U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

ADVISORY COMMITTEE

BLOOD SAFETY AND AVAILABILITY

TWENTY-EIGHTH MEETING

VOLUME II

Friday, January 6, 2006

9:06 a.m.

Salon I and II
Marriott Crystal Gateway
1700 Jeff Davis Highway
Arlington, Virginia 22202

P A R T I C I P A N T S

COMMITTEE MEMBERS PRESENT:

Arthur Bracey, M.D., Chairman

Judy Angelbeck, Ph.D.
Julie Birkhofer
M. Gregg Bloche, M.D., J.D.
William Duffell, Jr.
Karen Lipton, J.D.
David Matyas, J.D.
Glenn Pierce, M.D., Ph.D.
Glenn Ramsey, M.D.
Susan Roseff, M.D.
G. Gerald Sandler, M.D.
Merlyn H. Sayers, M.D., Ph.D.
Linda Thomas
John Walsh
Wing Yen Wong, M.D.

Jerry A. Holmberg, Ph.D., Executive Secretary

James S. Bowman, III, M.D., CMS
Jay S. Epstein, M.D., FDA
Matthew Kuehnert, M.D., CDC
CDR Michael Libby, Department of Defense

COMMITTEE MEMBERS ABSENT:

Harvey Klein, M.D., NIH
John McGuire
Gargi Pahuja, J.D., M.P.H.
Pearl Toy, M.D.

C O N T E N T S

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P R O C E E D I N G S

CHAIRMAN BRACEY: The committee will come to order, please.

DR. HOLMBERG: I had a request from several people for the roster of the new people and for the total committee, and so last night I went home and put this table together so that you have it in front of you, and what I would like you to do is I'm also sending around a copy for you to make any corrections, to add your address, fax number, e-mail, all the information that we can put down.

Yes?

MS. LIPTON: Jerry, I also had asked Renee yesterday, and she said she'd do this, but the presentations, a couple of them yesterday that were not handed out, those would be wonderful to have.

DR. HOLMBERG: Okay. What I will do, especially for the new committee members, to give you an idea of what we try to do is to send out a CD on the meeting shortly thereafter once the transcripts are out, and so we will include all the presentations, the transcripts, the

recommendations, and hopefully there will be also some of the comments from the recommendations, at least from the previous meeting.

Any other questions concerning the roster? And just please make sure that gets around the table, but each one of you should have a copy.

I would like to do a roll call this morning. I'd like to open the meeting, the second day of the Advisory Committee for Blood Safety and Availability.

First, Dr. Bracey.

CHAIRMAN BRACEY: Present.

DR. HOLMBERG: Dr. Angelbeck?

DR. ANGELBECK: Present.

DR. HOLMBERG: Ms. Birkhofer?

MS. BIRKHOFER: Present.

DR. HOLMBERG: Dr. Bloche?

DR. BLOCHE: Present.

DR. HOLMBERG: Dr. Duffell?

DR. DUFFELL: Present.

DR. HOLMBERG: Ms. Lipton?

MS. LIPTON: Still here.

DR. HOLMBERG: Mr. Matyas?

MR. MATYAS: Here.

DR. HOLMBERG: Ms. Pahuja is absent. Dr. Pierce?

DR. PIERCE: Here.

DR. HOLMBERG: Dr. Ramsey?

DR. RAMSEY: Present.

DR. HOLMBERG: Dr. Roseff?

DR. ROSEFF: Here.

DR. HOLMBERG: Dr. Sandler?

DR. ROSEFF: Present.

DR. HOLMBERG: Dr. Sayers?

DR. SAYERS: Here.

DR. HOLMBERG: Ms. Thomas?

MS. THOMAS: Present.

DR. HOLMBERG: Dr. Toy is absent. Mr. Walsh?

MR. WALSH: Here.

DR. HOLMBERG: Dr. Wong?

DR. WONG: Here.

DR. HOLMBERG: Dr. Kuehnert?

DR. KUEHNERT: Yes.

DR. HOLMBERG: Dr. Epstein?

DR. EPSTEIN: Here.

DR. HOLMBERG: Dr. Klein is absent. Commander Libby?

CDR LIBBY: Here.

DR. HOLMBERG: And Dr. Bowman? I'm sure Dr. Bowman will be here shortly. We'll recognize him when he comes into the meeting.

As most of you realized yesterday, Dr. Beato was to speak to the committee, and unfortunately circumstances came up and she was not able to be here, and she sent her regrets and asked me if I would please read her comments that she wanted to make to the committee.

So I will do that now, and then what I would like to do is also to follow up with an e-mail that Dr. Agwunobi has sent to the Office of Public Health and Science, and since you are all part of the Office of Public Health and Science, I think it's appropriate to share that with you.

As you know, Dr. John Agwunobi has been confirmed by the Senate to be the next Assistant

Secretary for Health. He was sworn into office on Tuesday of this week. This committee is a valuable one and one upon which the Department relies. I have reviewed the topics that you have looked at in the past and I remain impressed with the work you have done.

You began in the 1990s with the issues related to hepatitis C and then tackled mad cow disease and its human component, VCJD. And as you know, this is an issue that still is not settled.

You made recommendations regarding leukoreduction. Along the way, you have made recommendations to establish a blood monitoring system, to establish a national blood reserve. These two ideas in which I am vitally interested and will pursue.

Most recently, you have addressed the IVIG issue and I would like to talk with you for a few minutes, though, about IVIG availability and its reimbursement. I want you to know that within the department, we have taken several steps to ensure availability and to reduce the risk of compromised

health care to bona fide patients.

We have had discussions with each of the IVIG manufacturers and have determined that their release of IVIG has not declined, and that the government is not delaying lot release of products through regulatory processes.

In fact, the manufacturers increased available inventories for three consecutive months, August, September and October, and this pushed the available inventory into the green zone as measured by the Plasma Protein Therapeutic Association.

Unfortunately, however, I believe that the availability of products actually dropped in November. Be that as it may, the manufacturers in response to our discussions with them have created emergency inventories and toll free numbers so that the physicians can talk directly with the manufacturers' medical directors for emergency needs.

Allocation of products is a thorny issue, especially when there is a network of distributors and group purchasing organizations that set limits

based on quantities available. This multi-layer system seems to make it difficult to ensure that products are going to those facilities that truly need it for each individual patient care.

As we know, the increase in hospital and outpatient services have seen an increase as patients are moved from the physician's office to these settings.

I know that you have been concerned about reimbursement for IVIG. Let me say that the issue of CMS reimbursement of IVIG in the current marketplace is complex. The Medicare payment for IVIG administered in physician's office is determined by averaging the IGIV manufacturers' quarterly sales price as submitted to CMS.

The payment limit for IGIV is 106 percent of the average sales price as mandated by Congress. CMS recalculates the average sales price each quarter based on the previous quarter's data reported from the manufacturers. Separate payment is allowed for physician administration of IGIV.

Beginning in 2006, reimbursement for IVIG

in hospital outpatient departments will also be based on 106 percent of the average sales price. The payment of IGIV is in addition to the payment under the outpatient prospective services for outpatient services.

In addition, the department's Office of Inspector General is assessing reimbursement and Medicare beneficiaries' access to care. Based on your recommendations for immediate steps to address reimbursement for IVIG and our ongoing work with patient groups, manufacturers and other stakeholders, we continue to be concerned about reports of providers experiencing difficulties in obtaining adequately priced IGIV on a consistent basis to meet their patients' needs.

In response, CMS is establishing a temporary add-on payment effective January 1, 2006, to cover the additional preadministration related services required to locate and acquire IGIV and prepare it for infusion during this current period of market instability.

In the face of these factors, as

potentially increasing IGIV demands and manufacturer allocation of many formulations, physician office staffs and hospitals have to expend extra resources in locating and obtaining the appropriate product and scheduling patients for infusion.

Thus, for the calendar year 2006, only physicians and hospitals will be permitted to bill an add-on code to compensate for the administration burden associated with IGIV administration.

We have heard from some stakeholders who have indicated that the infusion of IVIG in physicians' offices is more complex and resource intensive, particularly during the actual infusion than many other types of infusions currently reported using the CPT codes used for similar drugs established by the American Medical Association CPT Editorial Panel.

As you know, CPT codes are common procedure codes used by the physicians' offices and clinics to obtain reimbursement. We have encouraged these stakeholders to discuss their

concerns with the CPT Editorial Panel to assess whether alternate coding or additional CPT guidance would be appropriate.

During the upcoming year, CMS and other agencies and the department intend to work with the IGIV patient community, product manufacturers, distributors, physicians and hospitals to develop a common understanding of the evolving IGIV marketplace to assure the continued collection of accurate average sales price data and to focus attention on the medical necessity for the utilization of IVIG.

We anticipate that these steps and other ongoing corrections in the marketplace will help to ensure the supply volatility stabilizes in the next year.

Please be assured that we are monitoring the status of IGIV supply and the factors that influence its availability. If I need additional specific recommendations on the issues or similar issues, I will bring the topic and appropriate questions to the committee.

On another note, your recommendation for coordinated strategic plan to ensure blood safety and availability are excellent, and support the Secretary's 500 day plan for the department. Working groups within the department are being formed that include a cross-section not only of blood interests, but also organ, tissues and cellular products.

We have considered your recommendations in the elements of our strategic plan as we move forward for the future. Today, you will be hearing from quite a number of people who are interested in how government and industry can work together to assure the safety and availability of blood and blood products in the event of an influenza pandemic.

This is an excellent forum for the exchange of information between the private sector, government, and the American people. I am sure that you will consider what your presenters have to say and make valuable recommendations.

I'm also sure those recommendations will

be of usual high quality you have delivered in the past, and I look forward to receiving them. Thank you. I hope you have a good day.

CHAIRMAN BRACEY: Thank you, Mr. Executive Secretary. Are there comments on the statement that's been read?

I had one question. Dr. Epstein.

DR. EPSTEIN: I think that the record should reflect the committee's appreciation of the steady support that Dr. Beato has given to the blood issues during her tenure as the acting ASH.

CHAIRMAN BRACEY: So let the record state that. I would assume that the committee is in unanimous agreement. Thank you.

There is, as I see it, two potential issues. The one issue is the issue of availability of the IGIV product, and the second issue is the issue of access to the IGIV product. In our deliberations, we hear in the public commentary regarding issues related to access. Is there a system that we can put in place?

I know there are call numbers, but how can

we hear about access aside from public comment?

DR. HOLMBERG: That's a very good question, and one that I will answer in several ways. First of all, we do have the various mechanisms through the FDA product shortage response number and e-mail capability. Dr. Nippin and Dr. Weinstein monitor those on a regular basis.

The three of us get together very frequently. I would say at least once a week we're talking about the issues, and we're following up with letters or e-mail responses back to people that have raised questions.

We are constantly monitoring those complaints that come in. Also, CMS has their 800 number, 1-800 Medicare. We have found most recently that we have had to rewrite the script for them because they were not obtaining the appropriate information, and so we learned that from the consumers, and when the consumer says that they're not getting the response, appropriate response, or the telephone person says I don't know, that's not our issue, or take it to your

regional contractor, we want to follow up on that.

And once again, we are in direct communication with CMS. Dr. Bowman has been a super-star in really trying to make sure that the people at CMS have been very responsive. Most recently even in response to some of the phone calls and that, there has been an active dialogue with the user community, and CMS.

Ms. Amy Pisano, who has addressed the committee back in May, held the meeting, and there was some very good outcomes of that meeting, even in the way that potentially the user community could interact with the regional contractors for Medicare and I don't know if a lot of you understand how Medicare reimburses through the regional contractors, but if you have an elderly parent, you quickly realize that those letters that come from some bizarre looking insurance carrier is actually the Medicare reimbursement and that these are really the contract and insurance, regional insurance carriers for Medicare.

But those are two of the mechanisms, and

then I have to say that working with the user community, my office is very much aware of some of the situations. Let me just say that I could probably have predicted that November was not a very good month, even before PPTA got their information up on the Web site, primarily because of the number of calls that I got at the first of the month.

And so we're continuing to operate and to look at those issues. Some of the other things like the 340B set-asides are real problem, and I think that in the letter or the comments that Dr. Beato mentioned, she also addressed the multi-layers of allocations, and we talk about allocations with the system with the way the manufacturers are allocating to the distributors, but then you have to understand that the distributors are allocated, are told what their allocations should be to the individual hospitals based on the GPO, the Group Purchasing Organization.

So there is a lot of dynamics going in

here, and that's why it has been very beneficial to have the IG, the Office of the Inspector General, do an assessment of the current situation because they have been able to get to the bottom of some of the issues and they will be reporting back directly to Congress on this.

So the Office of the Inspector General has interviewed my office. They've interviewed CMS, FDA, and we have talked about this. And we have identified other areas, for instance, like the 340Bs is handled by HRSA, and when I talked to the person that was responsible for the 340B IGIV, this person said that at a most recent meeting in which there was also an officer of the Office of the Inspector General present at this public meeting, that they asked if people were having problems getting IGIV.

And unanimously they said, no, there's not a problem in getting the product. The next question was are you finding it difficult to get the product at the price that you want to pay for it, and of course all the hands went up.

The question also came out do you get product--is there any product available under the 340B or is any place experiencing problems obtaining product for the 340B plan? And all the hands went up, and as far as what was related to me that the majority of hands went up in the audience, that there was difficulty and that primarily there was almost no product available through the 340B channel.

So we are very eager to hear what the Inspector General's Office will uncover. We are constantly monitoring it through numerous mechanisms, and on those particular situations that I've even talked to the user community. The Immune Deficiency Foundation has been fantastic at open communication, and they have even set up a triage mechanism, especially as we went through starting the first of the year with the new price structure, and so there is a triage mechanism that they have established. And the cases that they cannot resolve, they are referring to me.

CHAIRMAN BRACEY: Thank you, Dr. Holmberg.

That's a very good report. I would hope that as these new measures have been set forth that we can continue to look at these issues to assess the impact.

DR. HOLMBERG: I just wanted to, if there aren't any other questions on that--yes, Jay?

DR. EPSTEIN: I just have a comment which is that quite a number of issues that this committee has deliberated in the last few years revolve around the economics of the blood system and these are always very difficult issues to address because there haven't been very many comprehensive studies of the health economics related to blood products.

Just to name a few, you know, we've talked about the difficulty of funding safety advancements such as leukocyte reduction or pathogen inactivation, and we've talked about the cost and supply issues of clotting factors and more recently the cost and supply issues of IVIG. And I just wonder whether it might not be suitable for the committee to address the general problem of an

examination of how market forces and market constraints affect our blood system, both at the level of safety and supply, and I would just note that Paul Haas left us with his outgoing service an essay on this subject, which is very thought-provoking and I think warrants further consideration by the committee.

CHAIRMAN BRACEY: I certainly would second that. I was very impressed by the material included in the essay of Paul, Mr. Haas, and I would suggest that we invite experts that can help us address these issues in a future meeting.

DR. SANDLER: As the representative of the American Hospital Association on this committee, I strongly endorse the comment made by Dr. Epstein. I think that this is a central issue because any new safety issues that come our way are going to require an amount of money that's just not in the system for hospitals to implement, and we have to be much more proactive in looking at this, because we don't want to be in the position of not being to pay for safety issues when they come up.

CHAIRMAN BRACEY: Dr. Sayers.

DR. SAYERS: Thanks. I'd also like to endorse what Dr. Epstein said. At a time when there should be particularly constructive relationships between hospitals and blood programs, they are anything but. Bearing in mind that good relationships could promote the safe use of blood and bearing in mind that good relationships could encourage positive attitudes toward blood donation in the community, where we find ourselves at blood programs is unable to charge hospitals what it costs us to provide the product because we know that the hospitals are not appropriately reimbursed.

And this is a source of unnecessary tension between the user and the provider and acts to the detriment of the safety and the availability of the blood supply.

DR. HOLMBERG: I hear those comments, and what I will do is take those recommendations back to Dr. Agwunobi and we will see about having that as discussion points at the next meeting. I think

that at the next meeting may be very timely because there are several surveys, not only the IG survey that most recently took place with the manufacturers, but also I think other surveys that are taking place, other reports that are being written, that could be very beneficial for us to explore and for the committee to potentially comment on.

CHAIRMAN BRACEY: Thank you.

DR. HOLMBERG: I have one--I would like to read to you. Again bear with me with my reading. And I would like to read to you the e-mail that was sent out just yesterday by Dr. Agwunobi. This e-mail serves as a primary--I'm sorry--again, I should have maybe had four cups of coffee.

This e-mail serves as a preliminary and informal greeting to all of you now that I am officially a member of the Office of Public Health and Science family. Secretary Leavitt swore me as the Assistant Secretary for Health yesterday morning.

I am eager to finally drive the work at

OPHS. The President has honored me by appointing me to this position. I am further humbled knowing that the OPHS family is expected to bear great responsibilities on behalf of the President and the Secretary to improve the health and well-being of every American.

I recognize long-standing experience and expertise of the OPHS staff in the area and your enthusiasm for the mission. It is my plan to draw upon the dedication and commitment of all of you and further empower OPHS to achieve excellence in HHS and provide for better public health and safety for all.

Principal Deputy Assistant Secretary Cristina Beato has ably served as acting ASH and I want to express my gratitude for her. I am thankful that I can benefit from the knowledge of her and others here who have helped direct OPHS.

Ms. Diane Membo will be serving as my administrative assistant. Through the rest of the month, I will be meeting with the office directors as well as visiting each of the OPHS offices to

meet the staff. I look forward to seeing you, learning about your work and discussing your opportunities for the future. John O. Agwunobi.

CHAIRMAN BRACEY: Thank you. We certainly hope that we look forward to a two-way communication and look forward to meeting the new Assistant Secretary.

Now, for the agenda for this morning, our first speaker is Dr. Louis Katz. Dr. Katz has been very active in the field of blood banking and serves as the Executive Vice President for Medical Affairs at the Mississippi Valley Regional Blood Center.

Dr. Katz has been chair of the AABB Transfusion Transmitted Diseases Committee. He is a member of the FDA BPAC committee, and he currently is chair of the AABB Task Force on Pandemic Preparations and Risk Communication.

He will speak to us today on the activities of that group.

DR. KATZ: Let me thank Drs. Holmberg and Bracey for the invitation. This is very much a

work in progress. This task force has met by conference call I guess twice over about the last month and we're just getting our arms around the scope of the task that Karen Lipton has dropped in our laps.

I think yesterday was a superb prelude to the remarks I'm going to make, underscoring as they did, what we don't know and need to know to do an effective job of planning. Nevertheless, as is the case in public health most times, we need to proceed in the absence of the kind of evidence that would be optimal and that really is the major task that we've been charged with by Karen Lipton and the board at AABB.

So these are the members and it's the usual suspect organizations, the American Red Cross, America's Blood Centers, AABB, and Blood Centers of America. In blue, you see the liaisons from the federal agencies, Alan Williams and Indira Hewlett from FDA, Matt Kuehnert from CDC and Jerry.

And staff from AABB, Caryl Auslander and Theresa Wiegmann, and I forgot Kay Gregory, who is

sitting here. I apologize, Kay.

So what do we have to accomplish? Well, broadly speaking, we can look at the HHS Pandemic Plan and see that we along with everybody else involved in public health planning need to develop plans that will be living documents, that is updated frequently, exercised at some intervals to demonstrate what we haven't thought about, and across all that activity, to engage all our stockholders to the degree that we can identify them.

I think that's a fairly straightforward sort of planning menu. More specifically, what we think we need to accomplish is here, and we're really at the first bullet at this point which is to develop an outline of the issues that we can think up in brainstorming sessions that we'll need to be paying attention to.

Subsequently, to identify range of options for response to those issues and provide guidance to collection facilities and transfusion services. Now if I've left out plasma or tissue or organs, I

apologize. They're not perhaps directly our mission. I think that will be qualitatively--the planning process for those organizations will be qualitatively very similar.

The issues will be very similar. There will certainly be differences in details and whatever work product comes from our group will be freely shared with anybody who wants, and then at least at this point, we believe that the most appropriate role of the task force is to brief the Interorganizational Task Force on Domestic Disasters and Acts of Terrorism to allow them to be the focus of responses if and when or when pandemic influenza has an impact on the blood supply.

This is one of our primary planning maxims, and basically, as we have looked at disaster planning in the past as the blood community, we have looked at a paradigm of the rest of the system pulling together to respond to those areas that need help.

We don't think that's probably a correct model for pandemic planning, and the reason is

here, and I think you heard this from Dr. Schwartz yesterday, that the speed with which pandemic flu can envelop the country is so substantial that the idea of regional resource sharing from unaffected areas to affected areas is not likely to be an appropriate model for this activity.

Here's the--this is basically the Interorganizational Task Force on Disasters basic outline of response. I'm sure that the members of the committee who have been at prior meetings have seen this, but essentially an event occurs, the affected blood centers communicate with their customers, primarily at the hospital level, assess needs, contact AABB, that then convenes the Interorganizational Task Force on Disasters for developing an assistance plan and communication planning in partnership with HHS in the broadest sense.

We think that most of this, at least from AABB on, is appropriate, but for pandemic influenza, we will very likely to be required to think a little bit differently about the upper

left-hand corner.

Well, I'm a lumper so I try and make things into short lists that are kind of inclusive. All due respect to what we've heard about the transfusability of influenza, as a clinical virologist over a long period of time and a blood banker over a somewhat shorter period of time, it is clearly not the highest priority of this task force to address the issue of transfusability.

It may occur. How common or not common I don't think we know, but that is a work in progress, and in the absence of any more than a single asymptomatic contact out of 29 studied, we don't, we're not going to focus primarily on this issue.

The next two bullet points, we believe are where we need to focus our efforts. In the short-run, the impact on the donor base, and the impact on operations, both in blood collection facilities around the country and the transfusion services that we source with life-saving products.

Again, this is a quote from Dr. Schwartz

at this meeting in May, and this has kind of been the conventional wisdom, that those of us who have been sitting in our blood centers thinking about this have been faced with: a decrease in the blood supply but also a decrease in demand and capacity. No major impact on the safety of blood itself.

In the broadest strokes, perhaps this is true, but I think the task that we're faced with in our group is to be a little bit skeptical about such a simple paradigm.

The impact of pandemic flu--this is again from the HHS plan from November--and you can see that Asian or Hong Kong type pandemic in the left column and something more akin to 1918 in the right, and I just want to point out that in our worst case planning scenarios which is 1918 and may be bad enough as a worse case or may not, we're looking at estimates from HHS of almost ten million admissions, a 1.5 million admissions to intensive care units, and almost 800,000 individuals on ventilators as direct or secondary result of pandemic influenza.

This is an enormous burden on the health care system and our surge capacity. I think we all recognize this, and we need to at least be thinking and modeling what's the impact on the requirement for blood.

So that any assumption regarding a relatively balanced decrement in supply and demand needs to be questioned very carefully as we proceed through this planning process.

So we're assuming that donors and staff will be impacted much like the general population so that both donations and our ability to process donors may not be robust. Elective surgical needs will decline. Virtually every hospital or hospital system surge plan that I have seen has very explicit mention of some set of more or less detailed triggers that will cancel elective surgery and elective admissions to the hospital.

So I think we know that that is true. However, some things like platelet needs to support hematologic malignancy, hematopoietic progenitor stem cell transplants, complex cardiovascular

surgery, et cetera, will not decrease. These are not elective procedures, and many situations these activities are going to need to proceed and represent some of the most intense blood product needs that we see.

Some assume that flu victims will need few products, but I think this is likely incorrect, and I've showed you some estimates from HHS regarding ICU admissions and ventilator care. Those of us who have spent long hours day and night in ICUs know that acute respiratory failure, apart from trauma or hematologic malignancy or any of the things we classically associate with transfusion, in fact, require blood transfusion support quite frequently.

So assumptions that demand will decline need to be very, very carefully reconsidered.

What issues have we identified so far, and I'm going to go through basically an outline that we've produced over the last month so that you can see our thought processes and so that I can solicit input from the committee, either at this meeting or

offline.

Are there valid models for the impact of pandemic flu in the blood supply? The short answer to my mind is no. Of the range of impacts of pandemic flu on our ability to collect and process blood? No.

Of blood use in pandemic given the levels of medical care that we expect to provide the population in 2005? No.

You will hear from the Red Cross and blood systems a little later about some early efforts to develop models that will help answer these questions--most welcome.

What issues regarding the availability of donors? Obviously, attack rates. 30 percent is an oft quoted figure, and it's probably in the ball park. So there will be sick donors.

