
9 particular organ and how many have turned it
10 down, for whatever various reasons?
11 DR. HOLMBERG: Exactly.
12 MEMBER BOWMAN: I don't know the
13 answer to that. I am sure we could get that
14 kind of information, unless Dr. Metzger knows.
15 DR. HOLMBERG: And I guess it
16 raises another concern that I have that you
17 just mentioned or that Donna mentioned. That
18 is the two entries. Does this indicate that
19 we are double-counting off the waitlist?
20 MEMBER BOWMAN: I will let Dr.
21 Metzger answer that first, and then we can get
22 to the double-entry.

1 DR. METZGER: As to the first
2 question, the transplant center will get a
3 list of their patients that come up, and there
4 will be asterisks for patients from previous
5 centers that have turned down that organ. So
6 they will know that there has been some
7 turndowns. They won't know why it was turned
8 down, but they will know that there have been
9 some turndowns, depending on where they are on
10 the list.
11 And registrations and actual
12 recipients are different. Registrations are
13 always over and above the number of actual
14 recipients waiting on the waiting list because
15 the registrations are counted as well as the
16 number of recipients. We are paid for every
17 registration, not per candidate.
18 MEMBER ISON: I think it is
19 important to point out that the turndown is a
20 center/patient decision, not a center
21 decision. So, just because a center doesn't
22 want to -- and correct me if I am wrong -- if

1 the center feels that this organ is not
2 appropriate for this patient who came up as,
3 let's say, No. 6 on the list, and they turn
4 that down, it may be right for their same
5 patient that is No. 7. It is something that
6 is unique to that center and patient pair, not
7 necessarily a reflection on the actual quality
8 of that kidney.
9 MS. LEUBKE: Another issue is that
10 she had only consented to a local ECD,
11 expanded criteria, and she was led to believe
12 that expanded criteria meant that the donor
13 could be a little bit older than her. So she
14 was not fully -- you know, that was not
15 explained to her. This was a national ECD.
16 This was not a local. This kidney was out
17 there for about 24 hours.
18 DR. METZGER: Could I make a
19 comment on that? No, that patient wouldn't
20 have come into the ECD classification. ECD
21 for kidney are all patients over the age of 50
22 and any patient over the age of 50 who has two

1 out of the following three criteria: they
2 developed or they died from a cerebral
3 vascular event; they have a creatinine final
4 of 1.5 or greater, and they have any history
5 of hypertension. Those are the criteria for
6 saying that a kidney donor is ECD.
7 CHAIR BRACEY: Thank you.
8 Additional questions or comments?
9 Dr. Bowman?
10 MS. LEUBKE: Excuse me. I thought
11 ECD also had to do with their hemodynamic
12 instability and the non-heart-beating donor
13 issue.
14 DR. METZGER: No.
15 MS. LEUBKE: Okay.
16 DR. METZGER: The ECD definition
17 is very specific, but there are other risks
18 and overlaps in donors. That is something
19 that nationally we are working on very
20 closely, and we are coming up with what we are
21 calling a donor profile index. The ECD system
22 will then be eliminated and the transplant

1 center will be given a specific donor profile
2 index based on variables calculated by the
3 Scientific Registry for Transplant Recipients.
4 CHAIR BRACEY: Thank you.
5 Let's have Dr. Bowman and then Dr.
6 Halpern, and then perhaps we will close, so
7 that we can move on.
8 Dr. Bowman?
9 MEMBER BOWMAN: Yes, just very
10 quickly, I want to thank Ms. Leubke for coming
11 here this morning and presenting this
12 information. A picture is worth a thousand
13 words. Also, thanking her for presenting it
14 to the CDC and to our HRSA.
15 But the picture is very important,
16 I think, that she presents. She gave a very
17 graphic description of what often a typical
18 donor looks like when they appear at a
19 hospital, and they have to evaluate that donor
20 under duress, you might say. So the
21 information is limited, which puts an
22 extraordinary burden on that particular OPO

1 staff to try to elicit the kind of information
2 that will tip them off that it could be a
3 problem.
4 She mentioned that the donor may
5 have had clotting factor problems, or
6 whatever, Often, that has to come from a
7 family member or a friend that is familiar
8 with that donor's medical problems.
9 Dr. Acusni in the article that was
10 circulated to the Committee members touched on
11 some of this. All the tests in the world, we
12 are not going to be able to screen out all the
13 infectious organisms that are out there.
14 There are hundreds and hundreds of them, as
15 Dr. Ison and Dr. Kuehnert have informed us.
16 But a lot of times it just gets
17 back to good, old-fashioned basics of high
18 touch, talking to the family, touching the
19 patient, eyeballing the patient, whether it is
20 the physician or transplant coordinator or ICU
21 nurse, or whoever. And it is just plain, old,
22 good-fashioned, old-fashioned medicine.

1 Often, that time just is not there, but it
2 does put an extraordinary burden on the OPO.
3 Again, Ms. Leubke, I want to thank
4 you for pointing out the problems with
5 informed consent. This is an excellent
6 dovetail to Dr. Halpern's presentation.
7 Some of those issues have been
8 addressed by the subsequent CMS conditions of
9 participation for transplant centers that came
10 out in 2007, with the dual-stage informed
11 consent and especially the second stage that
12 requires the transplant center and surgeon to
13 let the potential recipient know of any donor-
14 specific factors that would affect the safety
15 of that organ.
16 So, again, thanks.
17 CHAIR BRACEY: Thank you.
18 MS. LEUBKE: I would just like to
19 thank Dr. Bowman and Dr. Kuehnert for talking
20 to this woman. But it was the second hospital
21 where she second-listed. So she actually
22 feels sort of betrayed that she was not told

1 that hospital No. 1 felt this was a poor-
2 quality kidney for her, and that hospital two
3 took it without full disclosure of that
4 information.
5 CHAIR BRACEY: Thank you.
6 Dr. Halpern?
7 DR. HALPERN: Thank you, Donna.
8 I was just wondering, it seems
9 that there are full discrete areas where one
10 might imply that errors occurred in this
11 process. I think probably most of us could
12 agree that better accountability once the
13 transmission was ascertained, we could
14 probably all agree that that was in order.
15 And I think we could all agree
16 that a better, more robust informed consent
17 process, so that the patient understood what
18 she was getting herself into, and that all
19 patients understand what they are getting
20 themselves into when they put themselves on a
21 list, or in this case multiple lists, for
22 transplantation.

1 I think what is less clear to me
2 is that an error in decisionmaking to provide
3 the organ was made here. I was wondering, if
4 those other two errors had not happened, if
5 you, in your conversations with this woman,
6 would she have perceived that an error in
7 decisionmaking occurred?
8 MS. LEUBKE: Decisionmaking to
9 accept that kidney for her?
10 DR. HALPERN: Yes.
11 MS. LEUBKE: Yes, because she felt
12 that if a surgeon at one hospital felt that it
13 was a poor-quality kidney, and she was stable
14 on dialysis and taking care of her family, why
15 was there urgency for her to go to transplant
16 with that kidney at that time?
17 So she feels it set up this whole
18 circumstance in which the exposure presented
19 itself because -- I think she just wants
20 answers, and part of the frustration is she
21 believes she went to every agency or group
22 that is charged with a duty to get answers,

1 and nobody cared to really be there and
2 support her, and that it has basically taken
3 five years.
4 Personally, I don't know that it
5 should have ever come to my attention. You
6 know, I am here as a private citizen
7 representing her to protect her privacy, but
8 I feel that we have a real problem with the
9 system if it takes five years later for it to
10 be delivered to Medina, Ohio, and that is how
11 it comes to the attention of the CDC.
12 CHAIR BRACEY: Thank you.
13 Dr. Holmberg has a statement.
14 DR. HOLMBERG: You can go ahead,
15 Mike, and get set up.
16 I just want to make the Committee
17 aware of another set of emails that came in to
18 me from a patient family. I don't want to
19 read this into the record, but I do want to
20 draw your attention to it. I have given you
21 copies of it.
22 It is in response to a kidney

1 transplant on a patient. This is from Shirin
2 Platt on March 14th, 2009, but just to
3 highlight that the patient received the kidney
4 from a woman that came out of the country,
5 that was originally from a South American
6 country. After transplantation, the patient
7 developed Strongyloides and it was related
8 back to the kidney.
9 So what I will do is I will have
10 this transcribed into the record, but will not
11 read this at this time.

1 To the Advisory Committee on Blood Safety and
2 Availability:
3
4 My husband, Peter C. Platt, was the
5 recipient of a kidney transplant on March 14,
6 2009 at New York Presbyterian Hospital. I
7 would like to inform you of the process that
8 led to his transplant and his untimely death.
9 While under the care of his
10 nephrologist, Dr. Alan Haratz in Eatontown,
11 NJ, it was determined that Peter would need to
12 begin dialysis due to his failing kidneys and
13 also to go through the process of being
14 accepted on the New Jersey transplant list
15 through St. Barnabas Hospital in Livingston,
16 NJ. All the testing was completed and he was
17 accepted on the transplant list. He was on the
18 list for almost three years before, upon
19 recommendations he decided to go through the
20 process in New York at New York Presbyterian
21 Hospital. He was accepted there in January of
22 2009. Upon their suggestion, his wait time was

1 transferred from New Jersey to New York, and
2 he began receiving calls about available
3 kidneys shortly thereafter. Even though he
4 wasn't listed as wanting to be considered for
5 a kidney which would be an "expanded criteria"
6 kidney, he started receiving calls fairly soon
7 after being accepted on the list. One was even
8 from an IV drug user from California, which
9 Peter declined.
10 A call came in on March 13 concerning a
11 kidney that would soon be available, the donor
12 being a 58 year old woman from Las Vegas,
13 Nevada, (originally from Honduras) with
14 asthmatic complications, and her family would
15 be donating her organs upon her death. Early
16 on the morning of March 14, we received a call
17 that Peter was a good match and he decided to
18 accept the transplant.
19 The transplant was performed at New York
20 Presbyterian Hospital by surgeon Dr. Lloyd
21 Ratner. It was forty hours between the removal
22 of the kidney from the donor to Peter

1 receiving the kidney. The surgery took a
2 little longer than the surgeon expected, but
3 we were told that it went well. .Peter was in
4 the hospital until Wednesday evening, when he
5 was discharged.
6 Following Peter's discharge from the
7 hospital, his care was overseen by Dr. R. John
8 Crew at New York Presbyterian. The kidney was
9 very sluggish and we were told that sometimes
10 it took quite a while for the kidneys to "kick
11 in." He received various treatments for the
12 following three months. The treatments
13 included, among other things, two biopsies of
14 the kidney, ultrasounds, injections of
15 Arinesp, IV immunoglobulin, Zenopaz and
16 Neupogin, as well as continuous blood tests
17 and monitoring of his creatinine level and
18 other cultures. He seemed to be doing well
19 during this time except for the slow start of
20 the kidney and a low white blood count.
21 However, during his appointment with Dr.
22 Crew on Monday, June 15, following a weekend

1 of not feeling well, it was determined that he
2 was extremely ill. Because a room wasn't
3 available in the MICU, he was sent to the
4 emergency room. He rapidly grew weaker and
5 weaker and was vomiting "coffee grounds"
6 colored blood, a gastric levage was performed
7 and he started receiving blood transfusions.
8 His breathing became so labored that he was
9 sedated and intubated. Finally, after 22
10 hours, he was rushed to the MICU. From this
11 time on, he never woke up.
12 After many tests and some time, it was
13 determined that the blood in his lungs and
14 stomach and the severe rash on his torso, both
15 front and back, and partly on his legs and
16 arms, was being caused by the parasite
17 strongyloides. Dr. Brian Scully of Infectious
18 Diseases treated Peter with Ivermectin and
19 Albendozole for the parasite, along with
20 additional treatments for the many ensuing
21 infections that continued to develop. He also
22 received many blood transfusions. Following

1 the month-long treatments, Peter never
2 regained consciousness and passed away, with
3 his family by his bedside, on July 15, 2009,
4 after two EEGs determined that there was no
5 brain function and that none of the treatments
6 could save his life. I was asked if we wanted
7 to have an autopsy performed but I declined,
8 feeling that my husband and family had been
9 through enough.
10 It was made clear to me by medical staff
11 treating my husband that the parasite came
12 from the donated kidney. After the
13 strongyloides was diagnosed, the New York City
14 Department of Health and the CDC became
15 involved because of the infected transplanted
16 kidney. I have written to both the CDC and the
17 New York City Department of Health. The CDC is
18 still investigating my request for information
19 and I have been in phone contact with Dr.
20 Sally Slavinsky of the city department, who
21 informed me of the ongoing studies and this
22 meeting.

1 The concerns of my family and friends
2 lies in the procurement of donated organs and
3 how the organs are tested prior to being
4 considered for transplant. We understand that
5 time is an issue from donation to transplant,
6 but certainly this tragic turn of events in my
7 husband dying following the transplant of an
8 infected kidney warrants further
9 investigation. And perhaps another question
10 would be why the kidney was transported from
11 Las Vegas to New York, thus delaying the
12 surgery. Are the risks from organs not
13 completely tested worth the chance of
14 infection, and the untimely death of my
15 husband of almost 43 years? Certainly, from
16 our perspective, it is not.
17 Hopefully, the studies of these
18 procedures will begin to change organ
19 procurement, or, at the very least, make sure
20 that possible recipients know more of the
21 dangers from transplants.
22 Thank you for your time. I hope that I

1 will be informed of further studies.

2 Sincerely,

3 Shirin (Sha-reen) Platt

4 45 Sunnybrook Drive

5 Freehold, NJ

1 To the Advisory Committee on Blood Safety and
2 Availability
3 Attention: Jerry Holmberg
4 My brother, Peter C. Platt, was the
5 recipient of a kidney on March 14, 2009 at New
6 York Presbyterian Hospital.
7 You have received communication from his
8 wife, Shirin Platt, outlining the process of
9 his transplant and subsequent untimely death
10 on July 15, 2009. Please allow me to share
11 some additional comments:
12 The loss that Shirin and our family has
13 suffered cannot be measured. During the month
14 that my brother was in the MICU at New York
15 Presbyterian Hospital, my husband and I made
16 a total of five trips to NY from Virginia,
17 each time hoping and praying that we would see
18 some improvement in his condition. Although
19 the hospital staff was excellent, they were
20 not able to offer much encouragement. His
21 wife, sons, daughter, siblings and close
22 friends lived a nightmare for the entire

1 month.

2 We can only go forward from here and

3 pray this never has to happen to another

4 recipient. It is our hope that new guidelines

5 and procedures for testing blood products and

6 donated organs can be developed so that

7 parasites, such as Strongyloides, can be

8 detected before organs are transplanted. While

9 we are aware of time factors in harvesting

10 organs and transplantation, it appears that,

11 in this case at least, my brother was placed

12 at great risk given the lack of testing of his

13 donated kidney.

14 We respectfully request that the

15 concerns raised by my brother's tragic outcome

16 will be thoroughly addressed by this committee

17 as you meet on November 19-20, 2009. Thank you

18 for your attention to our concerns.

19 Sincerely,

20 Donna Platt Whitney

21 5715 Lakemere Drive

22 Richmond, VA 23234

1 CHAIR BRACEY: Thank you.
2 Dr. Kouides?
3 MEMBER KOUIDES: Excuse me.
4 Before Dr. Ison begins, could you just clarify
5 with the first testimonial, Pam Alesescu, she
6 mentions in her text, and as she said, about
7 guidelines of the FDA, that the tissue
8 processor's actions remain within the
9 guidelines of the FDA regulations.
10 Do we have that for review, those
11 regulations? Did I miss that? Were they
12 somewhere for our -- were they disclosed to us
13 at the beginning of this meeting, those FDA
14 regulations?
15 CHAIR BRACEY: Yes. Actually, I
16 don't think those were distributed.
17 Dr. St. Martin, did you --
18 MEMBER ST. MARTIN: Well, I just
19 wanted to comment because I had asked for that
20 clarification. In 2001, if it was regulated
21 as a device, the regulations we presented
22 yesterday would not have been applicable, and

1 they were not in existence at the time of the
2 implant anyway. So they would have been
3 devices at that time. Now they are under the
4 tissues rules. The same for dura mater. Dura
5 mater used to be a device; now is it a tissue.
6 CHAIR BRACEY: Okay.
7 So we have Dr. Ison. Dr. Michael
8 Ison is a member of this Committee, and he
9 will present to us on the donor risk
10 assessment and the role of the OPTN Disease
11 Transmission Advisory Committee.
12 Dr. Ison is an Assistant Professor
13 in the Division of Infectious Diseases and
14 Organ Transplantation at Northwestern.
15 MEMBER ISON: Right. Thank you
16 very much.
17 I do want to thank our last
18 speaker because it highlights, I think, the
19 importance of this Committee of evaluating and
20 investigating, or helping to investigate,
21 potential disease transmissions.
22 So what I thought I would do today

1 is give an overview of the policies that are
2 present in the OPTN that help us recognize and
3 investigate these potential disease
4 transmissions; present to you the data that we
5 have to date with a focus on what we have
6 learned from that data.
7 I think it is important to
8 recognize that this Committee is changing its
9 focus from being a bean counter, counting how
10 many cases of which types of infections, to
11 looking critically at the data, to what can we
12 learn from this data and what can be done
13 about that education. Then I will conclude
14 with what is going to be my opinions of
15 current gaps that we have identified through
16 this process.
17 So you have seen a wide variety of
18 policies that have been put up, and this
19 Policy 4 I think is the third or fourth time
20 it has been presented. This is the policy
21 that deals with donor disease transmission
22 that specifically states that, when a

1 transplant program is informed that an organ
2 recipient at that program is confirmed
3 positive or has died from a transmissible
4 disease or medical condition for which there
5 is substantial concern that it could have been
6 from donor origin, the transplant program must
7 notify by phone and provide available
8 documentation as soon as possible, and not to
9 exceed one complete working day, to the
10 procuring OPO.
11 It further goes on to require that
12 the OPO will communicate all of this
13 information to all recipient transplant
14 centers and tissue banks. They will manage
15 the investigation. They will notify OPTN as
16 soon as possible and submit a final written
17 report to the OPTN 45 days after the initial
18 report.
19 This is the current makeup of the
20 Disease Transmission Advisory Committee. As
21 you can see, we are a broad range of
22 clinicians and OPO staff that represent the

1 entire nation from East Coast to West Coast,
2 and represent experts in transplant pathology,
3 nephrology, infectious disease, transplant
4 surgery, as well as adult and pediatric
5 representations, as well as representatives
6 from several different OPOs.
7 We have ex officio representation
8 from the CDC. We also have ex officio
9 representation from HRSA, as well as a number
10 of members from UNOS that sit in and
11 participate in our call.
12 Thinking through how we actually
13 do our work, once a report is made to the
14 OPTN, one of our liaisons prepares a summary
15 of events and redacts all pertinent materials,
16 so that there is no patient OPO or transplant-
17 specific identifiers.
18 This is, then, uploaded to a
19 password-protected share-point server, and an
20 email is sent to all members with a query and
21 with information and a link to the folder on
22 the share-point site. People then log in,

1 look at the information that has been provided
2 to them, and respond with queries and
3 recommendations over the course of 24 to 48
4 hours. This is, then, collated by the
5 liaisons and fed back to the transmit centers
6 and OPOs, and ensuing rounds of data and
7 discussion continue from there.
8 On situations in which it is a
9 reportable disease or a disease for which
10 there is the potential epidemiologic
11 importance recognized by the Chair, report the
12 case to the Centers for Disease Control and
13 recommend reporting to the local public health
14 services.
15 From time to time, we have event-
16 specific conference calls. This is generally
17 held in the case of one of two situations.
18 One in which it seems that one or several of
19 the involved groups is not moving forward in
20 what is felt to be a quick-enough fashion or
21 is kind of blowing off the report, but, more
22 typically, in the setting of a reportable

1 disease in which it is felt that the need for
2 sharing information needs to be real-time and
3 rapid.
4 We then review day 45 reports, and
5 on a monthly basis, about every second
6 Thursday of the month, have a conference call
7 that lasts about an hour, where we discuss in
8 detail each of the cases reported over the
9 last month to discuss, basically, what the
10 Committee thinks up to that point, what
11 outstanding issues and queries remain.
12 We also have just recently
13 established a system to review the 45-day
14 reports and, hopefully, close out or make
15 final determinations about the current status
16 of a potential case.
17 From time to time, there's
18 outstanding queries that may come back to the
19 Committee for discussion at these monthly
20 conference calls.
21 In addition, we meet twice a year
22 and review all the cases over the past six

1 months, trying to finalize the status of the
2 case, whether it is proven transmission,
3 probably, possible, or indeterminate, or
4 excluded, if that has been the determination.
5 We try to come up with a finalized
6 categorization of all those events for
7 reporting purposes.
8 We then look at the data and try
9 to understand if there is a need to recommend
10 change in policies to enhance safety, and then
11 do things such as make recommendations about
12 leadership and membership.
13 We are currently reporting at each
14 OPTN/UNOS Board meeting, present at as many
15 national and international transplant meetings
16 as we possibly can, and are in the process of
17 trying to do annual publications of the
18 lessons learned, the first of which came out,
19 as referenced here, in The American Journal of
20 Transplantation in August of this year.
21 I think it is important to look at
22 where we have come and where we are going as

1 far as number of cases reported. You can see
2 from this that there has been an exponential
3 increase from seven cases in 2005, the first
4 full year in which reporting was required, up
5 to what we are estimating to be 152 cases this
6 year. As you can see, to date, we are at
7 actually 135 cases, which is higher than any
8 previous year.
9 Interestingly, as I will show you
10 in the next couple of slides, the reliability
11 of these reports, i.e., what proportion of the
12 total reports represent actual proven
13 transmissions, has increased substantially
14 from year to year. I think that this is
15 important to recognize because it suggests
16 that there is probably underreporting, not
17 really an increase in disease transmission.
18 We also recently took a look at
19 the data to see, is everyone doing their fair
20 share of reporting cases? And my feeling is
21 anytime there is significant variability,
22 there's lessons to be learned to improve

1 reporting.

2 So we first looked region to

3 region to see if there was variability.

4 Clearly, there is, although that variability

5 is slightly less significant than we initially

6 thought that we would see.

7 But when you look at the specific

8 DSAs or OPOs, there is huge variability, from

9 zero reports in the case of 16 donor service

10 areas up to almost 5 percent of total organs

11 transplanted for that DSA.

12 I would submit that the 16 DSAs

13 that aren't reporting anything clearly are

14 underrecognizing the potential transmissions.

15 Because, over a two-year period, I find it

16 hard to believe that there isn't even a single

17 case in which there's a concern of potential

18 disease transmission.