There will be donors who are well but are staying home to take care of their family. Avoidance of public venues. Probably a better word is "fear," at least initially. Subsequently, avoidance of public venues may be a public health

recommendation.

Immunization of donors. Very important issue that we can talk about afterwards if you'd like. There is not insubstantial resistance to the concept of immunizing donors in blood centers over liability issues.

The use of antivirals on donors. Facilitating the access of donors to antivirals will require that this become a priority at the level of HHS, as I think I said in my comment yesterday.

And then the issue of FDA-promulgated deferrals whether related to exposure or concerns regarding the potential transmissibility. And that's all I'm going to say that. We just don't have enough information, I think at this point to be much more explicit than to say it's on the table.

Collection facility and transfusion service issues. Again, some of the same stuff. Attack rates. Absence to care for family. Education to prevent transmission. That is

something that can't be done one time. If the pandemic comes next year, the in-service that I do next month of my employees regarding standard precautions may be useful, but if it comes five years from now, if I've only done it one time, it's not going to be useful. I know that from extensive experience as a hospital epidemiologist.

Getting people to wash their hands or use masks when appropriate is an extraordinarily difficult ongoing task.

Work rules. This is a huge issue. Under what circumstances are we going to ask employees to stay home who, for example, might have been exposed to influenza? At what level in the pandemic would which work rules be implemented?

Mandatory immunization of staff versus encouragement of immunization of staff. Many emergency rooms now as a condition of employment require influenza immunization. Hospitals all over the country require immunity to measles, mumps, rubella, Varicella and immunization with HBV. But the resistance in early discussions that I've

gotten, the mandatory immunization of staff, whether at the collection facility or transfusion service, with an appropriate influenza vaccine have been substantial.

Once again access to antivirals and their use in our personnel and then triage of blood and component use at the transfusion service level that we need to deal with. There are many places that have suffered under blood shortages over long periods of time, who have triage rules in place.

There are many hospitals who have never suffered a blood shortage and have never considered triage. And getting those sorts of consensus rules is too strong a word, but consensus guidelines available in a relatively short period of time is a substantial effort.

Supply chain issues are huge. Those of you who have been in collection facilities understand that in our relationship with our vendors of bags and alcohol swabs and test kids and leukoreduction filters and reagents and what not try quite hard to adhere to a just-in-time delivery

scheme.

What happens to that if there's a 30 percent attack rate at the facility where Abbott manufactures, let's say, prism reagents or Pall manufacturing filters suffers a 30 percent attack rate in their main facility in California?

We have not brought our vendors into this activity yet, but we'll be doing so at some level so we need to know their planning.

Liaison with local and regional emergency management agencies. Local and state, federal public health. We need seats at the planning table. We need their ears for advocacy and we need consistent messaging in cooperation with public health. The ear for advocacy seems to me a major role of this committee. If there is consensus around the table that this is a high priority activity in the enormous scheme of pandemic planning, we believe that that is a top down activity that's going to need to come from this committee to HHS and down to the state and local jurisdictions.

Planning for limited blood supply. Are red cells an issue? They have a 42 day shelf-life under most circumstances. We really don't know what the impact on red cells are going to be and that needs to be modeled.

Platelets, we think are a critical issue. With a five-day shelf life and the non-elective predominance of indications for platelets, we think that this could be a major issue and are beginning to discuss in brainstorming sessions things like immunization and antiviral access for committee plateletpheresis donors.

And then what is the role of blood organizations and disaster task force in coordinating regional and national movement of components and controlling messages?

We thought we had a very nice message during Katrina about the blood supply, and I think those of us who do blood for a living realized that with the offhand comments of a single individual on national television, all that messaging was bypassed and many blood centers had long lines of

donors showing up where no need existed.

Communications planning. You heard about this from Dr. Wolfson yesterday, so I'm not going to get into too much detail. First of all, what is the message? What are we trying to tell people during a pandemic? How does it differ for a different agent or a different magnitude?

How do we all agree to use the message, whatever an agreed upon message is, and how do we partner with the media to disseminate the message and I think there were excellent comments on that issue yesterday. So I won't expand my thoughts.

International cooperation. I only throw this up because it has been discussed. Pandemic is worldwide. It's not just the United States.

Can we minimize patient mortality by sharing priorities and problems and approaches? The answer to that is probably yes. The EU, Australia and Canada are undergoing this same thoughts that we are at this point and we don't need to reinvent the wheel five, six, seven, eight times. So we need to be talking and those

discussions are beginning to occur.

And in the event of catastrophe, just as a brainstorm, is there a way to move supplies or components internationally if it's feasible to do so?

Well, so that's pretty much an outline of where we're going. The process that we will do is to take those issues that I've identified and the new ones that come up as we continue to think about them. Parcel those out to members of the committee, asking them to begin to develop option lists so that we can start to flesh out how collection facilities and transfusion services might respond with a range of options, and during that process bringing in all the subject matter subject experts that we need from government, public health, industry, elsewhere.

This is a pretty sobering statement from a guy who knows a lot about influenza that was published very recently in Emerging Infectious Diseases. The January issue is available on-line and I encourage you all to download that issue of

Emerging Infectious Diseases and look over it very carefully.

There's an enormous wealth of information in that publication that might help us. Basically, we all recognize that the keystone is vaccination. We have heard that vaccination in pandemic situations is not a matter of throwing a light switch.

Is it reasonable to believe that prophylaxis will work in a large vulnerable population? Probably not. But for containment and for critical infrastructure, perhaps.

So with that, I will take any questions, and more to the point would appreciate the discussion of the committee and any other issues that they identify.

CHAIRMAN BRACEY: Thank you, Dr. Katz. Questions. Dr. Sayers.

DR. SAYERS: Thanks. Lou, one of the questions that this group was posed was what strategies should be considered encouraging immunization of regular repeat donors?

So has your group had any thoughts on that?

DR. KATZ: We haven't had detailed discussions. As you know, Merlyn, I, during the vaccine shortage last year, advocated high priority for certain classes of donors, mostly regular plateletpheresis donors.

And the docs seem to think that's a decent idea, but the people that ensure us did not. So there's an enormous range of discussions. I absolutely support it. I believe that we will be remiss, if we do not when appropriate vaccines are available, to argue about which groups, but if we don't offer access to vaccines one way or another, whether we immunize on site or give them vouchers, or whatever, I don't know. But I think it ought to be a very high priority for blood centers during pandemic planning.

DR. SAYERS: So do you see then offering vaccination just to selected groups of donors, pheresis or negative individuals?

DR. KATZ: Well, I think that it depends

on all kinds of things like the availability of what we think is an effective vaccine and how much. My first thoughts about this came when there was a vaccine shortage and I said, well, who do I want to get it to first? And it was clearly in my center for a variety of reasons committed plateletpheresis donors that we couldn't afford to take out of the supply if, in fact, there was a lot of flu activity in the community.

So I think they're the easy group. I want to give it to everybody, you know. I think in my clinic we don't get consent for influenza vaccine. We sneak up behind my patients and shoot them.

[Laughter.]

CHAIRMAN BRACEY: Question from Dr. Sandler.

DR. SANDLER: Actually two questions, Dr. Katz. Your third slide from Dr. Schwartz reads that this is a disease that spread so fast that resource sharing isn't going to work.

It wasn't clear to me whether you accepted that or not. I'd suggest you don't accept it, and

the reason I think that is things like vaccines aren't the primary focus, it seems to me, of this committee. I think there are other people that are going to worry about keeping people healthy. I think what we should be focusing on is very, very specifically the blood supply, and if we're thinking specifically of the blood supply, I think resource sharing is the keystone of where we can go, and I don't accept that premise of Dr. Schwartz' presentation.

My second question relates to a presentation yesterday which was the first time I heard that there was a suspicion of some observations about prior epidemics of influenza where there was a hemorrhagic component, and if in fact, that is a fact, that would change some of our considerations. I've never heard of anything and there is nothing in my clinical experience that would cause me to even suspect it, and I'm wondering if your committee was aware of that, and if there is any data that we could kind of put the kibosh on that, if I can say that?

DR. KATZ: With regard to resource sharing, my primary purpose of that slide was to demonstrate where the conventional wisdom is at this point. When you look at the 1918 pandemic, for example, decent data available, in fact the spread was quite quick, and early on had transfusion been widely available in 1918, I think the possibility of moving product would have been very real.

This is why I think models are critical. What are the range of possibilities for how quickly how many communities would be affected and what can we do about it? And in fact, the Interorganizational Task Force on Disasters is really set up in large part on that model of resource sharing and if it's feasible I think that that can be done through that group.

As regards to hemorrhagic manifestations, I think what was being referred to was pathologic diagnosis of hemorrhagic pneumonia, and how much that per se would contribute to transfusion need, I don't know. I've never seen a high prevalence of,

for example, DIC associated with influenza.

CHAIRMAN BRACEY: Question from Karen Lipton.

MS. LIPTON: This really kind of a response to Dr. Sandler about the issue of resource sharing. When we did our modeling in the Disaster Task Force for other types of disasters, we actually ran numbers and figured out that we could cope with two major cities being down at the same time.

If you look at the modeling that they're talking about here potentially hitting a place like Washington, D.C., LA, New York City at the same time, we would not have enough blood under a normal circumstance. So then what we have to do is look at it and say, well, how much does the demand actually drop in those places, you know, given that, as Dr. Katz said, some of these things really aren't elective surgery.

I mean transplants take an enormous amount of products and probably the biggest usage in our country, and those are not really elective. So I

think that we do, Dr. Sandler, need to challenge the assumption that we can just move things across the country. I think we have some good mechanisms, but I think we need to--I really think we need to do a lot more study about the modeling and what might happen as this attack rate goes throughout the country.

CHAIRMAN BRACEY: There's--sorry.

DR. KATZ: Dr. Bianco just made a very important point that I really hadn't thought about, and the pace at which influenza spread across the states in 1918 is well recognized and there weren't any airplanes in 1918. So given the way we travel now, my suspicion is that resource sharing is going to be difficult. I think the models need to tell us that.

CHAIRMAN BRACEY: With regard to that, there are several questions. I'd like to make one comment, and that is that a real problem, as we experienced during 9/11, is the availability of transport. Our system now has been decentralized and we're depending on moving samples from Point A

to Point B, and I would think that finding assets, particularly federal assets, might be useful.

I think we've learned from Katrina and other disasters that relying on state support may not be the answer. There may be some federal assets that would be helpful. Has that been looked at in the task force?

MS. LIPTON: Yes.

DR. KATZ: Yeah, it's been talked about several times. Right now it's probably not on the top of our list because the nature of pandemic flu is substantially different than 9/11 or similar things and we don't think the impact on transportation communication infrastructure will be as gross as it was then. It will come up somewhere in the plans at some point.

CHAIRMAN BRACEY: Yeah. Again, one of the things I was thinking about was perhaps related to quarantine and I don't know if that would present an issue.

Dr. Kuehnert, in essence, would there be the potential for shutdown of transport between

regions?

DR. KUEHNERT: Possibly. I mean I think that's something that, you know, we can talk about societal disruption and snow days has been mentioned, and, you know, there is a gradation of that from asking people to stay home from having it be mandatory, but that certainly needs to be incorporated in the models. If you think about the most severe circumstances.

CHAIRMAN BRACEY: Executive Secretary Dr. Holmberg.

DR. HOLMBERG: Yeah, Dr. Katz, I know that we've had some of this discussion on the phone and you made a very good point about the number of individuals that would be on ventilation devices. I think that in comment with what was mentioned about the hemorrhagic respiratory part of a potential pandemic influenza, can you comment on whether or not that we could model in how much utilization could be anticipated for those people on respirators?

DR. KATZ: Yeah. I, in preparation for

the work of the task force and actually for this address, have tried to find some credible information about the incidence of red cell and platelet transfusion in ARDS, acute respiratory distress syndrome, and I really can't find anything that is terribly convincing.

There's a range of estimates from a few percent to 25, 30, 40 percent, that I think reflects the variation in medical practice around the country, and in my own experience I would guess that somebody with a respirator stay longer than five, six days, getting to a week and beyond is going to have somewhere between a 20, 25, 50 percent chance of being transfused under current approaches.

This gets in, as well--it doesn't mean that's all appropriate transfusion, and this enters very nicely into this issue of triage at the level of the transfusion service which other clinicians around the table can agree or disagree. I don't think we're ready for at this point.

CHAIRMAN BRACEY: There are several

questions pending. I'll try to take them in order. Dr. Ramsey.

DR. RAMSEY: Jerry, my question yesterday about the hemorrhagic complications potentially was actually with a reference to, if I may be specific, in the spirit of Dr. Likos' historical presentations yesterday, I would certainly defer to the real virology experts here, but what I was alarmed about was the passages in John Barry's book, to be honest with you, about the great influenza where there were descriptions of hemorrhage which sounded like both epistacksis [ph] and GI hemorrhage, and there's a footnote in there about whether this might been due to vascular toxicity or platelet dysfunction.

It sounds like from your comments on the cases so far that that's not been an issue so I was relieved that that doesn't seem to have come up in the H5N1 cases to date. That's where I was coming from with that question.

DR. KATZ: And I think the bets are off. I don't know whether the pathogenesis of H, X and Y

is going to be the same as H3N2 and H2N2 that I have any direct experience with. So, yeah, I think this is why the modeling is so difficult that we so desperately need.

CHAIRMAN BRACEY: Dr. Epstein, you had a question?

DR. EPSTEIN: My point was addressed.

CHAIRMAN BRACEY: Okay. Dr. Sayers. Sorry. Dr. Pierce was holding. Sorry.

DR. PIERCE: Lou, a question about transmission. You've indicated that it's highly unlikely in blood products. Is there any sera-prevalence data of the population base that supports that for any of the influenza outbreaks we've had?

DR. KATZ: I think actually you saw the data. It's the same data that I was able to dredge up and it's weak. So that's why I said probably not. I don't think it's a major issue, but if I'm wrong, I'll admit it, and I think that the studies that Dr. Hewlett is proposing will go some distance towards answering the question.

CHAIRMAN BRACEY: Follow up?

DR. PIERCE: But what about just historical sera-prevalence data from other outbreaks? So donors come in, recipients receive. During an outbreak, is there an increase in antibody titre?

DR. KATZ: I've never seen any such data.

CHAIRMAN BRACEY: Dr. Sayers.

DR. SAYERS: Thanks. This is going to sound selfish. Nonetheless, at our blood center which serves a large metropolitan area where we've had discussions about our role might be should there be a pandemic, the consideration is that it would only make sense to perform resource sharing if we could confidently predict that we were going to be protected for one reason or another from the pandemic.

We don't think that that's at all possible. So what we do assume, though, and granted there are risks even in this approach is that if there was evidence, say, of the pandemic emerging in Europe, then that might give us a

period of a few days during which we could encourage the community to donate, thereby bolstering the local blood supply to use during that period of time that the pandemic might subsequently hit.

DR. KATZ: I think that that is an obvious solution with regards to red cells. To ramp collections of red cells as we enter stage five, stages five and six, I guess, of that tiered system of alerts. For platelets, I think you and I can agree that a five-day shelf life makes that a difficult strategy to use effectively.

I'm not sure that red cells are going to be the major issue. I'm absolutely certain platelets are going to be a problem.

CHAIRMAN BRACEY: Dr. Wong.

DR. WONG: I'm just a little concerned int terms of the clinical manifestation of predicting the clinical manifestations as best as we can based on the experience in Southeast Asia that we have so far and the deaths there.

The understanding that I had was that

there's hemophagocytic syndrome associated.

DR. KATZ: And I have no data regarding transfusion utilization in hospitalized cases, any activity since 1997. So I don't think we know. I'm very concerned. The conventional wisdom is, well, there's influenza; there's not going to be a lot of transfusion needs. And I think that may be a problem, but certainly putting 800,000 people on a ventilator in some kind of a worst-case scenario is going to consume products.

DR. WONG: Well, dealing almost daily with hemophagocytic syndrome from a hemic viewpoint personally, that impacts your liver function, so if your FFP and the DIC-like picture may come in, as well as, you know, decreasing platelets and affecting the bone marrow's ability to make their own cells. So you're going to impact various types of blood products that you're going to need.

DR. KATZ: Yeah, I agree.

CHAIRMAN BRACEY: Are there plans to study the experience and the hematologic data of the patients in Southeast Asia--

DR. KATZ: Well, I've started making some inquiries to see if we can get that. If you look at what's been published so far, it's not explicitly there, which doesn't mean that they didn't transfuse, or that if they didn't transfuse, that they wouldn't have had they been here where availability is a different issue.

CHAIRMAN BRACEY: One of the groups that we heard of yesterday and I think a point that you made that's very important is the point of communication because one misstatement can change the entire picture, and we did identify that within HHS there is a pandemic communication team, and I think it would be essential for us in our deliberations to consider whether someone from the blood industry or this committee would be inserted within that group.

Additional questions for--Dr. Ramsey?

DR. RAMSEY: Well, I guess we'll go on through the day here, but just a couple of comments as we go on. One was the possibility of recruiting donors in an emergency setting like we have seen in

other cases might help counteract some degree of shortage that we are seeing, that we would see.

In other words, if this could be, from just exactly what you were saying here, if there are messages ready in the event that the community would want to try to increase donor recruitment and try to tap into donors that have not been donating before, that might be something we'd want to have depending on obviously the capacity in the blood centers to do that, collect those collections.

DR. KATZ: Right. I think that the thing that blood centers do really well despite spot shortages around the country is recruit donors, and if I'm trying to recruit donors during a critical need like a pandemic, I don't think there's going to necessarily be a shortage of willing people, given that they're well, but at high attack rates, and the possibility of deferrals and shortages and what not, how effective it will be in terms of product on the shelf, I don't know.

I think that those messages are something that we can do extraordinarily well with what we

know already.

CHAIRMAN BRACEY: One more comment. To have effective communications, we need information regarding stockpiles or inventories. It's my understanding that within ABC and perhaps ARC, that there are mechanisms for determining current inventory. Could you comment on that?

DR. KATZ: Well, the Red Cross has a single FDA license and what not. And a single system. Has a pretty good handle on their inventory day to day for the obvious reason. They're supplying customers and need to know where the blood is.

ABC is little less detailed perhaps, but we use what's called the stoplight in which our centers report on a daily basis a very simple inventory measure, red, green or yellow. Red being more than three days supply, and--did I say red--green is more than three days supply; red is a day or less; and yellow in between. And it has tracked very nicely over several years now what we hear in terms of blood shortages and what not. It's

reasonably effective and HHS has a system that they're getting ready to roll out and, Jerry, I'm sure you can brief people on where that is.

CHAIRMAN BRACEY: Dr. Holmberg.

DR. HOLMBERG: Yeah. Let me just say that we're pleased to announce that we're going to have our beta version rolling out pretty soon with some of our sites that have already been reporting to us, and this is--I've seen the modeling of it, and it's going to be very effective.

I think the benefit of both, of all of the systems that you have mentioned so far are very good. The only thing is that I think what adds to the dimension of the HHS monitoring system is that it will also include the hospitals and so that we will get an idea of what is the supply, what is the demand and it will have different capabilities of being able to look at geographic locations and see how things are happening in those.

So I think collectively, we will be able to get a very good picture of what will happen.

DR. KATZ: And as an example of how

serious Jerry and his staff are, they've offered to come to Iowa in February to show me the system for our center.

CHAIRMAN BRACEY: Dr. Kuehnert.

DR. KUEHNERT: I just wanted to ask Dr. Katz just a couple of questions about vaccination. You know there is this sort of thought which seems reasonable that, you know, donors are, you know, good people and they want to help out and they'll go and get vaccinated, but do we know if donor vaccination rates for seasonal influenza is any different from the general population controlling for, you know, the ages and other demographics and the other question I had is what's the precedent for blood centers to offer vaccination?

Has that been done before?

DR. KATZ: Not to my knowledge. I've been contemplating it since last year when there was a vaccine shortage, and I think the medical directors of the centers I've talked to think it's a decent idea, but as I explained the liability issues are occupying some administrators and blood center

counsel.

I have a very scientific survey of walking through my platelet room for about a week and a half last month, and 80 percent of our platelet donors had had or plan to receive flu vaccine, and the N on that must be like 60.

CHAIRMAN BRACEY: Dr. Fitzpatrick.

DR. FITZPATRICK: Thank you. Mike Fitzpatrick from ABC. Just to follow up on Dr. Katz' comment about the monitoring. Our board approved yesterday a new draft plan on monitoring that in the state of an emergency or a disaster or at the request of the task force consolidates the monitoring of our centers between ourselves and Blood Centers of America, BCA, and consolidates all those organizations so that in that event, there would be reporting by all centers to a single entity and logistical control from an inventory coordinator from a single inventory coordinator and then policy management from a single policy manager, all within ABC and BCA.

CHAIRMAN BRACEY: Thank you. Dr. Alter.

DR. ALTER: Thank you. Harvey Alter, NIH. Lou, I thought that was a beautiful summary. It really was. Despite that, I'm not going to come to Iowa in February.

[Laughter.]

DR. KATZ: You ain't invited.

[Laughter.]

MR. ALTER: But you underestimated or you downplayed the transportation problems, and I think that that will be significant. I think it may be more so than 9/11 because it will be the entire country, and you're going to have at least a 30 percent, if your attack rate is right, you're going to have at least a 30 percent hit on all airport personnel, pilots, et cetera.

And we're highly dependent on this because Red Cross and everybody else is shipping everything for testing to distance sites. Manufacturers are shipping everything everywhere, and I think it's going to be very important to, one, not underestimate it; number two, to have manufacturers in early because as you're stockpiling Tamoxifen

and vaccines, you should be stockpiling test reagents. And--

DR. KATZ: We're beginning the contacts with the vendors. With regards to transportation, I don't think that our priority list is in any way carved in stone, number one. It's on the list. We so far in the discussions I've had with other members of the task force, the designation of the blood community in some sense is critical infrastructure. We are hoping will finesse the issue, that we will have access to, priority access to transportation, recognizing transportation will be affected, but that we will have priority access to what is available.

And that's again dependent on our getting some sort of designation from HHS and on down the food chain as critical infrastructure.

DR. ALTER: Just one other little point. Were blood banks to have control of vaccine, this would be an enormous incentive to getting blood donors, but it would raise all the issues of incentives. So it's a tricky--

DR. KATZ: It's very tricky.

DR. ALTER: --tricky issue.

DR. KATZ: And it's one of the reasons I used twice when I brought this up the term "committed" donors. That we're thinking to avoid that magnet effect, we probably will require some limitation that the donor has demonstrated an interest previously in donating.

CHAIRMAN BRACEY: Dr. Kuehnert.

DR. KUEHNERT: I just wanted to follow up on Dr. Alter's comment about the transplantation issue which I think is important. These patients get a lot of transfusions, and I just wondered if there has been any discussion that you're aware of in blood centers in reaching out to transplantation personnel as far as what they're doing in pandemic planning?

DR. KATZ: It will happen. As you're aware because you're on the group, we haven't brought them in formally yet because we were trying to get a framework. Transplantation, trauma, there's a variety of groups that we think probably

need to be brought in at some point.

DR. KUEHNERT: You said the task force level. I meant at the individual hospital level. I mean I don't know if our AHA representative is aware whether within hospitals, whether there are discussions between transplant center personnel and blood center personnel or with administration?

DR. SANDLER: I'm unaware of those discussions.

MS. LIPTON: I could actually add something. Just to tell you, AHA is on the task force and so they are aware of these, and they have their own plans and we're trying to make sure that those are coordinated. So this issue would get raised.

DR. KUEHNERT: Great.

CHAIRMAN BRACEY: Dr. Epstein.

DR. EPSTEIN: Yes. Well, first, I'd like to echo Dr. Alter's comment thanking Dr. Katz and this task group for a very coherent and enlightening summary of what we may face in the blood system and just to remark that anticipating

recommendations of the committee, I think that we need to identify the Interorganizational Task Force and this subgroup as playing a national role in preparedness for the pandemic in this area.

CHAIRMAN BRACEY: Thank you. Speaker from the floor.

MS. ELIS: Yes. Hi. My name is Bridget Elis and I'm from the Plasma Protein Therapeutics Association. I just wanted to address some of the issues that Dr. Katz cited because the plasma industry was not recognized in this.

We just want to let you know PPTA is aware of the issues and we have read the President's plan and familiarized ourselves with HHS' plan. We've also familiarized ourselves with what the blood centers are doing and we do believe we have some of the same issues that will come up.

We need a healthy donor population and we need a healthy workforce to ensure that our therapies get to those people who need them. However, we do have different issues that may come up.

There's been a discussion that there may be a decrease in blood supply, a decrease in demand for blood supply, but we don't believe this would happen for our patients who are using our therapies. There may be an increase in demand for those needs. So we need to make sure that models that we look at do have that entailed.

We also--Julie reiterated--I want to reiterate what Julie said earlier yesterday about us being included in a tier one vaccination process because it's important that our therapies are available to all our patients.

CHAIRMAN BRACEY: Thank you. Ms. Birkhofer, you had a comment?

MS. BIRKHOFER: No, sir.

CHAIRMAN BRACEY: That's it. Okay. Dr. Bloche.

DR. BLOCHE: Dr. Katz, could you speak to what your task force has done and will or may do with respect to principles and priorities for rationing of the blood supply if these shortages develop either locally or nationally?

DR. KATZ: I think that I kind of finessed it a little bit by putting one bullet point about triage. But I think that as our discussions have gone on over the last six weeks or so, it's very, very clear that the potential to need--I don't know about require--the potential to need triage in hospital transfusion services around the country is a very real thing.

And at this nascent stage of what we're doing, I think that the options will be relatively limited that we'll be able to list. I think that anticipating a consensus of my group is that we're going to say to transfusion services that are members of AABB that they need to have in place prior to a pandemic a set of criteria of some sort that they're going to use for triage, and we probably need to assemble some triage plans from places that have done it before for other reasons and say here's the kind of structure that people have found useful for other events.

DR. BLOCHE: So I take it from what you're saying that you'd be reliant on local providers to

make their own perhaps quite different decisions with respect to rationing?

DR. KATZ: Well, it's really an interesting question that gets to the core of how we do business in American medical care delivery. That's the model. Whether you're talking about doing heart surgery or transfusing blood, for some reason, is that the doc makes a decision in consultation with whoever he has to do it with, and it results in enormous variations in practice all over the country.

I think there's a buzz word in development of quality benchmarks in health care that reducing variation is probably a good thing. Are we there? Do we have any consensus around the country about what are the appropriate transfusion triggers? More perhaps than we did ten years ago. But they are by no means consensus.

And I think Art Bracey is or Jerry Sandler are probably far more capable than I to talk to you about variations in transfusion practice. Can we tell people, no, you can't have blood? At the

individual hospital level, I believe that's true.

At that blood center level, probably. Probably I can sit by the phone at my blood center serving 40 some hospitals and say why do you need those platelets; no, you can't have them.

But I might be willing to do that and somebody else may not. So the level of variation related to the nature of medical practice in this country is huge.

DR. BLOCHE: The model variation isn't necessarily the model with respect to some allocated functions. For instance, there are regional or national principles with respect to organ allocation.

I do think I would caution, I think it could become controversial to say the least, and potentially even explosive, if in the event of acute shortages, allocation or rationing were done very differently from doctor to doctor, from hospital to hospital. A measure of due process in this area, at least with respect to large principles, is I think essential.

DR. KATZ: I think those are superb points.

CHAIRMAN BRACEY: Yeah. I think that speaks to what we have discussed at the previous meeting in terms of the need for a strategic plan to address issues of availability. There are nations, the UK has such a system, such a plan that's been developed and I think one of the outcomes of this, our deliberations, should be to make sure that we are cut with a plan rather than without one.

CHAIRMAN BRACEY: Dr. Roseff.

DR. ROSEFF: I'd like to reiterate what we talked about yesterday. I think this is an important time to do that. I mean this may be the impetus to let us go forward with that part of the strategic plan and use this as an opportunity to get together and not necessarily, as we talk about mandate what you do in times of blood shortage, but have a plan and some great guidelines that are sort of universally available so that we can use these locally.

I'm always very heartened to see when we have a blood shortage how little blood people really need, and I don't see that there are problems associated with that. And I'm also unhappy when I hear that, well, we are cutting platelet doses in our hospital, across the street, they're using a dose of 10 randoms as their dose.

We have to take this as an opportunity to try to address some of those issues, I think.

CHAIRMAN BRACEY: Thank you. Dr. Ramsey.

DR. RAMSEY: A couple. Why we're talking about inventory issues, I had a couple of other thoughts as you were talking. One was the possibility of stockpiling FFP in advance as an outbreak would begin to occur, both from the standpoint of a supply issue and the standpoint potentially of the health of the donor and the transmissibility, but that may be secondary. But that would be another opportunity to consider being prepared.

The other issue that might merit some thought from a regulatory standpoint would be

contingency plans for looking at the outdated platelets, under what circumstances the out date could be extended in a real national critical emergency. I just offer that as a thought.

DR. KATZ: Yeah, Alan Williams, Alan Williams on the task force is in fact--there's a draft guidance as you're aware for automated collection of platelets that has some substantial, suggests some substantial new restrictions, but Alan is already looking at that plan which in some form that guidance will come out. Whether it will have the restrictions that are being talked about is not clear at this point, but he's looking at the plateletpheresis guidance with an eye towards how would we change the picture in the event of a pandemic.

Different donor deferral criteria perhaps. He has mentioned to me a seven day outdate instead of a five day outdate now that we're doing bacterial testing, those sorts of things. So we're really looking forward to hear some of Alan's thoughts on those issues.

CHAIRMAN BRACEY: Thank you, Dr. Katz. That's a very clear and thought-provoking presentation. Our next presenter is Dr. Shimian Zou. Dr. Zou is a Senior Specialist with Transmissible--excuse me.

DR. HOLMBERG: I apologize for the interruption. First of all, Dr. Katz, I do want to thank you for your presentation and also I want to thank AABB for taking the lead on putting together this task force. This task force has been very important and I also want to invite you back to address the committee in the future so that we can get a better idea of where this task force is going.

I think that's it.

CHAIRMAN BRACEY: Sorry. I was out of place there. Our next presentation is actually Dr. Philip Norris. Dr. Norris is Associate Investigator and Director of Immunology at Blood Systems Research Institute. He's a visiting scientist with the Gladstone Institute of Virology and Immunology. Dr. Norris will present to us

today on Influenza Virus in Blood Donors and the Potential Transmission Through Transfusions and Transplantation.

DR. NORRIS: Okay. Well, thanks for the introduction and thanks to Dr. Holmberg for inviting me here to present today. This is an interesting group and I think that this talk should speak to a lot of the issues addressed by Indira Hewlett yesterday, and I think that you'll find that the plan studies that we have are complementary to what she and Dr. Alter are planning.

So what I'm going to present is similar to what we presented at REDS-II working group which is an NHLBI funded blood safety working group, and we're working this project through an expedited review process to perform the project as soon as we can, and what we hope to do is, first, to find the scope of the problem and that will open doors to new research in blood safety and influenza.

So before I launch into what the scope of the problem is I think we could just briefly go

over a little basic biology about influenza, and looking at the screen up there, it's difficult to read what the writing is. But you see the circles represent Influenza A, B and C, and we'll focus on Influenza A on the upper left, and it's a segmented genome with eight components.

The nuclear protein which you can't read up there is one of these components and each of the genetic elements is wrapped around a nuclear protein in the virus, and the three components on the left are all polymerases that are virus-encoded polymerases important for the viral replication.

There's a non-structural protein in gray there as well, and that is important for viral replication and also for immune evasion of host immune responses, and then we get to sort of the main event. There's the matrix protein which is important in coating the inside of the viral capsid and also for adjusting the pH endocytic vesicle, so what happens is influenza attaches to cells, gets endocytosed into an endocytic vesicle.

The pH is lowered through the action of

pores created by the matrix protein. Then the influenza can uncoat and migrate to the nucleus.

And then saving the best for last, there's the HA and the NA so the hemagglutinin protein, and what this does is it binds to sialic acid and it's also responsible for the host tropism of the virus so we know that there's influenza that affects avian species, influenza that affects swine, and influenza that affects humans.

And the hemagglutinin gene is responsible for that, and what it does is it binds to sialic acid that's bound to galactose and there's an alpha-2-3 linkage that is used by the hemagglutinin from avian species. So the avian species prefers to bind to a sialic acid that's attached to a glucose via an alpha-2-3 linkage, whereas the human-tropic strains like to bind to a sialic acid that's bound to a galactose by an alpha-2-6 linkage. So these are the two different types of linkages, alpha 2-3 and alpha 2-6.

And very few mutations in the hemagglutinin gene changes tropism, and what's

interesting is in swine, and this is the theory of how viruses were passed at least in the past was that swine viruses or swine can host both types of virus, the virus that prefers the alpha-2-3 or the alpha-2-6 linkages.

So for a long time, people thought that these outbreaks came from birds into swine and then into people. Now, it's apparent through a lot of the recent transmission events that people can get infected directly by avian viruses and we've seen that in Hong Kong and throughout Southeast Asia recently.

So it's possible that the recombination events between influenza from avian and human species can actually occur in people. So with that I'll move on to a little more about influenza. These are the history of the pandemics and you may have seen these similar slides in the previous talks.

But it looks like each of these went through probably avian sources for the H2N2 and H3N2 in between their human outbreaks and H1N1, if

you look at the phylogeny of the virus, the sequence, the hemagglutinin gene from H1N1 and what they see is that it groups with mammalian viruses and it groups very near the root of the tree meaning that it's not very distant from the primordial influenza viruses in people or in swines, and depending on how the analysis is done, it groups as either a swine virus or a human virus in the hemagglutinin gene and that's the 1918 Spanish flu, which had the extremely high virulence.

So it's interesting that it's slightly different. It doesn't look as if it was from an avian source, that hemagglutinin gene compared to other, the Asian flu, the Hong Kong flu, appear to be of avian sources.

So the question that we want to address, and I know this has been talked about earlier in the conference, does viremia occur in Influenza A? So we do know that viremia is rarely detected during symptomatic influenza infection. And in fact, if a lot of cases are looked at, it's very

rarely found. So there are plenty of studies showing that none of 20 individuals have influenza viremia.

These studies were typically done with chick egg inoculation, so it's sort of an older technique of detection though there have been some PCR studies looking for viremia. That being said, there are some isolated case reports of viremia detected during symptomatic influenza infection.

What's more interesting and I think I'll walk through in some detail is does viremia occur during a pre-symptomatic or an asymptomatic phase? And there is some thought that this probably does occur. So one of the studies I wanted to present in detail was done by Stanley and Jackson back in 1966. So this was a long time ago. 15 subjects were infected by nasal challenge, and these were actual prison volunteers who had volunteered to be infected with influenza. It's not a study we'd repeat today probably.

[Laughter.]

DR. NORRIS: But anyway, they volunteered

and they were infected. And a number of them--so from these 15 people, they looked at blood and nasal secretions and they tried to culture virus on a Rhesus monkey kidney tissue culture system. It wasn't a very sensitive system because only one sample was positive. It was a nasal sample, but all the rest of the nasal samples were negative and the blood samples were all negative.

And they thought, well, that's probably not an accurate enough or a sensitive enough test because six of the subjects did seroconvert after nasal challenge. So they had specimens left over from four of those subjects, not from any of the others, so of the four seroconverting subjects, they had sample left over and were able to inoculate an amniotic sac of a chicken egg, which is a more sensitive culture technique. And interesting, of the four individuals that they were able to test, all four had detectable viremia on day one after challenge.

By day two, it had faded to half of them and by day three, a quarter of them were still

viremic, one of four, and they stopped looking at that point. They didn't check again for another week or ten days or so. So we don't know exactly how long this viremia persists, but it's probably in the one to three day range.

And that fits with what we've seen because when people become symptomatic at day three, we really can't detect much viremia, so it's probably in the pre-symptomatic phase, and of note the person who was viremic for three days was actually asymptomatic in spite of seroconverting. So people can be viremic not only in a pre-symptomatic phase but asymptomatic infection can also be viremic.

So this is the study we'd like to do as part of the REDS group, and we'd be leading it out of BSRI, but it would be part of the REDS II working group. What we want to do is determine the prevalence of Influenza A viremia or antigenemia during periods of outbreak among healthy donors.

And the other thing we'd like to do is measure the relative sensitivity of RNA and antigen detection assays in different blood compartments.

So the first part is getting the assays to work on blood fractions. So the approved antigen or RNA detection assays are all approved for use on nasal secretions or oral pharyngeal swabs or some sort of respiratory secretion because that's where they're used in point of care diagnostics.

And none of them have been validated on blood yet. So we started talking to the companies that make the assays, in particular Gen-Probe and Prodesa make either a TMA or a PCR-based assays for detection of influenza RNA, and they're both willing to try to get these to work on different blood components, and I'll tell you a little more about how we plan to do that.

They're working in-house right now just to take the assays and get them working on different blood fractions. Once they have their assays up and running, we plan to spike influenza into different blood components at our facility, send them samples in a blinded fashion and compare the sensitivity of their assays for detecting influenza.

And I think this is a really a necessary step to do before we start looking in the blood supply. We really need to make sure the assays work, find out what their limits of detection are. So that's the first part of the study is to validate the assays.

The other interesting part of the project, I think, is to translate detecting not only the prevailing H3N2 virus in our own blood supply but to be able to detect H5N1 virus. Talking to Prodesa, they have two different PCR assays, one of which detects H5N1, one of which does not.

So we would want to see how good are these assays at picking up H5N1 virus? Now, of note, these assays don't differentiate whether Influenza A is H5N1 or not. There has to be a separate set of primers to specifically amplify the H5 hemagglutinin.

So to do that, we have a collaboration with Dr. David Kelvin at the University of Toronto, who is able to infect ferrets with H5N1 and longitudinally measure the virus in each of the

blood components to see if they also have a viremic phase which we do suspect they will.

So for the detection of Influenza A, I have mentioned the techniques have improved since chick egg inoculation. PCR is reportedly more sensitive. I can't tell you exactly how much more sensitive. The folks at Prodesa were supposed to get back to me on that, and I haven't heard from them yet, but they do tell me it's more sensitive.

And I think our planned studies will help answer that question. Then PCR and TMA are highly sensitive and specific. Direct antigen detection is also possible, but as I'll show you, it's less sensitive than the RNA detection assays.

So Gen-Probe gave us some data. This is published on their Web site. Of Influenza A, TMA specificities, they looked at a number of different viruses. I don't have a laser pointer here, but I can tell you the big box on the left there are all viruses that--adenovirus, human coronavirus, peri-influenza, RSV--none of these came up positive on either their Influenza A or Influenza B TMA tests.

The box, the smaller boxes, there are about four or five viruses there on the lower left--are all Influenza A and they're all positive on the Influenza A test, and unfortunately the slides are a bit small; you can't see them that distance, and then finally, the bottom two viruses are Influenza B, which positive in Influenza B but not on Influenza A tests. So there's good specificity of this assay using the panel of viruses that they have published.

This is unpublished data from Gen-Probe just showing the sensitivity limits of detection, and looking at 250 copies per ml is the lowest copy number that they've used, and they get a positive signal with down to 250 copies per ml of Influenza A.

BD is a company that makes direct antigen tests. So Directigen EZ, the sensitivities you'll see is a lot lower. If you can read the numbers there, the ten to the fourth, ten to the third range, one of the samples was detectible at almost ten to the third and ten to the second range.

So the antigen sensitivity is less. The reason we want to look at antigen or at least antigenemia as opposed to just viremia is it's possible that there will be more antigenemia than viremia. So that might actually compensate for the lack of sensitivity to the antigen assays. We may actually pick up a few people with antigen that we wouldn't otherwise if we were just using a PCR or TMA based assay.

Finally, these are looking at animal strains so the BD test also detects various bird flus and swine flus, so that's what delineated here. So there is good specificity for animal strains as well. Now, I'm going to shift gears a little bit and talk about the ferret model of avian influenza that's being worked on by Dr. David Kelvin.

So what he's done is infected ferrets with H5N1 virus. It's a Vietnam isolate. And what he found was that the virus was widely dispersed in tissues. He has not looked in blood yet because the original experiments they didn't get blood.

But what they find in their model is that at seven days there's 100 percent mortality infecting ferrets with the avian influenza, and this is the clinical course of a ferret that's infected with avian influenza.

There's weight loss that's progressive over the seven days. These end at day six because at day seven all the ferrets had died. They get a fever early on and then it spikes down to lower temperature in a pre-morbid state by day six.

The pathology of this, the top shows nice healthy lungs from a control ferret, and there's a progressive hemorrhagic infection. Day two, four and six are pictured here, and you can see there's increasing hemorrhage within the lung tissues in each of those days.

And they did, while they have not tested blood directly yet, they have looked at a number of tissues. The black bars here are nasal tracheal aspirates. The white bars are lung. The gray bars, the darker gray is brain, and the lighter gray is spleen. So we can see that there is virus

detected in all of these various tissues implying that the virus is widely disseminated and it's almost certain there is a viremic phase in these ferrets in his system.

And finally this segues a little bit into some studies we would like to do if we do, in fact, detect viremic donors, and I'm an immunologist. I've worked most of my background in HIV immunology, but what we'd like to do is see is there an immune predictor of how people will do a priori when they present with influenza.

So looking at the blood bank model, it gives us the unique opportunity to capture people in the pre-symptomatic phase. If we can detect antigen or RNA before they know they're infected, we can then look at them at that first time point and say are these people going to go on to live, are they going to go on to die, and what defines an effective immune response?

One of the interesting things I think that's coming out is the T-cell response against influenza virus. In our vaccine development, we

always focus on antibody, eliciting antibody to the prevailing strain, we try to measure which hemagglutinin molecule is out there, which H and which N, and then we try to tailor our vaccines to that.

But if we could make a T-cell vaccine to more conserve regions of the virus, can we then prevent some of the pathology or prevent mortality that's seen with influenza? So one of the things we hope to do is if we can capture these people early, we can then look at their T-cell responses against the whole virus and say, well, these people that went on to do well actually had a very robust T-cell response at the time of their infection implying that prior infections are vaccinations had elicited this.

And what we're showing here on this slide is looking at intracellular phosphorylation of some of the proteins, of one of the proteins that's in the T-cell activation pathway, and we see that there is immense immune activation going on even by day two after infection, which actually fades by

day six. So day four, there is sort of this peak of the immune activation, which then fades by day six in these mortally infected parrots--I'm sorry--ferrets.

So what do we plan to do in the short run? What I was discussing with the immune monitoring is sort of a second phase of the study, so what we intend to do to address the issue of viremia prevalence is to try to detect RNA and antigen in blood donors during periods of epidemic outbreaks.

So, we're fortunate in that the REDS working group has made a repository. It's called the--oh, boy--RADAR--thank you. I was trying to decipher the acronym. It's the REDS Allergen Egg Donor and Recipient Repository. It's quite a mouthful.

But anyway, the RADAR repository is unique in that it has donors and recipients. We're not using that part of it. They also have a number of unlinked donor samples and they have donor samples that are linked by zip code. So with that information, we can then go back and look at time

periods so we know when each of the samples was frozen down. We know which zip code it was collected in.

And then we can look. If you look at this graph, you can see there is a base level of influenza activity and then we can look at certain years, 2004 is the second to last year listed there. See, there's a big spike in mortality and this is influenza pneumonia associated with mortality which--that excess mortality is almost all due to influenza or influenza and secondary pneumonia.

So we can look at periods like this in collaboration with the CDC. We've been working with Anna Likos to really look at a fine level where is influenza breaking out and when. Now, we can go back to this repository which spans all of these years, and go back and say, okay, this is the zip code and this is the time when there was high influenza activity. So we want that 30 percent attack rate time.

We want to look at the very highest time

because we know that the viremia period is short, so to detect any appreciable levels of influenza in the virus, we're going to have to target the very highest levels of influenza activity and with a combination of the REDS repository and the CDC's cooperation, I think we'll be able to do that.

This is a map showing at a gross level where influenza is breaking out in the week ending December 6, 2003, and you can see that there are these red zones. We can get much more detailed information from that from Anna who is here at the meeting and combine that with our repository data to really target the right specimens.

So I think this is going to be key to completing this study and I've gone through here and listed each of the sites that's in the REDS repositories and you can't read that from there probably, but there is the Chesapeake Red Cross, Southeastern Michigan Red Cross, Southern California Red Cross, our own cited blood center is the Pacific, Oklahoma Blood Institute, Institute for Transfusion Medicine in Philadelphia, and

Florida Blood Services.

So anyway looking at those and going back to those gross maps that we had the slide before, we were able to correlate which weeks during each of the years where there was outbreak activity. So this is just showing that we have the data and the ability to target the blood supply once we get the assays optimized from the commercial makers of the assays.

Our sample size that we anticipated studying was a thousand patients. And if there's a two percent prevalence of influenza during these outbreak periods, which is not a horrible estimate, we would expect to see 1.23 to 3.07, 95 percent confidence intervals around that two percent.

So we're hopeful that we will be able to detect influenza if it exists, and we're also hopeful we don't detect influenza for the sake of the blood supply.

So in conclusion, viremia likely occurs during a pre-symptomatic Influenza A infection, and I have focused on Influenza A here, but I should

mention there are documented cases of Influenza B causing viremia as well. Because it's not quite as serious a disease, the manifestations of Influenza B, I really focused on A.

But what we find for A probably will translate to B. The incidence of viremia during influenza outbreaks is really unknown. People haven't looked in a systematic fashion, and now we have the tools that we can address this question, whereas we really didn't until quite recently.

If we do detect appreciable Influenza A viremia, I think that will have implications for blood safety and will raise a number of questions that I think we'll discuss here, and if we detect donors who are viremic, I think we can certainly study the donors to see how they do. That will be easy.

Studying transmission I think will be much more difficult. There will be a lot of ethical questions. I think we'll have to interdict those units. So it will be difficult to design the study in humans to determine whether transmission of

Influenza A virus occurs and I think that's where Indira and Harvey's studies probably will be very helpful to us.

And I think the other thing that we haven't talked about a lot is the ability to detect H5N1 viruses could present a valuable public health monitoring tool, and we've been in contact with the Deputy Director of the National Blood Bank in Vietnam whose eager to collaborate. If we can get our assays adapted to blood as we are, they have repositories of 30 to 50,000 patients per year from the Hanoi area and also out in the countryside where people are living with the chickens.

And we can then look at that blood supply to see is there H5N1 in that blood supply which I think would have real implications for the U.S. if the pandemic moved to here. So I think we have an opportunity to look not only at domestic influenza and safety and transmissibility but also at the avian influenza in the human blood supply.

So with that, I'll end, and take any questions if there are any.

CHAIRMAN BRACEY: Thank you, Dr. Norris. Questions for Dr. Norris? Dr. Sandler.

DR. SANDLER: One of the very important issues is the one that you say you'd have such a difficult time evaluating which is is the virus which is present in an asymptomatic donor transmissible by blood?

DR. NORRIS: Uh-huh.

DR. SANDLER: And I'm just wondering why would it be so difficult to get samples from recipients of persons who donated blood who were infected? It seems to me if there's 100 people who are infective and they donated blood and you collected 100 samples from recipients who got their blood, you would have some information and I'm trying to figure out why that key issue can't be somehow or other included in your study?

What we were talking about yesterday was the importance of not having to put in barriers to donation so the issues is really a key issue for us to look at.

DR. NORRIS: Yeah. I agree with you. I

think the trouble, why is influenza more difficult than say HIV where we can go back to these repositories like the RADAR and say there is linked donor and recipient samples? Well, the influenza is transient so it doesn't stick around like HIV or hepatitis, you can go back and find it in the recipient still. And if the recipient has positive antibodies to influenza, well, did they get that from this transfusion event or was it transmission in the community, which is also, you know, during outbreak periods is intense.

So I think it's difficult to do using existing repositories with any degree of certainty. I mean I guess you could statistically look and see do these recipients have higher influenza rates than other people that were in the hospital at the time, but I think to get a conclusive transmission, to really publish this in peer review and convince ourselves that influenza is or is not a threat to the blood supply, I think you'd have to demonstrate in a prospective fashion that there's transmission.

And the trouble with that is if you

identify people with influenza in their virus, you probably wouldn't want to transmit that--or transfuse that into people knowing that there is influenza in there. Even though we don't test routinely now, if we did in a research protocol, I think it would be very tough to get by an IRB to say we're going to put this in anyway and see what happens.

So we can't do that. So I've been thinking about this a lot and one of the things we could do is not look in the donors as current standard of care, and just prospectively test for viremia two days after transfusions in recipients. I think that's a study that probably could be done and then go back and test the donors using aliquots that are left over.

CHAIRMAN BRACEY: Dr. Fitzpatrick has a question.