19 Now, looking specifically at what

20 data we have collected, for each of these

21 there's going to be two sets of slides. The

22 first two sets are 2006 to 2008, which are all

1 data that have been fully reviewed, fully
2 categorized by the Committee.
3 The subsequent slide will be the
4 current year data, which is 2009 data, for
5 which only about the first six months has been
6 appropriately categorized. So we need to look
7 at it from that lens.
8 From a malignancy standpoint, we
9 have had, in 2006 to 2008, a total of 99
10 reported cases, nine confirmed transmissions,
11 and four associated deaths related to those
12 transmitted malignancies.
13 As you will see, and this is a
14 recurring theme, the most common malignancy
15 that has been recognized is renal cell
16 carcinoma. I will talk a little bit more
17 about that in a second.
18 Looking at 2009, we have seen 36
19 reports of malignancy, with renal cell
20 carcinoma, yet again, being at the top of the
21 list. There have been eight confirmed
22 transmissions, with one associated death

1 currently recognized this year.
2 So what can we learn from this
3 data? Well, really, there's a group within
4 DTAC that has specifically been pulled
5 together that includes members of DTAC as well
6 as outside malignancy experts to start looking
7 at the issue of malignancy.
8 I think that it is important to
9 recognize that our current reporting system
10 has a clear flaw when it comes to malignancy.
11 A day 45 report, I would submit, is
12 essentially useless in investigating a
13 malignancy transmission because the natural
14 history of malignancy is such that 45 days may
15 pass and a malignancy may have been
16 transmitted, but just not recognized in a
17 hospital. Based on current policy, it is hard
18 for us to actually go back and look at that.
19 To overcome that, we are actually
20 looking at the information that is required to
21 be reported to UNOS related to any malignancy
22 that is present in the recipient. There's

1 challenges with that because it is categorized
2 in one of four categories and not further
3 clarified. So it is either donor-derived, de
4 novo, pre-existing -- and I am blanking on
5 what the fourth category is. But, basically,
6 if it is donor-derived and listed as that, we
7 don't know if it truly is, what type of
8 malignancy it is.
9 Likewise, the thing that we are
10 concerned with and we are looking at is, if
11 you have multiple recipients of the same donor
12 that actually have the same, let's say, colon
13 cancer that is presenting, is that de novo
14 colon cancer in the recipients or is it
15 disease that has been transmitted through the
16 organ?
17 So we are trying to get at that
18 through kind of a backdoor approach. We are
19 thinking about policy changes to allow
20 expanded followup of these individuals.
21 I think the biggest concern, as we
22 have heard, that there is a significant need

1 for organs. In the case of renal cell
2 carcinoma, this has resulted in discard of
3 organs, which this year outnumbers the number
4 of cases reported to us.
5 This is challenging because,
6 again, anytime you have variability in care,
7 it suggests that there is the potential for
8 improvement. It is not as though there is a
9 consistent approach across the country or from
10 case to case. Oftentimes, it is the cases in
11 which there's probably the lowest likelihood
12 of concern for disease transmission that the
13 kidneys are discarded.
14 So the working group is actually
15 looking at different ways that we can identify
16 challenges to the system and provide guidance
17 to the transplant community about how to best
18 evaluate kidneys and other organs for these
19 malignancies and, when recognized, how to
20 manage the situation.
21 This was initially presented at
22 the Organ Donation Congress in Berlin just a

1 month ago, and actually was well received by
2 the Europeans, who, it should be noted, I
3 think are a little bit ahead of the United
4 States on the whole issue of malignancy.
5 We are in the process of
6 completing a resource document that will be
7 approved by the UNOS Board at the spring
8 meeting.
9 Now looking at disease
10 transmissions related to infections, this is
11 data from 2006 to 2008. The four most common
12 reports are for hepatitis C, bacterial
13 transmission, HIV, and tuberculosis. You will
14 see many of these are recurrent themes as we
15 move into this year.
16 I think it is important to
17 recognize that, in the case of hepatitis C,
18 there are two instances of transmission. One,
19 which is well-known, with the co-infection of
20 HIV and hepatitis C from one high-risk donor
21 to four recipients who acquired both
22 infections. The second occurred from a non-

1 high-risk donor who resulted in transmission
2 to three patients of just hepatitis C alone.
3 What this actually showed us, and
4 I will speak a little bit more in a few
5 minutes, is that screening for recipients is
6 a challenge and not completely done, as I will
7 show you some information later in the slide
8 sets.
9 But, more importantly, most
10 clinicians are actually using the wrong test.
11 In every case of hepatitis C transmission that
12 has been confirmed through organ donation, the
13 recipients have been sero-negative, NAT-
14 positive to confirm the transmission. In many
15 cases, including the HIV/hep C case, in which
16 the index patient was tested three times
17 serologically for hepatitis C, and had
18 negative testing, giving a false sense of
19 comfort to the team that was evaluating that
20 individual.
21 The majority of those cases,
22 though, I think are very important because the

1 remainder of the 17 cases minus the two
2 confirmed transmissions, and 11 of the 12 HIV
3 cases, are generally false-positive or non-
4 reproducibly positive nucleic acid testing.
5 Most of these instances resulted in loss of at
6 least one organ from use. So, again, we are
7 losing organs for no significant safety
8 benefit in these situations.
9 But I think it is more important
10 because it raises the question of, what is the
11 true false-positive rate as NAT is used in the
12 OPOs in the United States currently?
13 Then I will talk a little bit more
14 about bacterial transmissions in a few minutes
15 when I move into our current data, which, as
16 you will see, is a significant increase in
17 numbers; likewise, with tuberculosis.
18 So, in 2006 to 2008, we had 115
19 unexpected disease transmission reports
20 associated with 36 confirmed transmissions and
21 12 associated deaths.
22 Looking at the data for 2009,

1 there is some change, although the top three
2 at least are still essentially the same. We
3 have seen a significant increase in the number
4 of bacterial transmissions with more cases
5 with confirmed transmission and associated
6 death. What is important is many of these
7 cases have also resulted in loss of organs.
8 Likewise, we have a significant
9 uptick in the number of confirmed tranmissions
10 of tuberculosis in this year and a significant
11 increase, although it is spread out, of fungal
12 infections, if you total up cocci, crypto, and
13 zygomycetes.
14 So, so far to date, we have 81
15 reports of infectious disease transmission,
16 resulting in 18 confirmed transmissions and 10
17 associated deaths.
18 So I thought it would be also
19 important to highlight a few things that we
20 have discovered this year. One, we have
21 recently become aware of hepatitis C
22 transmitted through the use of cadaveric donor

1 vessel, in which an HCV-positive donor vessel
2 was used in a hepatitis C-negative living
3 donor recipient. This resulted in
4 transmission of hepatitis C, as is documented,
5 again, with sero-negative, NAT-positive in the
6 recipient on evaluation.
7 The real challenge is this was
8 only identified through a DEQ evaluation and
9 took three months after the transplantation to
10 recognize the disease transmission. As a
11 result of this, further investigation is
12 ongoing, and there are a number of other cases
13 that are currently undergoing evaluation.
14 To mitigate this, we and other
15 groups are actually looking at what needs to
16 be changed from a policy standpoint, and we
17 have prepared and submitted and sent a formal
18 notification to the members for the need to be
19 diligent in labeling and checking of vessels
20 and the need to perform appropriate consenting
21 of recipients of these tissues.
22 Now moving on to the issue of

1 bacterial transmission, so we have seen a
2 significant increase in the number of reports
3 and, as mentioned, an increased number of
4 transmissions and deaths and organ losses, the
5 result of these transmissions.
6 All of the deaths this year have
7 been the result of two separate Pseudomonas
8 cases and highlight one of the common
9 features, that oftentimes it is actually
10 resistant bacteria that result in
11 transmission, suggesting that some of our
12 patients may be acquiring these hospital-
13 acquired pathogens that may be resistant to
14 the standard antibiotics that are used as part
15 of routine prophylaxis in these patients.
16 We have also identified a
17 significant challenge of pre-donation culture
18 issues. What you have to recognize is that
19 most of the donors are considered patients in
20 the hospital cared for by one team. Then,
21 once they are declared brain dead and consent
22 is obtained, transfer of care is done to the

1 OPO or organ procurement organization. The
2 way that this is handled at an individual
3 hospital is quite variable. Some hospitals
4 actually close the account and technically
5 discharge the patient and readmit them under
6 a new account number for accounting purposes.
7 What this may do at some hospitals
8 is that it actually causes the lab to throw
9 out some of the ongoing cultures. In other
10 situations, it may make it harder to link the
11 patient chart back if someone is looking in
12 the computerized record because there is now
13 a dislink from the hospital discharge process.
14 It also raises some challenges
15 that have been highlighted by others with the
16 issue of handoff. So, if a patient has a
17 positive culture, standard of care would be to
18 start treatment and repeat cultures to ensure
19 that the pathogen has cleared. In a few
20 instances, that subsequent culturing has not
21 occurred until the required culture is
22 obtained at the time of procurement, which may

1 take up to five days to become positive.
2 Additionally, there are
3 significant communications issues. All of us
4 come to appreciate the ability to look at our
5 own hospital medical record, but I think we
6 all recognize that identifying where the
7 critical bits of data are is sometimes a
8 challenge, even when you know how to use your
9 system.
10 These OPO people are coming to
11 different hospitals every day potentially and
12 are logging into systems that they may be less
13 familiar with. Further, there's different
14 degrees of information access that these
15 individuals are given. So their ability to
16 have a complete history may be challenged,
17 actually, by some of the systems that we have
18 been put into place to enhance the history and
19 access to this data.
20 Likewise, there are some
21 challenges with communicating information from
22 the transplant centers to the OPOs. This is

1 better highlighted in the PPD cases, but also
2 there's challenges to communicating
3 information from the OPOs to the transplant
4 centers.
5 There's no standard approach of
6 who is responsible for those results at the
7 transplant centers and in many cases at the
8 OPO. Oftentimes, what is happening is the
9 information is being called to a pre-
10 procurement coordinator, who may not even
11 realize how important that information is, and
12 is not directly caring for the individual.
13 We are in the process of
14 developing a guidance document related to
15 bacterial transmission, at the request of the
16 MPSC, as a result of one of these transmission
17 events.
18 Next, mycobacteria, clearly, as
19 you can see from this graph, has increased
20 significantly year over year, such that there
21 are now at least 12 reported cases with a
22 significant number of potential transmissions.

1 There are huge challenges with
2 recognizing TB in these individuals. There
3 are currently no approved donor screening
4 methods. The PPD, for a variety of reasons,
5 can't be placed on these individuals because
6 they may be procured before that test could be
7 read.
8 And laboratory-based assays, such
9 as the interferon-gamma release assay or the
10 ELISPOT assays, have never been studied in
11 this population. Because there's disregulated
12 cytokine release, they may not be effective or
13 result in significant false-positive rates
14 that would rule out potentially donors.
15 There's challenges with
16 outstanding cultures. Sometimes the OPOs
17 don't even recognize that the culture has been
18 sent, particularly if it was sent in a prior
19 hospitalization. This is important because TB
20 cultures may take up to six weeks to turn
21 positive.
22 There are also challenges in

1 linking the positive culture to the donor. We
2 have had now several instances where the
3 information is provided to the public health
4 service in the local region, and they have no
5 idea that the patient has become donor. So,
6 although they begin an investigation into that
7 TB transmission, or TB positivity, they don't
8 know to contact the OPOs to give them that
9 important information.
10 Likewise, there's no data that has
11 been collected on what markers may give
12 indication of potential TB transmission in
13 these individuals.
14 Another thing that we have seen a
15 significant uptick this year is the number of
16 fungal infections, particularly
17 coccidioidomycosis. This is particularly
18 important because every case in which the
19 cocci has been documented to transmit to a
20 recipient, there's been at least one death in
21 those individuals.
22 It really raised some significant

1 questions about whether or not we need
2 guidance to areas that have endemicity to do
3 screening of these individuals, how to use
4 that screening test. But another issue that
5 was raised is, what would happen if you had a
6 patient from an endemic area travel to a non-
7 endemic region and die in that area and become
8 a donor? Would that area know what to do?
9 I think it is important to
10 recognize, although not captured by DTAC, a
11 similar transmission of histoplasmosis in
12 which a donor from the histo-endemic Ohio
13 River area was traveling in the Northwest,
14 became a donor, and transmitted histo to a
15 number of recipients in an area where histo is
16 not typically seen.
17 So, again, we have a working group
18 that is trying to put together some guidance
19 documents for addressing these issues.
20 We have seen a couple of other
21 diseases that have been recognized as well,
22 none of which have been recognized as

1 transmitting disease.

2 An issue that came up yesterday

3 is, are we doing a good job of testing

4 recipients for infections post-transplant? We

5 only have data on a very short period of time

6 in which we documented that, of the 8.8

7 percent of recipients of high-risk donors,

8 only 3.7 percent had any HIV post-transplant

9 testing, and only 5.9 percent had any

10 hepatitis C testing. Almost all of that was

11 serology, which would have clearly missed

12 disease transmission.

13 I feel that it is actually a major

14 problem that we are informing patients that

15 they have a receiving organ for which they

16 have potential risk of acquiring infection,

17 and then abandoning them by not doing the

18 post-transplant testing to show whether or not

19 they had that transmission, particularly since

20 early therapy in these individuals may be of

21 benefit.

22 Lastly, I thought I would

1 highlight a case from the past before DTAC was
2 in existence to show that these two fields,
3 organs and tissues, are inextricably linked.
4 This is a case of hepatitis C transmission
5 that was, unfortunately, first recognized
6 several years after an organ transplant had
7 occurred and resulted in significant hep C
8 transmission. But it was only when one of the
9 recipients of the tissue was recognized to
10 have hepatitis C that they went back and did
11 some additional testing.
12 I think this case actually
13 highlights a couple of issues. If we had been
14 testing these recipients of the organ
15 transplants for the disease transmission, we
16 would have caught it, and none of these
17 tissues probably would have been exposed to
18 the potential transmission.
19 Further, is it really acceptable
20 that, when we transmit hepatitis C, that there
21 is a two-year gap before that first patient is
22 identified as having an infection, when, in

1 fact, we have infected a significant number of
2 the recipients of these organs and tissues?
3 This, I think, raises one of the biggest gaps
4 in our current safety system.
5 Coming to the end, which is, what
6 do I see from the information that we have
7 acquired as significant safety gaps and
8 challenges? Well, the first deals with donor
9 medical and social history. Everyone in the
10 transplant community looks at this as the end-
11 all, be-all in making decisions about the
12 infectious disease safety of these patients.
13 Yet, no one has a standardized
14 approach that has been validated. Further,
15 there is no way of knowing, as was the case
16 that was presented earlier, of a mother who
17 hasn't even had contact with the patient to
18 know whether or not when they say they aren't
19 using IV drugs, how valid is that history?
20 Yet, that is a huge driver
21 currently at determining whether or not the
22 person gets NAT testing, whether or not they

1 are listed as high-risk, and whether or not
2 they in some centers get post-transplant
3 testing.
4 Further, as I have tried to
5 highlight, there are significant challenges to
6 medical and laboratory data; particularly, it
7 may be in an instance where our electronic
8 medical records may be a hindrance, instead of
9 in the past when you just had that big pile of
10 paper that it just took time to go through.
11 We currently, as was highlighted
12 with the handing out of Policy 12, have no
13 policy in place at the OPTN for living donors
14 screening. I think that is an important gap
15 that warrants addressing in the near future.
16 The high-risk donor criteria,
17 which we will be hearing about in a few
18 minutes, is slightly oversimplistic and
19 outdated, and needs to be updated.
20 Thankfully, that is occurring. It was
21 designed to exclude HIV, but has been used for
22 a broader purpose.

1 Then the real question is, how
2 valid are they? How good are they at picking
3 up patients that have latent blood-borne
4 pathogens in them? Or are we just identifying
5 patients at increased risk of having these, in
6 which our existing screening methods may be
7 appropriate?
8 We have other challenges related
9 to donor laboratory screening. Although there
10 is clear guidance for hemodilution in the
11 tissue population, these are not formally
12 codified by the OPTN as far as standards for
13 what defines hemodilution.
14 Serology is the mainstay of the
15 screening of our recipients. And as has been
16 highlighted, there are real challenges to the
17 availability of platforms and tests that are
18 appropriate for the OPOs, as has been
19 documented by the HTLV issue recently.
20 There's ongoing threats to the
21 availability of these platforms. Every year
22 over the last two years, at least one platform

1 has gone off the market and is no longer
2 available to us. There are no mechanisms to
3 really encourage companies to develop and
4 maintain these platforms and, more
5 importantly, to identify and study when new
6 pathogens need to be screened for or tested
7 for.
8 NAT, as has been highlighted,
9 there is currently no uniform policy in the
10 United States, and as a result, there's
11 significant variability. Each OPO,
12 essentially, has their own approach that is
13 different. Clearly, this needs to be
14 addressed in the near future.
15 But, importantly, this has to be
16 balanced with the issue that it may result in
17 organ wastage, and we have to really make an
18 assessment of, what is more important, as was
19 presented in the earlier presentation,
20 preserving the number of organs and the
21 benefit from that, or preventing an incredibly
22 rare transmission of a treatable infection?

1 Next, it is important that we have
2 a number of pathogens that other groups are
3 starting to think about screening, and yet, we
4 really don't have that yet on our radar
5 screen. We are starting to think about these
6 issues.
7 But, really, behind that is, how
8 will we determine how to add these, and what
9 funding mechanisms will document the safety
10 and efficacy of the specific tests as they
11 apply to this very unique population?
12 Lastly, there is currently no
13 global collection or presentation of data on
14 all donors. We only collect data on screening
15 results when at least one organ is procured
16 from a donor.
17 This is challenging, especially
18 when you look at things such as what's done in
19 the blood bank, where you can look at a map
20 and see where you have positive serology for
21 this or that pathogen. I think it is time
22 that we think about more proactively

1 collecting the appropriate data.
2 These are just other ideas that I
3 think we need to think about, how can we
4 enhance communication, both to improve
5 recognition, but also disseminate information
6 when it occurs?
7 Really, in part, this gets back to
8 some of the issues that the tissue discussion
9 revolved around. It really is that many
10 transplant centers don't take this seriously.
11 When we ask for information, it may take a
12 week to get information back on, even if they
13 are going to do testing of their recipients.
14 That is really not acceptable, in my opinion.
15 We need to do further education to
16 improve reporting, look, as Donna pointed out,
17 at systems issues to improve safety, and
18 really do a better job of capturing data.
19 Really, in my opinion, that is best done
20 through a prospective study.
21 So, with that, I think I have
22 presented a lot of information, and would be

1 more than happy to answer any questions that
2 you have.
3 CHAIR BRACEY: Thank you. That
4 was a very comprehensive overview.
5 Questions and/or comments? Dr.
6 Kuehnert?
7 MEMBER KUEHNERT: Thank you, Dr.
8 Ison. That was an excellent presentation, a
9 lot of issues that you brought up.
10 I wanted to clarify one thing. We
11 actually do not have a national database for
12 blood donor results. That is something that
13 would, in terms of biovigilance, would be
14 important to do. Of course, there are major
15 blood centers that publish their data on that
16 from time to time, but not a national
17 database.
18 MEMBER ISON: Although, though,
19 there is like the Chagas and West Nile that
20 actually do, from the AABB, have that publicly
21 available.
22 MEMBER KUEHNERT: Yes, for

1 selected pathogens, such as West Nile Virus
2 and Chagas, AABB had gotten voluntary results
3 on those particular pathogens, but not for HIV
4 and hepatitis viruses, for instance.
5 I wanted to ask you, it sounds
6 like there are a lot of initiatives for organ
7 safety ongoing within UNOS, but they are in
8 different areas. There's DTAC. There's
9 Operations. You mentioned DEQ and MPSC. I am
10 just wondering if you have suggestions on how
11 these groups could best work together, and is
12 there a role for perhaps organizations outside
13 UNOS to play a role now and in the future in
14 organ safety, given that, apparently, the UNOS
15 contract does not include any discussion of
16 organ safety? And therefore, right now, they
17 are basically operating somewhat out of their
18 purview, but, clearly, doing the right thing
19 by trying to address these issues.
20 MEMBER ISON: Yes. So, actually,
21 I would probably turn that over to Bob or Mary
22 D., since I know what is being done in the

1 purview for DTAC and am a member of the
2 Operations and Safety Committee, but for how
3 to coordinate that and who has priority, I
4 would have to defer to someone else.
5 Sorry to put you on the spot,
6 Mary.
7 CHAIR BRACEY: Introduce yourself,
8 please.
9 DR. ELLISON: I am Mary Ellison.
10 I am an Assistant Executive Director on the
11 staff at UNOS.
12 Mike is right, and Walter
13 mentioned yesterday that the contract has no
14 specific provisions for activities in this
15 area. And Matt is correct that staff operate
16 in this area in a number of sort of different
17 departments. They do coordinate with each
18 other.
19 Their activities are driven by
20 what the policies require and by some
21 operations that have been established to
22 support the Disease Transmission Advisory

1 Committee.

2 We have identified recently the

3 ability and the need to coordinate some of the

4 operations. The Research Department receives

5 the vessel tracking and disposition forms.

6 The Department of Evaluation and Quality

7 inquires with members when questions of policy

8 compliance are raised or to find out whether

9 information submitted to UNOS is accurate.

10 So now we have got the Research

11 Department talking to Evaluation and Quality

12 about observed information, the validity of

13 information, whether policies have been

14 complied with. Then those two groups are

15 working with the patient safety staff to pull

16 in the processes that they use to look into

17 whether or not there has been a potential

18 transmission.

19 So we are doing the best we can,

20 but it is driven by policy, No. 1, and

21 activities of specific committees, and most

22 specifically, the DTAC. And until and unless

1 we've got a dedicated -- well, I mean most of
2 our operations are dictated, actually, by
3 policy and committee activity. That is sort
4 of the way we work. So we think we are doing
5 pretty well with what we have got, but it is
6 not perfect, yes.
7 MEMBER KUEHNERT: Thank you.
8 CHAIR BRACEY: Dr. Triulzi, then
9 Dr. Bowman.
10 MEMBER TRIULZI: Can you describe
11 what are the adverse events or transplant-
12 related complications that are collected
13 outside of disease transmission? I am
14 thinking of things like graft versus host,
15 hemolysis from passenger lymphocytes,
16 thrombosis of an organ, hyperkalemia from the
17 preservative solution. Is that collected and
18 is that part of the Patient Safety Committee?
19 What is the scope of what is being collected
20 outside of what DTAC does?
21 MEMBER ISON: Right. So, again, I
22 would ask if either Dr. Metzger or Mary D.

1 would be willing to address that.

2 MEMBER TRIULZI: Sorry.

3 MEMBER ISON: So, just to give you

4 some information, the main way that

5 information is collected is through a

6 requirement to complete certain forms of the

7 recipients at fixed time points.

8 And what is on those forms are

9 approved every three years through a process

10 within UNOS, and then by OMB. What is

11 contained on those is variable. I would say,

12 for example, from an infectious disease

13 standpoint, the quality of the data and the

14 robustness of that data is somewhat limited.

15 DR. METZGER: As it is for most of

16 the other things you mentioned. They aren't

17 collected.

18 What we are primarily collecting

19 is data that substantiates patient graft

20 outcomes overall, and not specific patient-

21 indicated complications and things such as

22 that. They may be collected at various

1 transplant centers and reported in the
2 literature, but they are not collected in
3 general at the OPTN.
4 MEMBER ISON: So, if there were in
5 the contract a directive to collect patient
6 safety information that includes those items,
7 would that be helpful driving the centers to
8 complete the forms? You know, would that give
9 the teeth needed to get that information?
10 DR. METZGER: Yes, as long as it
11 would be funded both at the OPTN as well as at
12 the transplant center. Because a lot of the
13 issues are the funding that is available at
14 the transplant centers to provide the data to
15 the OPTN, and that is where there's a lot of
16 resistance to the amount of data you can
17 collect.
18 MEMBER ISON: At the OPTN?
19 DR. METZGER: The resistance is at
20 the transplant centers and the OPO because
21 they don't have staff or the resources,
22 either, under the current reimbursement

1 policies for providing those services to the
2 OPTN.
3 CHAIR BRACEY: Dr. Bowman?
4 MEMBER BOWMAN: Just a quick
5 clarification. I appreciate that, Dr.
6 Metzger.
7 Data collection is a fairly
8 cumbersome process that is subject to a number
9 of federal regulations involving the Office of
10 Management and Budget that requires that
11 Office's approval. It is done every five
12 years for the data collection forms for OPTN.
13 It is very cumbersome.
14 It is done on a five-year cycle.
15 The next cycle will end, I believe, in 2010.
16 Preparation has to be made well in advance.
17 So, given that, there has to be a
18 clear imperative for every single piece of
19 data that goes onto those forms that are
20 submitted to the OPTN that the UNOS contractor
21 develops. So, given all that, once the
22 process is in effect and certain data elements

1 are identified as necessary, they are put into
2 the OMB submission for that.
3 As a clarification for what the
4 UNOS, being the contractor for the OPTN, does
5 regarding patient safety, the absence of a
6 clear, specific directive in the OPTN contract
7 itself doesn't, obviously, mean that the
8 contractor is not engaged in patient safety
9 initiatives and concerns, as hopefully the
10 Committee has seen from the last two days.
11 The fundamental reason that OPTN
12 is what it is is to allocate appropriately, in
13 accordance with the statute of NOTA, solid
14 organs that are suitable for potential
15 recipients. That includes medical
16 suitability, obviously. That is inherent in
17 the process of what the OPTN is tasked to do
18 and what the UNOS, our contractor, is doing.
19 So I am not sure that we may not
20 ever see patient-safety-specific directives in
21 the contract with the OPTN contractor, but I
22 think you can see by the fact they've got a

1 Patient Safety Committee, a Disease
2 Transmission Advisory Committee, and
3 Operations Committee, and the Member and
4 Professional Standards Committee, it is
5 clearly inherent in just about everything that
6 the UNOS staff are doing.
7 CHAIR BRACEY: Let's take one last
8 question or comment from Dr. Williams. Then
9 we will need to move on.
10 MEMBER WILLIAMS: Just a couple of
11 comments on the donor history questionnaire
12 from the blood world.
13 After a decade-long process under
14 AABB's sponsorship, the donor history
15 questionnaire was reformulated. I think what
16 was accomplished was an evaluation of the
17 cognitive understanding of the questions,
18 logical organization, and a method for
19 addressing new questions, so that the
20 questionnaire didn't simply become a pathwork
21 again.
22 You mentioned the word

1 "validation". True validation of the
2 predictive value of the question to identify
3 a risk has been elusive and I think will
4 continue to be.
5 What we have been able to do
6 through extrapolation is estimate that
7 probably the positive predictive value overall
8 is somewhere between 80 and 95 percent, just
9 by extrapolating some other data.
10 But cognitive understanding and
11 organization of the question have been two
12 achievements, but validation is very, very
13 difficult in that setting.
14 MEMBER ISON: And then can I ask a
15 quick question, as a Committee member, to Dr.
16 Bowman?
17 If the patient safety is not part
18 of the contract, is that something that can be
19 supported through the federal funds or would
20 it have to become part of the contract to
21 increase financial support to support that
22 work?

1 MEMBER BOWMAN: Well, I don't
2 write the contract. So let me make that very
3 clear.
4 What I meant in my remarks earlier
5 is patient safety, especially as it relates to
6 identification of a medically-suitable organ
7 that can be allocated and distributed in
8 accordance with the statute of the NOTA, and
9 as it is codified in the final rule, is
10 inherent. So that is what I meant by the fact
11 that we may never see patient safety as a
12 specific item, line item, in scope of work for
13 the contractor.
14 But certainly the contractor and
15 OPTN are entrusted with identification of a
16 medically-suitable organ before that organ can
17 be allocated and distributed, in accordance
18 with the statute.
19 CHAIR BRACEY: Okay. Our next
20 speaker, then, is Debbie Seem. She is an RN
21 and Master of Public Health, and she comes
22 from Health Research Analysts at the CDC. She

1 is going to present an update on preventing
2 transmission of infectious disease through
3 transplantation of human tissue and organs.
4 Thank you.
5 MS. SEEM: Thank you.
6 What I will be talking about here
7 is giving a little information on the process
8 that we are using to help update these
9 guidelines and where we are in the process.
10 To a certain degree, these
11 guidelines are updating the 1994 guidelines
12 for HIV prevention of transmission through
13 transplantation, but we do have some major
14 differences in that the 1994 version addresses
15 organs and tissues and, to some degree, banked
16 breast milk and semen, and then the
17 recommendations for preventing transmission
18 are specifically for HIV only.
19 The newer recommendations will
20 address organs only. They will address
21 prevention issues related to transmission for
22 HIV, HBV, and HCV. We are also using an

1 evidence-based process.