DR. FITZPATRICK: It's a great talk and fits in very well with Indira's talk from yesterday. I just wondered what the publication of CDC's public health research protection guide for

public comment that came out last month, if this is an opportunity for the committee to work with Dr. Kuehnert and for this committee to have input to the long-range plan on that research guide to include the studies that Indira has talked about and studies that Dr. Katz talked about to provide funds and work with CDC to develop a format and a process for including the things that we've talked about here that are needed for the blood supply into that guide that CDC is now working on?

CHAIRMAN BRACEY: Dr. Alter.

DR. ALTER: Yeah. I had gotten up and then sat down again because Phil answered all the questions that Jerry--your answers are exactly what I wanted to say, but the only way you could do what you're asking, Jerry, would be a prospective study and we have one ongoing called TRIP study, where we have the saved donor samples and we have recipient prospective follow-up.

The problem is the likelihood of finding in the small numbers that we can follow, the likelihood of finding a positive donor is low, and

using up the precious samples to look for it is risky. So we may do that, but I'm not sure that we're going to find anything.

DR. NORRIS: I have one more comment on that. To do a prospective study, I think you'd have to really target turning on the study to make sure it coincides with the time when influenza is really breaking out. So again, we have to have the CDC really closely involved saying okay, now you can turn it on in this area.

And recognize, if influenza is transmitted by blood transfusions, it's obviously gone unrecognized, and that's not surprising. I as a clinician had a case of TRALI but didn't know what it was. We had a person who as transfused and had pulmonary edema, young healthy guy who had head and neck surgery, and, you know, we did a echocardiogram and all sorts of cardiac stress tests and everything was fine.

So I think it again may be something that is occurring. People with bone marrow transplant who get a transfusion, have a fever a couple days

later, well, was that influenza? We would never know because it's not something we look for.

So I think we would need to do it during periods right after an influenza outbreak in a prospective fashion.

CHAIRMAN BRACEY: Dr. Kuehnert.

DR. KUEHNERT: I just want to make a general comment. I think that really speaks to the need to incorporate recipient surveillance when you have a situation of an adverse outcome and it's not fully explained, to broadly consider possibilities, and one of them if the season is appropriate would be influenza. So you know I think all the prospective studies we're talking about I think are really good ideas but also just thinking more broadly about surveillance strategies, that would be something that could be considered.

CHAIRMAN BRACEY: Dr. Epstein.

DR. EPSTEIN: I was having a similar thought which is post-donation information is another way to get at the potentially exposed recipient. You get a call back that the donor got

sick, sounds like influenza, maybe there's a confirmatory test on nasal swab, and then you look at the recipient.

DR. NORRIS: That's a good idea.

CHAIRMAN BRACEY: Thank you, Dr. Norris. Any other questions for Dr. Norris? Dr. Epstein?

DR. EPSTEIN: You drew attention to the ferret model which is, of course, a well-established model for infectivity of influenza, but I wondered if you might comment on the development of the primate model and the potential advantages of the primate model? For instance, in looking at the natural history, humans don't have 100 percent mortality, so you would think that there's a difference then in the immune response.

Humans don't seem to have predominantly a hemorrhagic pneumonia. Ferrets invariably have a hemorrhagic pneumonia. So the ferret might not be the right model to look at the immune response or perhaps also not appropriate to study the transmissibility.

But on the other hand, the primate model

is much less well developed. So have you had any thoughts about the relative merits of the two models?

DR. NORRIS: I have my own biases about the models. I come from an HIV background where there are really pretty good primate models, but I work only in humans for the most part, so, you know, I think that the ferret--I think the primate model probably will be better than the ferret model, but I think the real model that we want to study is the humans.

So what we would like to do is prospectively capture folks and we're trying to build collaborations with the folks in Vietnam to look at avian influenza.

I think the primate model is certainly worth developing and Indira's project is interesting. I would be supportive of that. But I think to really get a good idea whether it be vaccination or looking at immune responses to determine what's good and what's bad, each of the species are different enough that I think you

really need to look in humans, but that's my own bias. I'll certainly say that.

CHAIRMAN BRACEY: Comment from Dr. Katz?

DR. KATZ: I'm kind of interested in, there's a lot of focus on H5N1. And I don't think we know whether H5N1 or HXNY is the next one, so tell me what you think we learned from studies with one strain and how in any way we generalize that to other strains? And one technical question, in the ferret model, was it positive sense or negative sense RNA being detected?

DR. NORRIS: Okay. So two questions. I'll go to the second one first. I don't know if he was detecting positive or negative sense, so that's an easy one.

And the second one--what was it?

DR. KATZ: How do we generalize from H5N1?

DR. NORRIS: Yeah, how do we generalize? Well, that's a good point. I mean I think it's very difficult to do that, and we don't know what the next strain is going to be, so I think we know that H5N1 is out there and it's caused a number of

human infections. So that gives us the opportunity to study it.

And I think that probably what happens with H5N1 is going to be more similar to a bad pandemic than what we currently have with the H3N2 infecting humans. We intend to study both and that's what we'll do, and whether it will be translatable, I don't know, but I think it will.

I mean influenza varies in its degree of pathogenesis, but it is the same virus with a lot of the proteins are conserved, especially the internal proteins amongst these different viruses so I think we will see, for example, T-cell immune responses to internally conserved proteins.

I think there will be a lot of translatability to that and some of it will not be translatable when we get the new pandemic whatever it may be.

CHAIRMAN BRACEY: Thank you, Dr. Norris. We will take a 15 minute break and reconvene at 20 after the hour.

[Recess.]

CHAIRMAN BRACEY: I'd like to resume the presentations. The next speaker is Alfred DeMaria. Dr. DeMaria is the Chief Medical Officer and the Director of the Bureau of Communicable Disease Control and State Epidemiologist with the Massachusetts Department of Public Health.

Hello. We're trying to reconvene here. Dr. DeMaria's responsibilities incorporate medical direction, consultation, communicable disease surveillance and control, as well as bioterrorism preparedness and a wide variety of dealings in infectious diseases.

Dr. DeMaria will speak to us today on State and local Preparedness for an Influenza Pandemic.

DR. DeMARIA: Thank you. Thank you very much. Good morning. And I appreciate the opportunity to speak on behalf of the Council of State and Territorial Epidemiologists who are in most cases taking the lead on pandemic planning at the state level, and I just want to cover some of the things that are going on at the state, local

and federal level, because I think I've been sort of surprised in preparing for this how little is going on in terms of the blood collection agencies in collaboration with local and state public health around the planning in most states, and I think that's something that needs to be addressed.

We have been working on pandemic planning in Massachusetts for the last ten years, and I think in most states, it's been a number of years, but obviously with all of the attention now towards avian influenza in Asia, things have really picked up obviously. So you know I think it's time for the blood collection agencies and the health care facilities--I think a little--there a lot of things that are going on in terms of HRSA funding to get health care facilities prepared for emergencies, bioterrorism originally but pandemic influenza now, that need to be addressed.

So I just want to briefly review some of the issues that we're facing, and I think I'm not going to spend too much time on this or any time at all, but basically say we tend to think that a

pandemic is inevitable. I found my slides, my influenza and pandemic influenza slides from 1980, and I could still use them today to talk about pandemic influenza.

So I think that there's been a lot of refinement, but the bottom line is it's in the nature of Influenza A viruses to cause pandemics as it is to have antigenic drift and to change from year to year, and that it's very different from SARS or other things we were planning for, for example, smallpox, in that the serial interval for transmission in the community is two to four days because the incubation is two days.

So the rapid spread means a lot of people get sick very quickly and are very infectious, not only when they get sick maximally, essentially when they get sick, but even before they get sick.

So it makes quarantine in terms of identifying people exposed and quarantining them probably not something that's not very effective.

The other thing is that there is no set way a pandemic occurs. We've had three pandemics

in the 20th century. There were presumably--there seem to have been three in the 19th century. When two out of three people who died died of an infectious disease, you probably wouldn't notice too much that there was an influenza pandemic, but in point of view, it does seem to occur every 20 to 40 years, and each pandemic has been different.

In 1918, it was differential mortality in the 15 to 45 year olds, and overall a two to four percent mortality rate, population mortality rate, which was an enormous number of people obviously.

But then if you go to 1968, it was really ordinary influenza the way it behaved. The curve, the case fatality curve by age could have been 2003 or 2004 basically differentially affecting the very young and the very old.

In 1957, it was peculiar but peculiar in that it differentially affected children under one. So whatever the pandemic does, it can do it in a variety of different ways. That makes doing the projection--I mean people really get into numbers, but doing the projections, they're very broad

parameters, and you can see from the CDC and these numbers have changed many times, and whether it's 9,348 or 6,937 is not going to make much difference. It's bad.

A pandemic is bad whether it behaves like 1918 or 1968, and the other point, although we're focusing on H5N1, it was brought up a little while ago, you know, I think I can make a better case that H7N7 is going to be the pandemic strain because that's even more adapted to human infection, although it caused mild infection in the Netherlands.

All of these viruses circulating all of the time, and avian influenza is something that's very, very common worldwide in birds.

And H5N1 I know, you know, obviously this is what has focused people's attention, and we have to differentiate between avian influenza and pandemic influenza. They are two separate things. Avian influenza is a disease of birds that occasionally affects humans. It's fairly easy to deal with although I think the public reaction

wouldn't be easy to deal with if we had a case in the United States.

In point of fact, it doesn't present a significant public health danger, whereas--and we can handle as indicated on this slide--whereas, pandemic influenza is human influenza that is highly adapted to spread in humans and that's the whole point of the pandemic.

So we're really looking at the possibility, and when you look at Influenza A viruses, all of them can infect birds. So in a sense, all Influenza is avian influenza and just some of the strains are adapted to humans.

So when we do our planning, it's basically planning for an overwhelming epidemic that will occur simultaneously across the world and across the country, and obviously one of the big issues will be the demand for health care which has changed over the years, and, you know, I remember years ago when I was in practice, you go see a patient in the morning and you say, well, you're doing very well, I think you can go home today, and

they say, well, you know, I don't really--can I rest for a few more days, and you say okay, you can stay. That doesn't happen any more, people have moved in, moved out, and there's no surge capacity in health care delivery system, and there is no outside help in a pandemic, so you can't wait for help--you know, in Massachusetts we can't wait for the Kansas National Guard to come and help us because they're having the pandemic at the same time.

So key to the planning has to be consideration that this is going to be overwhelming regardless of how severe the actual strain, how severe disease is caused by the actual strain that causes the pandemic, and that there is going to be no outside help, and there could be up to 35 percent absenteeism over a 12-week period, let's just say. In a wave of pandemic influenza, there's going to be a time where up to 35 percent of people are going to be out of work, either because they're sick or their family member is sick, or they're afraid to leave the house because this is also

going to be the first pandemic on 24/7 news coverage.

So there's going to be this persistent constant coverage of this, and it's not going to be, you know, how the brave and heroic public health people are doing their job; it's going to be like people dying and people lying outside of emergency departments.

So all this planning has to take into consideration that that's the reality of what happens now, and we've seen it a number of times with West Nile and white powders and so forth. And that the public systems are going to be impaired so we're not going to have enough police, we're not going to have enough fire.

Health care personnel obviously is going to be a big issue. As the demand goes up, there's going to be fewer people to take care of the patients, and then we live in a just-in-time economy, and it's really the first pandemic that's occurred in this kind of setting where everything is delivered in a just-in-time way, so that when

you get a hurricane in Miami, even though it didn't cause a lot of physical disruption, it caused a lot of disruption of the inventory system so that the store shelves are empty, the drug stores are empty, health care supplies aren't delivered to health care facilities, so that has to be an important consideration.

So a lot of what we're doing now has been shifted from sort of simplistic, you know, how are we going to take care of people on ventilators to how we're going to have continuity of operations of state agencies, the private sector and so forth, in the face of the demand presented by the pandemic, which I think is the major issue in terms of blood collection because donors are going to be sick, workers are going to be sick all simultaneously and we have to maintain essential services.

And as I said, you know, I think it's amazing to me, and I started to meet with our local blood collection agency and attending their medical advisory meetings, and how little that consideration has entered the planning so far in

terms of this essential health service, providing blood.

So we're at pandemic stage three, and we're looking at various elements in a pandemic plan, and I think that every state has pretty much now posted their pandemic plan. They're trying to track the federal pandemic plan. Ultimately they all have to agree because we can't have a different approach to pandemic influenza in one state versus another, and there are essential elements to these plans, and key elements are how we're going to maintain societal function in the face of absenteeism and how we're going to take care of the people who are going to require care at the same time reducing transmission of virus in the community because that's another issue.

And because of the nature of the influenza virus, and there are two excellent reviews by WHO in this month's Emerging Infectious Diseases, that really talks about what information we have about non-vaccine, non-antiviral approaches to influenza and I can tell you they don't--you wouldn't be

enthusiastic about, you know, after looking at what the data are about what we're going to do with isolation and quarantine and those kind of interventions that we use with SARS to some effect, but influenza is a very different disease than SARS.

The vaccine has to be matched to the strain so no matter what we do now, there's not going to be enough vaccine for four to six months. It's going to be available slowly, and if the pandemic happens before the next five years, it's going to depend on an egg-based production system for vaccine. The vaccine that's already been developed is 12 times less potent than ordinary influenza vaccines, so the supplies are going to be limited, if that's what we're left with having.

And we're already dealing now, we're having these public participation processes, to get the public to understand how we would prioritize vaccine, but in a sense, the vaccine is going to be anticlimactic because most of us are going to experience the brunt of the pandemic before there's

a vaccine available, and I think we need to have that in our consideration. Unless we're very lucky, and there's enough advance warning, it's always going to lag behind the response.

So the response plan has multiple components prior to vaccination, and that's maintenance of health care. Doing what we can with antivirals. There's never going to be enough antivirals. There's a lot of magical thinking about antivirals. I think if they were so great we would have been using them a lot, you know, up till now we haven't. So but I think they're critically important and critically important to use correctly in terms of tactical and strategic use of antivirals.

So that needs to be developed. People, if you're going to take them for prevention, if the plan is you're going to protect your staff and blood collection sites by treating with them antivirals, they're going to have to take their antivirals every single day while they're exposed and not miss because the irony is if they miss a

couple of a days, and they're exposed, they might have attenuated influenza, they're going to be infectious, but they're not going to be recognizably sick with influenza.

So it might actually present more of a danger rather than less of a danger, so we need to sort of refine what we're doing here, and I think the industry needs to get on board in terms of this planning in terms of what it means, in terms of business continuity.

The other thing is using the CDC's flu surge software to do protections, and again I don't think the numbers are important, but the shape of these curves I think are very important because this sort of looks at what would happen in terms of inpatient care, that there would all of a sudden be a surge in patients related to influenza.

We wouldn't sort of recognize that for a few weeks, so we wouldn't be reducing other hospitalized patients by canceling elective surgery and so forth for a little while, so I think we have to recognize. And then there would be a peak and

there would be a significant decrease in the number of patients hospitalized for non-influenza reasons, but then there's going to be--they're going to surge back again after the first wave of the pandemic.

So I think in terms of looking at the blood supply, planning has to take into consideration sort of this curve and the shape of the dynamic here because the demand for blood is going to be related to not only the fact that there's going to be a lot of people with influenza and who are going to have complications that might require transfusion, but that elective surgery is going to go down, but that elective surgery is going to have to be made up and some of the things that are going to keep going on, for example, bone marrow transplants and so forth are going to have to keep going on. The demand for blood under those circumstances is going to continue.

What we're doing for the public is basically what we did around SARS. I think we have more empiric evidence that it does have an impact

to do these things, so it's not only that our mothers told us to wash our hands and cover our nose and mouth when we cough. There is now evidence that actually viral respiratory illnesses do go down when you do all these things, so I think we need to sort of keep this message going because initially people are going to--we're going to need people to reduce transmission and people are going to need to know they have to do things to reduce transmission.

And in terms of public preparedness for the kinds of societal disruption, people really need to have a plan in place for their own home. And your employees need to have plans for how to deal with the pandemic because they're going to have to deal with the pandemic and hopefully still do their jobs at the same time.

So a lot of what we're doing at the state level and local level is trying to put into place these prepackaged messages for the public so that people understand what they can do related to this.

Finally, the ongoing, you know, I said all

these things as if we already had a plan that's going to work, and we're getting there. I think we're much better off than we were a few months ago, and hopefully we'll be better off a few months from now. The pandemic can happen any time, and it doesn't necessarily have to happen in the winter either. It could start any time of the year.

So this planning is ongoing. It's always going to be ongoing, but the big issues are the absenteeism, surge capacity, how we're going to take care of people at home or alternate care sites, how we're going to do that, how that's going to be feasible, maintaining public order, and how we're going to effectively use antivirals and vaccine.

One of the things we're doing, we're trying to enhance ordinary influenza vaccination because it builds capacity to vaccinate people when there's a pandemic, but it also drives the market in terms of demand and getting the manufactures to make more and more flu vaccine. You know, unfortunately, we've been in trouble the past few

years in terms of supply, but if we can really get the public used to getting flu shots, it will help when the pandemic comes, and there's now increasing evidence that there's some cumulative effect of getting flu shots over time that might be helpful in a non-specific way with influenza later on.

But, you know, I think just for the sake of driving the market it's going to be useful because the capacity for manufacturing is nowhere near what we would need for a pandemic.

The other thing is we're trying to get everybody who needs a pneumococcal vaccine to get vaccinated against pneumococcal disease because that's something that can be done now. We're not going to have time during the pandemic to do that, but since 75 percent of the pneumonia that tends to complicate influenza is bacterial, and about half of that is pneumococcal, the more we do now to provide for that, the better off we'll be in the future.

We already know we don't do a good job of--a good enough job of vaccinating people against

pneumococcal disease. So these are the elements. You know I think--I don't want to go into this in detail because I think people should look on the Web site. They should be meeting with their public health agencies to get involved in this planning. I don't think it's just enough to go to the Web site and read what's going on.

I think you really need to have representatives and this committee should be recommending that blood collection agencies and a variety, other parts of the industry, the industry that supplies the blood collection agencies in terms of supply. Everything is on just-in-time inventory, but blood banks were the first just-in-time inventory, and so even your supplies, your supply lines are going to be impacted by this, because the truck drivers are going to be sick, the workers and the manufacturing plants are going to be sick all at the same time.

So I think it really, you really need to get involved in through the health department because when this does happen, a lot of things are

going to be managed in terms of how, what's being done, through the public health system.

So what I would suggest is this review of the materials. I've been sort of surprised by talking to people and pointing them to Web sites that this hasn't gone on. I think that needs to be done and people need to get involved.

Everybody has to have a continuity of operations plan. I think that's key. The big impact is going to be maintaining society with absenteeism. That's going to be, you know--everything else is going to be difficult, but that's going to make it even more difficult.

And HRSA is funding hospitals for preparedness. And so that has to include blood collection and transfusion services and transplant programs as well. And then Secretary Leavitt is doing these summits, and I think in each state--he's going to all 50 states--and the blood industry needs to be represented at those summits so that you can hear what's going on and perhaps develop some guidelines that are specific for the blood

collection industry.

And then what I would recommend to everybody is to read one of the books about pandemic influenza because I think John Barry's book is particularly interesting in terms of the politics of influenza, but the classic is Crosby's book, and there are a variety of other sources of information. But everybody here probably spends a lot of time on airplanes, and this is good airplane reading.

Thank you.

CHAIRMAN BRACEY: Thank you, Dr. DeMaria. One of the questions that I have is that in the Secretary's plan, there is a significant involvement at the state level in terms of addressing this pandemic, and it appears, at least in my state, that the response is somewhat spotty, and your state may be in the vanguard. We will clearly try to send a message regarding the blood industry that we're part of the critical infrastructure.

Again, I guess my question is boiling down

to what is it going to take to make all of the states become active and what are your comments on federal response versus the state response?

DR. DeMARIA: You know I think, you know, all the states have to do this because we have to do pandemic preparedness because the pandemic could happen at any time, but that's been true for the last 20, 30 years. So you know I think that right now there's substantial federal funding, and on the state level, there's state funding now too as well to address pandemic planning, and I think we have to take advantage of that to do the best job we can with the resources that are available.

Obviously, the public health infrastructure has always been stressed by a variety of things, so this is an add-on that's going to need--it needs to be done whether we get the funding or not, but it's going to be done better if we have the resources to do it better, and I think that one of the things that we haven't done very well is we tend to meet with the same people all the time.

So we're meeting with local public health which is obviously extremely important whether it's county system, or in Massachusetts we have 351 independent health jurisdictions. So they're very big meetings. And you know that has to continue, but I think we're also realizing we have to be meeting with private industry at the state level. We have to be meeting with a variety of community-based agencies, the blood banks, because it's all connected, and because the pandemic is not just, you know, the pandemic is going on, somebody is responding to it. It's all of us.

It's happening to all of us simultaneously and that's how it differs from the other situations we face. I think that the blood banks have to be very sort of proactive and just insert themselves in the process and just go to, find out where the meetings are. Every state is having a variety of whether they call it a surge committee or the preparedness and response committee, and just get involved and then push the agenda and just say what are we going to do?

I think we've in Massachusetts, we've gotten a lot of push from outside agencies and I think that's good. I think the more we're pushed, the better. We can sort of promote what we need to do with the people who need to give us what we need to do it. So I think the blood banks need to be doing that too because it's an essential service that as far as I can tell hasn't really been prominently represented in this planning process so far.

CHAIRMAN BRACEY: Thank you. Dr. Sandler.

DR. SANDLER: Dr. DeMaria, I looked at the graph that you had that was very interesting where the pandemic would come and the number of hospitalizations goes up and then comes down, and then lagging that by a week or two comes the surge on the blood supply.

From that I took home that maybe one of the messages to blood donors would be if you've had the flu and you're going back to work now, would you be a blood donor? In other words, the target of one of the blood industry's messages would be to

people just getting over the flu going back to work and what have you. Is that an appropriate, given the caveats, of course, that go into models, is that an appropriate message?

DR. DeMARIA: You know I think, you know, it gets to a bigger issue because we're not going to have vaccine for a few months, so there is no way to immunize people against flu except by getting flu. So the experience of influenza is probably better than immunizing someone, and so we really need to have, we really need to have a plan to deploy the immune.

When I first started talking about it, I said deploy the survivors, and our public relations person said oh, no, that sounds terrible, don't say that. Deploying the immune. Because most people are going to just get over it, but they're going to be golden. You know it would be a shame--the example I always use, if you have a nurse who's working in the colonoscopy suite during the pandemic, he or she gets influenza, they come back to work after a couple of weeks, it would be silly

to have them sitting somewhere where there is no elective colonoscopies going on, rather than taking care of a patient with influenza because they're going to be immune to influenza.

They're going to be immune to that specific H and N that is causing the pandemic. So I think not only the donors but employees, you don't want to waste employees who are immune by doing things that are not critical in terms of relating to people with influenza.

CHAIRMAN BRACEY: Other questions? Otherwise, thank you Dr. DeMaria. Okay. Our next speaker is Dr. Steven Anderson. Dr.--let me just get my papers here--got it here. Dr. Anderson is an Associate Director for Risk Assessment in the Office of Biostatistical Epidemiology at the FDA CBER.

At CBER, he uses computer modeling and risk assessment techniques to address critical policy assumptions to the safety of blood and blood products and vaccines and cellular tissues as well as gene therapies.

Dr. Anderson will speak to us today on his model for blood supply modeling with smallpox vaccination as an example and applications for pandemic influenza.

Dr. Anderson.

DR. ANDERSON: All right. Thank you very much. I wanted to thank Dr. Holmberg and the committee for inviting me to share some of the work that we've been doing at the Center for Biologics on blood supply modeling.

I'm going to start out basically with a smallpox example and this basically is a model that we developed approximately two to three years ago looking at the impact of a nationwide smallpox vaccination campaign on the blood supply.

And then I think there's some very valuable lessons and methodologies that we can take from that work and apply it to the issue of pandemic influenza and the impact of influenza on the blood supply.

So let me sort of do a compare and contrast between the example that I'm going to talk

about, which is smallpox vaccination and then pandemic influenza, because I think it's important to highlight some of those differences as I go along.

First of all, smallpox vaccination that I'm going to be talking about, basically we were looking at in this modeling the effect of a 21-day vaccination campaign on the blood supply, and I sort of labeled this in bold that this is really an acute challenge, and it's something of very short duration.

And what do I mean by that? The period of vaccination impact that we were looking at on the blood supply was relatively short, about 45 days, and I think another important factor, at least for the smallpox example, the smallpox vaccination example was that there was certainly more certainty implementing a vaccination campaign, sort of in a pre-event or very early in a smallpox event than there will be with pandemic influenza.

For instance, pandemic influenza could be upon us and we could be in the middle of it before

we know that we are, in fact, in the middle of it. So I would highlight for pandemic influenza there is significant uncertainty, and whenever I see the word "uncertainty," as a modeler, I say, well, wherever there is uncertainty, you need a model to sort of help guide you in viewing the problem and then viewing solutions and potential interventions to deal with the issue and some of the risks.

I think the effect of a pandemic influenza on the blood supply is going to be sustained and long term so we're not talking about a 45 day or 60 day, but something more along the lines of six months to 18 months.

As everybody, I think, has mentioned, in this type of modeling we're going to have to incorporate effects on the blood centers, their support, the transportation system perhaps, a lot of the infrastructure for the reagents that are needed, and also on the demand side, I think several of the presentations earlier have mentioned, and just the previous presentation, that there's going to be health care setting issues, and

on the demand side, it's going to be drastically affected by a pandemic influenza.

And that's something we need to consider in the modeling as well. So I just wanted to emphasize, though, that our modeling efforts at this point are in their very early initial stages, at least for this pandemic influenza issue.

So let me talk about smallpox vaccination as our example. So in 2001, government agencies were developing plans to vaccinate the U.S. population should smallpox occur. And why is smallpox an issue? Well, the smallpox vaccination is an issue because live virus vaccine--it's a live virus vaccine basically, which specifically is a vaccinia virus which offers cross-protection against the smallpox virus.

The issue here is that an individual that's been vaccinated has viremia. If they donate blood, they could potentially transmit--and that blood is transfused in an immuno-compromised individual, that individual could potentially have serious life-threatening consequences as a result

of that.

So in our modeling, we assumed a minimum of 21 days if individuals are vaccinated, that would be required for a recovery from the vaccination, and then during that period, they would be deferred from blood donation. So our blood supply modeling question that we attempted to answer was what would be the impact of a 21-day smallpox vaccination campaign on the U.S. blood supply?

And I'm going to be talking about just in this modeling a more sort of global approach, and this is a national type of model, not a local level model. We can add that level of specificity to these types of models, but right now I'm just talking about sort of a global U.S.-wide blood supply model.

And our modeling approach for the smallpox vaccination was sort of we had two models within the larger model, and one was an infectious disease model where we looked at the number of donors that were affected by vaccination and deferred, but we

were also interested in the people that hadn't been vaccinated as potential donors and then as was mentioned just in the previous question and answer session, interest in recovered individuals because those are where we can draw our collections from and get those individuals targeted for donations in these situations.

So we take that infectious disease modeling results and then link it with the blood supply model. Our blood supply model is actually fairly simple and straightforward. We have a supply and demand type of model. On the supply side, we have collections from capable donors which are the donations that are in the system and coming into the system.

And that turns over on a daily basis. And it's a very dynamic system, and then we have demand side which is need from health care providers, and this is basic utilization of blood by patients. So we have these two components to the blood supply model, the supply and demand.

I wanted to sort of show the various types

of populations that would be impacted potentially, and this is not only valid for our smallpox vaccination but also for a pandemic flu type of event as well.

This is a typical, if you know anything about infectious disease modeling, this is an SIR model. I'm calling it an SVR model, and what that means is we're looking at populations of susceptible individuals, individuals that are vaccinated and then the population of individuals that are recovered from vaccination.

So on the left, this really is a continuum that goes from left to right. On the left, we have the susceptible population. If we have a 21-day vaccination campaign, about five percent of those individuals on a daily basis are going to move over to the newly vaccinated group, and they're going to--and it says under there in those arrows, there's going to be a 21 day recovery. And then a 21 day deferral from blood donation in which they can't donate blood during that time.

But after the 21 days, we're going to

assume that those individuals are recovered and then capable of donating blood. So again think about this as this continuum. It's going to be very important in our concept and thinking about the pandemic influenza situation.

And I wouldn't be a modeler if I didn't have some equations or some variables. So this is math 101 for blood supply modeling. I'm going to keep it pretty simple. So don't worry. Our basic key variable in the model that we're actually graphing in some of the subsequent slides that I'm going to be showing you is that we're going to be showing you the total amount of blood available in the system during a potential smallpox vaccination campaign.

And that blood availability is a function of several things. It's a function of the amount or rate of daily blood collected, and that blood is collected from susceptible individuals as I mentioned, and then also from those recovered individuals which are represented by S and R variables.

Okay. And then finally, we not only have collections to worry about, but we have utilization to worry about, so we basically take our collections, subtract what's being utilized and that's the blood that we have available in the system.

I'm showing you a sort of simple representation of this. It's actually a little more complicated because we have a little bit more math going on, but I didn't want to put everybody to sleep before lunch. I'll wait till after lunch.

And here's a summary of the equations that we used. B sub-a is on the left and then I have collections highlighted under, so we have the blood being collected from the susceptibles and the recovereds, and they're subtracting out the B sub-u to get our blood availability.

Now, the model if you go down further down the slide provides graphical output of available blood units for the United States and this modeling was done using Microsoft Excel.

I wanted to sort of talk about some of the

basic assumptions in the model. So approximately 14 million units of blood are donated on an annual basis. That was our underlying assumption and what that works out to is approximately 38,500 units donated on a daily basis. That's our B sub-c, and then we have utilization, which is 30,500 units we estimated were utilized on a per-day basis.

We have some other factors in here to consider because we have approximately five percent of the population donates on an annual basis. We know that approximately 60 percent of the population is qualified to donate, not the entire population, and then we have these turnover issues going on that we can--the product is perishable. We can only store whole blood for 42 days, and individuals can only donate blood once every 56 days.

So those are considerations in the model. Now, for the smallpox model that actually goes over a short period of time of 45 days, those last two factors are going to be almost irrelevant in the short-term model, but they become very important in

the model as you go to a longer term like a six to 18 month type of scenario.

Those are going to become very important factors in the model. So I thought this was a useful graphic because it shows what happens to the donor population in a 21-day campaign. This is a donor availability graph, and basically on the left on the Y axis, we have the percentage of available donors and then what happens over the period of time in 21 days.

You can see in the middle by the 21st day, we have essentially no donors that are capable of donating because they've all been vaccinated, but by the 22nd day, you can see that dip in the middle. We start getting recovered donors that actually can build back, that we can draw on to build the supply back up.

I think it's very important that as a risk assessor you look at those very low levels between, say, you know, ten and approximately 35 days where we have essentially low levels of blood coming into the system, if any at all. So what do we do about

that if we have very few donors coming into the system?

We've tried them--from my perspective, we model interventions and look at possible policies that we can implement to preserve the blood supply. So in this case, we used the model to evaluate interventions to do that. And the two interventions that we looked at was a policy that increased donation rate by 200 percent, and we assumed that that occur for just a short period of time of approximately 30 days and then the second policy we looked at was an emergency utilization policy which involved in a 50 percent reduction in utilization.

And what that would actually entail was perhaps some sort of emergency order to hospitals or treatment facilities, blood transfusion centers, saying only transfuse blood for lifesaving purposes.

So let's go into looking at not the interventions, but what would happen if we just had a 21-day vaccination scenario going on for smallpox

without doing anything to the blood--without doing anything, issuing any orders to preserve the blood supply and what we would find is--this is going to be tough to orient you without a pointer--but I think I should orient you on these graphs too before I go through several of them.

But that line at zero represents, is the point at which supply equals demand. So at that point of zero, supply is just meeting demand. Anything above that line represents a surplus in the blood supply. Anything below it represents in this case a dramatic shortage, and what we're plotting is B sub-a which is our blood available in the system.

So this is under normal donation rates, normal utilization rates. Our donations are decreasing because we're losing five percent of our donors up until that 21st day when we lose them all and start building them back up.

And what you can see is we have a dramatic--the model predicts a dramatic shortage and it predicts in this case up to 500,000 units.

Now, you notice up in the header I put, it's probably an unlikely scenario because what would happen is you probably wouldn't reach, you know, a need of 500,000 units in the system. There would be self-limitation by hospitals already saying, well, if blood is not available, we're not doing elective procedures and postponement of a lot of procedures.

This is really just a visual to show you the potential impact of a worst-case type of scenario. We can end up in a situation where definitely the blood supply wouldn't be there to meet the demand.

All right. So there are things that we can do. If we increase the donation rate by 200 percent for 30 days, and have normal utilization levels, what you see is that we have a situation in which there would be a surplus available almost throughout the entire duration of this smallpox campaign of 45 days overall.

What we see is that huge sort of hump up there is where we built up enough surplus by asking

more and more donors to donate before they are vaccinated. We build up that surplus and then that surplus is able to take us pretty much through the entire situation, this acute situation.

You'll see around days 37 to 40, though, that we do have a situation where we have a little bump down into perhaps shortages, but that seems pretty minimal given sort of the direness that would be experienced otherwise, given our previous scenario.

All right. So what happens if we imposed the 50 percent utilization rate as a policy, 50 percent utilization rate as an emergency type policy and what you can see is this again also keeps us in the territory where we at least have a surplus of blood available throughout the entire vaccination campaign.

Okay. So the next question that I thought was a very valuable question to look at is what duration of vaccination program would result in little or no disruption of the U.S. blood supply? I think that this slide generally is sort of

illustrative of even things that could happen during the pandemic influenza.

I put down numbers here so that five percent--I need to sort of orient you again on this. Remember we're not looking at 45 days now. We're looking at about 120 day period. So where I put that number 45 percent was from our previous scenario where we had that huge deficit if we took away five percent of our donorship up until 20 days. If we only took back--did a 60-day vaccination campaign shown by the next line up at 1.7 percent, you can see that we'll still have a dramatic effect and a shortage, but it would be less of a dramatic impact versus taking out five percent.

And then if we did a 90-day campaign, only taking about one percent of our population, affecting that at any one time, again, probably less of an impact on the blood supply. Again, there would be an impact. And I think what I wanted to point out was that I think it's very valuable that even if you sort of do a perturbation

where we're affecting the donor base by one percent, two percent or so, it's going to have a dramatic potential, potentially dramatic impact on the blood supply.

All right. So just summarizing this part of the presentation, modeling can provide important information for decision-makers under the impact of, in this case, a smallpox vaccination or an infectious agent on the blood supply.

Models can be used to identify the strategies to mitigate the impacts of vaccination on the blood supply in this case that we used for this smallpox vaccination example, and then smallpox vaccination campaigns greater than 21 days might--greater than 20 days might require one or a combination of interventions to prevent--I'm sorry--to prevent shortages and maintain the supply.

What I didn't show you in this graph, and we've also done considerable other modeling in this, is that you can do combinations of those two interventions I showed you in case there is some sort of dire, dire type event and you can preserve

even more of your blood supply by not only doing the--trying to take more donations in advance, but also cutting back on the demand side and issuing some sort of emergency policy.

And then that last slide, it showed that the campaign that was greater than 90 days might have little impact on the blood supply.

So I think models are pretty illustrative. So we're moving in this sort of virgin territory here with pandemic influenza. So some of the considerations that I put up here for modeling pandemic influenza, it's sort of the real estate mantra, which is location, location, location. I would say uncertainty, uncertainty, uncertainty.

Because that's the type of situation we're facing. And that's not a daunting way to look at it because as a modeler I see that as well that means we need to really be careful and develop a number of scenarios by which we can predict possible outcomes to situations and then have in our pocket from the modeling ideas about interventions that we can use to deal with those

potential risks to the blood supply.

So now the questions that came up yesterday and today, of course, is viremia an issue? Is it possible? If so, what's the duration of that? Pathogenesis and attack rates, you know what are the issues surrounding mortality rates? AIDS specificity of this potential pandemic?

If we have a pandemic like 1918, as the previous speaker had mentioned, you know you're targeting individuals from age to 15 to 50 to have high mortality rates. That's the demographic of your blood supply donorship as well, so that might be a consideration in the modeling.

And then the types of deferrals that we put in place which are for individuals that might have flu symptoms, for exposure and those types of things are all going to have impacts on the blood supply. And probably the last two, which are sort of separated out, was fear, because that's a big unknown. So we've been talking about that for the last two days which is even though only at one time ten percent of our population may actually have the

flu, you know, we had 20, 30 percent of the people may actually hunker down and stay home because they have fear of going out in public.

So, you know, if the blood donors do that, then we may have a significant issue on our hands about the supply.

And then again sort of mentioning this issue again about the effect. We need to consider in these models the effect on blood collection centers, the supportive infrastructure for those centers, and the reagent providers for those centers, and then the health care providers. What's happening on the demand side with patient care?

So, again, our approach here would be and it has been to combine our infectious disease modeling with our blood supply model, just like we did for the smallpox example. We want to know the numbers of donors affected by influenza. We'll calculate the numbers of susceptibles, infecteds and recovered populations based on historical trends and there are also modeling results in the

published literature. Some of those are from Ira Longini and Elizabeth Halloran's group in Atlanta and then Martin Meltzer at the CDC and the French, Jacques-Alain Valleron also has done some nice modeling work in flu. We could import those results into a blood supply model and make predictions on the blood supply from those estimates.

Again, some of the issues that we need to consider in this aspect of the model is the incubation period which it seems would be very short. Looks like one to two, maybe up to four days. The duration of the epidemic is the huge thing. Is it going to be six months? Is it going to be 18 months? That will be a huge consideration.

Again, the blood supply model is just going to be the supply and demand model that I just have showed you results from for the smallpox.

All right. So what's our approach going to be in the infectious disease modeling aspects? We're taking our results actually from the

Department of Health and Human Services Pandemic Plan and we're going to assume up to one-third of the U.S. population potentially could be affected and that would be approximately 100 million people.

And what we would do with working with a number of groups, working with the department and other government agencies, stakeholders and then some other partners as well, is we would work to develop some multiple epidemic scenarios based on the historical trends and the published literature and try to figure out what are some of the most likely sort of ways that a pandemic might evolve, what are some of the worst case ways that that might evolve so that we can use that for planning, and then what are some of the interventions that we can use to reduce the risks to the blood supply from a pandemic outbreak?

An example scenario would be just to do a proportional fit of these 100 million influenza cases to previous infection or mortality curves, for instance, from the 1918 influenza, and then to determine the impact of that on the U.S. blood

supply.

I believe Dr. Schwartz also showed you this epidemic curve and these are the mortalities from the 1918 influenza outbreak for three cities, Boston, Washington, and San Francisco, and we would basically take those curves, and you can see the bimodal type of distribution. We have the peak, largest peak, and then a smaller shoulder out to the further right, and then fit those to our 100 million cases and then look at the potential impacts on the blood supply.

Again, we wouldn't be characterizing people just based on this type of model, who's susceptible, who's already been infected, and who's recovered. The questions that are going to arise is, you know, things like the days of recovery from flu. We're also going to have to possibly input vaccination and drug therapy in this model as well, and I haven't done that for this presentation. But that's a consideration for us as well.

Just some possible assumptions. Again, we're going to be taking it from the department's

pandemic influenza plan. Susceptibility will be assumed to be universal. Again, a large population affected. Perhaps one to ten percent hospitalized. That could affect the health care and blood demand side of things. Infection provides immunity and then several other assumptions as well.

I wanted to talk a little bit about what components we're going to consider in addition, just in our infectious disease model, we'll of course consider perhaps antiviral treatment and vaccination, although our earlier models probably won't deal with that because basically I think that the supply of antivirals for one or two percent of the population, that's not going to really have a huge impact if the problem is larger, if the outbreaks are larger.

And vaccination, again, there's not vaccination--there's not vaccine in the supply chain right now, and so that might take, you know, up to six months or a year to get that vaccine produced. So that wouldn't be an issue at least early on in the modeling.

But we could potentially add those later on, and then the blood supply model. We have a very simple model right now, but we can add some complexity to that as well. Again, we need to add the impact on blood center staffs and support facilities and collections into this model, and we need to add the health care components as well and consider that in the modeling.

We may need to add age specificity to the model. If our donor is between the ages of 18 and 65 or 50 are affected, we may need to consider that in our modeling. If there is a higher mortality or infection or attack rate in those groups, that would have to be considered. And then the other things that we've also considered in adding into these models is ABL and RH plus and minus groups.

We have a global model right now. We could make it more geographical based, break it up into five regions, do a more localized model. I think that we would hear feedback from our stakeholders and then try to figure out what the best approaches would be for modeling.

And then seasonality might also be an issue that we could consider in addition in the model.

All right. So potential outcomes from the model. Pandemic influenza again may have this sort of sustained long-term impact on the donor population and the blood supply. From this modeling, though, I think modeling, at least what I tried to show with the smallpox vaccination example is that it can estimate the potential effects on the blood supply if we do have pandemic influenza occurring.

Again, we can use that to identify interventions to maintain the supply during this long-term pandemic type of event. And I think in the previous talk, one of the committee members mentioned interventions and some of those interventions may actually target the flu recovered population as we were discussing earlier as potential donors.

And that would be especially key in the sort of later stages of the pandemic. You know

initially everybody is going to be susceptible, but you know, as you get a third of the way through or so, you're going to start having a significant size recovered population, and you could potentially target messages to those individuals to donate and try to get those individuals into the donation system.

All right. Just to sort of summarize again, modeling of these--we can actually do the modeling and that's in the initial stages. Again, uncertainty, uncertainty, uncertainty. Considerable uncertainty in the course and evolution of the pandemic and its effect on the supply, blood supply. There are a lot of unknowns at this point.

Blood supply modeling with require input from any sources. I mentioned the department, other government agencies, stakeholders, academics and just other partners, to get feedback on the types of scenarios and concerns they have. And also probably eventually to bring in other products.

For instance, platelets are very important issue. We've done some platelet supply modeling issues for the smallpox vaccination and then also plasma as well and some of the other blood products could be included in this type of modeling.

I think as was mentioned yesterday, this type of modeling work does require a lot of data and research. So it was mentioned by Dr. Hewlett yesterday, the viremia types of questions really need to be answered through research because that's a whole different type of modeling that would need to be done versus are we looking at viremia and the impact on the donor supply and deferrals for those populations in addition to the fear factor that's going to take place where people don't want to donate.

So we've essentially got two things going on. If we can remove the viremia question from the table, either know that we have to include it or remove it, that would be a great help in sort of doing the modeling.

The other thing I wanted to mention was

that and remind people is that modeling is research, so we rely on resources, and I think the other speakers will probably echo that concern as well, that we do need resources to put into this type of effort. It's a gargantuan effort.

The effort for the smallpox work took approximately a year and a half to actually get that work completed, so that was a significant effort. And I think our final goal though is to generate a useful product and outputs to inform planning efforts and decision-makers in their efforts to maintain an adequate blood supply. And I'll end with that.

Thank you.

CHAIRMAN BRACEY: Thank you, Dr. Anderson. Questions from the committee? Dr. Epstein.

DR. EPSTEIN: Steve, thank you very much for that very informative presentation. Dr. Katz drew our attention to the fact that the world looks very different for platelets and could you just comment on the feasibility of modeling this also for platelet?

DR. ANDERSON: Right. Well, we did develop models for platelets and platelets are an entirely different story. So, the turnover rate for platelets is not 42 days; it's five days. You would have extreme shortages in sort of quick time with platelets if you didn't identify those specific platelet donors that you need to have protective measures in place for.

So you would have to target vaccination and then possibly, you know, the antivirals and those type of protective therapies for those individuals specifically to keep the platelets in supply because otherwise it's just not, they're going to be largely affected by a pandemic.

So I don't have the results. I actually should have brought some of the results and showed that as well, but just limited by time here.

CHAIRMAN BRACEY: I had a couple of questions. One is we have to be cognizant of the other needs. That is the blood product, the derivatives. And I would hope that perhaps if we can get the funding which we certainly need for

this that perhaps the modeling of that area might be considered as well.

And then actually that's more of a comment. But the other question is that as this pandemic, if it were to come, business would not be usual, and so your modeling is based upon routine donor criteria. If we want to really examine policy, would we be able to look at or we would consider at least looking at things like lowering the hemoglobin threshold a bit, the impact of that; perhaps shortening the interval of donation?

DR. ANDERSON: From a technical standpoint, I mean we can do all that in the modeling. So I mean we would have to sort of determine what characteristics and parameters we want to look at. If we want to look at, you know, maybe donors can donate, you know, once every 30 days--I don't know. But those types of things can definitely be put into these models. It's usually, you know, just a simple matter of the mathematics.

So but we would probably work with partners at FDA and try to define what types of

interventions could actually, you know, by rolling back some of the current standards that we have in place just to kind of as what if scenarios.

CHAIRMAN BRACEY: Right. Thank you. Other questions? Dr. Kuehnert.

DR. KUEHNERT: Thanks for the presentation. I wondered just now seeing that curve a second time on 1918, and I can't remember from Dr. Meltzer's paper whether they took it into consideration as far as separating out the viral pneumonia from bacterial pneumonia? Because they're interspersed in there obviously and at the present time, the impact of bacterial pneumonia is going to be different, and I just wondered if that's put in the model as far as the efficacy of antibiotics?

Of course, there's now antibiotic resistance to take into consideration. But that should be considered.

And then secondly, the effects of that treatment, which could have hematologic complications. For instance, you know, Linezolid;

even beta-lactams may have some hematologic complications requiring transfusion.

DR. ANDERSON: You know again all of that can be put into the model. I wanted to sort of just mention some of the work that we're also doing. We know there's considerable data on the supply side of things, so actually our efforts--we have a project going on now where we're looking at Center for Medicare and Medicaid Services data and looking at more of the demand side of things and trying to figure out, you know, what are the top procedures that require blood and those types of things.

And there was a question that came during Dr. Katz' presentation about ventilation. Well, ventilation actually in our current study that we have ongoing is about number 15 as far as high mechanical ventilation is really about 15th out of the top 20 procedures that we looked at as far as blood utilization.

So and the question came up, well, can we look at the need for that? People that need blood

and ventilation versus the regular ventilation patients and what percentage of ventilation patients actually need blood and we can do that with the Center for Medicaid and Medicare Services data.

And so what our goal is is to actually try to incorporate some of that information into the demand side of the models so we can take and, let me see, break out some of these curves, for instance.

This is not a good curve to use, but we can say break that down and we know that 20 procedures make up about 50 percent of that curve on a normal basis, and so that would be our goal. Our goal is, well, what would be the impact of putting in an emergency utilization policy, and right now elective procedures number about 30 percent of the blood supply. So you could get there to 50 percent maybe if you had some drastic policies.

But again, we think that sort of the demand side needs to be looked at as much as the

supply side, so we were focusing our efforts on the demand side. Because we think those questions are important as far as--and also therapies as well, that you speak of.

DR. KUEHNERT: I think when you look at ventilated patients, I mean they're not a very homogeneous group, so you just need to look at why they're ventilated. But that subset would be very useful to know.

DR. ANDERSON: Well, we can pull that out of our data set and then look at those a little bit closer as well so--

CHAIRMAN BRACEY: Question from Dr. Pierce.

DR. PIERCE: I've got a two-part question about the fear of leaving home. First, how would one go about quantitating that kind of parameter in the model? And then, secondly, would you be able to consider the excess fear that might be a part of this model from actually going to the blood center to donate and the fear of acquiring the infection at the donation center?

DR. ANDERSON: You could do surveys to determine, you know, people's fear to go out during a pandemic. I mean you would have to get that all through survey information, and then, you know, and also query people about their fears, but, you know, until we're actually in the pandemic, that's, you know, when the hypothetical becomes real.

So you could get some prior information through surveys, but you know that may be sort of meaningless because you know if it's really severe, you know, and this has a high mortality rate, you know, more people aren't going to want to go out.

But if it's like, well, you know, you could get sick, but your chances of mortality are less than one percent, then people might be more willing to venture out in public. So it's more of a function of the actual event and so again it's that uncertainty issue. And we would, actually in the model, we would probably have to say, you know, a ten percent, 20 percent, 30 percent, you know, drop or fear rate and include that in the model and consider that.

So that's how I would address it because I just don't think like prior to the pandemic, we can really get at that, and the committee can discuss that as well, because we'd like input on that as well. How do we actually incorporate that into the model at this point is a big question of ours as well?

So--

CHAIRMAN BRACEY: Question from Dr. Sayers.

DR. SAYERS: Actually can I ask Dr. Norris a question if he's still here?

CHAIRMAN BRACEY: Yes.

DR. SAYERS: Is he still here?

CHAIRMAN BRACEY: You may.

DR. SAYERS: I'm sorry.

CHAIRMAN BRACEY: Just a second. Any other questions, though? Let's finish up with Dr. Anderson. Any other questions for Dr. Anderson?

Dr. Ramsey?