2 We have some good reasons to

3 expand it to address HBV and HCV. As Mike had

4 pointed out earlier in his presentation, HCV,

5 HBV, and HIV are three of the five most

6 reported pathogens that are suspected as

7 donor-derived transmissions. This does not

8 mean they were actually transmissions, but

9 suspected.

10 This data are approximations

11 where there were, between 2005 and 2009, 28

12 reported cases for HCV, approximately 14 for

13 HBV, and 12 for HIV.

14 We have already talked about the

15 2007 case where there was a transmission of

16 HIV and HCV to four organ recipients. This

17 brought up a lot of discussion about whether

18 or not testing should be performed with regard

19 to HIV, HBV, and HCV.

20 So the question is, are current

21 serology tests sufficient? This is one of the

22 issues that will be addressed in the

1 recommendations.

2 Also, as was pointed out, the

3 risk, exclusionary risk factors in the 1994

4 guidelines for HIV are already being applied

5 in some cases to HBV and HCV. This has

6 resulted in inconsistencies in risk

7 assessments by the OPOs and then possibly

8 recipient management.

9 The goal of the guidelines is

10 based on targeted, systematic review of the

11 best-available evidence with explicit links

12 between the evidence and the recommendations.

13 We also are using grades to rate

14 the quality of the evidence and to also rate

15 the strength of the recommendations. The

16 value of using this evidence-based process is

17 that it makes the whole procedure transparent

18 and reproducible.

19 Just as with the 1994 guidelines,

20 CDC is taking the lead for the PHS agencies,

21 and we are also contracted with the Center for

22 Evidence-Based Practice at the University of

1 Pennsylvania Health System and the ECRI
2 Institute. These institutions both have a lot
3 of experience in developing guidelines using
4 the evidence-based practice.
5 We have two advisory groups. One
6 is the expert panel. They have expertise in
7 transplantation, organ recovery, laboratory
8 medicine, HIV and HBV, and HCV content, and
9 also expertise in consent issues.
10 The advisory group is comprised of
11 representatives from the PHS agencies as well
12 as members of the transplant community,
13 pharmaceutical manufacturers, a patient rep,
14 and also state health departments.
15 The difference between these two
16 groups is that the expert panel provides a
17 little more in-depth review of the materials
18 as they are produced versus the review
19 committee.
20 There are five phases to this
21 guideline development methodology. We
22 basically have one foot in phase four and the

1 other in phase five and leaning more into
2 phase five.
3 Where the expert panel and review
4 committee became involved is, after
5 development of the key questions and inclusion
6 and exclusion criteria for these guidelines,
7 they were able to review them and make
8 recommendations.
9 We have now, just the other week,
10 sent them the evidence report. It is probably
11 over a 500-page document for them to review.
12 I can see it is going to be a bit
13 of a struggle for some.
14 Then they will be, then, involved
15 also in reviewing the strength of the
16 recommendations in the actual guidelines.
17 Two, evaluate the evidence on
18 preventing blood-borne pathogen transmission
19 to recipients. We examine data addressing 10
20 key questions. These 10 key questions fell
21 under various key topic areas.
22 The first key topic area was the

1 risk of disease transmission through solid
2 organ transplantation. Our first question
3 was, what is the prevalence and incidence of
4 blood-borne pathogens among potential organ
5 donors? The second question, what is the rate
6 of transmission of these infected organs to
7 unaffected transplant recipients? And does
8 the rate of transmission vary by organ, and
9 does it vary by when the donor was infected?
10 The second key topic area was
11 potential risks and benefits of
12 transplantation of solid organs from infected
13 donors. We had one key question here. That
14 was, what are the clinical outcomes of
15 recipients of infected organs compared to
16 those who remain on the transplant waiting
17 list?
18 Another key topic area was about
19 the methods to mitigate the potential risks of
20 transplantation of solid organs from infected
21 donors. We had four key questions in this
22 area.

1 The first being, what are the
2 behavioral risk factors associated with
3 increased probability of infection? And what
4 is the prevalence of these risk factors among
5 potential solid organ donors?
6 The next key question was, what
7 are the clinical risk factors associated with
8 increased probability of infection? And what
9 is the prevalence of these risk factors among
10 potential solid organs?
11 We also wanted to know what were
12 the test characteristics of screening methods
13 to detect infection in the potential organ
14 donor, and some of these characteristics we
15 are looking at are sensitivity, specificity,
16 and the window period involved with each of
17 the tests.
18 The next question was, what were
19 the methods of inactivation that can reduce
20 pathogen transmission from infected donors to
21 infected recipients?
22 Another key topic area was the

1 potential risks and benefits of interventions
2 to mitigate transmission of transmissible
3 diseases.
4 Our first key question was, what
5 are the clinical outcomes of recipients
6 receiving organs from donors with behavioral
7 or clinical risk factors -- or how do these
8 clinical outcomes of recipients receiving
9 organs from donors with behavioral or clinical
10 risk factors compare to those who remain on
11 the list? What is the impact of excluding
12 potential donors with behavioral or clinical
13 risk factors on the organ donor pool? And
14 then, lastly, what is the impact of false-
15 positive tests on the organ donor pool?
16 This leads us to the production of
17 the evidence report, which is part of phase
18 four. The first three steps in this phase
19 were to conduct a systematic literature
20 search; create inclusion criteria for each of
21 the questions, and then screen the studies
22 that were produced for inclusion and exclusion

1 criteria.

2 Actually, this didn't come out

3 very well, but, basically, we conducted an

4 electronic search of 12 databases -- these are

5 the 12 databases that we used -- looking for

6 relevant information related to the 10 key

7 questions, using certain terms or specific

8 terms.

9 We then developed the inclusion

10 criteria. We had some general inclusion

11 criteria, such as it had to be in English,

12 peer-reviewed journals and studies for this

13 process.

14 Then we also had specific

15 inclusion criteria for each of the 10 key

16 questions. This purpose was to basically

17 eliminate bias in the evidence that was

18 produced.

19 Actually, I am having a little

20 trouble seeing this one.

21 So we started out with over 3500

22 articles that the abstracts were reviewed.

1 Through the process, then, a number of these
2 articles were eliminated. Then the actual
3 full texts were brought up of a smaller number
4 of these articles, and we ended up with 167
5 articles that met the inclusion criteria.
6 And I don't know if you can see
7 it, but for each of the key questions, various
8 numbers of articles supported the questions,
9 ranging anywhere from it looks like about 59
10 articles for Question 2 to some of the key
11 questions we weren't able to find any evidence
12 whatsoever in the literature.
13 The next two parts of phase four
14 were to extract data and assess the quality of
15 the studies. So the data was extracted from
16 the relevant studies.
17 Then, as I pointed out, where we
18 are is to have the evidence report reviewed by
19 the expert panel and the review committee.
20 This, basically, just shows an
21 evidence table. The value of these tables,
22 multiple tables were developed for each of the

1 key questions, depending on the type of
2 information we were gathering. It was able to
3 put the various studies in a format that we
4 were then able to do some comparisons.
5 And this goes to the grade table.
6 For each of the findings, a grade was
7 developed, and it was based on the quality and
8 the type of the evidence.
9 So trying to explain here, for the
10 finding -- let me just pull this up. Okay.
11 For the finding of -- this is
12 about the relationship of HIV infection to men
13 who have sex with men. If you look at the
14 bottom one for HIV association, we found two
15 observations. What they found was that there
16 was a high association.
17 Now the first grade that was given
18 was that, it started with a low grade, and
19 basically, randomized control studies were
20 given high grades; observational studies,
21 which most of ours were, were given low
22 grades, and expert opinions start out with a

1 very low grade.

2 Then the grade of the evidence can

3 go up or down depending on what is found in

4 the study. So, for the very last one, for HIV

5 and its association with men who have sex with

6 men, we started with a low grade and ended up

7 with a moderate grade of evidence.

8 These basically show you what

9 these grades represent. So, if you ended up

10 with a high grade, it meant that further

11 research is very unlikely to change confidence

12 in the estimate of the effects. Then you have

13 a moderate and low grade, very low grade

14 meaning any estimate effect is very uncertain.

15 So next steps: we are basically

16 looking at what goes on in phase five of the

17 guidelines development. We estimate it is

18 probably going to take two to three months or

19 more to get through this last step.

20 In phase five, we will write an

21 evidence summary for each of the key

22 questions. We will derive recommendations

1 from these evidence summaries. We will draft
2 expert opinion issues.
3 The review committee and the
4 expert panel will review all of this data, and
5 then the information or the guidelines will be
6 submitted for clearance and publication.
7 There were a number of issues or
8 points that were not amenable to a formal
9 review, and these fell under this other key
10 topic, which is approaches to how recipients
11 can be informed about the risk of disease
12 transmission and be evaluated for possible
13 exposure post-transplantation.
14 Actually, these are two of the
15 four points that we want to address in the
16 guidelines, the first one being discuss when
17 there may be a specific informed consent
18 process concerning risk of disease
19 transmission from the donor, and another being
20 propose when testing of the recipient should
21 be done to delete disease transmission from
22 the donor. There are two others here, but I

1 don't have them listed.

2 We have talked with our expert

3 panel, and they will be providing or writing

4 up the information for these various points.

5 And then, lastly, this is the

6 scheme that will be used to grade the strength

7 of recommendations. A Category 1 means that

8 it is a strong recommendation. Category 2

9 means it is a weak recommendation. Then,

10 within Category 1, you have various degrees of

11 the quality of the evidence.

12 I am not sure how we will be

13 applying these for 1A, B, and C. According to

14 the grade documentation, typically, if it

15 receives a Category 1, the strength or the

16 expectation is it is as high or as strong of

17 a recommendation as 1A as it would be to a 1C.

18 Then, in some cases, I think,

19 well, we will have cases where we will have no

20 recommendations. Then, also, we will be

21 making recommendations for further research.

22 Thank you.

1 CHAIR BRACEY: Thank you.
2 Questions or comments? Yes, Dr.
3 Ison.
4 MEMBER ISON: Debbie, thanks.
5 As someone that has gotten to look
6 at this 500-and-I-think-13-page document, it
7 is very impressive, but it is going to be my
8 Christmas reading or Thanksgiving reading, I
9 guess.
10 The question that I have, what
11 proportion of the information or questions do
12 you think there's actually quality evidence to
13 support a recommendation? And if it is the
14 substantial portion that aren't, what can we
15 recommend to help support getting that
16 information?
17 And then just a second point, I
18 think, that this last issue, that there's
19 nothing to guide evidence for when and how to
20 inform consent, I think suggests that this is
21 an area of need for research.
22 MS. SEEM: Yes. I, like you, have

1 not weeded my way through the entire document.
2 So it is hard to say at this point in time how
3 strong or how weak some of these
4 recommendations are or if there is sufficient
5 evidence.
6 I think, with that, that would be
7 part of this process, and that where we see
8 there is weak evidence or no evidence is when
9 we start devising and working with the expert
10 panel and review committee on deciding what
11 type of research is needed to answer some of
12 these issues.
13 MEMBER ISON: And then, as a
14 corollary to that -- and maybe Matt can answer
15 this -- since this is a Public Health Service
16 product, is there intention to put Public
17 Health Service money behind addressing some of
18 these gaps?
19 MEMBER KUEHNERT: Well, I can
20 answer part of the question. One is that we
21 went into this thinking that there would be
22 very little data to work with. Actually, we

1 were surprised that the contractors came back
2 with the over 500-page document on basically
3 the literature on organ safety, which really
4 tells you something. When we really look
5 rigorously at something, there is more
6 published than you think.
7 That being said, there is going to
8 be areas where there is, quote, "no scientific
9 evidence, no recommendation", but we assembled
10 the expert panel and the review committee in
11 order to gather opinions on each of the
12 questions because we need to answer all these
13 questions in the guideline.
14 I don't anticipate that we are
15 going to have an issue where we are going to
16 say, well, we just don't know what to say. We
17 really do need to have some recommendation on
18 each of the issues.
19 I think it is also important, even
20 though it was a 500-page document, to
21 anticipate that there's going to be a lot of
22 gaps and a lot of areas where research needs

1 to be done. We can point those out as part of
2 the value of the guideline.
3 What we cannot do, I think, is be
4 able to say where the resources will come from
5 to fill those gaps. I think that is something
6 that maybe the Committee could help direct the
7 Department to help do.
8 CHAIR BRACEY: Actually, that is a
9 segue into a broader discussion because,
10 actually, one of the things that occurred to
11 me is thinking of the Committee's role in
12 these deliberations and discussions, one
13 potential hazard is that we might become too
14 prescriptive. That is not really our role in
15 this, using the analogy of the FDA versus our
16 interaction with them on blood.
17 Clearly, what seems to be an
18 overriding theme is the lack of adequate
19 resources in order to acquire information
20 needed. I think this could be an important
21 element of what we do as a collective group to
22 address the needs.

1 MEMBER KUEHNERT: I just wanted to
2 say one more thing about the guidelines, which
3 is it certainly is going to be a
4 public/private partnership of the kind that I
5 was talking about in a different way, I guess,
6 in terms of identifying the scientific
7 evidence and having it lead to
8 recommendations.
9 In the end, there are going to be
10 PHS guidelines, but the expert panel and the
11 review committee are going to be very
12 important participants. Clearly, it is a lot
13 of work because it is an evidence-based
14 approach.
15 I don't know how many of these
16 sort of guidelines have taken this approach of
17 being both evidence-based and also involving
18 this sector outside PHS to engage in creating
19 this sort of thing.
20 I think that what I would ask the
21 Committee to do is think about whether this
22 could be a successful model for other efforts

1 as well.

2 The reason why we chose to do this

3 for organs first was because we think the need

4 is most urgent. Because of the factors that

5 have been presented here in the last two days,

6 the donor risks are ever-increasing.

7 One abstract that we didn't

8 present concerns the possible yield of nucleic

9 acid testing for high-risk donors, as defined

10 by the 1994 guidelines. The prevalence for

11 hepatitis C is between 15 and 20 percent.

12 This is far beyond anything that would ever be

13 seen for blood and tissue donors.

14 So I just want to give the

15 Committee a sense. And even looking at

16 donors, regardless of risk, we are looking at

17 a prevalence for HCV by serology of around 5

18 percent. So this is orders of magnitude

19 beyond anything I think the Committee usually

20 considers.

21 So I just ask you to keep that in

22 mind in terms of the urgency to really address

1 some of these gaps.

2 CHAIR BRACEY: Thank you.

3 Additional questions? Dr. Bowman?

4 MEMBER BOWMAN: Yes, Debbie,

5 thanks for the very nice and concise

6 presentation.

7 Just a point that I think the

8 Committee might be interested in, and maybe

9 you can shed some light on this, or maybe

10 Matt.

11 To the best of my knowledge, I

12 don't think we have any idea of the actual

13 true status and characteristics of those

14 potential donors that are not selected to be

15 donors by the OPOs, the ones that are sort of

16 pre-screened out or screened out in advance

17 before they are evaluated, worked up, and

18 reported to the OPTN.

19 MS. SEEM: Yes, that information

20 is not collected.

21 MEMBER BOWMAN: So there is a

22 whole universe out there, whether the HCV

1 prevalence is 5 percent per serology or 15
2 percent per NAT. Dr. Ison just presented data
3 that there have been two donors in the last
4 three years, I believe, with HCV that has been
5 transmitted. So that is a remarkable track
6 record, considering we sort of our groping in
7 the dark, I think, considering that that is
8 probably a denominator of about 25,000 donors
9 over the course of three years.
10 CHAIR BRACEY: Dr. Ison?
11 MEMBER ISON: I think it is three
12 hep C transmissions in the last year-plus.
13 CHAIR BRACEY: Okay. Any other
14 questions?
15 MEMBER ISON: I guess there is
16 another thing to point out, too The paradigm
17 that the transplant community is currently
18 using I think is flawed when it comes to hep
19 C. Everyone thinks in terms of high-risk
20 versus non-high-risk. Clearly, at least two
21 of these hep C transmission events have been
22 from non-high-risk donors.

1 MEMBER KUEHNERT: Yes, and we are
2 going to redefine those terms because in this
3 area, if you are comparing to other healthcare
4 settings, it would be high-risk and really,
5 really high-risk. So I think we have to
6 change the terminology.
7 CHAIR BRACEY: Dr. Pomper?
8 MEMBER POMPER: For my own
9 education, so 20 percent HCV versus three
10 patients in 25,000, the math doesn't add up
11 there. Could you clarify that?
12 MEMBER KUEHNERT: Yes. So those
13 -- and I am sorry we didn't have time to
14 present this abstract to give it really the
15 full description it needs.
16 But, basically, what we did is we
17 looked at a convenient sample of organ
18 procurement organization data, to look at the
19 serology results of donors that were screened.
20 About 10 percent of donors are high-risk
21 donors, as defined by the OPO. Of those,
22 between 15 and 20 percent were detected as

1 having HCV by serology.

2 From that and from extrapolation

3 from blood donors, you can model the incidence

4 and look at what the possible benefit of using

5 NAT would be. Clearly, there is a very

6 evident benefit of using NAT, particularly for

7 HCV, where you can decrease the window period

8 by 90 percent between serology and nucleic

9 acid testing.

10 MEMBER ISON: It is also important

11 to point out, for hep C at least, unlike HIV,

12 those hep C-positive organs still can be used

13 by the organ community because there's clear

14 outcomes data for most of the organs that use

15 of hep C-positive donors into a hep C-positive

16 recipient really has minimal difference in

17 outcomes from using a hep C-negative donor.

18 MEMBER KUEHNERT: And that is why

19 we considered this in the key questions for

20 the guidelines.

21 CHAIR BRACEY: Okay. Pardon me.

22 I think, if the Committee is ready, we need to

1 talk about moving toward a recommendation or
2 perhaps a set of recommendations. Because, at
3 this juncture, we have heard the evidence or
4 the presentations of all presenters on the
5 topics of safety with respect to tissues and
6 organs.
7 Just to sort of frame the
8 discussion, what I would look at is that we
9 have changed our schedule and we will have the
10 discussion carry on up until approximately
11 3:15, and we will have shuttles at 4:00 and
12 4:15.
13 If it is okay with the Committee,
14 I would suggest that we have an abbreviated
15 lunch break of perhaps 30 minutes, if that is
16 okay with the Committee. Okay?
17 So, that said, I think that what
18 we, at this juncture -- as I see it, the
19 framework, again, and I will just start this.
20 Let me start the discussion.
21 What we want to address are the
22 broad public policy issues with respect to

1 safety of tissue and organ transplantation.
2 We discussed yesterday a number of gaps or a
3 number of recurrent themes that were
4 associated with these interventions.
5 We did break the groups down into
6 recognizing -- I think one of the principles
7 that we thought about is that there really is
8 a tiering, so that consideration of these
9 issues would, in essence, be better focused on
10 specific areas, rather than lumping them
11 automatically all together. We may migrate
12 back toward a set point.
13 So we then set forth groups to
14 consider the different areas. So I think
15 perhaps what we can do now is to discuss from
16 the various subgroups their considerations,
17 based upon all the data that we have heard.
18 The question first is, Rich, do
19 you have information from subgroups?
20 MEMBER ISON: So the organ group,
21 basically, sent information around last night,
22 but hasn't actually met to discuss what our

1 recommendations are, just as a point back.
2 CHAIR BRACEY: Right. So why
3 don't we start the discussion? Because what
4 we will do is we will break at 1:00, but we
5 will go ahead and start the discussion now.
6 Then, during lunch, the subgroups can convene
7 and firm up what the discussion will be.
8 Ms. Birkofer?
9 MEMBER BIRKOFER: Thanks, Dr.
10 Bracey.
11 Can I just ask a high-level
12 question with regard to communications? Is
13 there like a national organ donor month that
14 HHS and the Secretary support?
15 CHAIR BRACEY: Dr. Bowman?
16 MEMBER BOWMAN: There is. I don't
17 know what it is, though.
18 DR. HOLMBERG: I think it is
19 April. I want to say April.
20 CHAIR BRACEY: Okay. All right.
21 Yes, Dr. Lopez?
22 MEMBER LOPEZ-PLAZA: I would like

1 to make a comment before we continue. I just
2 want to point out the fact that the
3 presentations on the organ transplant program
4 have been outstanding. We have very
5 comprehensive information.
6 However, I think we need to
7 recognize the lack of such equitable
8 information coming from tissues or stem cells
9 that will be the tissue side. I think we have
10 had some presentations, but they have been
11 very limited.
12 For example, I mean going to both
13 tissues and stem cells as a group of tissues,
14 we did not have any presentation regarding
15 maybe an MDP experience, fact experience.
16 Then, from the tissue point of
17 view, again, we had a very good presentation
18 coming from the tissue banking side, but from
19 the recipient side I think that we have not
20 really heard, except the fact that some of us
21 have the impression that there is a lot more
22 that can be done.

1 So I just wanted to state that
2 kind of handicap in our deliberations.
3 CHAIR BRACEY: All right. Dr.
4 Holmberg?
5 DR. HOLMBERG: Yes. You point out
6 the peripheral stem cells and the National
7 Donor Marrow Program. That is under HRSA, and
8 we specifically tried to separate that out.
9 So we were trying to deal with the tissues
10 that FDA regulates, as we did in the gap
11 analysis. So that is the rationale behind
12 that. But I hear your comments.
13 MEMBER ISON: Is there someone
14 that is focused on the safety issues on those
15 cells?
16 CHAIR BRACEY: Go ahead.
17 MEMBER BOWMAN: Yes, I can answer
18 that for HRSA. HRSA does have contracts under
19 the C. W. Bill Young Stem Cell Transplant
20 Program of 2005. Those contracts are through
21 the National Marrow Donor Program and also
22 through CIBMTR. I can get you the full name

1 of that organization, if you need that.
2 They are extremely focused on both
3 donor safety, because all these stem cells
4 basically do come from, if it is cord blood,
5 it comes from mothers who have just delivered
6 babies, umbilical cord blood. If it comes
7 from bone marrow or peripheral stem cells, it
8 comes from living donors.
9 So these are procedures that are,
10 by virtue of coming from living donors, they
11 are elective in nature. Even those urgent
12 indications for leukemia and lymphomas are
13 still semi-elective.
14 So the donors undergo an
15 extraordinarily complete and comprehensive
16 evaluation workup. So the focus is primarily
17 on the donor safety, but it is also devoted to
18 tracking any transmitted infections and
19 diseases from those donors that might have
20 somehow escaped the rather comprehensive
21 workup.
22 We did not present the bulk of

1 that in the sessions yesterday and today, but
2 a lot of that is included in the full
3 biovigilance test group report.
4 CHAIR BRACEY: Dr. Holmberg has a
5 comment, and then Dr. St. Martin.
6 DR. HOLMBERG: Yes, I just want to
7 make a comment on the scope of the white paper
8 and the fact that, just like Dr. Bowman just
9 mentioned on the donor aspect, the donor
10 health, I think that that raises a real big
11 issue with the living donors for organs. So
12 I would just challenge the Committee, when you
13 look at your recommendations and, as we think,
14 I think we have been focusing primarily on the
15 recipient, but especially in the living donor,
16 we have to think of the donor health.
17 Remember the title of the gap or the white
18 paper: "Patient Safety and Donor Health".
19 CHAIR BRACEY: Okay. With that,
20 oh, so I'm sorry, Dr. St. Martin, yes.
21 MEMBER ST. MARTIN: Sorry. I just
22 wanted to clarify. In my presentation, I kind

1 of glossed over it, but I did mention the
2 CIBMTR. They do a lot of data collection, but
3 I also mentioned that we specifically excluded
4 products that were regulated under 351 or
5 under additional regulations. So peripheral
6 blood stem cells and cord blood would be
7 subject to additional regulations and so were
8 not included in the scope of the gap analysis.
9 I also wanted to dovetail onto
10 what Jerry Holmberg just mentioned about donor
11 issues. The tissue rules do not cover
12 specifically donor safety issues, and it isn't
13 something that we are looking into. Although
14 most of the HCTPs from deceased donors, you
15 know, other than the cells, there are some
16 living tissue donors of skin, living bone,
17 although I think the surgical bone has
18 decreased, but there are some living skin
19 donors from after surgery from weight loss,
20 after weight loss.
21 So we are concerned about those;
22 also, the reproductive donors. We have been

1 trying to look at what we can do to try to
2 address those types of issues, but they are
3 not within the scope of the authority we use
4 for the tissue regulations.
5 DR. HOLMBERG: Laura, could you
6 clarify for me, I notice that when Debbie
7 spoke, she mentioned that in this round of the
8 donor criteria, that it did not include breast
9 milk. I think that that is something that has
10 raised some concern over the last couple of
11 years.
12 Is that under your jurisdiction?
13 MEMBER ST. MARTIN: Breast milk is
14 specifically excluded from the HTCP
15 regulation. That is one of the items that is
16 specifically excluded. It is not a tissue.
17 I think I can say that the
18 Department has been discussing oversight of
19 human breast milk, and there probably will be
20 some decisions made soon.
21 MEMBER ISON: I think it is also
22 important to point out that, if we are talking

1 about gaps in what we have learned about, we
2 haven't heard anything, actually, about living
3 donors from organ transplantation. So I think
4 it is hard for us. Personally, I think that
5 it would be hard for this Committee to make
6 comments related to living donor safety
7 issues, since we haven't heard anything about
8 that.
9 CHAIR BRACEY: Right. Good point.
10 Dr. Lopez, did you have another
11 comment?
12 MEMBER LOPEZ-PLAZA: Regarding
13 that, no.
14 CHAIR BRACEY: Okay. All right.
15 The point being made by Dr.
16 Holmberg is, if the Committee wishes to hear
17 more about living donor issues, then that is
18 something that can be brought and maybe
19 something that we can consider.
20 With that, Dr. Sarode, are you
21 ready to discuss the tissue elements?
22 MEMBER SARODE: We met last night

1 and we came up with some points which have
2 been projected on the screen.
3 Do you want me to go into detail
4 or we can read it?
5 CHAIR BRACEY: Yes, if you could
6 just sort of talk us through the concepts?
7 DR. HOLMBERG: Primarily to read
8 it into the record.
9 MEMBER SARODE: Pardon?
10 CHAIR BRACEY: Yes, read it. Yes,
11 you read it, yes.
12 MEMBER SARODE: Okay. Last
13 evening when we met, we talked about our task,
14 and we came up with some ideas which I put in
15 there.
16 Basically, there is a general
17 consensus regarding safety of tissue
18 recipients because the process of tracking
19 from donor to the recipient, and vice versa,
20 has several gaps.
21 The biggest gap is that there is
22 no accurate data on infectious disease

1 transmission via tissue transplants. Now this
2 may be due to the fact that the end-users do
3 not perceive tissue capable of transmitting
4 infectious diseases. They think that the
5 tissues they are getting, they are sterile
6 objects.
7 The Committee identified the
8 following issues: I think the most important
9 thing is we don't know what is the extent of
10 the problem. So there is need to get more
11 accurate data on number of recipients who are
12 affected by tissues.
13 The data that consists right now
14 is primarily of the numerator and anecdotal
15 case reports. Now current tracking of use of
16 these products is so informal that any attempt
17 to identify recipients is fraught with
18 difficulty.
19 And I believe we are supposed to
20 insert that New Jersey incident, but we
21 couldn't get it.
22 So, really, the evidence for a

1 problem would consist of risk assessment
2 consisting of the numerator of adversely-
3 affected persons and the denominator of
4 persons with risk, in this case, exposure to
5 products of concern like various tissues;
6 corneas we talk about.
7 Now, currently, there is great
8 concern about adequacy of the numerator and
9 denominator are not available.
10 Now there are many options for
11 numerator. Mandatory reporting versus
12 voluntary reporting. Linked versus unlinked.
13 Infectious disease versus a broader definition
14 of other adverse events. Lab assessment of
15 donor versus disease diagnosed in the
16 recipient.
17 The second point that we wanted to
18 discuss was tracking. A major step to resolve
19 issues regarding the evidence of a problem is
20 to develop a universal tracking system for all
21 products, whether organs or tissues, harvested
22 from a single donor. Now this could be based

1 on a universal unique donor identifier, such
2 as a ISBT-128, so that all implanted products
3 can be linked.
4 No. 2, there should be a tracking
5 system that traces every product from the
6 donor to the recipient, and vice versa. I
7 think this is one of the key central
8 recommendations of the Subcommittee.
9 Now every patient who receives an
10 implanted donor tissue product should be
11 identified. Anecdotally, we have heard that
12 in some instances products might be split
13 among different recipients. For instance, one
14 patient might receive a transplanted kidney,
15 another patient might receive excess vascular
16 material left from the kidney, and there is no
17 link between the two.
18 MEMBER ISON: I think you have to
19 be careful with that fact because, No. 1, both
20 the kidney and the vessel are not tissues per
21 se, and they actually are linked through the
22 OPTN tracking system.