DR. RAMSEY: I don't know who to address it to exactly, but would there be some data from

SARS in Asia about, that could be addressed in terms of the impact on society and going out and, you know, fear and so forth?

DR. ANDERSON: Yeah, I guess I would be more hesitant to use that type of data just because of cultural differences perhaps. Asians actually, you know, you see a lot on Tokyo trains as well and buses where people are not hesitant to wear masks.

And during SARS, you saw, you know, pictures of entire trains where people all had masks on on their faces, and in the United States I have yet to see that, even--so I think there's going to be cultural differences. So I'm not necessarily sure I would rely completely on that data, but--

MR. WALSH: Is there any data from Toronto experience with SARS?

DR. ANDERSON: Maybe somebody else can answer that because I'm not sort of an expert on SARS and up to date on SARS. So--

CHAIRMAN BRACEY: We see no expert on SARS. There's a question in the back. Is this for

Dr. Anderson?

MS. STARKEY: Yes, it is. This is Jane Starkey with America's Blood Centers. I just wanted to ask you to consider the fact that there is probably no normal donation rate and what reminded me of that was your graph where you talked about age groups.

It's not as if every donor has a five percent chance of donating. High schools will all be closed, which will wipe out all high school donors at once. It's not as if, because those donors will probably not come to a blood center. So my suggestion is maybe consider something like access to donors in addition to the donor rate.

DR. ANDERSON: Right. Right now that's actually an average so all those numbers are averages and we can add that variability in. And you're correct. I mean, you know, there's going to be--

MS. STARKEY: And flu season is the high school donation season.

DR. ANDERSON: So definitely we can add

that in, and, yeah, I mean again we're going to need input as to what's not--what's the system going to look like under a pandemic situation. Because, you know, I can just run the numbers of scenarios that people that tell me.

I'm not--I don't have any special magical powers to sort of make that prediction or a crystal ball, and I don't mean that facetiously.

MS. STARKEY: No, I understand, which was why I was making the comment.

DR. ANDERSON: Yeah. I mean I think that's very important to consider that, you know. We don't have all the answers as well, and there are certain things that we will need more information on.

People's willingness to go out in public. People's willingness to donate is going to be a huge factor in this. So--

CHAIRMAN BRACEY: Question from the executive secretary, Dr. Holmberg.

DR. HOLMBERG: Yes. That raises a good point, Jane, and I was wondering if Dr. Katz or Dr.

Bianco has a figure of how many or what percentage of the donations are from high school students during the school year?

What is the percentage of donations from high schools during the school year? I'm just thinking during the high school--during the school year.

DR. KATZ: The percentage from high school donors--you know, it varies so much even in our system from subcenter to subcenter and mobile staging site to mobile staging site, I would guess, if I tried to average it over a month from September through April, ten percent, maybe closer to 15. It depends. I mean we do some huge mobiles at high schools and in a given week, it may be half our blood supply in September when we're gearing up again as kids come back to school.

So that's probably a ball park, but I don't know if it's precise.

CHAIRMAN BRACEY: Question from the audience.

MR. ZOU: Shimian Zou from the Red Cross.

Just a comment on the earlier question. There was a survey in New York City of health care workers. One of the components was about SARS, even it says how willing or how able are you going to report to duty? Up to 50 percent said they may not be able to or they may not be willing to report to duty.

Just information.

CHAIRMAN BRACEY: Thank you. Are we finished with questions for Dr. Anderson because we have another question for the previous speaker? Thank you, Dr. Anderson. Very good.

DR. ANDERSON: Thank you.

CHAIRMAN BRACEY: Your question?

DR. SAYERS: Yeah, thanks, Art. This is really a stretch. It's a question for Dr. Norris. I know we transfuse viruses by transfusion. We transmit viruses by transfusion. Given three million patients that are transfusion dependent a year, given 40,000 donations a day, I have no doubt that over the past decades, we have unwittingly taken blood from individuals who are infectious for Influenza A, asymptomatic but maybe viremic, and it

just seems intuitively right that somebody would have identified post-transfusion influenza in individuals, particularly bearing in mind so many of those transfusion recipients are immuno-compromised.

It just seems intuitive that somebody would have identified influenza as being a risk for transfusion. So I'm just wondering if there is anything unique about influenza that renders the circumstances under which we store blood and components hostile to the virus' survival?

DR. NORRIS: Yeah. That's a good question. So the question really gets at the viability of influenza with our current storage techniques.

I mean there are parallels for this. If we look at syphilis transmission, transfusion transmission, the refrigeration of the red cells seems to kill of the spirochetes.

I don't know that that exists for influenza and intuitively, you know, it's a virus, I think it probably should survive the storage

techniques. I don't know of any studies that have looked at the viability and I think that's something we could address certainly with animal models such as the macaque model that's being talked about right now. It's a good question.

In terms of us having identified it, I think that even if existed, we probably wouldn't have identified it because we're really not looking for it at this point. So that's the second answer to your question.

CHAIRMAN BRACEY: Thank you. In the interest of maintaining the nutritional needs of the members of the committee and the public, we'll take our lunch break now and resume with the two speakers in one hour's time, so that will be at 1:40.

Thank you. And those members of the writing subcommittee, we will have lunch here. Thank you.

[Whereupon, at 12:35 p.m., the Advisory Committee recessed, to reconvene at 1:49 p.m., this same day.]

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

[1:49 p.m.]

CHAIRMAN BRACEY: Welcome back. Our next presentation is by Brian Custer. Dr. Custer is a scientist in the Epidemiology and Health Policy Research Section of the Blood Systems Research Institute. Dr. Custer has been involved in REDS II and has done extensive literature review of economic analyses of blood safety and transfusion medicine interventions.

In addition, he developed a community blood supply model. This model allows for considerations of multiple factors related to the quantity of safe blood in the blood supply, and the specific talk will be the community blood supply model and its potential role in planning for pandemic flu.

Dr. Custer, thank you.

DR. CUSTER: Thank you. First, I'd like to thank Dr. Holmberg for inviting me to speak. So you just sort of heard the overview and what this talk is really going to be composed of is sort of

describing this model and then looking in a very simple sort of first pass approach at how it could be used to think about the impacts with relation to pandemic flu.

So as kind of already indicated, the idea behind developing this model was to try to develop a model that could be used to look at tradeoffs between safety and sufficiency of the supply and then also incorporate in cost factors in terms of procuring blood from different donors and what the implications might be because there are cost differences for different donors, and then of course, to try to roll that out and use it in a meaningful way with respect to looking at threats to the supply.

So to start, what I actually want to do is unfortunately these plots are not easy to see, but I wanted to just sort of describe sort of how one starts to work through the issue of the donor base.

So what these plots represent is actually obviously at the top of each little plot is sort of a stratification. You have eligible female donors

who are repeat donors in the very upper left, and then what happened is actually this is a whole donation year's worth of data plotted on the X-axis and the age of the donor is on the Y-axis.

And so what you kind of see is sort of the space, the relationships that might or might not exist with respect to donors. The red line is incredibly hard to see, but there is a red line that goes across all of these plots. That is the mean age of the donors on that given day.

You can also see sort of some white striations. You can see days where there were not collections collected. So days when the blood center wasn't collecting.

The purpose of this plot, and it's actually really difficult to see, is that when you look actually at first time donors, you start to see that there is a mean age that changes throughout the course of the year, and that's particularly in relation to school-age donors who donate during the school year, but then during the summer the mean age of first-time donors goes up in

reflection of those donors not being present at school blood drives.

Similarly if you look instead of at eligible donors but short-term deferrals, and short-term deferrals I'm defining those as deferrals between one and 56 days in length, not post-donation deferrals, but actually deferrals related to eligibility, you can also see this mean age is easier to see now that there are less data points. Mean age fluctuates particularly for first-time donors. Once again, attributable to school differences, differences with donations with respect to school year.

Okay. So the schematic of this model is to first start by stratifying the donor population into relevant age and gender groups. That then is actually input into the sort of core of the model which I'll describe which goes through a process of saying through probability equations, whether you're eligible to donate, whether collection is obtained, and then also infectious disease marker screening.

The next point then feeds back to sort of some summary estimates, and then finally going back into actually representing to donate again at another time in the donation year, and what happens then, though, is you restratify the donor base because it involves repeat donors and then also new donors coming in, but all of those people aren't obviously necessarily presenting at the same time.So I hope to make that a little bit more clear in just a second.

So what is this design and what is this model? So all model parameters are estimated using year 2000 Blood Centers of the Pacific data. It's a cohort simulation. Probabilistic sensitivity analysis through Monte Carlo simulation. It's not a micro simulation, and what I mean by that is that I am not counting the individual experience of individual donors. Instead, we're using those stratified age and gender groups to make broader statements about general groups in the population.

Costs or results are determined from both the societal and the blood bank perspectives. In

this particular iteration of the model, the focus is whole blood donation from allogeneic donors, and the time horizon is one year.

The key factor in the model, of course, is the 56 day post-donation deferral interval, and what we used that to do was we took that, cut that into instead of being 56 days to two month intervals and created six cycles over the course of a year to look at. So the model was intentionally designed this way so that you could either look at events throughout an entire year or acute events during a two-month interval.

I should say that the model is scalable. I will show you a little bit of the model. I can set the initial cohort to whatever is the relevant value, from the purposes of Blood Centers of Pacific data, that's about 120,000 presenting donors in a given year, but that could be a million or it could be a thousand, and you can still sort of, at least, determine scale effects.

So and then finally through what if analyses or sensitivity analyses, you can look at

different--how different parameters, changes in different parameters might influence the number of units that are obtained.

I'm not going to spend any time on this. Suffice it to say this is the core model. There's a little bit better indication of it here. What happens in this model is that you're making a decision between Policy X or Policy Y or perhaps thinking about an event. Donors come into donate. From then on, what happens with each individual demographic group, the probabilities are different, but the model structure is the same, and that's as presented right here.

So you can see the first time donors. There's a similar line that would be for repeat donors. First time donors are either eligible to donate, determined to receive a short-term deferral, a long-term deferral which we define as between 57 and 365 days in length, or a permanent deferral which are true permanent deferrals, three-year deferrals and up to five year cancer-related deferrals.

From then, you're either able to donate or not, meaning you faint, the phlebotomist can't locate a vein, these kind of issues. After that, if a unit is successfully collected, it goes into screening. If it then meets the screening requirement and also then meets sort of appropriate weight requirements, it's not a short, then it actually can be a unit that's cleared for release or processing into other components.

Okay. So this by way of just example is to try to demonstrate that truly there are differences in the risks of people being classified as a short-term deferral, a long-term deferral or a permanent deferral based on age and demographics or age and gender and specific.

So in this table, I'm using the referent group as males who are 55 years or older, who are repeat donors, and then you can see relative to that category some donors such as actually first-time donors who are older have a much higher likelihood of actually being deferred, permanently deferred even.

So to just kind of go back to the actual structure, it's eight demographic groups based on 15-year age intervals. There are nine outcome parameters estimated for each demographic group within each two-month period for the model year, and there are the six cycles over the course of the year.

All of the model probabilities reflect the frequency of events observed in two-month intervals of BCP data, and the model then has 432 event probabilities in the baseline.

Okay. So, results can be generated in terms of two-month intervals or any multiple thereof with respect to transfusable units obtained, deferrals characterized by duration, miscollections, underweight or overweight units, disease marker positive units, and then also total and per unit cost for blood bank perspective and an estimated cost for the societal perspective.

I am not going to talk about the costs today. I think that the focus is more on issues of the sufficiency of the supply with respect to

pandemic flu.

So once again, this is just a slightly complex table, but the idea is to just sort of say when you break down the demographic groups, the donor base into demographic groups, you then see differences in impact. It's difficult to see here. I think I won't spend any time on it, but you can get output for all those various kinds of categories, a short-term deferral, the unit cost for individual donors, and so on and so forth.

Now, this slide is not really about model validation, but it is about kind of toward validation, so we developed this model using BCP data. You then run the model and you hope that the model then reflects what the actual data was. And so the purpose of this is just to show that generally speaking, the model tracks what you actually observe in BCP data pretty well.

There are some divergents and I believe that you were provided with the paper. There are some further explanations for why we believe those divergents happened particularly with respect to

first-time donors collections screened.

So what doesn't the model do? The model with respect to costs looks at mean costs and not incremental costs. I think that it would be really interesting to think about what are incremental costs of replacing deferred donors, but this model can't do that, given the way that it's structured. It's a supply model. It does not address demand or utilization. And also the model doesn't fully track the experience of the most dedicated donors who come in in that 56 to 61 daytime period.

I will also just make a comment that I understand the model well, and I'm going to show you a few of the details in the model. I think you might find it a little bit confusing so it could benefit from a little more user friendly interface.

With respect to some additional limitations, it doesn't include components. It doesn't include outdates. Once again, the model parameter specific to BCP. The cost parameters may overestimate the cost of obtaining whole units of blood. And there are some issues with respect to

whether it fully accounts for societal costs.

Okay. So what I wanted to do is spend sort of the remainder of the time, after having kind of introduced the model, talking about how the model then might be useful in thinking through pandemic flu. So these are some of actually the assumptions in the DHHS documentation that I've seen.

The community will be affected for six to eight weeks. That's particularly convenient from the standpoint of the way that this model was developed and that it looks at two month intervals. Multiple waves could occur so that you could go into a new cycle, but in specific, about what I wanted to show today as sort of preliminary data, looking at the attack rate of overall 30 percent, but perhaps higher for children, in the case of the model I'm calling children 16 to 24-year-olds. Some might disagree. But then for working adults, a 20 percent attack rate.

So what does that mean? Could we put that in the model? Well, I did, and I will perhaps see

if I can--now, I'll show you the model. So I've definitely tried to blow this up, and the disadvantage of doing this is that you cannot see the whole page at one time, but for a given theme, we could actually set, once I set--like I said, the actual presenting donor cohort to whatever appropriate size. That cohort is then broken down based on the percentages observed in any given data source into the age group and then gender specific things, and then moving over, you have the cycles, and you have the percentage of donors within that demographic group that present in that cycle, and then here actually is where I started to try to incorporate pandemic flu assumptions.

I used the January-February interval as an example, and these were the assumptions that I made. Most likely, loss would be 40 percent in 16 to 24-year-olds, 20 percent in other age groups. Always trying to incorporate some level of uncertainty with respect to it, I actually said, well, what if it was 30 percent to 50 percent in 16 to 24-year-olds and ten percent to 30 percent in

other age groups?

So that feeds into a series of pages that look like this. And so what happens is you then break, and this is sort of that core structure that I showed you, you then break the donors into first time versus repeat donors, and then there is a series of probabilities that follow from whatever happens with respect to what you observe in the data.

That then goes back to the output file and the output file actually includes all of these various parameters that I had talked about. Number of successful donation attempts, number of first-times who visit during a certain cycle and so on and so forth, so going all the way through.

Okay. And that's probably enough of the model for right now. So, with those assumptions specifically focused on the January-February time period, in the normal year, Blood Centers of the Pacific sees about 17,000 16 to 24-year-old donors during that time period. There's an uncertainty around that. Fairly tight uncertainty in that year

in, year out, but there's not a lot of variability unless we try to scale up and recruit more donors.

However, then in the face of pandemic flu, actually you see a pretty significant donor loss. I'm sorry. I think I've made a mistake. In January through February, you have a total of about 17,000 total donations. That's not specific to the 16 to 24-year-old groups. That's total donations. Overall, you then actually with pandemic flu and those assumptions that I described, you see a loss of around 3,500 to 4,000 donations. That would represent a 22 percent loss. Incorporating that uncertainty of those values I gave you, that would be about 20 to 26 loss within that interval.

And it shouldn't be a surprise at all to think that if you've broken the demographic--the donor base into demographic groups, essentially what this is it's a very fancy weighted average calculation of what the impact would be.

I didn't go through and model whether there would be recurrence since you would think about what might happen in the March to April

interval at this point. It's just sort of a preliminary look at this to see whether there's interest in using these kind of techniques to think through pandemic flu.

But I think there's an important point to make, which is I think it might lead to an acute shortage over the course of the year. If you look at annualized year results, you're going to see a relatively minor impact as things return to normal, and I think it's always that time interval is going to be critical in terms of thinking through what the impact is going to be.

Okay. So I'm going to finish up just saying that right now the model is undergoing an update, and that update is actually using blood systems data from 14 blood centers and we're redoing the model adding those parameter values so that it has greater generalizability.

In addition, we're actually incorporating double red blood cells. At this point, specifically because we will still define demographic groups in terms of their eligibility to

donate, but then you're either shunted into a sort of double red cell collection module which has a different time interval, 128 post-donation deferral, or the standard whole blood collection, and I just wanted to acknowledge people who have participated and provided data for this, and with that actually I will take questions.

Thank you.

CHAIRMAN BRACEY: Thank you, Dr. Custer. Are there questions from the committee? Dr. Sayers.

DR. SAYERS: So this model then would enable you to predict how you would have to enhance double red cell collections to make up for whatever losses you might anticipate during the first wave of the pandemic?

DR. CUSTER: I think that's correct. The intent would be to then look at those tradeoffs, so if you saw once again that someplace there was evidence that pandemic flu was coming, and you tried to shunt as many donors as you could into double red cell collections during that acute

interval, you would at least begin to offset that supply to some degree, and this model would be capable of looking at those tradeoffs.

It also, you know, with respect to that, you could also think of if you really do, as you model things out, think that there's going to be a severe impact perhaps, you think of altering deferral criteria and any sort of decision that's made in terms of altering deferral criteria that might up eligibility to donate in a certain interval could be incorporated into this model and looked at also what the implication would be in terms of the available supply.

CHAIRMAN BRACEY: Dr. Bloche.

DR. BLOCHE: Could you say some more about how you estimate the reduction in donors or number of donations?

DR. CUSTER: Sure. Are you meaning specifically with respect to that slide that I sort of estimated?

DR. BLOCHE: Yeah. For instance, the 20 percent amongst the so-called adults, the above 24

years?

DR. CUSTER: Yes. What I did there is actually I ran the model as though there weren't the pandemic flu assumptions. Then I ran the model with the pandemic flu assumptions and it was just a question of calculating, adding up the total number of units that were lost in the face of actually with the pandemic flu assumptions and then just doing a percentage based on the standard supply.

DR. BLOCHE: And when you refer to the assumptions, are you talking only about people getting sick or are you incorporating hunkering down kinds of responses, various subjective or panic responses or the other factors?

DR. CUSTER: I haven't thought through it more formally than just include sort of those estimates of the attack rate. So only the attack rate, only the assumption that those people who are sick, either do or don't come into donate. Exactly what's driving that, this doesn't get at sort of that finer information and it doesn't explicitly incorporate sort of people's unwillingness to come

into a center to donate.

DR. BLOCHE: So to the extent that people are more reluctant in general to go out into the public space, the model underestimates the reduction?

DR. CUSTER: The model would definitely underestimate that because if you just have people who are unwilling to come to a center for whatever reason, then the impact would be more than just perhaps the people who became sick.

DR. BLOCHE: Right.

DR. CUSTER: And the impact could be even more severe, and an acute shortage of whole blood.

DR. BLOCHE: It does strike me that perhaps looking at the SARS experience or other recent experiences, one might be able to come up with some numbers to very crudely estimate the hunkering down effect.

DR. CUSTER: Uh-huh.

DR. BLOCHE: Then you could factor them in and come up with some other final estimates of the loss of--

DR. CUSTER: Yes, definitely you could.

CHAIRMAN BRACEY: Dr. Epstein.

DR. EPSTEIN: In a sensitivity type analysis, how much does the age stratification and the time stratification really get you in terms of the effect on the estimate? In other words, there's a cruder cut yet, right, which is you just take the averages across.

DR. CUSTER: Well, I guess part of them showing that sort of changing mean age of blood donation over the course of the year is trying to get at that. In the case of something like pandemic flu, I don't think that it's wise necessarily to just make broad averages because I think that you have differential impact and belief in differential impact, and also you see that you have differential kinds of donations from the different age groups.

In something that's a different kind of policy or event that more broadly affects all individuals the same over a longer time period, you may not need that careful stratification.

DR. EPSTEIN: Yeah, I understand that, but I'm asking a quantitative question. What I'm saying is having done all this stratification, how much of a difference does it make compared to the average calculation?

DR. CUSTER: I haven't done the average calculation, so that's a difficult thing for me to say. What I can say different question altogether, but even using these same kind of modeling technique, and this is not going to exactly get at your question, but it is I think relevant, you can see a demonstratable difference in the cost of obtaining transfusable unit of blood from the different demographic groups.

And so I think that there is at least suggestion of evidence there that the finer stratification can be relevant and may be relevant, but I have not formally looked at it.

CHAIRMAN BRACEY: Given a limited quantity of vaccine, we may not be able to vaccinate all blood donors, and so one of the discussions that we had was, in essence, trying to develop strategies

for vaccinating committed donors.

Would your system or your analysis be able to tease out estimates of where we might target those vaccinations?

DR. CUSTER: Well, certainly from the perspective that if you were going to target your most productive donors, your most productive repeat donors, one could further stratify and actually say not losing them from the supply based on the fact that you had previously vaccinated them would lead to "x" percentage increase so I think it's feasible.

I haven't thought through formally how you would exactly incorporate that additional bit of information, but if you had specific demographic groups that you wanted to focus on, the model is definitely capable of doing that at this point.

CHAIRMAN BRACEY: Okay. Other questions from the committee? Thank you, Dr. Custer. Thank you.

The next speaker will be Dr. Shimian Zou, who I mistakenly introduced earlier, and let me do

that again. Dr. Zou is the Senior Scientist with the Transmissible Diseases Department of the Holland Laboratories of American Red Cross Biomedical Services located here, well, in Rockville.

Dr. Zou has been very active in the study of transmissible diseases, and Dr. Zou today will speak to us on Assessing the Potential Impact of Pandemic Influenza and Other Emerging Threats on the Availability and Safety of the U.S. Blood Supply.

DR. ZOU: Thank you, Dr. Holmberg, for inviting me. I guess it's going to be difficult for me to do this talk after so many good talks, especially the ones by Steven and Brian because we're basically talking about the same thing.

The topic of my talk is Pandemic Influenza and the Blood Supply. It's only a study proposal. I think for the completeness of my talks, I'll still go over these issues even though I know you have heard a lot and you may be tired of hearing this again.

So as we know, pandemic influenza can be caused by--that's what I was told when I was in school--by antigenic shift, which is caused by a reassortment and mixing infections in pigs. That's the theory at that time.

But now it's apparent than even humans could be mixing vessels. So we have a direct jumping across species which is a newer phenomenon, and avian flu and highly pathogenic avian influenza, H5N1 and H7 and others.

The pandemic potential of existing avian viruses in humans. As we have heard so many times, the viruses can directly infect humans, but the transmission from human-to-human is very inefficient. But even so, it does occur.

So to me the existing avian viruses have a low epidemic potential I have to say as they are, but they can change. I was going to say the risk is these viruses can mutate very rapidly because they can cause severe disease in humans already. So if they do mutate and further adapt to an efficient transmission among humans, so that's the

real risk we are talking about right now.

So in terms of the blood supply, as you know, the Red Cross has 35 regions across the country. We have about four million donors annually donate over about seven million units.

So the challenges to the blood supply, not only Red Cross, but the whole blood supply, has been safety which has been very safe right now, but we paid a higher price as well.

And then now we focus on, I'll talk about also availability, especially in difficult times and also for certain products. So this has relevance for modeling for prediction. And of course, contingency planning and accommodation is always a difficult issue like following the September 11 attack, but I think this time after Katrina, we did a much better job.

So what could happen to the blood supply when pandemic influenza occurs? First, let's look at safety. We have heard that viremia can occur among infected individuals, but the chance may be low, especially in asymptomatic infections, and

also to me a very important issue and we have heard again and again, is the influenza's normally is transmission is through a respiratory tract, and can also occur through epithelium cells, but whether the virus transmitted through transfusion can cause infection or can cause the same kind of impact infection we don't know.

So the only way, according to the information we have right now, so I think the potential impact on safety side should be small. Of course, I cannot say it's zero.

Now, let's look at the potential impact on the availability side. I did a very, very crude calculation based on a model which was prepared by CDC published in 1999 by Martin Meltzer and others, so in a model the assumption was attack rate from 15 percent to 35 percent and also a lower intervention was included in another model.

So when I used the model, I didn't use assume any self-deferral by potential blood donors and also I didn't include, make a reduction in donations due to a panic or unwillingness to come

out and donate, and I didn't include any additional deferral by FDA. So just basically plug in the age distribution of regular blood donors into the model and come out with a number which is eight to 19 percent of blood donors could be infected, and 97 of those would have no need for hospitalization.

And I also tried the same thing for Red Cross employees. At that time, I only used the employee data from one region. Actually last night I got the data from the whole Red Cross, but I didn't have time to do the calculation. So assume I used the same model, same attack rate, 15 to 35 percent, the same assumption, no intervention, and also I assumed no reduction in reporting to duty due to panic or unwillingness to come out and work, and no additional loss due to quarantine by disease control authorities. So the result was eight to 18 percent of blood supply workers could have been infected and could not report to duty.

However, as I said, some of the blood donors and blood supply workers may have to stay home to care for family members who are sick

because they are infected by influenza. More donors and workers may be unable to or be afraid or unwilling to show up for various reasons.

And also I would like to mention in the rough calculations I did, I didn't break down like for blood donors, for example. Blood donors of certain components like platelets may be different from others because the demand may be different. The impact during a pandemic may be different.

In terms of staff who are working in blood collection, process and delivery, I didn't break down into like here, for example, critical staff like myself. Even if I'm working for Red Cross, if I'm sick for eight weeks during a pandemic, it doesn't impact the Red Cross blood collection at all, but if some people in the central testing are sick for eight weeks, that will have a huge impact, so that hasn't been built into the very crude calculations. So those numbers just give you a kind of ball park.

We just talk about the supply side, so also, as we have heard many times, we need to look

at the recipient side, the demand for blood side, because during a pandemic there will be an impact as well.

So that could be reduced. Admissions to hospitals, and hence reduce the need for transfusion. So if there is an impact, how much? And also as we heard, delayed elective surgery stuff. There could be also reduced need for transfusion among hospitalized patients who are already in hospital but because of pandemic, so there could be a reduced need because of cancellation or postponement of surgeries, et cetera, et cetera.

And even the hospitals may not have enough staff to do all the work. So, just one point I'd like to mention is I did look at the data available, I think in the U.S., roughly half of the blood was for medical treatments and half of the blood is for surgery, very rough data.

I was trying to get data about elective surgery, how much of the blood was used for elective surgery. I couldn't find it. And I was

trying to contact the Agency for Health Care Research and Quality because they, I am glad to find out, they have established a system. It's called the Healthcare Costs and Utilization Project, which basically has random sample of hospitals across the country, so they collect some data, but I haven't looked at the data yet.

I got an e-mail last night, but I didn't get time to look into the data elements to see what's available, what's not. So from what I have found so far, if we assume like half of the surgery is for elective surgery, for example, that could be, during the pandemic, we could have a reduction in demand by a quarter, because half of the blood is for surgery, half is for medical.

If we assume that medical treatments are essential, we cannot delay at all. If we can assume half of the surgery like treatments are for elective surgery which could be delayed, so that's a quarter reduction, but just a ball park. As I said, I haven't looked at the real data from the Agency for Health Care Research and Quality, so I

can't really say.

So to me, the questions are by how much will the reduced need for transfusion be including for different components? And by how much were staff absence affect the blood supply? And by how much will various factors affect the donors' donation? Here we can single like donor demographics and also collection size, sponsoring groups. These are also important because if many groups cannot sponsor collection anymore during the pandemic, if many sites are not available, this will have impact as well. And how much impact will different intervention options have on blood availability?

So we can propose a lot of intervention options, especially in emergency or during a crisis like pandemic flu without enough time to assess impact. The impact could be huge. As I was talking to Steven during lunch, like when we did risk assessment for CJD, at that time, based on a very rough survey of donors who traveled to UK, we estimated the impact could be one percent, but as

we all know, like the impact, the true impact is much more than one percent because we didn't take into account those people who self-deferred because of the policy.

So these are important issues. When we propose new policies, we have to think about this carefully.

So what's needed? So to me we did a model that can incorporate many unique aspects of the blood supply system including like the donor donation, donor deferral, blood collection, screening, processing and delivery. We have heard like delivery will be important as well and not only for supply but also for products. And staff attendance and production capacity. Recipients and their transfusion needs for different components. And also mitigation efforts such as inter-region transfer of certain products could be limited but may still be possible. And also we heard a lot about the uniqueness or importance of platelet availability and platelet apheresis collections.

And also the model should be able to allow

ready assessment of impact of changes in various elements that may affect supply or demand and assessment of intervention options such as what we heard--antivirals, vaccination, provision of care for sick family members of key staff members, and reduced admission of certain patients to hospitals, and postponement or cancellation of certain medical procedures, and additional donor deferral options.

So we proposed a study. Actually the idea was generated in the late 2004. At that time, the idea was to develop a model for the blood system and then to use the model to describe the successful story of West Nile. You know we can learn from mistakes. We can learn from failures. We can also learn from great success like the West Nile control is a great success.

So I wanted to use a model to describe the success we have had so far with West Nile, and we did include the pandemic flu as once we have done with West Nile. We can use that for pandemic flu and other things once we have a model established.

But I didn't--I never got time to work on

it because we got other things to do. But anyway, the idea we had was to establish a model for the blood supply system. The model should be based on widely available software and also based on existing data from Red Cross and other sources and also have a multiple components, but these components are also linked to each other, and the model should be validated so testing in different populations.

This just gives an overview of what we thought about that. We didn't really have even a picture of the model. So the idea was to start from the general population to the recipients. So for the general population and for blood donor population, and also blood components and also patients need in hospitals and all those kind of probabilities from one group to another or from one stage to another. It is the balance of blood supply to demand by components.

Just to give you an example of some of the components. For example, this is about elements of the blood donor component of the model. We have

gender, age, race, education, composition of U.S. population because they have different donation rates.

And also the change in pattern over time. At that time, I was interested in the seasonal and also the long-term impact because we did a study, kind of internal study, there is a change over time, both long-term and of course seasonal. We heard about seasonal today.

And also composition of first/second time donors, and the repeat donors and the regular donors or more committed donors. Retention rates, donation frequency and blood drive type, and sponsor type, and the staff capacity, gender, age, contingency capacity especially for key operational units.

Donor health history deferral rates of different donor categories, and also infectious disease and marker positive deferral rates of different categories. And also impact entry for reduced presentation during a crisis such as pandemic flu.

This is another example of the medical exam and health history deferral component. The elements could include like donation interval. As we heard today, there could be changes over the interval as well. Could have a shorter interval or could have a longer interval, like as we heard for women, for example, some proposal, a longer interval, so there could be changes so I would like to incorporate that into the model as well.

And also we have physical deferrals like temperature, blood pressure, pulse, weight, hemoglobin and inspection of arms, and deferral for donor safety questions, deferral for general blood safety questions, deferral for specific bloodborne or sexually transmitted infection questions, and deferral for potential new or emerging threats for which there is no screening test, deferral for other questions.

And also deferral like different deferral periods, and also the changing pattern over time as well, seasonal and long-term, and deferral rate for different categories. And also donor reaction

following donation and other related factors.

And for the blood demand side, for the recipient side, these are the elements we thought of, like utilization of different blood components by recipients and the composition of recipients by demographics, disease categories, procedure categories, impact in entry for reduced admission or demand during a crisis such as pandemic flu and also entry for proportion of transfusion that can be delayed or canceled in a crisis situation.

So once a model is established, the plan was to or is to use the model to assess the likely impact of pandemic influenza.

This part of the modeling might be different. Something would be built based on the model I just talked about for the blood supply system, but because of the dynamic nature of flu pandemic, we may have to introduce some new different components, maybe a dynamic component, and the likely impact on both supply; that means donor and blood center. Also demand; that means recipients and also hospitals.

And infection of blood donors. Further reduction of donation due to other reasons, and infection of staff and further reduction of staff for other reasons, and also impact on transfusion needs by components, and of course the risk of transfusion transmission. So it could be low according to the information we have so far.

Then we use the model to evaluate intervention options like we can evaluate whether reduced attack rates or how much will be the impact. So that will probably be done through general public health measures, and also if we have measures to protect blood donors, to protect supply workers, antivirals, vaccination and others, and also cancel or postpone certain transfusions, and of course to introduce new donor deferral options. Hopefully, we can have a chance to do the evaluation before we implement something.

So what are available? I think we should have general epidemiologic data on influenza. CDC is very good at collecting data. And also I guess WHO will have some data about the global picture.

And about donor donation data, we have the data and other presenters have the data as well. And donor deferral, same thing. Donation management, staff capacity, that should be available as well. As I said, I got some data even just last night.

And also utilization of blood products data. As I said, the Agency for Health Care Research and Quality has--HCUP, Healthcare Cost Utilization Program. But from talking to people briefly, the data may not be as good as I thought, so we may have to do some studies in hospitals, for example, find out how much of the blood is for elective surgery which could be postponed or delayed. This is important information for the modeling process if you want to get a balanced picture of the supply and the demand.

And, of course, the experience with related diseases such as SARS, which I would say a bit more about the comment I made before lunch. Actually afterwards, a lady talked to me. I think it's a very good point. The likely impact about

the SARS, which is different from influenza, because SARS as you know, the case fatality rate is very high, like 60 percent.

So with pandemic flu, I don't know. It could be, people may think it was staff missing, it's not as much as SARS, so they may be waiting to, more waiting to come out. We don't know. So I guess we may need to do more study to find out. But nevertheless, the experience with SARS should be very, very useful. And, of course, research results on health care providers.

So what's next? We plan to organize working group on pandemic influenza and blood supply and then this group will help us to lay out modeling framework, and then we, of course, need to seek advice and comments from relevant experts on the framework and to optimize the model design.

Here I'd just like to elaborate a little bit. I didn't do the modeling exercise myself, but I was involved a little bit. I think, actually you're the real experts to judge whether modeling is good or not. Don't even look at those fancy

equations. If you look at the input elements, if you look at all the four elements, if you look at the major key parameters, you can get an idea how good a model is.

As far as I can recall, from the history of epidemiological modeling, many of the modeling results are just junk. But a few cases, the modeling results did conflict with conventional wisdoms, which later on were found to be correct. So modeling is good in that it suggests important clues.

Also, like if the conventional wisdom is not good, it's not right, the modeling results would be very critical, but any results from any modeling should be verified no matter how fancy the model is.

So I think that's an important component, and then of course we want to model the blood supply system, followed by the impact on flu and other things.

So expected results. We hope to have a model for the system. That's what we wanted to do,

and I think this time for the flu purpose, we should do it. So the idea is the model will reflect the entire process from potential donor to recipient including major influencing factors or elements.

And the model can be used to assess the effectiveness of impact, an impact of intervention options, and can be applied with, of course, modifications to other situations. I'm sure there will be other events, other circumstances which we may be able to use the model as well. So of course, the second set of results will be for the estimated impact of pandemic flu on the blood supply.

And now I'd like to acknowledge, we have ARCNET Study Group which represents the Red Cross, a lot of work of interested researchers and people and staff. Roger, Chyang, Sue, basically they initiated the whole thing. I joined the Red Cross just a few years ago, so--and we have physicians from blood centers and also we have regional staff and also staff from my group.

Thank you.

CHAIRMAN BRACEY: Thank you, Dr. Zou. We have a question from Dr. Epstein.

DR. EPSTEIN: Thank you. I have both a comment and a question. We've now heard three different modeling system approaches, by Dr. Anderson from FDA, by Dr. Custer from Blood Systems, by Dr. Zoo from Red Cross, and indirectly we heard about the CDC model which was not actually presented to us. And I'm struck by the fact that these models have, of course, similarities and differences.

The major difference that I pick up on is one of stratification. In other words, the amount of stratification in the underlying variables, and it would seem that the stratification that you're hoping to develop in the Red Cross model is a bit more detailed than what we heard from Dr. Custer.

In terms of the modeling approach, it seems to be generally similar which is that you look at the different demographic strata, how they behave over the course of a year, which is to say

seasonality, and then you estimate the outcomes in terms of the yield rates from donation.

So my question really here is, well, how much cooperation can we expect among the different modeling groups? And shouldn't we attempt to foster that? And also one direct way of getting at this would be to see whether the model developed in one set of hands applies to the data set generated in another set of hands.

So, for example, would the Red Cross be willing to plug in the Red Cross demographic data and see how predictive the BSRI model is for the baseline behavior of the Red Cross system?

Because it would be very, very important, I think, to learn whether those systems really behave the same way or not, and of course, if they don't, then one thing we've learned is that we really need, you know, regionalized or system specific models rather than a national model.

And then I think that you've pointed out that it would be extremely useful also to try to validate these models by looking at how they would

have predicted actual behavior as was observed in the cases of SARS and I would add 9/11 disaster and also some of the shortages that we experienced. We've had in the last three or four years, a couple of periods of rather severe blood shortage, and you know what would the models have done in those epochs and isn't that a way to also test their accuracy?

So I'm all for this because I think we need to do as much of this as we can in order to understand the system and figure out the value of candidate interventions. I also generally speaking like the idea of redundancy. I mean, you know, two heads are better than one, four heads are better than three.

But I think we shouldn't miss the opportunity for a little bit of complementarity and, you know, test each other's models with each other's data and see what we can learn from the different modeling approaches.

DR. ZOU: Thank you, Dr. Epstein. I think I can tell there are three questions. The first

question is the difference of the models. Actually I talked to Steven during lunch already so I--and then I listened to the talk by Brian. Actually I got a paper of Brian's group. These models, as I mentioned to Steven during lunch, the idea I had initially for my model is Markoff process. Because that's the one I used for my hepatitis C modeling when I was in Health Canada.

Because especially the model is very straightforward, you can look at, you can change all the parameters, and once you change one, all the rest is changed. So because I'm not a modeling expert, I'm a medical epidemiologist, I find that kind of model is very user friendly. But I didn't develop the model. I used that model for my purpose. The model was developed by a company which gave us permission to use the model.

So that's the model I had in mine. But I haven't--as you can see, we haven't done the modeling for these purposes yet, but after I listened to the talks by Steven and then Brian, actually all the models, I should say, are the same

family. This kind of decision analytic type of model, and other models I have seen so far talk about basically deterministic type of modeling, no stochastic process has been incorporated, which in terms of influenza might be necessary.

So you are right. These models are very similar. They're different because Steve's model is classic way of proof, SIR type of model, which has been used many, many times for many, many diseases successfully.

Brian's model is decision-tree type of model. The one I had in mind was Markoff process model, but all of them are kind of decision analytic models. Okay. So that's the first question.

Second question, I think certainly we need to like learn from the each other. As I talked with Steve, I said I may have questions to ask you and my boss, Dr. Chang, even offers if FDA needs data, I will be happy to work together because we have plenty of data.

And then in terms of the redundancy, in a

way I think it's good. As I said, modeling can only give you a ball park. Modeling suffers from kind of inherited limitations. When you do modeling, most of the time you have an uncertain, like uncertainty for many, many of the parameters, for which you don't have data. If you have data, just a mathematical calculation, you get numbers right away. Because we don't have data for many of the parameters, we have to do modeling to estimate what it would be? If we assume this, what will be the case? If we assume that, what will be the case?

So I think in way it might be good to have two or three different models compare with each other. When you talk about the CDC model, that model is good in that. That's why I use it, but it's mostly designed for public health purposes, for the national level, for the state and for the local level.

I think as well I did use the model to get a ball park, a rough estimate like eight to 19 percent, eight to 18 percent. Basically I plug in

the age distribution. That's why there is a difference. Even so, the attack rate is 35 percent, from 15 to 35, but I only got eight to 19 or eight to 18 because the age distribution is different.

But there are some parameters in the CDC model which you can modify, but certainly not to the extent you can use it to cover the whole blood supply system from the population, that is the potential blood donors to the recipient side. So it's good as a starting point. And also may be important to use the results from the CDC's model to verify or to compare with the results from our three models, FDA one, the Brian's model and the Red Cross model.

So I think you're right. Certainly we need to work together, like, as you said, plug in the data from the different sources to verify the model. That's very important, as I mentioned in the presentation, but a couple more models may be helpful.

I think that's the--did I miss anything?

CHAIRMAN BRACEY: Comment from Dr. Custer or question?

DR. CUSTER: Actually it's a comment. First of all, coming from Blood Systems Research Institute which is, of course, led by Mike Busch, we are all about collaboration. Love the opportunity to actually look at different data sets, subject our model to validation against other data sets and everything like that. I think that that's the way you improve any given model. I just wanted to make one comment with respect also to Markoff processes and sort of the donation process.

It becomes incredibly complex because you've got this dynamic cohort of people coming in and so it makes it a very challenging question, but all power to you in trying to develop that model.

CHAIRMAN BRACEY: Yeah. One comment related to the dynamic of people coming in and perhaps it would serve as a reminder in terms of the importance of defining blood as a critical piece of the infrastructure, because I would imagine that as there are shortages in the

workplace, i.e., if only 80 percent of the workers be that can show up, then it's less likely that those places might be willing to sponsor a blood drive unless if they really understand that this is a critical element of our medical infrastructure.

So, again, as we discuss later on, how we'll position the blood industry in the pandemic, I think it is really important that we seek collaboration with our private partners as well as the public partners.

Any other questions?

DR. KUEHNERT: I just wanted to maybe make a suggestion. I see you were looking at the HCUP data from ARC and that is from my recollection state-based surveillance. It's nice because you can access it pretty easily, but it's somewhat limited, and I don't know if you've looked at a national hospital discharge data which has the advantage that it's free but is maybe a little bit harder to work with, but you might want to consider that.

The limitations of HCUP is that it's, I

don't think they're yet in 50 states, so it's only a select number of states, and if there's biases geographically, then you're going to--the data is going to be skewed.

DR. ZOU: Yeah, you're right. It's a sample of several hospitals. I think it's about 20 hospitals. Actually I got about half of the blood is for medical treatment and half is for surgery. I got that from the hospital discharge data from that agency. Yeah.

CHAIRMAN BRACEY: Question from Dr. Sandler.

DR. SANDLER: Actually, a comment. One of the data sets that you are missing and that you seem to feel is going to be important in your model was how much blood is used electively and how much is not elective in hospitals?

I'd like to caution you very much on that distinction. We've had decades of experience of blood shortages and every wintertime and every summertime I have the opportunity of trying to distinguish from the shored blood I have what's

elective and what's urgent, and common sense would say if somebody is just bleeding out there, that's not elective, and if someone has got a pain in the back or a pain in the knee and they want to get it fixed, that's elective.

I can tell you it doesn't work that way. When we're really short of blood, there are hospitals in this community that are doing elective surgery, that will say we're not going to close our operating room. We're going to pay our bills and we're going to take the cases in and we want our share of the blood. I've got doctors that I will go and say, you know, you got an average of ten units that you use for this type of back surgery, why don't we defer it? And the answer is you go to my patient and you tell my patient who's waited one year for this surgery, and has got his family all together, and you tell him that you don't have ten units of blood, so he can get his back fixed before he becomes paralyzed in his leg or so forth.

The obvious elasticity that you're looking for isn't obvious. And I would caution you when

you get your data to make sure it's harder than just someone surveying whether someone came in for a, quote, "elective" or non-elective because it's not that elastic.

DR. ZOU: Thank you.

CHAIRMAN BRACEY: Dr. Ramsey.

DR. RAMSEY: Thanks. I have a few other comments along those lines as well. And maybe this is just from the perspective of a tertiary care center and I would invite some of the other transfusion medicine physicians to sort of envision what might happen in their environment, but a few thoughts that I have about this would be that if the ICU beds are really full of influenza patients, then that's going to have a big effect on other types of treatments and surgeries that would normally use the ICU beds.

So for example, large scale procedures like liver transplants, if you don't have a place to put your liver transplant patient after the transplant, because the ICU beds are full of flu patients, then maybe you're not going to be doing

liver transplants for a little while.

I don't know. I'm just trying to envision what might happen here. There are, in fact, some, probably some stem cell transplants that would be somewhat deferrable in terms of lymphoma patients, myeloma patients, and Dr. Wong would have been able to address this better than I, in terms of being able to wait for a few weeks to have the procedure done.

There may also be issues in terms of obtaining donors or obtaining unrelated donors in the environment of a pandemic. And also in many tertiary care centers, patients are traveling from long distances. Would they be able to travel for their procedures? So those are a few things that came to mind to me.

And also chemotherapy that might be deferrable for at least a little while. So I guess there might be some value in sort of doing some Delphic analysis with clinicians about these issues in terms of what their priorities would be in the event and in all kinds of institutions, small and

large, what their priorities would be in terms of treating patients. We don't know exactly where our products go in the first place which is another issue, but trying to envision what would happen across the scale of the health care system.

The other--and there might be less trauma, for example, due to less traffic, less shootings except for the gun battles over the last dose of Tamiflu, of course. But the other serious point I had, just in passing, would be we're all focused on this pandemic issue, and the what's going to happen in the middle of this, but if there really is a lot of deferral of health care until that's over, then there might in the recovery phase, there could be a big pent-up demand for health care needs, surgical and medical and otherwise, in patients who have had to wait for the epidemic to subside.

So those are a few thoughts I had. We can, again, we can talk about these a little bit more in the open discussion session, I guess.

CHAIRMAN BRACEY: Yeah, I think we will discuss those, but I would comment on the issue of

elective surgery. I mean clearly that is an area where we need to better understand utilization patterns. We know that, at least in my facility routinely there are five percent of the patients that use about 40 percent of the blood. In specific, we also know that those patients that are generally more urgent procedures tend to use more blood.

So I think that issue of the elasticity of the elective cases really needs to get looked at because oftentimes there are elective cases that use a great deal, but a large number of them are sort of not so heavy uses. But that's an area where we could explore and gain much more information.

Dr. Bloche.

DR. BLOCHE: I think Dr. Sandler's comment underscores the urgency of coming up with national criteria for how we prioritize. If indeed the crisis comes and we're prioritizing based on the intensity of a doctor's advocacy on behalf of a patient who has "x" versus "y" family members

present for the procedure, then the sense of unfairness, if the public becomes aware of that sort of thing, is again potentially explosive.

So we really need more of a kind of national and equitable approach to this sort of allocation.

CHAIRMAN BRACEY: Could I ask are there any more questions for the speaker, Dr. Zou? Otherwise we can go into our committee discussion. Any more questions? Thank you. Thank you. Really appreciate it.

At this point, we have two options. Well, first option. Well, the first option is are there any members of the public that have a comment to make?

Okay, hearing none, so, then for the committee, our options are to proceed with the discussion which the chair would be in favor of doing. Or we can take a short break. Let's proceed with the discussion, and then after we conclude with the discussion, we can move into review of draft recommendations in terms of

recommendations to the Secretary.

So, discussion. Dr. Sayers.

DR. SAYERS: Thanks, Art. In the discussions of modeling, we've been looking at models for their potential value in anticipating threats to the blood supply, but there are circumstances where those models might be valuable as tools to manage occasional excesses in the blood supply, and I think of our own experience at a large metropolitan blood program when it was suddenly realized that a significant number of individuals with metastatic breast malignancy were no longer candidates for marrow transplantation.

And we totally underestimated the extent to which we would have to reduce pheresis platelet collection. So I'm just thinking there might be opportunities to use these models in both the deficiency and potential for excess direction.

CHAIRMAN BRACEY: Excellent point. Karen, Ms. Lipton.

MS. LIPTON: I just wanted to comment on the concept of national guidelines because I really

do think we have to be very careful about this. I understand that there's an issue of sort of fairness and equity and transparency, but I think coming up with truly national guidelines in our context is problematic.

First of all, the whole system that HHS has set up really does defer to the states and allows local decision-making, even in terms of whether they purchased Tamiflu or whether they're going to--who's going to get vaccinated. So there are some recommendations, but it's really basically left to the local level, and it becomes even more complex in the blood arena, because even if you set national guidelines, what could really happen in this situation is different communities could be affected disproportionately.

And we aren't in, we do not have the ability to everyday rationalize blood across every single community, and so I think that--I mean some of the blood organizations--we have a history in the past of trying to set very generic guidelines, but beyond that, I think it becomes very, very

difficult to try to, you know, legislate from a national level usage, and it isn't quite like organs. So--

CHAIRMAN BRACEY: Actually that's an interesting point. I think that clearly what usually happens in a regional environment is that there are medical societies that take responsibility for policies in terms of delivery of care. One of the things that I think, though, that can be done is that the blood banking organizations can foster an approach other than laissez-faire, because as it stands now, it's generally a hands-off approach from the suppliers and I can tell you, for example, in our region, we used to have conference calls when there were blood shortages but it became somewhat embarrassing because of the disparity in the supply between the various institutions.