1 MEMBER SARODE: Okay. Wrong
2 example.
3 Now No. 3 was reporting. All
4 adverse events possibly related to tissue
5 graft should be reported voluntarily through
6 a central repository charged with collecting
7 and investigating these reports. The reports
8 should be made using donor ID, ISBT, so that
9 the initial report can lead to an assessment
10 of other recipients of the product from the
11 same donor.
12 No. 4, transportation and storage.
13 We identified that this seems like an
14 important issue. I think there have been
15 reports of serious difficulties with
16 transportation and storage of some products.
17 The tracking system mentioned
18 above is the key because, with that, if there
19 is any problem with the product that are
20 consistently mishandled, then the product-
21 specific risk assessment can be identified.
22 CHAIR BRACEY: I have a question

1 regarding the transportation issue. That is,
2 those are truly anecdotal in the sense, again,
3 in terms of data that we have seen. You know,
4 we may not have enough to be really granular
5 about that.
6 MEMBER SARODE: Right, but there
7 can be some kind of tracer attached to the
8 product, so that you know if the product has
9 exceeded --
10 CHAIR BRACEY: So to enhance the
11 traceability and monitoring?
12 Dr. Holmberg?
13 DR. HOLMBERG: Maybe one way
14 around that would be to address this as the
15 distributor. You know, I think that we heard
16 clearly yesterday that the distributor was
17 part of the good tissue practices. So maybe
18 not get down to the granularity of the
19 transportation, but maybe stay at the level of
20 oversight or regulations concerning the
21 distributor inclusion into the GTPs.
22 CHAIR BRACEY: Dr. Williams?

1 MEMBER WILLIAMS: You could
2 probably also cover it efficiently by saying
3 management and tracking of the products.
4 MEMBER ISON: And I think the
5 other issue is, and Scott may want to comment
6 about this, there's standards for
7 transportation and shipping, and then the
8 issue before with regard to required
9 reporting, my understanding -- and correct me
10 if I am wrong, Dr. St. Martin, but it is
11 actually currently required to report that.
12 The big issue is the recognition and reporting
13 from the patient side, not so much the
14 industry side.
15 CHAIR BRACEY: Scott Brubaker?
16 MR. BRUBAKER: Yes, if I could
17 make a comment, please, absolutely correct.
18 ISBT-128, although the context that is
19 referred to here is incorrect, it is not a
20 universal donor number. It is actually
21 similar to what we use today. It is
22 establishment-specific coding. So it is not

1 a donor, universal donor, number.
2 For instance, a recovery agency,
3 if they would use an ISBT-128 coding system,
4 they would still send the tissue to up to five
5 tissue banks, say, but each tissue bank would
6 create their own establishment-specific
7 ISBT-128 code. So it is not going to change
8 your idea about a universal donor number.
9 That is not going to happen if you institute
10 ISBT-128, but what it would do, it would be a
11 global way of tracking tissue, where it is
12 machine-readable labeling that could be
13 actually read throughout the world in time, I
14 guess.
15 CHAIR BRACEY: Yes, I think the
16 principle, as I see it, is that you are right,
17 because when it goes to another entity, there
18 is a change that links it to that particular
19 entity.
20 MR. BRUBAKER: Entity number, yes.
21 CHAIR BRACEY: But, yet, you do
22 generate some uniformity, so that Entity X

1 doesn't create a number of its own that it
2 knows, but others don't.
3 MR. BRUBAKER: Yes, there will be
4 no duplication of numbers, exactly, yes.
5 CHAIR BRACEY: Right.
6 MEMBER SARODE: So I think that is
7 what we want to do, emphasize that there
8 should not be duplication of numbers then,
9 because currently it is possible.
10 DR. HOLMBERG: You know, one of
11 the things that I think has been obvious is
12 that the tissue working group from ISBT has
13 been very slow in coming to the table,
14 although they have been invited over 10 years
15 ago to do this.
16 The beauty of this is not so much
17 the bar code, not so much the 128 part of it,
18 but once again bringing the people to the
19 table to identify the data elements that need
20 to be moved from one location to another.
21 That is what has been missing, is the
22 standardization of data elements through a

1 common means, which in this particular case
2 you are referring to ISBT-128.
3 CHAIR BRACEY: Dr. Ison?
4 MEMBER ISON: I guess one
5 question, and maybe this is capturing what we
6 are intending, is I think the thought process
7 is perhaps having an ISBT-128-compliant
8 patient tracking system that incorporates a
9 uniform donor component in it. So that all
10 organs and tissues would have a four-segment
11 number, where the first segment is the donor
12 number; the second segment is maybe something
13 that tells you about the manufacturer, and
14 then the last set of numbers would be unique
15 to that particular -- and again, I don't know
16 if that is reasonable, but something where at
17 least part of the numbering system is a direct
18 linker to the single donor, so that you could
19 much more easily link all of the different
20 components back to one donor.
21 CHAIR BRACEY: Dr. Haley, then Dr.
22 Triulzi.

1 MEMBER HALEY: We discussed quite
2 a bit last night. At least my thinking is
3 that I don't know enough about the various
4 numbering systems out there to make a
5 recommendation on whether it should be an ISBT
6 number or something else. That is why we
7 qualified that as such as an ISBT number.
8 The point is we want some kind of
9 tracking from donor to recipient. Whether is
10 an ISBT number or some entirely new system, I
11 don't know. Well, I do know that I don't know
12 enough to make such a recommendation.
13 I think what we probably want to
14 do is, in that section two up there, is to put
15 in a specific recommendation to the Secretary
16 that the Secretary should -- I don't know if
17 the right politically-correct word is to
18 instruct the FDA to develop regulations that
19 will mandate a tracking system that tracks
20 tissues from donor to recipient.
21 I agree with Dr. Ison that I don't
22 think it is rocket science. It is probably,

1 like he said, a three-part number, something
2 that identifies the donor, something that
3 identifies the manufacturer, and something
4 that identifies the tissue involved.
5 But I see that as probably
6 something that is an FDA activity -- I don't
7 know exactly what -- that we can recommend to
8 the Secretary that the FDA do this.
9 CHAIR BRACEY: Dr. Triulzi, you
10 had a comment?
11 MEMBER TRIULZI: Yes. I think we
12 are getting a little too prescriptive. I
13 think the concept of traceability is clear in
14 the quality, what that means. I think what we
15 identified as traceability can occur today
16 from the source to the hospital door.
17 Traceability is lost or uneven from that point
18 on, and the only agency we heard that has any
19 regulation inside that door is JCAHO. We
20 heard that they don't reliably do tracer for
21 trackability.
22 So I think that we should

1 emphasize that traceability, as a quality
2 issue for tissue, is probably the No. 1
3 problem was identified, that that is primarily
4 related to the hospital piece, the end-user
5 piece. And we could decide if there is
6 specific recommendations, such as the
7 Assistant Secretary may want to contact in
8 writing the counterpart at JCAHO and recommend
9 that this be made a higher priority, and that
10 they do tracer studies.
11 Then you can get consent, maybe
12 item No. 2. But I wouldn't get too
13 prescriptive about it.
14 CHAIR BRACEY: Yes, I think one of
15 the things that we heard in general is, in
16 principle, there is traceability, but in
17 practice it is not operative. So we want to
18 make the traceability more robust. We want to
19 facilitate it to make it operative.
20 MEMBER HALEY: Could you look at
21 6.b?
22 CHAIR BRACEY: 6.b? Oh, okay.

1 Dr. Sarode?
2 MEMBER SARODE: Oh, you want to do
3 6.b now?
4 CHAIR BRACEY: Yes, Dr. Haley
5 -- yes.
6 MEMBER POMPER: Should he read the
7 whole list into the record.
8 CHAIR BRACEY: Yes, just go ahead
9 and continue.
10 MEMBER POMPER: He sort of never
11 completed reading it into the record.
12 CHAIR BRACEY: Where did you --
13 yes, so we will get to 6.b. So you were at
14 consent.
15 MEMBER SARODE: Yes, about
16 consent, it seemed there is no requirement for
17 informed consent at this stage, and that most
18 patients do not seem to know that they might
19 have been engrafted with a product which is
20 harvested from another person.
21 This makes any links between
22 subsequent illness difficult, especially if

1 there is a long interval between implantation
2 and onset of illness later on.
3 The consent may not be the real
4 issue, so much as making sure the patient
5 knows what has been implanted.
6 DR. METZGER: Can I make one
7 comment for a minute?
8 CHAIR BRACEY: Yes, Dr. Metzger?
9 Please come to a microphone.
10 DR. METZGER: I just want to say,
11 would you please strike the word "harvest" and
12 use "recovered"? Our donor families don't
13 like the idea that their organs are harvested.
14 MEMBER SARODE: Oh, sure. I mean
15 this is really, really the earliest draft. I
16 mean, you know, we haven't had a chance to --
17 CHAIR BRACEY: Sure. That's fine.
18 MEMBER SARODE: This was just
19 typed as we were thinking.
20 No. 6, oversight. It seems that
21 oversight is a little large, and primarily
22 seems to consist of -- it is terrible English

1 -- seems to consist of assessment within
2 hospitals. I think that is what Jerry was
3 referring to, that if the GSE emphasizes that
4 there should be more oversight within the
5 hospital system, so that all the tissues can
6 be tracked and traced -- because, as we know,
7 only 20 percent of the blood banks in this
8 country, they control tissues, and 80 percent
9 there's no good distribution or no records of
10 various tissues in the hospital.
11 CHAIR BRACEY: Okay. Dr. Lopez?
12 MEMBER LOPEZ-PLAZA: I just wanted
13 to make a comment about a comment about
14 traceability. I think that, of the three
15 areas, blood, solid organ, tissues, probably
16 tissues is the one that is behind what all the
17 other ones have accomplished. So that is the
18 big reason to emphasize that.
19 But whatever we say, I think an
20 important thing for the three areas, and now
21 with tissues and solid organs, is that we have
22 a way of tracking that will shorten the time

1 between finding and informing, and that
2 everyone else gets captured that might be
3 affected. I think that is a real point in
4 here.
5 CHAIR BRACEY: Okay. All right?
6 MEMBER ISON: So I have a
7 question. Correct me if I am wrong, but the
8 Joint Commission is a private company. It is
9 not a government agency. So I am not sure
10 that we can direct a private company to do
11 anything.
12 CHAIR BRACEY: Well, actually, but
13 they are deemed -- so, in other words, in
14 order for an organization to be paid by the
15 government, then they must be inspected by a
16 deemed organization. There is a linkage to
17 the government regulations.
18 MEMBER ISON: Then just Joint
19 Commission, correct?
20 CHAIR BRACEY: Yes.
21 MEMBER NETHER: Yes, that was
22 going to be my point in terms of we don't

1 accredit everything.

2 I actually had a question for

3 Scott. Since you had really most of the

4 analysis with regards to traceability, what

5 were some of the root causes and where this

6 was exactly dropped? And are we covering

7 everything, is the question.

8 MR. BRUBAKER: Well, I provided

9 some slides from our experience with different

10 major recalls since the 1990s. Process

11 improvements, it has improved. Changes have

12 been made, in reaction to what has been going

13 on over the years.

14 Back in -- gosh, I am going to try

15 to remember -- in the first HIV case, there

16 were only about five grafts that couldn't be

17 located. That was in the early 1990s.

18 When you look at hepatitis C in

19 the early 2000s, 2002, that case that was

20 described by Dr. Ison, I believe, again, there

21 were about five grafts that couldn't be

22 located.

1 When we get into the BTS issue,
2 there were 2,000 or so, under 2,000, from a
3 total of 48,000. The percentage has basically
4 stayed the same, around 7 percent, that
5 couldn't be located, couldn't be located to
6 the recipient.
7 In some of those cases, like in
8 the BTS case, it was a distributor who
9 couldn't even tell you where it was sent, much
10 less getting to the recipient.
11 But when we get to, then, the most
12 recent major recall of about 5,000 grafts,
13 Chryseobacterium and meningosepticum infection
14 with tendons, there was 100 percent could be
15 tracked to the recipient out of, I think it
16 was maybe 2,000 that were actually implanted.
17 So it has gotten better over time, and that
18 was a recall in 2006, which is a year after
19 the Joint Commission's standards went into
20 place for tissues and tracking throughout five
21 accreditation manuals, instead of just one,
22 where it started. It started in the

1 laboratory.

2 So we have seen a big progression

3 over time. It has gotten better.

4 Implant, hard return, I know that

5 is another question that is on another slide

6 I have provided for you, because I have to

7 leave soon. It is well over 50 percent, and

8 it has been improving ever since the Joint

9 Commission standards have come out.

10 So we are getting more -- and

11 again, that is all voluntary. The compliance

12 is getting better, but it is probably not over

13 80 percent on a routine basis, I should say.

14 MEMBER KUEHNERT: Could I just ask

15 a point of clarification with that because you

16 have presented that before? When you say 100

17 percent, do you mean that they had a recipient

18 patient name for every single one?

19 MR. BRUBAKER: For every single

20 one that was implanted, yes. I've got them on

21 a slide. If you want to see it, I have

22 provided it.

1 CHAIR BRACEY: Well, can we do
2 this, because we are getting really, really
3 close to the lunch hour? So what I wanted to
4 do is to make sure we at least have a look at
5 the document. There will be more discussion
6 of the document after lunch, but let's just go
7 ahead and read it into the record.
8 So can you finish with that, Dr.
9 Sarode?
10 MEMBER SARODE: Yes, I think I am
11 done.
12 CHAIR BRACEY: Oh, you're done?
13 MEMBER SARODE: Yes.
14 CHAIR BRACEY: Oh, okay. I
15 thought there was a 6.b.
16 MEMBER HALEY: In a later version
17 that we did.
18 CHAIR BRACEY: Oh, in a later
19 version? Okay. Well, we will do 6.b. after
20 lunch.
21 Dr. Lopez?
22 MEMBER LOPEZ-PLAZA: I just have a

1 request, and I don't know if that is possible
2 or not. Could the Joint Commission be able to
3 share with us, not today, maybe through other
4 sources, but what has been their experience
5 once they started with their requirements,
6 starting inspecting the different hospitals?
7 You know, what has been the gaps they have
8 found?
9 I think that would be a very good
10 source of information because that is the only
11 entity so far that actually looked at the
12 hospital side of tissues. We don't really
13 have any other solid information. It would be
14 nice to have that information.
15 CHAIR BRACEY: Mr. Nether?
16 MEMBER NETHER: Yes, we can look
17 at the compliance data.
18 CHAIR BRACEY: Okay. Let me
19 quickly -- quickly -- read. Are you ready,
20 Rich?
21 Yes, Dr. Holmberg.
22 DR. HOLMBERG: Excuse me. I am

1 taking my Executive Secretary privilege here
2 just to remind the Committee that I thought
3 that I heard some discussion about the uniform
4 donor questionnaire, and as being a deficiency
5 on the tissue side. Is that something that
6 the Committee wants to put into this
7 recommendation?
8 MEMBER ISON: Pointing out that it
9 crosses over, I think, to organs as well.
10 DR. HOLMBERG: Absolutely, but I
11 think what we have is we have a document that
12 may not have gone through the same process
13 that organs has gone through, as far as the
14 evidence-based.
15 MEMBER ISON: Well, organs,
16 actually, have been involved in that process,
17 correct?
18 CHAIR BRACEY: We are searching
19 for a document which is -- I'll tell you what.
20 Let me read the document.
21 Typically, what we will do is we
22 will have a preamble of sorts. The idea is to

1 discuss a preamble.
2 What we have talked about is the
3 notion of having tiered recommendations, one
4 set focused more squarely on tissue and
5 another set focused more squarely on solid
6 organs.
7 What I thought I would do now, or
8 at least what I thought I was doing last
9 night, is creating some very, very poor
10 English, but to frame the discussion.
11 "Decisions regarding tissue and
12 transplantation safety are complex and require
13 careful consideration of scientific/medical
14 risk versus organ/tissue availability.
15 Transplantation safety decisions should be
16 made using" -- use a term, but I said
17 "validated risk assessment tools in an open
18 manner to foster" -- here it gets a little
19 weak -- "a transparent, careful vetting of
20 data regarding the impact of proposed
21 interventions on patient outcome.
22 "This is especially true in the

1 case of organ transplantation" -- I think we
2 can strike the stem cells -- "organ
3 transplantation therapy due to limited supply
4 and the high risk for many potential
5 recipients if these life-saving transplants
6 are unavailable.
7 "Data on the risks of communicable
8 disease transmission and other serious adverse
9 events of transplantation of tissue and solid
10 organs are poorly characterized.
11 "Given the incomplete status of
12 information in this area, it is currently not
13 possible to accurately assess the benefit/risk
14 assessment or ratio of many donor-testing and
15 donor-screening strategies.
16 "Carefully-designed surveillance
17 studies would allow for improved decisions by
18 physicians and patients regarding options
19 available to enhance the safety of
20 transplantation therapy by providing numerator
21 and denominator data as opposed to relying on
22 case reports and anecdotes.

1 "In the area of transfusion
2 medicine, well-designed studies and
3 repositories allowed robust assessments of
4 safety measures. Similar efforts are needed
5 to advance decisionmaking in organ and tissue
6 transplantation.
7 "While many of the needed steps
8 will take a substantial amount of time to be
9 completed, there are several interventions
10 that can in the short-term lend to improved
11 transplantation practice."
12 So the English needs to get worked
13 on, but I guess the question is, is the theme
14 appropriate? Do we need to have something
15 like this and then the specifics underlay it?
16 Dr. Kuehnert?
17 MEMBER KUEHNERT: I think this is
18 great as background. I think the only thing
19 I would urge is to separate the concepts where
20 you say surveillance studies between research,
21 as we talked about, research studies and
22 surveillance.

1 CHAIR BRACEY: Good point. Correct.
2 MEMBER KUEHNERT: Because I think
3 those are separate --
4 CHAIR BRACEY: Right.
5 MEMBER KUEHNERT: -- but both very
6 important endeavors. Some keywords with
7 surveillance is like sentinel network,
8 something that is real-time and is not
9 something that involves a randomized control
10 trial or a study-type setup, but, rather,
11 something that is surveillance.
12 CHAIR BRACEY: Okay. So I guess
13 what I was just thinking is that we would have
14 a general background statement, and then we
15 would address, under the areas of
16 intervention, i.e., and concern, tissue and
17 transplantation, the various recommendations.
18 Does that seem fair?
19 Dr. Bowman?
20 MEMBER BOWMAN: Just a minor point
21 on the scope. At the very last sentence on
22 that top paragraph that you are looking at on

1 the screen --

2 CHAIR BRACEY: Yes.

3 MEMBER BOWMAN: -- where it says,

4 "data on the risk of communicable disease

5 transmission", I would certainly agree with

6 that, "and other serious adverse effects of

7 transplantation." I can't speak for the

8 tissue community. I think when you include,

9 and quote, "other serious adverse effects"

10 beyond the donor transmissible diseases, you

11 are getting into an area that has been studied

12 fairly extensively for three decades at least,

13 four decades.

14 CHAIR BRACEY:Oh, I see what you --

15 MEMBER BOWMAN: And that really

16 widens the scope of your preamble there, I

17 think.

18 CHAIR BRACEY: Right. I see what

19 you are saying.

20 MEMBER BOWMAN: Surgeons have been

21 living and transplant physicians have been

22 living with the effects of their mistakes and

1 crap work for decades in transplant, and I
2 think tissues can probably attest to that,
3 too.
4 CHAIR BRACEY: Okay. Yes?
5 DR. ELLISON: I guess I was going,
6 actually, before you even spoke, I was trying
7 to figure out if I was allowed to speak to say
8 that you might actually make a bigger
9 statement of going beyond infection. Because
10 there are, clearly, a lot of different kinds
11 of adverse effects, adverse events, that
12 occur, and in order to design the system to be
13 safe, to lead to the best outcomes for both
14 the donor and the recipient, I think there's
15 actually a much broader investigation that is
16 needed.
17 There is very little, very limited
18 epidemiologic literature on this. It is
19 really largely either expert panel -- we did
20 a search on this as well -- expert panel or
21 high-profile anecdotal evidence.
22 So enabling both the research,

1 which I think is an important point, targeted
2 research that can sort of guide the direction,
3 and then general surveillance based on what
4 you learn --
5 CHAIR BRACEY: So let me suggest
6 this: let's have a couple of more comments
7 and questions. And in the interest of making
8 sure that we maintain our physiology, we will
9 break for lunch. Then we will come back and
10 then we will start fleshing through what will
11 be the end product.
12 Dr. Triulzi?
13 MEMBER TRIULZI: I will just say
14 quickly I think, when we talk about
15 biovigilance as it applies to blood, tissues,
16 and organs, we meant more than just infectious
17 diseases or malignancy.
18 CHAIR BRACEY: Correct. Correct.
19 That is a good point.
20 MEMBER KUEHNERT: I think if you
21 look at some of the extra slides that I
22 included in my presentation, it explains at

1 least my viewpoint on biovigilance and what it
2 can encompass, which I think are a lot of the
3 things that were just mentioned, without
4 taking on everything in organ and tissue
5 transplantation.
6 CHAIR BRACEY: Dr. Ison?
7 MEMBER ISON: I think the last
8 thing that I was going to say is, maybe over
9 lunch, thinking about what we mean by adverse
10 events. Because I agree that there's a lot of
11 research that has looked at CMV, you know, the
12 risk of immune suppression, those kind of
13 adverse events. But really how about when the
14 vessel is cut wrong or when this or that?
15 There's other adverse events that actually
16 impact the safety of both the donor and the
17 recipient that I do think probably warrant
18 further --
19 CHAIR BRACEY: So perhaps a
20 qualifier to the unexpected? You know, we
21 will figure out some way to state it.
22 So let's break for 30 minutes,

which would mean that we would reconvene at 1:35. Is that right, Dr. Holmberg?

DR. HOLMBERG: Yes.

MEMBER ISON: And then for the organ group, if they can grab lunch and maybe come back here to sit down and chat, that would be good.

CHAIR BRACEY: Okay.

(Whereupon, the foregoing matter went off the record at 1:06 p.m. for lunch and went back on the record at 1:42 p.m.)

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

1:42 p.m.

CHAIR BRACEY: Welcome back, everyone.

We are just connecting the laptop. So what we have done is we have put the various elements, that is, the specific recommendations, under the preamble, recognizing that we do need to wordsmith the preamble, but I am not going to waste time on that right now.

What I want to do is to go to the beginning of the subsections. In essence, I think that there is some redundancy, so we can start deleting pieces.

So, right now, we are at the beginning, where you see, under the green, the tissue group, it says, "There is general consensus regarding safety of tissue recipients because the process of tracing recipients has several gaps."

I think that we actually cover

1 that. When we discuss this point here, we
2 have it as evidence of a problem. But I guess
3 what I was thinking is that we could,
4 basically, make the statement, and the
5 recommendation would be to improve the
6 tracking.
7 So I guess what I am thinking of
8 is that, do we need to have additional
9 information regarding the verbiage in this
10 paragraph? Do we need the verbiage or do we
11 just want to crank it down to a
12 recommendation? The verbiage being, "The
13 general consensus regarding tissue recipient
14 tracking is a problem."
15 So what we could do, here we are
16 talking about the decisions and safety, and we
17 haven't really focused on -- we talked about
18 the complexity of making decisions. We talked
19 about the need for a surveillance system, but
20 we don't necessarily talk about specific
21 problems.
22 So do we want to make a statement

1 in this about specific problems or do we want
2 to just go straight into a recommendation?
3 What is your sense?
4 Mr. Nether?
5 MEMBER NETHER: Yes, Dr. Bracey.
6 One of the things I would say is that I would
7 like to see a recommendation that, for
8 especially with traceability and some of the
9 other issues, if we could start to drill down
10 somehow and get data, what are the
11 contributing factors of why we have these
12 problems?
13 CHAIR BRACEY: Okay.
14 MEMBER NETHER: Because I haven't
15 heard that throughout these two days. I know
16 we have problems with traceability, informed
17 consent, but what are those contributing
18 factors? And can we get to that level of
19 detail? So the recommendations we make for
20 improvements will actually lead to
21 improvements and not just changes.
22 CHAIR BRACEY: Okay.

1 MEMBER POMPER: Just a little not
2 quite wordsmithing, but is it the biggest
3 gaps, as you know, are accurate data on
4 infectious disease transmission via -- is that
5 tissue and organ or just tissue? Just put
6 them all together?
7 CHAIR BRACEY: So what you are
8 saying is, if there is commonalities, fuse on
9 the commonalities. Okay. So what we could
10 say here is there is general consensus. There
11 is consensus or there is concern. Consensus
12 is consensus among the Committee members or?
13 MEMBER ISON: I think concern
14 would be an accurate word because I think we
15 all are actually concerned that there isn't
16 this data.
17 CHAIR BRACEY: Okay. So I am
18 trying to -- oops, I did the wrong thing.
19 DR. HOLMBERG: Art, do you need
20 help there?
21 CHAIR BRACEY: Yes, actually, I am
22 not the greatest typist. Okay, Rich.

1 So there is concern regarding the
2 safety and -- well, why don't we just, if we
3 just say there's concern regarding the
4 traceability, do we need to restate the issue
5 of it is a safety concern? Can we just
6 specifically go to concern regarding
7 traceability of tissue and organ recipients --
8 MEMBER ISON: Well, in my
9 thinking, there is no concern about the
10 traceability --
11 CHAIR BRACEY: Mainly for tissue,
12 okay. All right. So there is concern
13 regarding the traceability of tissue
14 recipients. I don't know if we need the other
15 verbiage. So if we just take it all the way
16 to "recipients"?
17 So there is concern regarding the
18 traceability of tissue -- there's concern --
19 MEMBER ARNOLD: Does that mean
20 something to everybody at the table except me,
21 traceability of tissue?
22 CHAIR BRACEY: No, it doesn't.

1 No. There is concern that the absence --
2 there is concern -- let me just talk it
3 through. There is concern regarding
4 inefficient or deficient traceability, but
5 don't type that.
6 MEMBER ISON: How about
7 inadequate?
8 CHAIR BRACEY: Inadequate
9 traceability of tissue recipients lending or
10 creating, causing -- what's the word?
11 MEMBER ISON: Well, I think the
12 thing is we are actually concerned about the
13 traceability of the tissue, not of the
14 recipient. We heard there may be some way of
15 recognizing that the recipient had a tissue,
16 but --
17 CHAIR BRACEY: So, yes, there's
18 traceability of tissues and impairing
19 surveillance, and impairing -- is that okay?
20 MEMBER ISON: But I think the big
21 issue -- this is my opinion at least -- is
22 that the traceability that we are concerned

1 about is that, if there is an infection in a
2 single donor, we may not be able to identify
3 all the recipients. Vice versa, if there's a
4 recipient that gets an infection, we may not
5 be able to trace all the way back.
6 So I wonder if just stating that,
7 that there is concern regarding inadequate
8 traceability of tissues, such that there is
9 not forward and backward, bidirectional --
10 CHAIR BRACEY: So there is no
11 bidirectional, okay.
12 MEMBER ISON: How about there is
13 no bidirectional surveillance?
14 CHAIR BRACEY: Well, "no" is kind
15 of strong because there is some surveillance.
16 MEMBER ISON: Bidirectional
17 traceability. Maybe just shorten it up to,
18 "There is concern regarding inadequate
19 bidirectional traceability of tissues."
20 CHAIR BRACEY: Right. Inadequate
21 bidirectional traceability. "There is concern
22 regarding inadequate bidirectional

1 traceability of tissues."
2 Then you want to link that to
3 something which would then impair --
4 MEMBER POMPER: Regarding the gap
5 analysis, the two themes through the 15 or so
6 gaps identified were infectious diseases and
7 adverse events. Those came up quite a bit.
8 MEMBER HOLLIS-PERRY: Can you link
9 that to inadequate patient followup?
10 CHAIR BRACEY: Inadequate patient
11 followup?
12 MEMBER HOLLIS-PERRY: Because that
13 ties, if one patient develops an infection,
14 you can't link that to other patients who
15 received tissue from that donor.
16 CHAIR BRACEY: Well, yes, I guess
17 the thing I was thinking about, though, is we
18 want to push really hard for the concept of --
19 MEMBER HOLLIS-PERRY: Because you
20 can't follow that patient if you can't find
21 him or her.
22 CHAIR BRACEY: Well, let's see,

1 Dr. Haley has a comment. Dr. Lopez?
2 MEMBER LOPEZ-PLAZA: In theory,
3 adverse events surveillance versus safety,
4 because what you are impairing is really the
5 adverse event surveillance, like you know --
6 CHAIR BRACEY: Yes, yes, adverse
7 event surveillance. Well, I mean I guess, to
8 me, adverse event surveillance includes
9 patient followup.
10 MEMBER ISON: Yes.
11 CHAIR BRACEY: Okay. So "There is
12 concern regarding inadequate bidirectional
13 traceability of tissues impairing adverse
14 event surveillance. The biggest gap" -- I
15 don't know. Do we need to be that specific?
16 No. So let's get rid of that.
17 "This may be due to the fact that
18 end-users do not perceive" --
19 MEMBER ISON: I think it is hard
20 to actually say that because we don't have
21 evidence of that presented at this meeting.
22 We have heard that we think that that is the

1 case, but we don't have evidence.
2 CHAIR BRACEY: Yes, and we are
3 going to have a solution for that anyway,
4 which is a more robust system for
5 surveillance. Okay, strike it.
6 So now what I was thinking is that
7 you would make a statement of the problem, and
8 then you would have a recommendation.
9 MEMBER SARODE: So that should be
10 recommendation?
11 CHAIR BRACEY: So what is the
12 recommendation?
13 MEMBER ISON: I think there's
14 multiple recommendations. I think it is
15 accurate, you need a unique identifier so that
16 you can do traceback. I mean, if you don't
17 have a unique identifier, you can't do
18 tracing.
19 CHAIR BRACEY: Yes, but isn't the
20 recommendation the unique identifier?
21 MEMBER ISON: That's one. Then
22 the second is that you basically need to use

1 that unique identifier to determine a
2 numerator and denominator of tissues collected
3 and used.
4 CHAIR BRACEY: So the question is,
5 when we discussed this in this format, the
6 basic point is that one of the things that we
7 discussed is that we need to have surveillance
8 -- and I used the wrong term -- study, but we
9 need to have a surveillance system that would
10 allow us to capture numerator and denominator
11 data.
12 MEMBER ISON: But that is actually
13 the second step, I think. At least this would
14 be my thought. The core of this is that we
15 don't have bidirectional traceability, and
16 that impairs adverse event surveillance.
17 The first step is we have to
18 develop that traceability, which means someone
19 has to come up with a --
20 CHAIR BRACEY: A system.
21 MEMBER ISON: -- a system to have
22 a unique identifier. And once you have that,

1 then you actually could get, theoretically, if
2 it is traceable, that information.
3 Then the second concept is that we
4 have incomplete data on the frequency and
5 characteristics of adverse events in the
6 tissue populations. Then the solution for
7 that would be do a focal study to pilot the
8 issues to identify the key processes that need
9 intervention and investigation.
10 CHAIR BRACEY: So perhaps, then,
11 we would move No. 2 to No. 1, switch those two
12 around? That is easy for me to say.
13 DR. HOLMBERG: But don't you think
14 that the elements under No. 1 are part of the
15 problem that should be up in the first part of
16 that?
17 MEMBER ISON: I think you need --
18 both are going together. That you need to
19 have the unique identifier and then use that
20 to define your numerator and denominator.
21 CHAIR BRACEY: So, I mean, what I
22 hear Dr. Ison saying is let's get a system

1 first. Then, after the system, we would state
2 that we then need to use that system to gather
3 data.
4 MEMBER AXELROD: What I hear Dr.
5 Holmberg saying is, what we have as No. 2,
6 whether the text in that belongs in the
7 opening paragraph as part of the statement.
8 CHAIR BRACEY: Okay. So, then,
9 yes, if you take that first sentence, so you
10 take the first sentence and put it after
11 surveillance?
12 Okay. So then, "There is concern
13 regarding inadequate bidirectional
14 traceability of tissues impairing adverse
15 events surveillance. There are no accurate
16 data on the number of recipients affected by"
17 -- should we say, "adversely affected" or?
18 Dr. Haley?
19 MEMBER HALEY: Because that is a
20 denominator statement, I would say, "in whom
21 tissues are implanted".
22 CHAIR BRACEY: So "There are no

1 accurate data on the number of recipients" --
2 oh, yes -- "in whom tissues are implanted."
3 Right. We need the total denominator.
4 "There are no accurate data on the
5 number of recipients", and then go, "in whom
6 tissues are implanted".
7 MEMBER KUEHNERT: So what would
8 follow would be "And thus, rates on adverse
9 events cannot be calculated."
10 CHAIR BRACEY: Okay. So then we
11 can scratch, then, "affected by tissues" and
12 "anecdotal reports". Okay.
13 "The Committee identified" -- so
14 here we want to say, "The Committee
15 recommends...."
16 MEMBER KUEHNERT: Yes, right.
17 CHAIR BRACEY: "The Committee
18 recommends...." Now you can scratch --
19 MEMBER SARODE: Or "The Committee
20 has the following recommendations."
21 CHAIR BRACEY: So, as an action
22 point, would we say, then, "The application"

-- "development"; pick a word -- "of unique identifiers," or what is the verbiage there?

DR. HOLMBERG: You need a system, a system which utilizes unique identifiers.

MEMBER HALEY: "The development of a system for...."

CHAIR BRACEY: Oh, not "for", but "using", "employing"?

MEMBER HOLLIS-PERRY: "Implementation"?

CHAIR BRACEY: What's the right word? "Developing a system...."

DR. HOLMBERG: Well, you want a system of bidirectional traceability, a system for bidirectional traceability. Then that bidirectional traceability would use a unique identifier.

CHAIR BRACEY: Okay. So a system --

MEMBER KUEHNERT: Make sure that you say where you are going from and to, you know, from donor to recipient. Otherwise,

1 people get --

2 CHAIR BRACEY: Yes, yes, yes.

3 Bidirectional traceability from donor to

4 recipient.

5 MEMBER KUEHNERT: -- people will

6 say, well, there's already regulations. But

7 we are saying to the actual recipient.

8 CHAIR BRACEY: So development of a

9 system by bidirectional traceability from

10 donor to recipient, and then the question is

11 "employing" or "using"?

12 DR. HOLMBERG: "Which would

13 use" --

14 CHAIR BRACEY: "Which would

15 use" --

16 DR. HOLMBERG: "Which would use a

17 unique identifier".

18 CHAIR BRACEY: All right. So then

19 we can scratch "There is a need...."

20 MEMBER ISON: And then do we want

21 to make a specific comment here where we,

22 basically, are -- I think the issue where that

1 identifier has to have some commonality for a
2 single donor, so that there's not like 10
3 numbers for a single donor.
4 CHAIR BRACEY: A unique
5 identifier --
6 MEMBER ISON: That is donor-
7 specific.
8 CHAIR BRACEY: Linking a single
9 donor to all tissue implants -- tissue and
10 organ implants. Linking a donor --
11 MEMBER ISON: I would just say, "a
12 single donor" --
13 CHAIR BRACEY: "A single donor", I
14 like that.
15 MEMBER ISON: -- "to all
16 subsequent organs and tissues".
17 CHAIR BRACEY: "A single donor to
18 recipients"?
19 MEMBER ISON: No, "to all
20 subsequent organs and tissues".
21 CHAIR BRACEY: "To all
22 subsequent"? It is subsequent.

1 MEMBER ISON: Whether the
2 "subsequent" is there or not, but, I mean, it
3 is basically all the organs and tissues that
4 are linked back to the donor.
5 MEMBER AXELROD: Yes, and
6 regardless of whether it went into a patient,
7 because you would want traceability even if it
8 was discarded. We have to do that for blood
9 products.
10 CHAIR BRACEY: Yes, okay. Good
11 point.
12 MEMBER HOLLIS-PERRY: Yes. Do you
13 call it a graft?
14 CHAIR BRACEY: Right, right. "To
15 all subsequent organs and tissues" because
16 they are, yes, they are subsequent to the
17 collection process, not harvesting.
18 MEMBER ISON: Could you add the
19 word "simple system", "simple"?
20 CHAIR BRACEY: Linking to the
21 recovery, do we want to incorporate linking a
22 single donor to all recovered organs and

1 tissues? Yes. So then you can scratch
2 "subsequent". "All recovered organs and
3 tissues". Okay?
4 MEMBER ISON: Could you add
5 "simple system" or "ease of use"? "User-
6 friendly system" or? I mean, if it is
7 immensely complex, then it is going to defeat
8 the purpose.
9 CHAIR BRACEY: Yes, exactly. A
10 "practical". No, not "practical".
11 MEMBER SARODE: I thought we don't
12 have to be too detailed. We don't have to
13 give all the details, right?
14 CHAIR BRACEY: Yes, okay. Let's
15 just leave it at this for now. Then we will
16 remember that we want to make sure that we
17 comment upon the ease of use because it should
18 facilitate the process.
19 So now we go down to, so we are
20 coming into tissues and we are focused right
21 now on traceability as task No. 1. Then we go
22 to task No. 2 here that says, "Current

1 tracking is inadequate". Well, we have
2 already addressed that. So we can strike
3 that, right?
4 MEMBER SARODE: Yes, we can
5 delete.
6 CHAIR BRACEY: That could be a
7 good thing. Okay. So now "reporting" -- so
8 this is another important point. So here we
9 don't actually have a preamble. So we have
10 discussed above the -- well, can you go up to
11 the paragraph above?
12 So here we say, "There is concern
13 regarding inadequate bidirectional
14 traceability. There are no accurate data on
15 the number of recipients in whom tissues are
16 implanted, and thus, the rates on adverse
17 events cannot be calculated."
18 So, in a sense, that is tied
19 nicely to No. 1, but No. 2, the question is,
20 should we develop a preamble for No. 2?
21 Yes? Dr. Lopez?
22 MEMBER LOPEZ-PLAZA: My

1 understanding from the discussion today is
2 that at the manufacturer level there is
3 something that is very well-established. It
4 is required, I guess, from the federal
5 agencies. But at the patient side, it is not
6 really developed.
7 So reporting of all events closely
8 related to tissue grafts, there should be
9 something that there has to be a program or a
10 standardized, development of a standardized
11 way of reporting those things from the
12 recipient's side to the --
13 CHAIR BRACEY: Right, but what if
14 we stated that the Committee is concerned --
15 again, there is a concern that is driving
16 this.
17 MEMBER LOPEZ-PLAZA: Uh-hum.
18 CHAIR BRACEY: And the concern is
19 that there is variable reporting or the
20 Committee is concerned about underreporting of
21 adverse events.
22 MEMBER LOPEZ-PLAZA: That is

1 common for all, for solid organs and for
2 tissues, and I don't know if that -- you might
3 want to address that in here, but I think that
4 should be discussed as an overall topic.
5 CHAIR BRACEY: Dr. Holmberg?
6 DR. HOLMBERG: I think what the
7 Committee may want to do is to expand maybe
8 the first or second sentence up there to
9 include impairing adverse events surveillance
10 and investigation. Then just get rid of the
11 word "reporting" in front. It would be "All
12 adverse events possibly related to tissue
13 graft should be reported."
14 CHAIR BRACEY: Okay. Yes, I like
15 that. Put the justification upfront.
16 "Surveillance" --
17 MEMBER ARNOLD: Well, I think if
18 you eliminate a lot of those words and just
19 put "biovigilance" in there, you would cover
20 a lot of future intended sins, you know. You
21 know, you leave the door way open there.
22 MEMBER KUEHNERT: I think part of

1 the thing we are struggling with here is we
2 are also talking about rapid communication.
3 So, in other words, we are saying that, yes,
4 there is piecemeal traceability; yes, there is
5 reporting. But the question is, if you have
6 an event that happens in a patient, and it has
7 ramifications for other patients who got
8 tissue from the same donor, or for tissue that
9 is about to be implanted into a recipient,
10 then is the system working as well as it
11 could?
12 Clearly, we are saying it needs to
13 be improved. So how do you talk about
14 timeliness of communication?
15 CHAIR BRACEY: So I think that we
16 could address that in the second piece, where
17 we state that all adverse events should be
18 reported in a timely manner; should be
19 reported -- yes?
20 MEMBER BOWMAN: I thought the TTSN
21 was the vehicle that was sort of designed and
22 planned to take care of the timely and rapid

1 coordination of communication and reporting
2 between providers, programs, recipient
3 centers, donor centers, that type of thing.
4 CHAIR BRACEY: Good point.
5 MEMBER BOWMAN: We don't need to
6 reinvent the wheel here.
7 CHAIR BRACEY: Right.
8 MEMBER BOWMAN: The preamble was
9 written by the TTSN folks several years ago.
10 MEMBER ISON: Yes, but is the TTSN
11 funded?
12 MEMBER BOWMAN: Well, that is a
13 separate issue, but you are looking for
14 solutions to a problem.
15 CHAIR BRACEY: Right, right. So
16 we talk about the funding piece, that would be
17 separate.
18 MEMBER LOPEZ-PLAZA: I think in
19 here, again, for just specific patients, what
20 you are looking at is the end-user side. That
21 is where we need a good tracking system, and
22 we need a way of being able to identify and

1 report those in a timely fashion to the
2 manufacturing side. I think that is where the
3 gap is.
4 CHAIR BRACEY: So let's go down to
5 the second piece here. So here let's just get
6 rid of reporting.
7 Then we want to say, "All adverse
8 events possibly related to tissue" -- this
9 should be plural, I guess -- "tissue grafts
10 should be reported."
11 MEMBER KUEHNERT: Can I make
12 one --
13 CHAIR BRACEY: Yes.
14 MEMBER KUEHNERT: -- in case we
15 sort of don't go back to the preamble?
16 I think what is missing there is
17 the efferent arm. So surveillance, yes, that
18 is important, but that is gathering data.
19 What about active intervention? So "impairing
20 adverse event surveillance and active public
21 health intervention"? I mean, isn't that what
22 we want?

1 CHAIR BRACEY: Yes, yes, you're
2 right.
3 MEMBER KUEHNERT: Okay.
4 CHAIR BRACEY: Yes. Please.
5 MEMBER ISON: How about "timely
6 public health intervention"?
7 MEMBER KUEHNERT: Yes, that's
8 good, "timely".
9 DR. LAZARUS: Can you hear me
10 through this one?
11 I am covering for Laura while she
12 had to step out.
13 I just had a question about
14 reporting, a comment and a question.
15 As you know, as I explained
16 yesterday, there are reporting requirements
17 that are specific to the manufacturer for
18 infectious disease-related adverse reactions.
19 So I am trying to be conscious of, and maybe
20 raise everyone's consciousness about, the
21 issue of duplicative reporting requirements.
22 I am wondering what your thinking

1 would be about how developing another
2 reporting system to a central repository about
3 adverse events that would include communicable
4 disease, mandatory communicable disease
5 requiring, would that create a duplicative
6 system?
7 Also, I wonder if this would
8 adequately address the concern that we really
9 want the end-user to provide information to
10 the manufacturer, and would requiring or
11 encouraging -- I realize the word "voluntary"
12 is there. But in developing a system whereby
13 the end-user reports to a central repository,
14 would that in any way be a disincentive to
15 providing the information to the manufacturer,
16 which is something that we have enforcement
17 tools that we can use if the information gets
18 to the manufacturer, whether or not the
19 manufacturer even forwards that to us, because
20 we can go in and inspect the manufacturer's
21 records?
22 MEMBER AXELROD: Yes, that is a

1 good point. I think what we heard was that
2 the point up to the distribution has a
3 tracking mechanism and a reporting mechanism.
4 Then, once it gets behind the doors of the
5 hospital, that communication from the issues
6 coming up to the manufacturer is where the
7 deficit is. So I understand what you are
8 saying.
9 So is really the question that we
10 have to get that reporting back to the
11 distributor, and then it gets into the system?
12 CHAIR BRACEY: Well, I guess one
13 of the things, that perhaps we may be getting
14 a little too prescriptive in terms of whether
15 it goes to a central repository. What we want
16 is to have all of the adverse events reported,
17 period. Leave it up to those who can manage
18 the process to figure out, well, how you make
19 that happen.
20 Dr. Triulzi?
21 MEMBER TRIULZI: Yes. The issue
22 with that is, unless FDA is going to put

1 aggregate data from all manufacturers, how do
2 you know the incidence of adverse events? And
3 would they agree to do that?
4 DR. LAZARUS: Right. Like are
5 these two separable issues? And maybe Matt
6 can help elucidate this. But, I mean, we are
7 talking about surveillance and acquiring
8 numerator and denominator data as one issue,
9 and then, also, the necessity to communicate
10 as close to real-time as possible important
11 events that require immediate actions. They
12 are kind of two different things.
13 I guess that is what I am
14 struggling to understand with point No. 2.
15 Like is No. 2 trying to encompass two
16 different ranges of activities, and maybe, in
17 doing so, creating some difficulties with one
18 or the other?
19 MEMBER KUEHNERT: Right. I think
20 this is part of what I was talking about,
21 having parallel systems, a mandatory
22 regulatory system and perhaps a voluntary

1 public health system, but they serve two
2 different purposes.
3 For instance, you can get data
4 from manufacturers on an event and say, well,
5 we need to change the screening tests because
6 they are obviously not sensitive enough, but
7 that doesn't help the patients in that
8 particular situation, for instance, as we saw
9 in the Tugwell article in HCV transmission, in
10 making sure that tissues are not implanted.
11 You would need a rapid communication system
12 that communicates the adverse event in an
13 efficient way.
14 So I think the repository term
15 maybe we could change and say, instead of
16 "central repository", perhaps have at least a
17 common mechanism, and also, integrated with
18 existing reporting. So that it is not that we
19 are trying to wipe out the existing reporting
20 mechanisms, but, clearly, there needs to be
21 something new on top of what we already have.
22 CHAIR BRACEY: So what we said,

1 "All adverse events possibly related to
2 tissues should be reported voluntarily and
3 aggregated to" -- you know, we want to bring
4 it all together.
5 MEMBER LOPEZ-PLAZA: Okay. Again,
6 I think we are talking about two different
7 levels of reporting or recognition. The first
8 one is, I think, in the tissue world, a lot of
9 the end-users assume that what they are
10 getting is a perfectly sterile product. So I
11 think there is the problem of actually
12 associating any adverse event with that
13 patient implantation.
14 I think, from the specific guide
15 for the tissues, we have to create some kind
16 of awareness or mechanism that that is going
17 to happen, so that adverse event gets
18 reported. Okay? That is from that point of
19 view.
20 The level of how fast we can get
21 all that into some kind of central
22 information, so all the persons that use that

1 donor can be linked together, that is at a
2 higher level that will include all the tissues
3 and organs.
4 So, I mean, for the tissues, I
5 think it is the recognition that what is
6 happening in that recipient might have to do
7 with that implantation.
8 CHAIR BRACEY: Right, and that we
9 can get to in terms of reporting back to the
10 end-users. Because if you report to the end-
11 users, they, then, would, you know, be made
12 aware.
13 But we definitely want to get all
14 of the adverse events reported. Where we are
15 getting hung up is on the issue of having two
16 systems, a redundancy.
17 So do we feel strongly about a
18 central repository?
19 MEMBER LOPEZ-PLAZA: I don't think
20 that should be discussed at that level. I
21 mean that should be discussed at the general
22 recommendations we are going to have.

1 I mean I think, whatever you want
2 to word it, I think right now for tissues we
3 have to have some mechanism that we can bring
4 the knowledge of the users of being able to
5 relate an adverse event to the implantation.
6 CHAIR BRACEY: So we had "All
7 adverse events possibly related to tissue
8 should be reported, investigated, and reported
9 back to end-users."
10 MEMBER ISON: Well, then, I wonder
11 if there needs to be a third component where
12 there is an education piece or something to
13 educate the end-users to think about,
14 recognize, and know how to report. Because,
15 I mean, I think the thing that we got is,
16 although there were a number of instances
17 where there was the manufacturer and someone
18 else, it was actually pretty rare that it was
19 just the user that was reporting an adverse
20 event in the case of tissue.
21 So, clearly, again, the reality is
22 the report should be coming from the users

1 because the manufacturers, clearly, are
2 getting that, hopefully, from the users.
3 CHAIR BRACEY: So let's separate
4 out the education piece, but let's just do the
5 reporting and recognize that there is a need
6 to have an educational piece.
7 Dr. Triulzi?
8 MEMBER TRIULZI: Yes. So I think
9 Ileana is heading in that direction, the right
10 direction, which is a reporting system that is
11 analogous to what we need to do, recalls and
12 consigning notification. It is rapid, right?
13 There is an adverse event identified --
14 CHAIR BRACEY: Yes.
15 MEMBER TRIULZI: -- in a
16 transfusion. It is communicated to the blood
17 center. The recall, the consigning
18 notification of any other products occurs.
19 We want that parallel process for
20 tissue. That is a rapid --
21 CHAIR BRACEY: Right.
22 MEMBER TRIULZI: -- process that

needs to go both directions, right?

CHAIR BRACEY: Yes, right. No one has to educate us about it because --

MEMBER TRIULZI: Right. That I think is the highest priority.

CHAIR BRACEY: Okay. So then --

MEMBER TRIULZI: Then the second is the reporting of adverse events into a central database, like REDS, or wherever, wherever that is. That is a lower priority. We would like that, but --

CHAIR BRACEY: So, if we rephrase this into "All adverse events possibly related to tissue grafts should be reported, investigated, and" -- the issue is the return to the end-user. I'm blocking on that.

MEMBER LOPEZ-PLAZA: No, not the end-user. Returned to the manufacturer, to the tissue provider.

CHAIR BRACEY: Okay. So "All adverse events possibly related to tissue grafts should be reported, investigated,

1 and" --

2 MEMBER LOPEZ-PLAZA: "Should be

3 recognized, investigated, and reported to the

4 provider." That really should be the --

5 CHAIR BRACEY: Reported to the

6 manufacturer?

7 MEMBER LOPEZ-PLAZA: Provider.

8 MEMBER TRIULZI: We have already

9 heard from FDA that the distributor is part of

10 the manufacturing process. So, if it is

11 reported to the distributor, then the chain of

12 communication has been initiated.

13 We have said that the distributor

14 is a manufacturer.

15 DR. LAZARUS: Right.

16 MEMBER TRIULZI: And so they have

17 a responsibility via contract with the source

18 producer.

19 DR. LAZARUS: Yes. The way the

20 reg is written is that the adverse reaction

21 must be reported to the FDA by the

22 manufacturer who made the tissue available for

1 distribution.

2 So most, you know, the vast

3 majority of reports we get are from the

4 manufacturer. I think, from a risk and public

5 health standpoint, it is very important to

6 consider -- and I know this has been discussed

7 -- that the manufacturer has to look -- it is

8 likely that, if there was a problem with the

9 tissue, the manufacturer would be in a better

10 position to do the investigation, to do any

11 other assessments about whether other tissues

12 might be involved, and the distributor

13 wouldn't.

14 MEMBER TRIULZI: I understand, but

15 the hospital may not know for that -- they

16 deal with their distributor, right? They

17 don't know where the source, just like a blood

18 center sends a unit to the hospital. We don't

19 know in the hospital what 15 blood centers

20 they import from. We let the blood center

21 that distributed the products know there was

22 a problem. It is their job to see which of

1 the 15 centers they imported that product
2 from.
3 DR. LAZARUS: It might be helpful
4 maybe to hear from some of the members of the
5 Committee who are involved in hospital tissue
6 services. The point I am trying to emphasize
7 is that the manufacturer that is in the best
8 position to do the investigation and take the
9 necessary follow-up actions would more likely
10 be the tissue bank.
11 MEMBER TRIULZI: I agree with
12 that. It is just the hospital probably
13 doesn't know who that is.
14 MEMBER SARODE: Yes, I think that
15 is right. So if something happens in my
16 hospital, I would only know the distributor.
17 I wouldn't know who manufactured it.
18 DR. LAZARUS: Yes.
19 MEMBER SARODE: So I would report
20 it to the distributor.
21 MEMBER AXELROD: Well, let me ask
22 a question. Maybe we are getting on

1 semantics.

2 Does that FDA regulation

3 automatically make the distributor contact the

4 manufacturer as a result of the reg? Because

5 that is really what our concern is.

6 So, for example, if we distributed

7 a product to a hospital that was gotten from

8 another blood center, and then there was an

9 adverse event that was reported back to us, we

10 were the distributor, but not the

11 manufacturer; we would immediately report back

12 to the manufacturer of that unit who sent it

13 to us.

14 So, if that is mirrored in tissue,

15 then it is just semantics. If it is not, then

16 it is an issue.

17 CHAIR BRACEY: You know, actually,

18 what I was thinking about is, when you report

19 it to the manufacturer, they must investigate

20 it, according to the regulations.

21 DR. LAZARUS: Yes.

22 CHAIR BRACEY: So the point really

1 is that, if all adverse events are reported to
2 the manufacturer, then that is it. That is
3 what you want to achieve.
4 MEMBER LOPEZ-PLAZA: But the
5 hospital doesn't necessarily have that
6 information. The contact person in most
7 hospitals is going to be the distributor. You
8 see?
9 CHAIR BRACEY: But if you just
10 say, "All adverse events are reported to the
11 manufacturer", so the manufacturer does not,
12 then, have to so inform the distributors,
13 others that have received the tissues?
14 DR. LAZARUS: Well, you are adding
15 another --
16 MEMBER AXELROD: You are going the
17 wrong way. The issue is the hospital has a
18 relation with the distributor, and not in all
19 cases; sometimes the manufacturer is the
20 distributor. The distributor has gotten that
21 product from the manufacturer.
22 So the question is, if the

1 regulation says that the manufacturer must be
2 notified, are all the distributors following
3 that regulation, that if they get notified, it
4 automatically goes back to the manufacturer?
5 If that is the issue, there is no
6 issue.
7 DR. LAZARUS: Yes, I can only say
8 that you are adding another step. This is an
9 issue that I am not sure I can answer it. I
10 can only tell you what the regs says, that the
11 establishment that made the product available
12 for distribution is the one that is
13 responsible for reporting to FDA.
14 DR. HOLMBERG: So would you want
15 to say the source, notification of the source?
16 CHAIR BRACEY: Notification of the
17 source?
18 DR. HOLMBERG: Of manufacturing?
19 Or the source of --
20 MEMBER HALEY: One of the issues
21 that we struggled with last night is that some
22 donors, cadaveric donors, will have products,

1 will have tissues and products that go to
2 different manufacturers. Well, the organs may
3 go directly to a hospital somewhere for
4 transplant. Some tissues may go to a
5 particular manufacturer.
6 I think that is why we talked
7 about a central repository, not specifying
8 where that would be because, if we notify the
9 manufacturer, if this is a patellar tendon, if
10 we notify the manufacturer, have we also
11 notified whoever did the kidney transplant or
12 whoever dealt with the kidneys?
13 CHAIR BRACEY: Right, right,
14 right.
15 MEMBER HALEY: And the reason I
16 use central repository is it fuzzed it up
17 enough that the FDA and the Secretary could --
18 CHAIR BRACEY: Figure it out.
19 MEMBER HALEY: -- could figure it
20 out, yes. I mean I am not smart enough to
21 figure this out.
22 CHAIR BRACEY: Dr. Bowman?

1 MEMBER BOWMAN: What the Committee
2 is describing over the last 15-20 minutes are
3 the functional requirements and the elements
4 of those requirements for a process in a
5 system. I don't think the Committee needs, on
6 a Friday afternoon, to get into all the nuts
7 and bolts of how to design a national system.
8 And again, I don't own stock in
9 TTSN. I am not paid by the TTSN. I don't
10 have a personal preference. HRSA does support
11 whatever the Department supports with TTSN.
12 But, to the extent that the TTSN
13 has already delved into these issues and has
14 come up with a pilot, and now comes out with
15 a request for information, I think it behooves
16 the Committee to go ahead and proceed along
17 the lines of in some way recommending support
18 of the TTSN and making that a large-scale
19 beyond the pilot stage.
20 DR. HOLMBERG: Well, just to give
21 you a little insight, what we are working on
22 at the present time is a concept of operations

for biovigilance. Really, not even getting to the level of the TTSN, because we don't know even know that that is going to exist. You know, it was only a pilot.

So I would end the sentence "should be reported", "should promptly be reported". And let the Department work on the concept of operation.

CHAIR BRACEY: Okay. That gets to the principle.

MEMBER HOLLIS-PERRY: "Reported and investigated"?

CHAIR BRACEY: "And investigated".

MEMBER LOPEZ-PLAZA: "Promptly".

CHAIR BRACEY: "Should be promptly reported and investigated". So, "should be promptly reported and investigated". Okay.

I did something wrong there. Okay.

So we are expanding. Now let's go down to transportation. Transportation, I mean in a sense, this is getting at -- I am

1 not sure we have enough data to really deal
2 with that. I think we should strike that.
3 MEMBER LOPEZ-PLAZA: I think I
4 would take that out because we don't have
5 enough information.
6 CHAIR BRACEY: Yes. And, really,
7 this gets to more along the lines of what
8 HRSA, oh, the FDA in this case, would review.
9 We have got traceability up -- it
10 is the same thing, yes. So let's strike that.
11 Consent is important. Discussion?
12 So what do we want to say about consent?
13 MEMBER HALEY: Could you break
14 this into two? You know, one would be
15 something along the lines of the uniform
16 living donor history questionnaire, and then
17 the other part would be patient consent, or
18 something along those lines. Maybe not.
19 Maybe one is not really consent.
20 CHAIR BRACEY: Well, I think what
21 we want to do, we want to remember the uniform
22 donor history questionnaire, but we want to do

1 consent as a separate issue.
2 MEMBER HALEY: The tissues are
3 implanted in people who have given consent,
4 but it is a general surgical consent.
5 CHAIR BRACEY: Correct.
6 MEMBER HALEY: So, when I wrote
7 this last night, I forgot to put in the part
8 about the general surgical consent, which
9 often includes a clause or usually includes a
10 clause about the specific tissues that might
11 be implanted, such as some bone material or a
12 patellar tendon or something like that.
13 CHAIR BRACEY: So wait a minute.
14 You lost me.
15 So you want to include that
16 reference to the general surgical consent?
17 MEMBER HALEY: I think Dr. Arnold
18 probably ought to because he actually does
19 this.
20 CHAIR BRACEY: Dr. Arnold?
21 MEMBER ARNOLD: Well, I don't
22 accept the statement that there is no

1 requirement for informed consent. I think the
2 concern, or at least as I understood it today,
3 is more about whether or not that could take
4 a better form with patients receiving
5 allograft tissues or tissues from other
6 individuals, that perhaps in its current form
7 consent is not as fully informed as this
8 Committee, with a little more insight,
9 believes is necessary to be ethically correct.
10 CHAIR BRACEY: So perhaps we would
11 recommend that the Secretary --
12 MEMBER ARNOLD: Advance language
13 for standardization of informed consent
14 wording, or something along those lines.
15 People could be more informed.
16 You know, again, we can't send them all to med
17 school, not that that is done.
18 MEMBER HOLLIS-PERRY: The consent
19 does not specify the risk of exposure to human
20 tissue.
21 MEMBER ARNOLD: And I disagree
22 with that. I mean ours does. But it is just

a matter of --

MEMBER HOLLIS-PERRY: Well, I mean in all cases.

MEMBER ARNOLD: Yes, that's right. There should be uniform language relative to receiving tissues.

CHAIR BRACEY: What about, what if we say that the Secretary assess the current state of consent with respect to tissue implantation and advance the standard?

MEMBER LOPEZ-PLAZA: It is more the language than the actual consent.

CHAIR BRACEY: What is that again? Use the microphone.

MEMBER LOPEZ-PLAZA: It is more the language -- I mean I think the consent exists. It is just the standardization of the language that is used that can be probably across the system.

So it is more looking at the details of the consent, not at just that there is a consent or not, but the language. No

1 matter where you are including it, it has a
2 standard language that would address risk and
3 whatever needs to be addressed.
4 CHAIR BRACEY: Well, yes. I guess
5 the question is it is language and process.
6 DR. HOLMBERG: Don't you think
7 that what you are saying is transparency?
8 CHAIR BRACEY: Yes, yes.
9 DR. HOLMBERG: That the informed
10 consent needs to be assessed for transparency?
11 CHAIR BRACEY: Yes.
12 MEMBER BOWMAN: I think what you
13 are asking for is the adequacy of informed
14 consent.
15 CHAIR BRACEY: So assess the
16 adequacy?
17 MEMBER BOWMAN: Adequacy and
18 transparency of informed consent --
19 CHAIR BRACEY: Assess the adequacy
20 and transparency.
21 MEMBER BOWMAN: -- as currently
22 practiced for allograft transplants.

1 CHAIR BRACEY: How about that?
2 MEMBER POMPER: I think the
3 problem statement is that, and then the
4 solution would be to advance language for
5 standardization of informed consent. So I
6 think the concern is inadequacy, and that
7 might be --
8 CHAIR BRACEY: Right, but if we
9 just ask them to assess it, then they would
10 follow on with the advancement of --
11 MEMBER BOWMAN: The Assistant
12 Secretary would report back to the Committee,
13 I think.
14 CHAIR BRACEY: Right.
15 MEMBER ARNOLD: I mean maybe
16 similar to the reception of blood products,
17 which are ubiquitous. It is essentially the
18 same concept in my mind, that perhaps going to
19 the OR and signing off on you can stick a
20 ligament in me should have a little bit more
21 of the language that has been infiltrated in
22 receiving blood products, the permits that we

1 sign these days.

2 CHAIR BRACEY: Right, but I think

3 that we should want to have the Secretary

4 evaluate the process. We don't have to tell

5 him how to evaluate the process. We just say

6 we think the issue is they should assess the

7 adequacy of the current practice of informed

8 consent for tissue implantation, without being

9 prescriptive.

10 "Assess the adequacy of the

11 current practice of informed consent for

12 tissue implantation."

13 Examples, I mean we could give an

14 example, use that as an example.

15 MEMBER ARNOLD: I don't see that

16 it is the practice of informed consent. It is

17 the language of informed consent.

18 CHAIR BRACEY: Current language?

19 DR. HOLMBERG: Well, not only

20 language, but I think what you are getting at

21 is --

22 CHAIR BRACEY: Well, how about

1 process?

2 DR. HOLMBERG: -- the transparency

3 and the understanding of the process.

4 MEMBER BOWMAN: The process as

5 currently practiced.

6 CHAIR BRACEY: Well, process would

7 include transparency.

8 So "Assess the adequacy of the

9 current language and process of informed

10 consent for tissue implantation." That's it.

11 Okay, then strike the -- okay.

12 Oversight. We don't want to beat

13 up on TJC too much there.

14 MEMBER LOPEZ-PLAZA: Can you put

15 CMS instead?

16 CHAIR BRACEY: No, no, I am just

17 thinking, so what we are really getting at is

18 that, while there are systems in place, there

19 is no way to audit activity. So what we would

20 recommend is an audit function to --

21 DR. HOLMBERG: To ensure.

22 CHAIR BRACEY: -- to ensure. So

1 establish audits to ensure compliance with
2 current tissue regulations, because the
3 regulations are there.
4 MEMBER KUEHNERT: I think they are
5 standards, aren't they? We are talking about
6 Joint Commission? Because there are no
7 regulations in the hospital for tissue, right?
8 CHAIR BRACEY: Well, we should
9 say, "ensure compliance with tissue standards
10 and regulations", because it depends on where
11 you are.
12 MEMBER TRIULZI: You've got to add
13 the word, you should add the word "hospital"
14 in there somewhere, I guess.
15 MEMBER NETHER: No, I would
16 disagree because I think we need to cast this
17 net a little bit wider. It is just not
18 hospitals. What about the ambulatory
19 settings?
20 DR. HOLMBERG: Well, maybe not
21 that, but what we also heard was that some of
22 this really goes into the dental office.

1 CHAIR BRACEY: Yes, right. So,
2 "Establish audits to ensure compliance with
3 current tissue standards and regulations".
4 So "establish audits", is that
5 right?
6 MEMBER LOPEZ-PLAZA: I don't know
7 how you could put "establish audits". Like at
8 the end-user or something that is reflecting
9 -- I mean we use hospital; we really mean
10 anyone that receives a tissue transplant. I
11 think that is where you really have to
12 establish those audits.
13 MEMBER AXELROD: Can we do it like
14 the one before and say something to the nature
15 of -- I mean, is there not a process at all or
16 is it to assist the sort of adequacy of the
17 current process to ensure compliance with
18 current tissue standards?
19 You know, is there a process and
20 it is just not being met in terms of the
21 oversight of compliance? Or is it that it
22 doesn't exist at all?

1 CHAIR BRACEY: So you would say
2 perhaps, because I was getting at assessing
3 adequacy through establishing audits, but
4 audits is perhaps prescriptive.
5 MEMBER AXELROD: Right.
6 CHAIR BRACEY: So you are saying
7 assess --
8 MEMBER BOWMAN: Why not something
9 like "Assess the adequacy of current oversight
10 mechanisms"?
11 CHAIR BRACEY: Yes, okay. "Assess
12 the adequacy of current oversight mechanisms."
13 MEMBER BOWMAN: Because, actually,
14 there are not specific regulations or
15 conditions for the patient in the Medicare
16 program for physicians' offices and hospitals
17 and ambulatory care centers and outpatient
18 departments and hospitals. They are not in
19 that level of detail for tissues, if I am not
20 mistaken, right now.
21 CHAIR BRACEY: So "Assess the
22 adequacy of current oversight mechanisms to

1 ensure compliance with tissue standards".
2 Instead of saying, "current", just "tissue
3 standards and regulations".
4 MEMBER KUEHNERT: You might want
5 to say particularly at the -- and I am being
6 careful how I phrase this -- particularly at
7 the healthcare --
8 CHAIR BRACEY: Facility.
9 MEMBER KUEHNERT: -- facility
10 level. Make sure that we include, you know,
11 we are not just talking about hospitals.
12 MEMBER POMPER: Yes, and a few
13 examples like, I mean, dental offices,
14 outpatient, ambulatory locations, patient
15 locations.
16 CHAIR BRACEY: But you say,
17 "particularly at...."
18 MEMBER KUEHNERT: Yes, I would end
19 with, "particularly at the healthcare facility
20 level".
21 CHAIR BRACEY: So that would all
22 go at the end, "particularly at...."

1 MEMBER KUEHNERT: At the end.
2 MEMBER BOWMAN: But the concern is
3 that there may not be current standards for
4 tissue at dental offices or physicians'
5 offices.
6 MEMBER NETHER: I was just going
7 to say that, in terms of I can only speak from
8 the Joint Commission side, that we have
9 requirements for tissues, but I can't speak
10 for every other accreditor. So I don't know
11 if tissue standards or requirements exist.
12 MEMBER KUEHNERT: I am sorry. I
13 meant that whatever is written here, that it
14 implies that there may be some situations
15 where there are no standards and there are no
16 regulations.
17 So, then, the mechanisms would be
18 inadequate, and there wouldn't be an issue
19 about compliance because there is nothing to
20 comply with.
21 MEMBER BOWMAN: What you really
22 want is the Secretary to assess the adequacy

1 of the current oversight with respect to
2 achieving the goals previously enumerated in,
3 I think it was, goal No. 1, I believe, or goal
4 No. 2 up there.
5 MEMBER AXELROD: It is almost, as
6 he is mentioning, it is almost to ensure -- I
7 don't know if the word is compliance, but
8 ensure meeting the goals established in one,
9 two, and three. That is what you want to make
10 sure, that you have an oversight mechanism
11 that is going to address the top three things
12 that we have talked about that relate to--
13 CHAIR BRACEY: So to ensure
14 compliance with the aforementioned concerns,
15 issues? Items?
16 MEMBER BOWMAN: It is just not
17 compliance. I don't know the exact word, but
18 it is not compliance.
19 MEMBER KOUIDES: And we also need
20 to put in there adequate regulations, right,
21 because it is not just compliance, but we
22 need --

1 CHAIR BRACEY: Oh, so you're
2 saying also make sure that, if there aren't
3 regulations, that there need to be. So, to do
4 assessment to adequacy of current oversight,
5 to ensure compliance -- it is not compliance.
6 MEMBER AXELROD: It is almost
7 ensure success of the recommended systems
8 above, or something like that.
9 MEMBER KOUIDES: I guess it is to
10 ensure patient safety.
11 CHAIR BRACEY: Yes, that's good.
12 Yes, keep it in the broadest sense, to ensure
13 patient safety, yes.
14 MEMBER BOWMAN: Maybe patient
15 safety, as identified --
16 CHAIR BRACEY: As identified.
17 MEMBER BOWMAN: -- in the
18 previously enumerated one, two, and three or
19 the objectives identified in recommendations
20 one, two, and three.
21 MEMBER SARODE: Well, there are
22 some other recommendations which are not

1 included in that, the original. So I think,
2 if we just specify those three, then we are
3 eliminating others.
4 CHAIR BRACEY: So some say keep it
5 broad; some say focus. How does the Committee
6 feel?
7 MEMBER SARODE: It should be
8 broad. It should be broad.
9 CHAIR BRACEY: Broad? So just
10 make it broad? Just patient safety.
11 MEMBER KUEHNERT: Okay. So, then,
12 you would need to say, because now that it has
13 been simplified, "Ensure patient safety in
14 tissue recipients" --
15 CHAIR BRACEY: In tissue
16 recipients.
17 MEMBER KUEHNERT: -- "as
18 identified in the aforementioned items."
19 CHAIR BRACEY: Well, we were going
20 to strike "as identified in the
21 aforementioned". Yes. Yes, just strike it
22 all the way to the end.

1 Okay. Now we have four specific
2 recommendations. Well, now the thing that is
3 missing is the uniform history questionnaire.
4 How about, as item No. 5, "Develop uniform
5 questionnaire for donor screening to ensure
6 patient safety."?
7 MEMBER POMPER: I just want to
8 qualify that all of this is under the original
9 problem statement that just talks about
10 tissue, so we are all on the same page.
11 CHAIR BRACEY: Right, right, it is
12 in the problem statement, but then we are
13 recommending.
14 MEMBER POMPER: I am just saying
15 this is all about tissue. So, if any of this
16 is intended to imply organs, it is not
17 referring to that.
18 CHAIR BRACEY: Right, right,
19 right.
20 So, for tissues, we basically have
21 five recommendations. One is traceability.
22 The second is adverse event reporting. The

1 third is the consent. The fourth is oversight
2 of, you know, the regulations.
3 MEMBER ISON: The process?
4 CHAIR BRACEY: The process. And
5 the fifth is screening.
6 So, then, are we ready to move on,
7 then, to organs? Okay. So, now under organs,
8 you've got to go down deeper.
9 MEMBER POMPER: Does that stay?
10 CHAIR BRACEY: No, it starts right
11 here.
12 So, Mike, do you want to --
13 MEMBER POMPER: Just another sort
14 of overarching concept to keep in mind, since
15 question No. 1 or item No. 1 from the
16 Assistant Secretary, the first part of the
17 question is examples of how might the federal
18 government leverages resources, to keep in
19 mind if we want to recommend any sort of
20 funding, et cetera, in any of these areas
21 because we haven't yet.
22 CHAIR BRACEY: Oh, okay.

1 MEMBER POMPER: Even in the
2 preamble or something like that.
3 CHAIR BRACEY: Okay.
4 DR. HOLMBERG: Art, I am not sure
5 if questionnaire is going to ensure patient
6 safety.
7 CHAIR BRACEY: Okay.
8 MEMBER ARNOLD: Perhaps
9 "questionnaires" should be "database" or "data
10 fields" because the tissues we are talking
11 about are typically harvested from donors.
12 CHAIR BRACEY: So data fields?
13 MEMBER ARNOLD: Yes, data fields.
14 I mean we have already identified that
15 sometimes families aren't even reliable. So
16 there may be whatever, questionnaire, it is a
17 nuance. It is nomenclature issue, but a
18 questionnaire implies somebody is going to
19 answer a bunch of questions.
20 CHAIR BRACEY: I will keep that
21 and we will come back. So the question is
22 whether to use questionnaire or data fields?

1 MEMBER POMPER: Uniform donor
2 data --
3 CHAIR BRACEY: Uniform donor data.
4 MEMBER POMPER: -- information,
5 yes.
6 MEMBER ISON: And we will get to
7 that in the organs stuff as well.
8 So, actually, just for ease, the
9 first bit is a bit of the preamble. But,
10 basically, specific to organs, it is
11 recognized that there are significant gaps in
12 identifying the risk of disease transmission.
13 Then we highlighted a couple of key areas.
14 First, donor medical and social
15 history. There are currently not standardized
16 approaches to collecting the medical and
17 social history.
18 This is critical to assess, as it
19 directly impacts classification of donors as
20 increased risk versus standard risk of latent
21 infections with blood-borne pathogens, which
22 directly derives additional testing of donors,

1 which may lead to increased use or loss due to
2 false-positive testing and additional
3 consenting, as discussed below.
4 And then this is a recommendation.
5 Specifically, the Secretary should develop a
6 funding mechanism to support development and
7 validation of such standard approach, meaning
8 uniform donor health, history, screening
9 questionnaire.
10 This approach should include an
11 internal validator or similar method to assess
12 the reliability of the data, and maybe that
13 should be, instead of "data", the historian.
14 Access to medical and laboratory
15 testing of donors. Currently, there are no
16 standard approaches to allow procurement
17 organizations to access and review the
18 comprehensive amount of data available on each
19 recipient. The Secretary should investigate
20 mechanisms to allow easier and complete access
21 to the appropriate records.
22 Next, currently, the OPTN policy

1 requires specific informed consent of
2 recipients of, quote/unquote, "high-risk
3 donors". There is significant variability in
4 how information is provided to potential
5 recipients, and research is needed to
6 understand gaps in clinician and patient
7 knowledge related to high-risk donors, in
8 particular, and all organ donors in general.
9 Further research is also needed to
10 understand the impact of the consent process
11 on how organs are used. The Secretary should
12 direct funding to understand the knowledge
13 gaps and impact of -- maybe just, instead of
14 the "special consent process" -- the consent
15 process as it relates to organ utilization.
16 There are currently limitations
17 related to donor screening, including lack of
18 standard policy defining hemodilution, the
19 availability of serologic and nucleic acid
20 tests in appropriate platforms to be used by
21 organ procurement organizations, methods to
22 optimize and implement appropriate use of NAT

1 in donor screening, and how to ideally study
2 novel pathogens and donor screening.
3 Further, there is no data
4 collected on donor screening results in
5 potential donors that do not yield at least a
6 single organ and for non-required testing,
7 such as NAT or other pathogens that aren't
8 part of required screening. Likewise, the
9 data on donor screening is not publicly
10 available and not presented in a real-time
11 fashion.
12 So that probably needs an action
13 item, too.
14 CHAIR BRACEY: Where is the action
15 item?
16 MEMBER ISON: We need one. I
17 didn't put that one. But, then, I guess the
18 action item would be something along the
19 lines: provide funding to both simulate the
20 continued availability and assess new
21 platforms, and then something along the lines
22 of collecting all data on all donors,

1 irrespective of whether organs are procured or
2 not.
3 There is an AOPO standard to
4 retain donor specimens for later testing for
5 10 years. There is currently no standard
6 about what type or volume of specimen to
7 obtain and how they should be maintained.
8 Further, there is no standard on recipient
9 specimen retention, and neither of these are
10 part of OPTN policy.
11 So, again, I don't know whether
12 this is something that is getting too
13 specific, but needing to develop standards for
14 both donor and recipient retention.
15 This is getting to the numbering
16 system.
17 Although there are unique donor
18 and recipient identifiers that are linked in
19 the proprietary UNOS system, and this allows
20 for both forward and backward tracing of
21 donors and recipients, this system is neither
22 contemporary, ISBT-128, for example, nor

1 linked to other tissues derived from the same
2 donor. So maybe linking that back up.
3 Although there is a policy for
4 reporting a proven or suspected donor-derived
5 disease transmission, the increasing rate of
6 reports suggests that there is significant
7 underreporting. Further, there is not a
8 formal system in place, such as the Transplant
9 Sentinel Network, to capture cases and
10 facilitate communication. Because of these
11 reasons, there is need to address the gaps as
12 outlined in the white paper and to fund a
13 prospective study to outline the risks of
14 disease transmission through organ
15 transplantation, similar to the Spanish
16 Resitra Cohort.
17 The Committee believes that
18 patient outcomes will be improved by
19 identifying preventable adverse events -- or
20 sorry -- adverse transplant-related events.
21 In addition to the disease transmission, there
22 should be a formal requirement in the

1 reporting system for transplant-related
2 preventable adverse events beyond infections
3 and malignancies.
4 Then the Committee noted that
5 there are no national policies regarding
6 living-related donor screening. There was
7 insufficient data presented for the Committee
8 to make these recommendations. Therefore,
9 additional information needs to be provided to
10 the Committee in this area in a future
11 meeting.
12 DR. HOLMBERG: Did you address
13 informed consent?
14 MEMBER ISON: Yes. That was up --
15 I think we just need to put a statement about
16 that, but the informed consent piece was up
17 here under the high risk. So we should
18 probably just get rid of --
19 MEMBER POMPER: So just an
20 observation that the concept of
21 bidirectionality is listed under tissues. So
22 we probably should consider some sort of

1 ability of not just bidirectional, but
2 crossover from solid organ to tissue, and back
3 and forth, so it doesn't get lost just in
4 tissues, and everybody is communicating.
5 MEMBER ISON: Yes, but I think the
6 one difference, though, is that we do have
7 bidirectionality in traceability from an organ
8 standpoint, and there is a mechanism to
9 communicate information back and forth with
10 tissues and eyes, although that is not
11 actually codified, how that is done. It is
12 just sort of we have kind of created this
13 email system.
14 CHAIR BRACEY: So maybe if we can,
15 then, go to the top and then your action
16 items? So the beginning is -- okay, so it is
17 specific to organs. Okay. So then that would
18 be a header.
19 MEMBER ISON: So it is, basically,
20 the way that most of these are laid out, it is
21 that this is the data, and here's the --
22 CHAIR BRACEY: So Rich might be

1 able to help.

2 So, basically, this would be a

3 header. Donor medical and social history.

4 Yes, as the header.

5 MEMBER LOPEZ-PLAZA: Can you put

6 that like under "donor risk" and then be

7 specific? Like, you know, donor risk

8 assessment, and then, first, the history, and

9 then like testing, and you can shrink that?

10 CHAIR BRACEY: What do you think,

11 Mike?

12 MEMBER ISON: Sure.

13 CHAIR BRACEY: So donor risk

14 assessment.

15 MEMBER ISON: Then, actually, we

16 could probably merge this and the history into

17 one topic as well.

18 CHAIR BRACEY: Okay. Yes, donor

19 risk assessment, right?

20 Okay. That all sounds good.

21 So, then, here you would say --

22 Dr. Holmberg, in order to make this uniform,

1 we will just say the Committee -- or
2 recommendations, or the Committee recommends,
3 yes, that the Secretary -- yes. You've got
4 the Secretary there, okay.
5 MEMBER LOPEZ-PLAZA: I have a
6 question.
7 CHAIR BRACEY: Yes?
8 MEMBER LOPEZ-PLAZA: Can we put
9 the recommendations all together at the end as
10 a summary?
11 CHAIR BRACEY: Yes. Maybe we can
12 just firm up on the recommendations first,
13 though, because we've got some action items we
14 need to generate.
15 "Recommends the Secretary develop
16 a funding mechanism to support development and
17 validation of" --
18 MEMBER ISON: So, then, of just "a
19 uniform donor health" --
20 CHAIR BRACEY: Yes.
21 MEMBER LOPEZ-PLAZA: You can just
22 put between parentheses maybe history of

1 testing. I mean I don't think that is needed.
2 MEMBER ISON: No, no, because I
3 think that that is different, the testing is
4 different, because this is the questions that
5 you ask of the family, similar to the blood
6 questions --
7 CHAIR BRACEY: Do we want to get
8 prescriptive in terms of the validative piece
9 and all of that, or do we just want to leave
10 that out?
11 MEMBER ISON: Well, I personally
12 think that we should make a comment that this
13 piece should have some sort of assessment
14 of --
15 CHAIR BRACEY: We can leave it.
16 Yes, we can leave it.
17 MEMBER ISON: I think the big
18 thing is that there is no way of assessing
19 whether or not this is a good or a bad
20 history.
21 CHAIR BRACEY: Unless it would be
22 validated, right.

1 MEMBER ISON: So quality of the
2 history?
3 DR. HOLMBERG: You already say
4 that up there, "to support development and
5 validation of a uniform health...."
6 MEMBER ISON: Yes, but the
7 validation is proving that the
8 questionnaire --
9 DR. HOLMBERG: Right. So I think
10 the validation takes care of that last
11 sentence.
12 CHAIR BRACEY: Yes, the principle
13 I think is there.
14 MEMBER BOWMAN: Mike, do you know
15 whether the OPTN has addressed this at all?
16 MEMBER ISON: No.
17 MEMBER BOWMAN: You don't know or
18 they have not?
19 MEMBER ISON: They have not.
20 MEMBER BOWMAN: They have not?
21 MEMBER ISON: I know that they are
22 part of the working group that AATB has put

1 together. I think Tim Pruett is part of that
2 group.
3 MEMBER BOWMAN: But this is in
4 reference not to tissues, but specifically as
5 an organ --
6 MEMBER ISON: But from the AATB
7 uniform questionnaire, the AATB uniform
8 questionnaire is designed specifically for
9 organ and tissue donors. There's problems
10 with it, I will point out, because there are
11 questions that are specific to Cruetzfeldt-
12 Jakob Disease, for example, that aren't part
13 of organ policy. But it does question all of
14 the high-risk issues and whatnot.
15 MEMBER BOWMAN: My question is the
16 specific recommendation is for funding, asking
17 the Secretary to fund the development of the
18 screening tool.
19 It may be more appropriate to
20 recommend the Secretary work through the OPTN
21 to develop the tool. Funding, if there is a
22 need for the tool, I think the Secretary and

1 our agency would somehow find the funding to
2 accomplish that. It would not be done
3 necessarily through the OPTN, but it would be
4 probably with their advice and
5 recommendations. That is the key point.
6 CHAIR BRACEY: So you would say,
7 "The Committee recommends that the Secretary
8 support development"? Just cut out --
9 MEMBER BOWMAN: I think that might
10 be more appropriate as a recommendation.
11 CHAIR BRACEY: Yes, okay.
12 MEMBER ISON: I guess the only
13 comment, though, is that the goal, when this
14 was brought up, was to actually have a single
15 questionnaire that would be used by both
16 groups since a third of organ donors are also
17 tissue donors.
18 MEMBER BOWMAN: Okay, that is a
19 different -- I think that should be
20 specifically stated in the recommendation, if
21 that is the goal, because, otherwise, that
22 will be interpreted as just develop an organ

1 donor screening tool.

2 MEMBER ISON: Right, right. I

3 think the point that he is making is, again,

4 because the way that this was conceptually

5 thought of -- and again, the Committee can go

6 one way or the other -- is that this was the

7 goal from an efficiency standpoint, since a

8 third of organ donors are also tissue donors,

9 that you would have one questionnaire that

10 would address both sides of the issues.

11 And you may have thoughts about

12 whether we should have two separate --

13 MEMBER BOWMAN: No, that's

14 certainly possible, and they probably can come

15 up with a common screening tool. I think

16 there may be specific questions that for organ

17 donors are going to be different than for

18 tissue donors.

19 MEMBER ISON: Right, exactly.

20 CHAIR BRACEY: I guess what I was

21 thinking, there is enough difference between

22 the two --

1 MEMBER ISON: As it is being
2 developed now, it is a single questionnaire
3 for both organ and tissue. So, basically, the
4 draft one that has been developed, basically,
5 addresses all regulatory requirements for
6 organs and all regulatory requirements for
7 tissue.
8 MEMBER BOWMAN: I guess I just
9 want to make sure the recommendation is set up
10 so that it leaves the Secretary the
11 flexibility to work through the OPTN, because
12 that is where this is going to eventually
13 fall, at least for organs. I am not sure for
14 tissues, to be honest with you.
15 CHAIR BRACEY: So is this broad
16 enough?
17 MEMBER ISON: Sure.
18 CHAIR BRACEY: All right. Then
19 the next point relates to when the screener is
20 onsite, the access to laboratory information
21 that was mentioned in Dr. Ison's presentation.
22 So here we would break out, under

1 action item, specifically --

2 MEMBER TRIULZI: Mike, can you

3 describe what you would like to see

4 practically?

5 MEMBER ISON: Actually, this may

6 be something where I am not sure exactly what

7 the true solution would be. But, as it stands

8 now, there is a lot of variability, and

9 perhaps maybe it is not the government, but it

10 is the Joint Commission or some other group.

11 But the reality is that different

12 hospitals have different policies about who

13 can access what and how much. So an OPO may

14 actually go into hospital A, have access to

15 everything in the system, go to hospital B,

16 where they only have access to a limited

17 amount of information, and go to hospital C,

18 where they have access to no information at

19 all.

20 MEMBER TRIULZI: Believing this is

21 a HIPAA issue?

22 MEMBER ISON: Correct.

1 MEMBER TRIULZI: Okay.
2 CHAIR BRACEY: So do you want to
3 make this, again, in the form of a
4 recommendation rather than specifically?
5 MEMBER ISON: Sure, yes.
6 CHAIR BRACEY: Okay. So then
7 break that out. "The Committee recommends the
8 Secretary" -- you've got it up there. You can
9 just delete. "Investigate mechanisms to allow
10 easier and complete access to appropriate
11 records." Okay?
12 All right. Then you have --
13 MEMBER BOWMAN: On that one, I
14 think you are referring to the OPOs, isn't
15 that correct?
16 MEMBER ISON: Correct.
17 MEMBER BOWMAN: I think I would
18 probably specify that, so it is clear.
19 MEMBER ISON: So, OPOs, yes.
20 CHAIR BRACEY: To allow OPOs --
21 MEMBER BOWMAN: And to some
22 extent, that might involve CMS. I think there

1 are some conditions of participation for OPOs
2 to have agreements with hospitals in their
3 DSA. So I don't know the specific language of
4 that, but it might mean strengthening those
5 conditions of participation.
6 MEMBER ISON: That is why I think
7 it is kind of vague as written because I am
8 not sure exactly what the solutions are, and
9 it may be something they have to put an
10 interdepartmental task force together for.
11 MEMBER POMPER: Mike, I didn't
12 have a chance to comment on this when you were
13 speaking, but it directly relates to this. I
14 mean you may shoot this down. Fine. But
15 something along the lines where you are there,
16 easier and complete access to appropriate
17 records, recognizing that -- and I am not
18 going to wordsmith this; I am just going to
19 kind of say it. Recognize that there is a
20 conflict or might be a problem between --
21 there is an inherent problem between donor
22 confidentiality and getting access to the

1 information.

2 It is a good thing to maintain

3 donor confidentiality, and it is a good thing

4 to get all the information. Sometimes these

5 things butt heads.

6 I know the name of the patient can

7 change, which is the donor, and then you

8 disconnect all that information.

9 MEMBER ISON: So it is nothing to

10 do with donor confidentiality because the

11 donor forms actually have the patient's name

12 all over it.

13 MEMBER POMPER: But in the

14 hospital medical record, that donor's name

15 ceases to exist. It becomes "donor". We

16 don't know what that was. If I have been

17 following patient Mary Smith --

18 MEMBER ISON: Got you.

19 MEMBER POMPER: -- then suddenly

20 it becomes "donor", I don't know that Mary

21 Smith is donor unless they let people know.

22 CHAIR BRACEY: Right, but I mean I

1 think in the broad sense what we are saying
2 is --
3 MEMBER POMPER: You are not going
4 to find the culture results on Mary --
5 CHAIR BRACEY: Right, right,
6 but --
7 MEMBER POMPER: -- if they are
8 relevant to the case, unless there is a way to
9 get through all that.
10 CHAIR BRACEY: Well, right, but I
11 am just saying, in the broad sense, complete
12 access to appropriate records, you have got
13 it.
14 MEMBER ISON: And I think part of
15 the problem is how it is handled at your
16 hospital is they become "donor". Some
17 hospitals, they may keep the name. There is
18 no consistent approach to what happens to a
19 donor and how to be able to search their data.
20 MEMBER POMPER: Exactly, and I
21 don't know if that is, again, a
22 confidentiality issue or what it is, but for

1 some reason I am just trying to -- I agree
2 with --
3 DR. HOLMBERG: I just want to
4 remind people we have 15 minutes.
5 (Laughter.)
6 No pressure, no pressure.
7 CHAIR BRACEY: Well, now the next
8 piece should really be informed consent as the
9 header and then the rest follows. So the
10 header would be informed consent.
11 MEMBER ISON: And actually, in
12 some regards, that might be kind of the last
13 section.
14 CHAIR BRACEY: So here we would do
15 the recommendation piece, break out the
16 recommendation for the Secretary. "The
17 Committee recommends the Secretary direct" --
18 oh, sorry. "The Committee recommends that the
19 Secretary direct funding to understand the
20 gaps and impact of the consent process," I
21 guess.
22 The organ donor?

1 MEMBER ISON: No, organ
2 transplantation.
3 CHAIR BRACEY: Okay. Yes,
4 transplantation. Okay.
5 So then we move down to -- is it
6 testing? This would be testing? Okay.
7 DR. HOLMBERG: I would also
8 recommend that, behind nucleic acid testing,
9 you use the acronym NAT, so that you don't --
10 right there. After "nucleic acid testing", in
11 parentheses, "NAT" after the "testing".
12 CHAIR BRACEY: Yes.
13 MEMBER ISON: After "testing",
14 just NAT, yes.
15 CHAIR BRACEY: Okay.
16 MEMBER WILLIAMS: I also recommend
17 some reference to confirmatory testing that is
18 needed, whether it is prospective or
19 retrospective, and accesses is a continuing
20 problem.
21 CHAIR BRACEY: So this would be
22 "availability of serologic" --

1 MEMBER ISON: So maybe that would
2 be -- I think there may be actually three
3 points under this. One would be just doing
4 things to maintain the availability and the
5 appropriate platforms. Two, study or
6 guidance, may be the right term, on how to
7 determine true versus non-reproducibly
8 positive, and then three is collection of
9 screening results on donors that have not
10 yielded organs.
11 MEMBER LOPEZ-PLAZA: Guys, I think
12 that you are being too specific. Could you
13 make more of a statement that, regarding both
14 the donor history and the testing, that you
15 need to have more standardized testing
16 reflecting your needs, as for example? That
17 might shorten it. Because you are getting
18 into details that they don't really know about
19 it. I mean it is important, but I think more
20 reflecting the mixture of needs, more than
21 anything else.
22 CHAIR BRACEY: So here we state

1 that the limitations of --

2 MEMBER BOWMAN: Mr. Chairman, I

3 think what Ileana is referring to is probably

4 a good suggestion. This is getting very

5 prescriptive that is going to involve FDA and

6 possibly CMS and possibly HRSA.

7 But what I think she is referring

8 to is that maybe the Secretary explore ways to

9 more effectively identify and utilize the most

10 optimal laboratory screening and confirmatory

11 testing, both current and future technologies,

12 or something to that effect.

13 That way, it encompasses just

14 about everything that Mike has in those

15 things.

16 CHAIR BRACEY: So, then, the

17 recommendation would be that "The Committee

18 recommends that the Secretary explore

19 screening and confirmatory testing" -- oh,

20 this would go at the end right here, instead

21 of that whole paragraph.

22 "The Committee recommends that the

1 Secretary explore" --

2 MEMBER BOWMAN: "More effective

3 use of screening and confirmatory laboratory

4 donor testing."

5 Or, Dr. Williams, maybe you've got

6 some suggestions on wording for that?

7 MEMBER WILLIAMS: Not suggestions

8 on wording. Where I was actually trying to go

9 with the confirmatory test issue is trying to

10 start some thinking about a national

11 confirmatory effort, national laboratory.

12 MEMBER ISON: The only thing that

13 I don't think is captured with this, and maybe

14 this is too prescriptive, but collecting

15 screening data on all donors instead of those

16 in which organs are procured. The last

17 sentence. Or, actually, the second-to-last

18 sentence.

19 For example, to really have an

20 understanding of what the true risk of disease

21 transmission, you have to know all donors, not

22 just the ones that are procured.

1 CHAIR BRACEY: Well, wouldn't that
2 be inherent in that last statement?
3 MEMBER ISON: No.
4 CHAIR BRACEY: In other words --
5 MEMBER ISON: Because that is just
6 talking about the testing platforms, not about
7 the results of the tests.
8 MEMBER BOWMAN: You could say,
9 "screening and confirmatory laboratory testing
10 of potential donors", and that would include
11 donors that don't ever materialize to yield
12 organs.
13 CHAIR BRACEY: And we are sure
14 that Executive Secretary Holmberg could take
15 that to the Secretary, in other words, the
16 issue, without having it specifically in the
17 recommendation.
18 MEMBER BOWMAN: But a further
19 statement on what Dr. Williams was suggesting
20 would be, I think, to explore options to
21 enhance innovation --
22 MEMBER WILLIAMS: Accessibility --

1 MEMBER BOWMAN: -- for the
2 technologies for organ donor screening.
3 CHAIR BRACEY: "And explore
4 options for" --
5 MEMBER BOWMAN: "To enhance
6 innovation and development of more effective
7 organ donor screening", something to that
8 effect.
9 In other words --
10 CHAIR BRACEY: "Options to
11 enhance" --
12 MEMBER BOWMAN: -- it may not be
13 direct research funding for corporations, but
14 it would --
15 MEMBER ISON: Small business
16 grants and things like --
17 MEMBER BOWMAN: Right.
18 CHAIR BRACEY: "Options to
19 enhance" -- you lost me -- "testing"?
20 MEMBER WILLIAMS: "Accessibility".
21 CHAIR BRACEY: "Accessibility and
22 development".

1 MEMBER WILLIAMS: "Development,
2 innovation" --
3 MEMBER BOWMAN: "Innovation" is a
4 big word that is used a lot in government.
5 CHAIR BRACEY: So do we need a lot
6 of the preamble?
7 MEMBER ISON: No, we can rid of
8 that whole paragraph.
9 Oh, and the other thing is
10 hemodilution, the reality is that that could
11 be made a new policy. The hemodilution issue,
12 I can actually take back as an action item for
13 DTAC to work on.
14 CHAIR BRACEY: Wouldn't you leave
15 "There are currently limitations related to
16 donor screening", period?
17 MEMBER ISON: Yes.
18 CHAIR BRACEY: So that would be
19 your preamble?
20 MEMBER ISON: Yes.
21 CHAIR BRACEY: Okay. Now the next
22 piece is AOPO.

1 MEMBER ISON: So this is just
2 standard sample collection.
3 DR. HOLMBERG: Excuse me. Go back
4 to the top again because donor screening would
5 also imply -- oh, okay, so you have testing as
6 the header? To be more specific to donor --
7 okay, never mind. Got you.
8 MEMBER ISON: Do you think we need
9 to be more specific on what the --
10 DR. HOLMBERG: Well, I am just
11 saying, no, donor screening would also include
12 the questionnaire.
13 CHAIR BRACEY: You could say donor
14 laboratory screening.
15 MEMBER ISON: Laboratory screening
16 would be better, yes.
17 DR. HOLMBERG: Donor laboratory
18 screening.
19 MEMBER ISON: And then I guess the
20 other question is, do we need to be specific
21 with serology and nucleic acid testing, since
22 currently there's no nucleic acid testing for

1 organs?

2 DR. HOLMBERG: Oh, I would leave

3 it broad, I think.

4 MEMBER ISON: Leave it broad.

5 Then maybe, as kind of another

6 recommendation, just to get rid of all of

7 that, that standards be developed for donor

8 and recipient sample retention.

9 MEMBER BOWMAN: You could say, "as

10 recognized in Gap No." such-and-such of the --

11 MEMBER ISON: Gap 16, I think.

12 MEMBER BOWMAN: -- yes, Public

13 Health Service, biovigilance report.

14 MEMBER ISON: I think the way that

15 it is written, though, is standards be

16 developed. So that includes how much, what

17 type, how to store it.

18 So, I think, to be honest with

19 you, this may be addressed in the tissue side

20 since it says both organ and tissue.

21 So this, I agree, is important.

22 This is basically where we are saying that the

1 Secretary needs to investigate funding a
2 prospective study to define the risk.
3 CHAIR BRACEY: So the heading
4 would be surveillance?
5 MEMBER ISON: So, Matt, do you
6 think it is surveillance or --
7 MEMBER KUEHNERT: Oh, yes.
8 CHAIR BRACEY: Good point.
9 MEMBER ISON: So funding a study
10 to -- I think it is risk assessment, isn't it?
11 CHAIR BRACEY: Risk assessment.
12 MEMBER ISON: Risk assessment
13 would be adequate.
14 So there's two things in this
15 paragraph. There is, one, to fund the
16 Transplant Sentinel Network and the other to
17 do a study to -- and I think that they both
18 fall under risk assessment because the
19 Transplant Safety Network is something that I
20 think we have previously backed, and that
21 would further define risk, and then doing a
22 prospective study.

1 MEMBER BOWMAN: You could make the
2 first two sentences I think more succinct and
3 just say, "Significant underreporting of
4 donor-derived disease transmission is
5 suspected." Then just proceed with the
6 recommendation, I think. Or follow it with
7 "There's no formal" -- the next sentence.
8 MEMBER ISON: I think it is
9 actually fine. We suspect that there is
10 underreporting and then two bullets for this,
11 that the Committee recommends funding the
12 Transplant Sentinel Network. I think it may
13 make sense to do it in flip. So fund the
14 study to define the risk, and then fund the
15 Transplant Sentinel Network is the secondary
16 action item, to continue to monitoring ongoing
17 risk.
18 CHAIR BRACEY: So what you are
19 saying is that we can just strike that
20 paragraph?
21 MEMBER ISON: Well, the last two
22 sentences, I think. So I guess it would be

1 that we "ask the Secretary to fund a
2 prospective study to outline the risk of
3 disease transmission through organ
4 transplantation". Whether we want to say,
5 "similar to the Spanish Resitra Cohort" or
6 not, that may be prescriptive, but at least it
7 gives a scope and concept that he can look up
8 in the literature.
9 Then, No. 2, to fund the TTSN.
10 MEMBER KUEHNERT: I like the tie-
11 in with the white paper. I mean that is
12 something, actually, that isn't mentioned on
13 the tissue portion which maybe should be,
14 since it was approved by the Committee,
15 because there's a lot of detail on Transplant
16 Sentinel Network in the white paper. So it
17 could just refer back to that.
18 MEMBER ISON: So maybe three
19 bullets? One, that we support the white paper
20 and advocate for addressing the gaps as
21 outlined -- or just addressing the gaps.
22 MEMBER KUEHNERT: Uh-hum.

1 MEMBER ISON: No. 2, funding the
2 study. No. 3, funding TTSN.
3 MEMBER KUEHNERT: Yes.
4 MEMBER ISON: So, No. 1, "The
5 Committee asks the Secretary to address the
6 gaps, as outlined in the white paper."
7 Actually, "ask the Secretary to"
8 and then colon and then, "One, address the
9 gaps outlined in" -- yes, the last sentence.
10 "Address the gaps as outlined in
11 the white paper," No. 1. That's No. 1.
12 No. 2 is to "fund a prospective
13 study to outline the" --
14 MEMBER KUEHNERT: No. 1 doesn't
15 look right.
16 MEMBER ISON: No, no, it is right.
17 "Address the gaps as outlined in the white
18 paper."
19 No. 2, "to fund" -- so it is
20 already there -- just "to fund a prospective
21 study to outline the risk of disease", and
22 then I think you missed some at the very end.

1 So cut "transmission" through
2 "Resitra Cohort". Yes.
3 And then No. 3 is to fund the
4 TTSN.
5 MEMBER KUEHNERT: Where is that
6 at?
7 MEMBER ISON: I think it is
8 probably -- get rid of that.
9 Yes, so that just needs to spell
10 out the Transplant Sentinel Network.
11 MEMBER KUEHNERT: Transplantation
12 Sentinel Network.
13 I guess one way to put it would be
14 -- I am a little uncomfortable, being the one
15 to suggest this, but "Provide resources for
16 national implementation of a Transplantation
17 Sentinel Network".
18 MEMBER ISON: Okay.
19 MEMBER KUEHNERT: The pilot has
20 already been --
21 MEMBER ISON: Yes.
22 MEMBER KUEHNERT: "Provide

1 resources for national implementation of a" --
2 MEMBER ISON: And this was
3 something that Darrell added about other
4 safety issues.
5 I guess the question is I wonder
6 if this should be something that is both
7 tissue and organ as well. Maybe something,
8 "Although the focus of our discussion today
9 has been on organ and disease transmission, it
10 has been recognized that there are other
11 adverse events. These need to be identified,
12 tracked, and investigated."
13 MEMBER TRIULZI: Right. As we
14 spoke, biovigilance is beyond just disease
15 transmission. It could be toxicity of agents
16 used to do pathogen activation of tissues. So
17 it is just meant to be broad.
18 MEMBER KUEHNERT: I think if you
19 are going to do that, because we are going to
20 get into the same discussion about duplicative
21 reporting, that maybe I would suggest
22 something like there should be an integrated

1 national system, or something like that, if
2 you are going to make this cover everything.
3 CHAIR BRACEY: "There should be an
4 integrated national system for capture of
5 outcomes" and then, "e.g., biovigilance"?
6 MEMBER KUEHNERT: I meant just to
7 put it in that bullet. But if you are going
8 to create it anew, then you could say,
9 "Capture of outcomes to identify preventable
10 adverse events and improve patient safety."
11 MEMBER TRIULZI: I would put
12 "adverse outcomes", right? We are talking
13 biovigilance, yes. We are not talking about
14 graft survival, and et cetera.
15 CHAIR BRACEY: "Capture of adverse
16 outcomes".
17 MEMBER BOWMAN: I wonder if this
18 wouldn't be a better topic for another session
19 of the Committee to devote at least
20 considerable more time.
21 CHAIR BRACEY: Well, I mean I
22 think, as a general statement, we could

1 incorporate that under the premise of
2 biovigilance without being specific. But I
3 don't know. What do you think? What does the
4 Committee think?
5 MEMBER BOWMAN: I mean patient
6 safety is a huge, prominent focus now, both
7 within the federal government and within the
8 entire medical healthcare system. I mean we
9 heard one lecture session this afternoon. The
10 federal government itself is funding huge,
11 millions of dollars in grants right now for
12 patient safety.
13 So it, conceivably, could involve
14 two full days of discussion of this Committee,
15 I think, given the expertise that we have on
16 the Committee.
17 CHAIR BRACEY: So, then, we would,
18 basically, recommend that we visit -- that the
19 Committee recommends review -- no, ACBSA
20 review.
21 MEMBER ISON: The one thing that I
22 would say, though, is I think if you look back

1 to our last meeting, we also had an update by
2 the AHRQ group. If you will remember, they
3 even admitted that the extent of focus on
4 organ transplantation is a single page, which
5 basically the only question being, "What organ
6 did you receive?"
7 So, yes, I think that there is a
8 lot of money spent on this. I am not sure
9 that any of it is being spent on at least
10 organ safety.
11 MEMBER BOWMAN: No, actually, you
12 are correct, and it might highlight the need
13 for some reasonable amount of money to be
14 devoted to patient safety in the organ and
15 tissue transplant field, and even maybe blood,
16 for that matter.
17 DR. HOLMBERG: Well, exactly what
18 you are talking about is that, with the
19 patient safety organizations and the data
20 elements, you know, there is just a one-page
21 placeholder right now, and this is the
22 opportune time to develop the data elements.

1 CHAIR BRACEY: All right. I guess
2 the consensus is we leave it?
3 MEMBER ISON: Yes, leave it. But
4 I think that that leaves it, actually, open
5 and broad enough.
6 Do you think that that is
7 adequate?
8 So I think we can get rid of that.
9 Then I think the last issue was
10 brought up related to living donation from the
11 organ and potentially tissue side. Again, I
12 am not sure that this has to be in a
13 recommendation to the Secretary, but maybe one
14 to Dr. Holmberg, to consider this as at least
15 a presentation or two at the subsequent
16 meeting.
17 CHAIR BRACEY: Okay.
18 MEMBER BOWMAN: Mr. Chairman,
19 maybe you could change that sentence, just
20 make it say something like, "Biovigilance
21 initiatives should be included in an
22 integrated national system", since we don't

1 have an integrated national system right now.
2 The focus of this Committee over the last few
3 days wasn't to come up with an integrated
4 national system for all adverse events.
5 MEMBER KUEHNERT: Wasn't that the
6 charge that the Committee gave to the work
7 group?
8 MEMBER BOWMAN: In relationship to
9 organ and tissue transplants, but the way that
10 is, that is our entire healthcare system.
11 MEMBER KUEHNERT: Oh, I
12 understand. Got you.
13 CHAIR BRACEY: Yes, we are not
14 going to generate an integrated national
15 system right now.
16 So "Biovigilance initiatives
17 should be included in an integrated national
18 system to identify preventable adverse
19 outcomes."
20 DR. HOLMBERG: Okay, we are
21 getting down to 3:30.
22 CHAIR BRACEY: Okay.

1 DR. HOLMBERG: So we need to start
2 wrapping up.
3 CHAIR BRACEY: All right. So we
4 have gotten to the bottom of the organ piece.
5 So let's take it -- that's at the bottom. Oh,
6 as No. 4? Yes. Well, not No. 4 under this
7 because, then, it gets -- just leave it as a
8 separate unnumbered piece.
9 All right, so we go up.
10 MEMBER ISON: So, Jerry, can I ask
11 you a question? The fact that we are saying
12 to address the gaps and the white paper, it is
13 under technically the organ side? Do you
14 think it is going to be clear enough to the
15 Secretary that would mean all of the gaps, and
16 not just the two that are listed under organs?
17 Or do you think that should be taken out of
18 there, and maybe we should have a separate
19 recommendation that we reviewed and agree with
20 the white paper and advise the Secretary to
21 address all of --
22 DR. HOLMBERG: I would like to see

1 it that way.

2 CHAIR BRACEY: I didn't -- like to

3 see it which way?

4 DR. HOLMBERG: Go ahead, Mike.

5 MEMBER ISON: So make a separate

6 section that states that "The Committee

7 reviewed the white paper and agrees that the

8 gaps are accurate and should be addressed by

9 the Secretary."

10 CHAIR BRACEY: Yes, we voted on

11 that, though.

12 DR. HOLMBERG: But I think we need

13 to get it down on a recommendation. I mean we

14 voted on it, but it wouldn't hurt to put it in

15 here.

16 CHAIR BRACEY: Okay.

17 DR. HOLMBERG: I would take it up

18 and put it up in the top.

19 CHAIR BRACEY: So "The Committee

20 reviewed and approved the gaps noted in the

21 white paper" --

22 DR. HOLMBERG: Why don't you just

1 say, "PHS working group white paper"?
2 CHAIR BRACEY: White paper, okay.
3 All right.
4 MEMBER ISON: And I think
5 specifically say that we recommend that the
6 Secretary address the gaps.
7 CHAIR BRACEY: All right.
8 MEMBER KUEHNERT: Just a little
9 wordsmithing, "The Committee reviewed and
10 approved the" -- I would just say not the
11 gaps, but actually "approved the PHS
12 Biovigilance Working Group white paper".
13 DR. HOLMBERG: Maybe we use the
14 exact title of that. I think that is better.
15 MEMBER KUEHNERT: Yes, actually,
16 that would be the best thing.
17 DR. HOLMBERG: I don't have it in
18 front of me.
19 MEMBER KUEHNERT: Just use the
20 title.
21 "Reviewed and approved the
22 findings".

1 MEMBER ISON: And then "recommends
2 the Secretary address the gaps and
3 recommendations listed therein."
4 CHAIR BRACEY: "And
5 recommendations listed therein."
6 DR. HOLMBERG: Do you want to
7 separate that out into a separate -- maybe a
8 period after "health" and then "The Committee
9 recommends the Secretary address...."? Break
10 that into two sentences.
11 CHAIR BRACEY: Yes. Yes, that is
12 a good point.
13 Okay, break that out. Yes, you've
14 got it.
15 You can put it back together.
16 That will work.
17 Okay. So now we have this is the
18 organ piece. Now, remember, we have the
19 tissue piece, which is separate.
20 Where would the tissue piece fit
21 with respect to the organs? Just a matter of
22 before or after? At the end? Okay. So we

1 will put the tissue piece at the end, which
2 you have in another file, I believe.
3 So, yes, just go from here. And
4 actually, I think that we will use this, and
5 we won't use the preamble because, really, in
6 your preamble you are just getting to the
7 requirement to review the white paper and the
8 gaps incorporated, and we don't need a lot of
9 additional verbiage.
10 MEMBER ISON: And the only other
11 thing that I would recommend that we add was
12 something we talked about yesterday, which is
13 a dashboard. So I think the specific
14 recommendation should be that "The Secretary
15 should ask", whatever the title is, "the
16 Executive Committee on Blood, Organ and Tissue
17 to, at regular intervals, review current
18 adverse event reporting from organs, tissues,
19 and blood and provide an update to the
20 Committee for each meeting on the current
21 status of these transmission events" or
22 "adverse events".

1 CHAIR BRACEY: Let's see, that
2 would go --
3 MEMBER ISON: Probably at the end.
4 CHAIR BRACEY: -- probably at the
5 end because that is incorporating both.
6 MEMBER ISON: And I think that it
7 should include blood adverse events in that
8 report as well. That is my feeling.
9 CHAIR BRACEY: So then, "The
10 Committee recommends that the Secretary
11 develop a dashboard for monitoring adverse
12 event reporting for tissues and organs" --
13 MEMBER ISON: I would do "blood,
14 organ, and tissue", all three.
15 CHAIR BRACEY: Good. "Blood,
16 organs, and tissues to be reviewed on a" --
17 MEMBER ISON: "Regularly".
18 CHAIR BRACEY: -- "regularly by
19 the safety" --
20 MEMBER ISON: What is the title,
21 Jerry, of the Committee or the group?
22 DR. HOLMBERG: The internal

1 committee?

2 MEMBER ISON: Yes, the

3 Executive --

4 DR. HOLMBERG: Right, it is the

5 Blood, Organ and Tissue Senior Executive

6 Council.

7 CHAIR BRACEY: And somewhere we

8 are seeking language to say that this would be

9 reported back to ACBSA.

10 MEMBER ISON: At every meeting.

11 CHAIR BRACEY: And reported to

12 each meeting, ACBSA, each meeting of ACBSA.

13 DR. HOLMBERG: That paragraph

14 above it looks strange. Is that staying?

15 CHAIR BRACEY: Let's see. Let's

16 go back.

17 Oh, no, this you can get rid of.

18 That is overage. Yes, that is some other --

19 yes, there are several pieces.

20 Do you want to go up?

21 MEMBER LOPEZ-PLAZA: Can I ask a

22 quick question?

1 CHAIR BRACEY: Go all the way to
2 No. 1 on this one because that stuff in the
3 middle just captures ideas. Right there.
4 Yes, now scratch.
5 MEMBER LOPEZ-PLAZA: Art?
6 CHAIR BRACEY: Yes?
7 MEMBER LOPEZ-PLAZA: When we are
8 asking about funding, you know, to look more
9 at the data and all those kind of things, can
10 we mention something about requesting
11 something similar to what the REDS study has
12 done or by what hemovigilance is doing? Can
13 we kind of be as specific that way? I mean
14 because we are telling like there is something
15 already established that has worked. Why
16 can't we do something very similar to that?
17 MEMBER ISON: So maybe at least in
18 the organ section where I would say, "the
19 Spanish Resitra or the U.S. REDS study",
20 something along those lines.
21 CHAIR BRACEY: Yes. So, if you go
22 back to the organ transplant piece, where they

1 talk about the Spanish study, there is a
2 reference to the Spanish -- what is it, the
3 Resitra study? There is a reference under the
4 organ safety to the Spanish study.
5 MEMBER ISON: Yes, it is, I think,
6 in this section. Oh, here we go, there.
7 CHAIR BRACEY: Right here, right
8 here.
9 Similar to --
10 MEMBER ISON: "The Spanish Resitra
11 Cohort or the U.S. REDS study". Is that what
12 it is called?
13 MEMBER KUEHNERT: Maybe, once it
14 is approved, you could look up what the
15 acronym stands for.
16 DR. HOLMBERG: Yes, but it has
17 changed, though. REDS III has changed now to
18 Recipient Epidemiology Donor Study.
19 It was retrovirus and now it has
20 changed to recipient. Okay.
21 CHAIR BRACEY: So we need to get
22 close to the point of a vote.

1 A quick readthrough. A quick
2 readthrough, so you don't vote on something
3 you haven't read.
4 All right. So up to the top.
5 "The Advisory Committee on Blood
6 Safety and Availability was asked during the
7 November 19th-20th meeting to address the
8 following questions:
9 "Please comment on the mechanisms
10 to identify and address information gaps
11 related to infectious diseases of organs and
12 tissues.
13 "Please comment on the types of
14 tools, the policy analysis that may be used to
15 enhance the current decisionmaking process
16 such as risk assessment and cost-
17 effectiveness/cost utility modeling."
18 Basically, this is, you know, what
19 was in there.
20 "The Committee reviewed and
21 approved the findings of the PHS Working Group
22 white paper Biovigilance" -- the title.

1 "The Committee recommends that the
2 Secretary address the gaps and recommendations
3 listed therein.
4 "Specific to organs, it is
5 recognized that there are significant gaps in
6 identifying the risk of disease transmission."
7 Bullet - "Donor risk assessment.
8 There is currently no standardized approach to
9 collecting medical and social history. This
10 is critical to assess, as it directly impacts
11 classification of donors as increased risk
12 versus standard risk of latent infection with
13 a blood-borne pathogen. Currently, this
14 drives additional testing of donors, which may
15 lead to increased use or loss due to false-
16 positive testing and additional consenting,
17 discussed below."
18 MEMBER ISON: You can probably get
19 rid of "discussed" --
20 CHAIR BRACEY: You can get rid of
21 that.
22 MEMBER ISON: Just the "discussed

1 below".

2 CHAIR BRACEY: Right.

3 "The Committee recommends that the

4 Secretary support development and validation

5 of a uniform donor health history screening

6 questionnaire."

7 There was some question about

8 whether we would use "questionnaire" or

9 "database".

10 MEMBER ISON: It is a

11 questionnaire. It is not a database.

12 CHAIR BRACEY: Okay,

13 questionnaire.

14 "Access to medical and laboratory

15 testing of donors. Currently, there are no

16 standard approaches to allowing procurement

17 organizations to access and review the

18 comprehensive amount of data available on each

19 recipient."

20 Is that "recipient"?

21 MEMBER ISON: Donor.

22 CHAIR BRACEY: Donor, that's

1 right, it should be "donor".

2 "The Committee recommends that the

3 Secretary investigate mechanisms to allow

4 organ procurement organizations easier and

5 complete access to appropriate records.

6 "Informed consent. Currently, the

7 OPTN policy requires specific informed consent

8 of recipients of `high-risk' donors. There is

9 significant variability in how information is

10 provided to potential recipients, and research

11 is needed to understand gaps in the clinician"

12 -- is that right? No. "Gaps in clinician and

13 patient knowledge related to high-risk donors,

14 in particular, and all organ donors in

15 general. Further research is also needed to

16 understand the impact of the consent process

17 on how organs are used.

18 "The Committee recommends the

19 Secretary direct funding to understand the

20 knowledge gaps and impact of the organ

21 transplantation consent process.

22 "Testing" --

1 MEMBER TRIULZI: Before you go on,
2 do we really need to pull out high-risk
3 donors? I mean, is just the whole consent
4 process as a piece of it? Or do we need --
5 MEMBER ISON: Well, I think that
6 we do need to -- this is my opinion -- I do
7 think we need to highlight that because there
8 was a change in policy that changed a huge
9 change in practice of giving special informed
10 consent only for recipients of high-risk
11 donors.
12 So there is a standard consent
13 process and then a kind of add-on consent
14 process just for the high-risk. And there is
15 concern at least that that -- and I think you
16 heard that from Dr. Halpern's presentation,
17 where he is saying we shouldn't even be doing
18 that. So I think there is enough controversy
19 to specifically focus on that, as well as the
20 consenting process.
21 CHAIR BRACEY: And when it is all
22 reviewed, it will incorporate those others, I

1 think.

2 "Testing. There are currently

3 limitations related to donor laboratory

4 screening. The Committee recommends that the

5 Secretary explore more effective use of

6 screening and confirmatory laboratory donor

7 testing of potential donors and explore

8 options to enhance accessibility and

9 innovation. The Committee recommends that

10 standards be developed for donor and recipient

11 sample retention.

12 "Risk assessment. Significant

13 underreporting of donor-derived disease

14 transmission is suspected. The Committee

15 recommends the Secretary address the gaps as

16 outlined in the white paper" --

17 MEMBER ISON: I think we can get

18 rid of that. I think we can get rid of the

19 "address the gaps" since we have already --

20 CHAIR BRACEY: Okay.

21 MEMBER LOPEZ-PLAZA: The first

22 sentence --

1 CHAIR BRACEY: "Significant
2 underreporting of donor-derived" -- what's
3 that?
4 MEMBER LOPEZ-PLAZA: There's
5 something on the sentence that is missing.
6 MEMBER WILLIAMS: There is likely
7 to be significant underreporting.
8 MEMBER LOPEZ-PLAZA: When we
9 suspect it, I mean a significant
10 underreporting of disease transmission.
11 CHAIR BRACEY: I mean I think the
12 intent is clear.
13 MEMBER LOPEZ-PLAZA: Okay, now I
14 got it. Okay.
15 MEMBER ISON: I think it is fine.
16 CHAIR BRACEY: Yes, I think it is
17 okay.
18 Okay. So "The Committee
19 recommends:
20 "One, to fund a prospective study
21 to outline the risk of disease transmission
22 through organ transplantation similar to the

1 Spanish Resitra Cohort or the U.S. REDS I
2 study.
3 "Two, provide resources for
4 national implementation of the Transplantation
5 Sentinel Network (TSN). Biovigilance
6 initiatives should be included in an
7 integrated national system to identify
8 preventable adverse outcomes."
9 Then this goes on. "There is
10 concern regarding" -- so we need a header.
11 "Tissues." Then we can underline it.
12 "There is concern regarding
13 inadequate bidirectional traceability of
14 tissue impairing adverse events, surveillance,
15 and timely public health intervention. There
16 are no accurate data on the number of
17 recipients in whom tissues are implanted, and
18 thus, rates on adverse events cannot be
19 calculated.
20 "The Committee recommends:
21 "One, development of a system
22 employing bidirectional traceability from

1 donor to recipient, which would use a unique
2 identifier linking a single donor to all
3 recovered organs and tissues."
4 MEMBER POMPER: So the only thing
5 there is, do you want to say, "and, when
6 applicable, crossover with solid organs"?
7 CHAIR BRACEY: But it is there
8 because it links organs and tissues.
9 "All adverse events possibly
10 related to tissue grafts should be promptly
11 reported and investigated.
12 "Three, assess the adequacy of the
13 current language and process of informed
14 consent for tissue implantation.
15 "Four, assess the adequacy of
16 current oversight mechanisms to ensure patient
17 safety in tissue recipients.
18 "Five, develop a uniform
19 questionnaire for donor screening to optimize
20 patient safety."
21 And then the last piece, "The
22 Committee recommends that the Secretary

1 develop" -- this really is general. Would
2 that be general? I don't know. It is kind of
3 hanging lose.
4 "The Committee recommends the
5 Secretary develop a dashboard for monitoring
6 adverse event reporting for blood, organs and
7 tissues to be reviewed regularly by the
8 HHS" --
9 MEMBER POMPER: You can put that
10 at the top as a general recommendation for
11 both, you know, overarching recommendation or
12 leave it at the bottom as an "in summary for
13 all", something like that. But I think it
14 should go at the top as a general.
15 MEMBER TRIULZI: And can we put
16 the biovigilance statement with it and make
17 both of those statements that apply to both
18 tissues and organs?
19 CHAIR BRACEY: Right.
20 Rich, can you help me? This is a
21 little beyond my skills.
22 MEMBER TRIULZI: And put them both

1 at the top.

2 CHAIR BRACEY: So we want to take

3 the biovigilance statement, which is at the

4 end of the tissue --

5 MEMBER TRIULZI: At the end of the

6 organs.

7 CHAIR BRACEY: At the end of the

8 organs. So you have to go down. Down. Okay.

9 So right there, get "biovigilance", okay, and

10 we want to take that to the top and put it

11 under "general". That is a new header.

12 MEMBER LOPEZ-PLAZA: Guys, I think

13 I tend to agree with Greg that somehow we have

14 to link, you know, the tissue infections,

15 transmission rates, to adverse events, to be

16 tracked down to the organ.

17 MEMBER ISON: It is.

18 MEMBER LOPEZ-PLAZA: Okay.

19 CHAIR BRACEY: Right there, yes.

20 So put "general"; type in "general", maybe

21 with caps. Just put "general" as a new

22 header.

1 Okay. So now you want to go down
2 to the bottom, to the very end, all the way to
3 the end. You want to capture this. Capture
4 that and then move it up to the top, right
5 under "biovigilance".
6 MEMBER ARNOLD: In that next
7 section where it says, "specific organs",
8 would you consider transplanted tissues versus
9 organs?
10 CHAIR BRACEY: Let's go back. So
11 on the specific organ, I was thinking that we
12 needed a header that says, "organs" then.
13 Right, where we say, "specific to organs".
14 So what was the comment, Dr.
15 Arnold?
16 MEMBER ARNOLD: Well, I think that
17 statement works to both questions that we
18 tried to answer below. It may be able to
19 remain in the general statements if you remove
20 the word or change the word "organs" to
21 "transplanted tissues". Otherwise, your new
22 heading is appropriate.

1 CHAIR BRACEY: Wait a minute. I'm
2 lost. I'm sorry.
3 MEMBER ARNOLD: It is a phrase.
4 "Specific to organs" is changed to "specific
5 to transplanted tissues".
6 CHAIR BRACEY: Okay.
7 MEMBER ARNOLD: It can remain
8 where it is without the new heading "organs"
9 listed above it.
10 CHAIR BRACEY: Oh, I see what you
11 are saying.
12 MEMBER ISON: But there is a
13 problem if you do that because, then, all
14 these things are organ-specific.
15 CHAIR BRACEY: Oh, right, that is
16 organ-specific that follows, yes, that is
17 right.
18 MEMBER ARNOLD: Yes, I recognize
19 it. When we transitioned into the organs kind
20 of out of the general meanings, we probably
21 need the heading "organs" in there someplace,
22 and whether we screw with that paragraph or

1 not is up to the Committee, but --
2 CHAIR BRACEY: So why don't we
3 just say, just delete all that and say, "It
4 was recognized that there are...."? Yes.
5 Right. Okay.
6 So that is the document. Are
7 people happy with it as it reads?
8 Can I hear a motion?
9 MEMBER HALEY: I move we accept
10 the document as written.
11 CHAIR BRACEY: Is there a second?
12 MEMBER POMPER: Second.
13 CHAIR BRACEY: Okay. Any
14 discussion? We've had lots of that.
15 (No response.)
16 All in favor?
17 MEMBER LOPEZ-PLAZA: Just silly
18 grammar, but "tissues" is in caps; "organs" is
19 in lowercase. I don't know if you want to put
20 them the same or not.
21 MEMBER ISON: I think that we can
22 trust Dr. Holmberg to do minor edits.

CHAIR BRACEY: Okay. All right. Further discussion?

(No response.)

Is that okay?

All right. So, then, all in favor say aye.

(Chorus of ayes.)

Opposed?

(No response.)

Abstentions?

(No response)

Then it passes unanimously.

DR. HOLMBERG: We have 12.

CHAIR BRACEY: All right. All right, thank you.

(Applause.)

Now we have exceeded the time to allow the discussion of updates.

DR. HOLMBERG: We have 10 minutes before the shuttle bus will be here, and I know that many of you need to get moving by four o'clock.

1 So what is your pleasure? We have
2 two topics. I have somebody waiting
3 potentially on the phone -- I need to call her
4 -- to give you an update on the H1N1 and the
5 guidances that have been distributed, which I
6 have notified you of, or the update on the
7 BPAC that happened at the beginning of this
8 week.
9 CHAIR BRACEY: What's the
10 Committee's preference?
11 DR. HOLMBERG: Or read a summary.
12 I will provide a summary.
13 CHAIR BRACEY: I would entertain a
14 motion to have a summary distributed.
15 DR. HOLMBERG: Okay, I will
16 provide a summary of both the H1N1 and, also,
17 I will rely on Dr. Williams to give me a
18 summary of the BPAC, and I will send it out to
19 the Committee.
20 MEMBER ISON: And there's slides.
21 DR. HOLMBERG: Oh, very good.
22 Okay.

1 CHAIR BRACEY: So is there any
2 other business?
3 (No response.)
4 Motion for adjournment?
5 MEMBER ISON: So moved.
6 CHAIR BRACEY: All right, we are
7 adjourned.
8 (Whereupon, at 3:54 p.m., the
9 proceedings in the above-entitled matter were
10 adjourned.)
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