And that is an end effort of laissez-faire, but if at that regional level, you know, policy could be made, I think that would be quite important.

Dr. Bloche.

MS. LIPTON: I was just going to say I think at the regional level, having the involvement of all the people at the table including the physicians and the hospitals, but that's the policy I think we should be setting. You need to be prepared for what happens, and you as a blood system need to come together and understand who the stakeholders are in making these decisions rather than setting.

CHAIRMAN BRACEY: Right. Dr. Bloche.

DR. BLOCHE: Having national guidelines and national policy is consistent with the reality of different intensities of local effects. If the national principles. If the national allocation principles take the form of priorities, then an area that's much more severely affected than another can apply those principles.

And, yeah, there are people who live in a severely affected area who are going to be denied blood by such principles while people in an area across the country that's less severely affected

will get blood. So I don't think there's the second concern that you voiced.

And with respect to the history of localism, yeah, that's inevitably some of that, and certainly we all know about the John Winberg studies and clinical practice variations, and the absence of evidence for most of the clinical decisions that doctors make.

But given that we're talking about a potential national crisis, it seems to me that this committee would be well advised to recommend that we go a bit more national and do a little bit less of this local deference, especially given the realities of fault lines of class and race, et cetera, by which allocation often occurs, when we opt for laissez-faire approaches.

CHAIRMAN BRACEY: Dr. Epstein.

DR. EPSTEIN: I want to come back to the point that Merlyn was making about dealing with excess because I think that there is both a paradox and an opportunity here based on what Steve Anderson told us which is that one of the candidate

strategies for dealing with an anticipated shortage is over collection.

Now, you know, it's harder to do for a short-lived product like platelets, but you could do it for FFP, you could do it for red cells, and what that's about is building surge capacity. Paradoxically, how you go about building surge capacity could be the very thing that enables you to deal with the hit that you'll take with, you know, the loss of staff during the outbreak.

So, for example, if you have more trained people, if you have more people who can be called in ad hoc, if you have more cross-trained individuals, then the robustness of your operation is much, much greater even when it downsizes.

So we focused a lot about, you know, what do you do with the obligatory downsizing, but I think we ought to also incorporate into that the whole notion of the strategy to expand capability on the model of, you know, surge capacity.

And that that is itself one of the candidate strategies to whatever extent the

outbreak can be predicted as, you know, coming in a week, coming in a month.

CHAIRMAN BRACEY: Dr. Kuehnert.

DR. KUEHNERT: It seems just in general we're talking about a lot of black boxes where we don't know exactly what we're dealing with, and I know in the setting of a pandemic that's reasonable, but in terms of, for instance, utilization, I think if we're going to consider guidelines, we need to consider evaluating utilization and a way to utilize it, because if you implement guidelines for the first time in the setting of a national disaster, you know, there's going to be some serious bumps in the road, and you don't want those bumps in that setting.

So I guess what I'm suggesting is that as a package, if we're going to consider guidelines, we should also consider evaluation of utilization, both before and after those guidelines are put out, or some sort of validation of those recommendations as really a prerequisite for that.

CHAIRMAN BRACEY: Well, one of the things

that I would envision, and I would hope that we will look at, we'll have further discussion of, but also consider in our recommendations, is in a way to tie into the strategic plan in terms of optimizing blood utilization and maximizing blood availability general strategy.

Because you're right. This is a black box. We don't know what's going to happen, but on the other hand, it could prepare us for another scenario which is yet unseen and unthought of, and I think that's where the real strength of this lies.

DR. KUEHNERT: And also building on what the Office of the Secretary is doing concerning monitoring availability. I mean one could also monitor utilization and also monitor adverse reactions, and so it all sort of fits together in the strategic plan.

CHAIRMAN BRACEY: Karen Lipton.

MS. LIPTON: One of the things that we have struggled with for so long, and you know the reason when we talk about guidelines, I mean as an

organization, the AABB has been committed to try and come up with practice guidelines for the last how many years, and every organization that's tried it has walked away from it because it's just, it's just very difficult.

And the real issue is measuring what are the outcomes you're trying to tie this product utilization to? And again, I think to Matt's point, I think we need to understand when we go into this what we're getting into if we're really trying to set guidelines.

I think maybe more what we want to talk about is not so much utilization in terms of specific types of illnesses or surgeries but really more setting broad categories--if we can define elective, if we can define medical use. But again when we looked at this, and we've looked at a lot of data on utilization, and transplant is just huge. And transplant is not generally elective, and it's going to hit you pretty, you know, it's going to hit you across the country and you're not even going to know when.

So when that liver patient is here and that liver or whatever is available, that person is going to get transmitted someplace else, or if it's a heart-lung transplant, because they're not going to waste that organ. They just can't. I just, I think there are a lot of issues, and I think it would be good to try to define what we want out of this.

I'm just saying I know from painful experience how difficult it is to get these practice guidelines in place.

CHAIRMAN BRACEY: Jerry.

DR. HOLMBERG: Thank you. I really appreciate the comments that have been made, and I think that--I think that what we're trying to do is to get at maybe putting out there that every state and local facility develop some strategy for triaging their blood supply, you know, instead of trying to dictate utilization.

And I agree with what Dr. Kuehnert said was, you know, at the time of a disaster in a pandemic, you don't want to be trying to validate

what your utilization guidelines are. And there is a lot of opposition, and I think, you know, to some of these guidelines, but on the other hand, I also appreciate what Dr. Bloche is saying, and that is, you know, in any guideline, how do you ensure in the practice and implementation that there is not disparity?

And so we want to make sure that, I think it's better that if we put that recommendation out there, that the committee could put a recommendation that at the local level or at the state level, maybe even at the state medical level, that they develop or look at ways of triaging the critical infrastructure of blood.

CHAIRMAN BRACEY: Maybe Dr. Sayers will speak to this because he's been actively involved with the Texas Medical Association's Committee on Transfusion, and it's a model that may exist in other states, but again there there is a body that's under aegis of the state medical society.

Dr. Sayers, would you like to comment on that?

DR. SAYERS: You caught me as I came in from a telephone call. Jerry, give me the essence of the question again.

CHAIRMAN BRACEY: Well, okay, Dr. Sayers.

DR. HOLMBERG: What I was basically saying was that instead of trying to establish criteria or guidelines for utilization of blood products that at a national level, that what we do is or what the committee could possibly do is to push that responsibility down to the state level and which the state is trying to, is in their pandemic plan looking at ways of strategy of utilization of decreased inventory.

DR. SAYERS: This may be idiosyncratic of physician's conduct in Texas, but I suspect that even the Texas Medical Association would have difficulty encouraging their membership to abide by state defined transfusion guidelines.

DR. HOLMBERG: Even if was the state medical association?

DR. SAYERS: Well, prefaced by this is Texas.

[Laughter.]

DR. SAYERS: I'd say even if.

CHAIRMAN BRACEY: But on the other hand, if it were following a recommendation from the Secretary, and that the Secretary has a vision of the management of the pandemic both at the federal and state level, then perhaps?

DR. SAYERS: You're right. I think that would make a difference, and I think then something like the medical, Texas Medical Association's Blood and Tissue Usage Committee would really try and promote the Secretary's opinion and counsel.

CHAIRMAN BRACEY: Dr. Pierce.

DR. PIERCE: I think I'm appreciating where you're going, but I want to clarify it a little bit. Are you suggesting, then, that some general recommendations come out through the Secretary's Office such as deferring elective surgeries, evaluating other surgeries or potential delay, without getting too specific, and then allowing it to be decentralized at the local level?

Because I guess I'm a little concerned

about just having a free for all at the local level with all the disparities that would occur there unless some general set of guidelines was issued nationally that would at least put some boxes around or walls around what good medical practice ought to be?

CHAIRMAN BRACEY: And the general thought is that we would not be too prescriptive, but that at the state level, they would develop a strategy and we would leave that strategy to the given folks at the state level, and that we would perhaps on a national level develop guidelines which in essence currently exist promulgated by different entities, but are often, not frequently followed, shall we say?

So the point would be to encourage the development of reasonable guidelines making it again not very prescriptive but at least attempt to have uniformity, but then in terms of application of issues at the state level, again, leave that to local managers.

Karen Lipton.

MS. LIPTON: What is the model that's being used? I can't, you know, think about it. In the HHS plan, how are they talking about the allocation, for example, of hospital beds or, you know, medical services to people? I mean is there any talk about rationalizing that or allocating that at a state level? Are there guidelines in there. I just don't remember.

Because that would be a model if they have guidelines. You know, you have a lot of people absent from a hospital, your 1,000 bed hospital is suddenly a 300 bed, well, how do you make that determination as to who gets treated? And is there some assistance in the HHS guidelines for that because we're really talking about the same issue. It's just a different type of resource.

DR. HOLMBERG: I think that the guideline that is out presently does not go into that depth of detail. And I think that that's probably why HRSA is giving money to hospitals to develop their strategic plans.

CHAIRMAN BRACEY: The one thing I was

thinking is that at present we are in a position to foster the development, the consideration of these guidelines in terms of a strategic plan. Beyond that, I don't see that we will be able to, you know, really go beyond that point.

So in terms of specifics, I think we won't get there, but I think the idea of maintaining some independence at the regional level I think would be important.

Dr. Sandler.

DR. SANDLER: Yeah, I think that our job for the first three points is to get the blood and make it available times three, and then when we fail the job that we're given, then we can tell people how with what we didn't do they'll have to do with what's there.

But I think the major message in our document ought to be how to get the job done that was supposed to get done.

CHAIRMAN BRACEY: Good point. Dr. Roseff.

DR. ROSEFF: Well, just to reflect, I wasn't going to talk about this, but one of the

models shows if you decrease transfusion, then you have more blood available. So they're not really totally distinct, just getting it versus not using it. I mean there is a model for each.

But guidelines don't have to be specific and they don't have to be mandated. You know guidelines are a framework, and I think it's very important that somehow we communicate that this is a part of disaster planning, and after 9/11, the disaster committees that I was on, this kept getting shunted.

You know, while we were busy with containment units and washing people in the street, this keeps getting pushed aside. And if there's anyway--I think that's what we keep hearing, to keep pushing this forward and one of the ways to do that is to have something that creates a guideline that has to be disseminated somehow, gives a broad brush stroke that you can use locally to define what you want.

But I still think something has to come that's required for each local entity to do

something as opposed to just say local entities, do something, this is what you have to do, these are the steps you have to follow.

CHAIRMAN BRACEY: Dr. Matyas.

MR. MATYAS: My point is just as a follow-up which is the notion of guidelines can be just that, guidelines for the goal of addressing the fact that there will be disparity as opposed to what I think the proposition was beginning, which was to eliminate disparity.

I think the idea of having a goal being to eliminate disparity in a pandemic situation, well, that might be a lofty goal, but we're not going to eliminate it, but if you set out guidelines to allow at the local level to address it, then we've done the best that we can do given the fact that history tells us in the blood community, you cannot mandate to the physicians and the hospitals exactly what the criteria will be, except to try and encourage the creation of criteria.

CHAIRMAN BRACEY: Dr. Bloche.

DR. BLOCHE: Thank you. I appreciate what

Dr. Lipton said about the difficulty of developing practice guidelines, guidelines for good medical practice. It seems to me that one way to kind of get over that hurdle is to frame this task as something fundamentally different.

These are, one might, I might dare say, guidelines for bad medical practice, or at least guidelines for desperate, more or less desperate medical practice, at a time of regional or national crisis. It seems to me, therefore, that the framing of principles for allocation can be kind of separated out and not, you know, separated from that Pandora's box of practice guidelines.

Second point I'd make is that however prescriptive or nonprescriptive the guidelines may be, national or regional, it seems to me the key point is that they really need to tightly limit the kind of discretion that Dr. Sandler really nicely laid out.

I thought you did a beautiful job of laying out the reality of allocation processes. A footnote to this. There is both a physician and

economist named Jeffrey Harris, who has written about allocation through internal queuing and advocacy by different doctors for different patients, and you really nicely set that story out.

That's exactly what we don't want to happen at a time of crisis, and so whether it's national recommendations for priorities that then get implemented and refined at the state level or whether it's a clear call by the Secretary for the state level to develop such priorities, either way I'm agnostic.

The key, I think, is to avoid the situation where you have two hospitals, one on one side of the tracks, the other on the other, and they're getting different allocations, and then different people depending on what color their skin is or how much they have in the bank are getting different things even within that given hospital.

CHAIRMAN BRACEY: Dr. Holmberg.

DR. HOLMBERG: And I would just agree with that, and one of the things that I would like to comment on is that that is clearly one of the

objectives of Secretary Leavitt is to decrease the disparity in medical care.

CHAIRMAN BRACEY: Dr. Bianco.

DR. BIANCO: Thank you. Celso Bianco, America's Blood Centers. I must say this is one of the most exciting meetings that this committee has had since I started attending them. This is important; this is serious and I'm very happy.

There were several points that were made and we are concerned, and we expressed that concern before, about that level, that is from the federal level to the local level, how things will happen.

And we know how complex the local level is. Maybe what you are all saying that I hear and I agree with 93 percent is that maybe the federal level, that is the Secretary, has to make the local level aware that there will be only 30, 40 percent of the blood that there was yesterday before the epidemic, and that they have to think on how they are going to manage this process.

And so the way that they will have to prepare is for not having the product that they are

used to have, and I think that that's the challenge to them. If we just tell them that instead of using eight grams of hemoglobin, you should use six or whatever, then we are not going to be able to resolve it.

But if we give them this to their hands and say now you have to do something about it, I believe that's one way by which the Secretary can help, by making it a national priority, by including blood into the major issues that have to be dealt with in a pandemic and saying, and predicting what is going to happen so that people can develop their plans.

CHAIRMAN BRACEY: Thank you. Dr. Bloche, did you have your--

DR. BLOCHE: No, I just forgot to turn it off. Sorry about that.

CHAIRMAN BRACEY: That actually segues, I think, fairly nicely into what I would like to propose as the next step, and that is that we would look at the recommendations to the Secretary because incorporated in the draft recommendations

is some language that addresses that.

So I would propose that we take a 15 minute break and then we'll come back and then we'll look at the draft recommendations based upon all the evidence that we've heard thus far. Okay. Fifteen minutes.

[Recess.]

CHAIRMAN BRACEY: Could the committee members take their seats and we'll have the draft, which again is truly to be considered a draft document. Prior to the time that we go over it, I think there were some key points that we should consider and make sure those are all in there, and one is that the blood supply would be considered an element of the critical infrastructure.

That, two, under our charter, we are obligated to assess the safety of the blood supply, and therefore the question of viremia needs to be addressed.

And another key point is to make sure that there's adequate representation of the blood industry or blood system, if you will, at the level

of policy development as it stands for addressing the influenza pandemic.

So that said, what I'll do is begin to review the draft document.

DR. PIERCE: Art, just a quick question.

CHAIRMAN BRACEY: Yes.

DR. PIERCE: What was the genesis of this draft?

CHAIRMAN BRACEY: Correct. The genesis of this draft was a review of the points that were submitted by the Executive Secretary for the committee to consider, and let me just go back over those.

Here it is. It's the page with the five points, and one was what strategies should be considered by DHHS to prepare the blood system for the possible flu pandemic? Considering immunization of staff, encouraging immunization of repeat donors, supply monitoring and management during an outbreak.

Two, how can DHHS help to resolve present scientific uncertainties underlying the potential

need for donor deferrals? And there again issues of viremia; value of deferrals for clinical exposure and/or use of Tamiflu; and potential for falsely positive donor screening tests following influenza infection.

Three and four had some overlap. Three is what new approaches to communication between public health, blood, organ and tissue communities would be helpful in order to enhance preparedness? And then four, which was what would be the most efficient interfaces with global and domestic influenza surveillance data, communication between collection, transfusion, local and state public health, communication between blood, organ and tissue communities.

And then five, what surveillance methods are needed for blood and plasma recipients in order to detect transfusion associated transmission pandemic influenza, need for adverse reporting, testing, evaluation, frequently transfused recipients and then surveillance and evaluation of vaccination and antiviral prophylaxis?

So with that as a lead-in, this is our draft, and again a draft, and please make comments, modify it. The first point is:

Whereas, evidence suggests that the possibility in the near term for a global pandemic of influenza, (a) based on recent highly virulent human infections with an avian H5N1 virus;

(b) where the HHS plan for pandemic influenza recognizes the priority to preserve critical infrastructure in our society--that was based upon the statement made yesterday by Dr. Schwartz from the Secretary;

(c) ensuring the safety and availability of blood and blood products including plasma products is a critical public health need central to the medical system;

(d) the availability of blood products is likely to be highly compromised during an influenza pandemic;

(e) data have suggested the possibility that influenza viruses may be present in the blood, organs and tissues of asymptomatic donors;

(f) influenza surveillance data, which come from diverse sources, are limited in scope, timeliness and integration--lost me there--that's all right--

(g) risk education and communication delivered by scientific and medical experts are essential components of preparedness for pandemic influenza.

So there are the sort of background statements. Before we talk about specific recommendations, let's maybe pan back, go back down. You know, the first point being that, yeah, there's evidence to say that we should be concerned about the evolution of this problem; (b) there is a plan, and the federal focus is to maintain a critical infrastructure; (c) what we're saying is that ensuring the blood and blood products is critical; therefore, we need to be part of that infrastructure; (d) we think that availability is going to be highly compromised; (e) there are questions about whether or not there's asymptomatic carrier states; (f) surveillance is key, and it's

somewhat--well, I wouldn't say fragmented, but it's multisourced at this point, and not guaranteed to be integrated.

As we heard from the communicators, the message has to be right, and the message should be both educational as well as a point of communication. And then, well, that was it.

So what's missing in terms of the discussions? Dr. Sandler.

DR. SANDLER: I don't see there the message that there is uncertainty. One of the messages I heard today was there's a lot of uncertainty in a lot of the data and the assumptions going forward, and it seems to me that (h) would have some message, and I can't wordsmith and I can't wordsmith it just right, but it would be to the effect that given the uncertainty, there is nevertheless the need to make some recommendations or something.

I don't have the right words for it, but uncertainty seems to be missing.

CHAIRMAN BRACEY: Dr. Holmberg.

DR. HOLMBERG: In statement (f), could that be worked in there about the uncertainty because which comes from diverse sources, are limited in scope, timeliness and integration. I mean could we put in uncertainty there?

CHAIRMAN BRACEY: But I think--

MS. LIPTON: I think it's more than uncertainty from the surveillance. It's really uncertainty in what we know about all of these issues.

DR. SANDLER: But I thought it was, if you go to (b) or (c). Can you go up?

CHAIRMAN BRACEY: Go up to (b), please. We really don't address the uncertainty specifically. I mean one other thing I thought of is perhaps if we put it up front in (a), but then we would sort of erode the message perhaps.

DR. EPSTEIN: Or perhaps we could just make it point (b), which is that there is great uncertainty in any predictions of the course and severity of such a pandemic.

CHAIRMAN BRACEY: And perhaps that--and

there's great uncertainty, and in some way that underscores the need to support, you know, studies or research initiatives to further clarify the current state of knowledge. Can you wordsmith?

MR. MATYAS: No, but I think the point is that it doesn't go between (a) and (b) even because we're not asking as much about the uncertainty of the pandemic influenza because there are others looking into that.

It's relationship to after (c) and (d) is the notion of there's uncertainty as to the impact it will have on blood and blood products and availability and the like.

DR. PIERCE: Maybe in (d), there could be a clause saying that although the scope of the pandemic is uncertain, the availability of blood products is likely to be highly compromised.

CHAIRMAN BRACEY: Yeah. I thought that was a good suggestion. Does the committee? So although--thumbs up--would you like to repeat that, Dr. Pierce? Although there is--

DR. PIERCE: Although the scope of the

pandemic--

CHAIRMAN BRACEY: Is uncertain.

DR. BLOCHE: You want to say scope and impact?

DR. PIERCE: Yes.

CHAIRMAN BRACEY: Yeah. Good point. Dr. Epstein.

DR. EPSTEIN: I think of the potential pandemic. This in fact may not happen.

DR. PIERCE: Sure.

CHAIRMAN BRACEY: Yeah.

DR. EPSTEIN: Potential.

DR. PIERCE: Is uncertain. That's a friendly amendment.

MR. MATYAS: I thought part of the comment that was also under (d), which is data have suggested the possibility, the notion of uncertainty there because we don't have enough data to even say that we're sure if it suggests, I thought.

DR. BLOCHE: That's why possibility.

CHAIRMAN BRACEY: Right. How would you

modify that?

MR. MATYAS: I mean is the notion that it's very limited; it's preliminary data? I mean I'm not sure from a scientific perspective, I'm not trying to, as a lawyer, wordsmith it. I'm trying to figure out what--that seems to indicate that we have data and it says it's possible, but--

CHAIRMAN BRACEY: Sorry.

MR. MATYAS: Yes.

CHAIRMAN BRACEY: But I think the point though is what you mentioned first, I think, limited data. I mean would that address your concern? Dr. Pierce. There was a question as to whether you were finished with your recommendation?

DR. PIERCE: I was finished with that one. I have another one, though.

CHAIRMAN BRACEY: Ah. Which number, which letter would that be?

DR. PIERCE: Well, I'm not sure it's a letter at this point, but this is very centric to H5N1. Is there a way of saying that, or is it useful to say that this is a model for disaster

preparedness for the blood supply for any potential pandemic?

CHAIRMAN BRACEY: I think that as we come down to the recommendations, there is a piece there that will address that. In fact, perhaps--so maybe what we could do, we have the "whereas's" now. We're sort of laying the background. Can we go down to the recommendations and then come back?

Okay. Let's try that. And I'll go where I can read this actually better. The committee recommends that the Secretary take immediate steps to:

(1) establish national recognition of the blood and plasma systems (collection, processing and use) as key elements in the critical infrastructure under the HHS plan, specifically including facilities, staff and committed blood and plasma donors;

(2) assure full funding of research to resolve critical scientific questions regarding the potential impact of pandemic influenza on blood, organ and tissue safety and availability.

(a) foster collaborations with investigators in countries affected by the current H5N1 influenza outbreak to promote studies of possible viremia in asymptomatic persons including recent case contacts;

(b) support studies of H5N1 virus in suitable animal models including non-human primates to investigate viremia and organ localization of infectivity in preclinical, clinical and convalescent stages of disease; transfusion transmissibility of virus if present in blood; and impact of infection and/or drug treatment on the accuracy of donor screening tests;

(c) support studies of influenza viremia during annual outbreaks of non-pandemic strains including studies on blood and plasma donors and product recipients;

(3) provide targeted federal support to enhance global and domestic surveillance for seasonal and pandemic influenza;

(4) recognize the central role of the AABB Interorganizational Task Force in the development

and implementation of a national strategy to address potentially massive blood shortages during a pandemic of influenza by (a) assuring blood organization representation on key federal policymaking and communication committees; and (b) promoting cooperation among state and local public health authorities and appropriate blood collection organizations, hospitals, medical professional organizations and patient advocacy organizations.

Those are the recommendations. And in a sense, in (4), though it's targeted for influenza, the notion is that as we address any potentially massive blood shortage, it really would go beyond the scope of influenza even though it specifically states it here.

Yes?

MR. MATYAS: Without being able to see the whole thing, I don't think we've addressed the communication aspect in there.

CHAIRMAN BRACEY: Okay.

MR. MATYAS: The need to develop the message.

CHAIRMAN BRACEY: Oh, I see. We did state it in the "whereas."

MR. MATYAS: We said it in the "whereas," but we haven't as a recommendation that it needs to be a task that's accomplished wherever, whoever--

CHAIRMAN BRACEY: Yeah.

MR. MATYAS: --and we develop the message now and the various messages which would be irrespective of what the issue is.

CHAIRMAN BRACEY: Ms. Birkhofer.

MS. BIRKHOFER: Thanks, Mr. Chairman. Under (4) in the recommendations, I'd like to ask you and Karen Lipton your thoughts, if it would be appropriate to add the blood and plasma protein therapeutic shortages or to assuring, you know, blood and blood product organization representation, to be more comprehensive in that recommendation?

I just would ask if that would be appropriate because I think PPTA does have a representative or liaison to that Interorganizational Task Force?

MS. LIPTON: Yes, there is a representative from PPTA on that.

CHAIRMAN BRACEY: And I think that again we tried to incorporate that above and I think it helps to add it below. So I appreciate that comment.

MS. BIRKHOFER: Thank you.

MS. LIPTON: Could I also just make a comment about the risk communication? I mean I think one of the things that we're trying to draw a fine line here is whose responsibility is what? And we did create something. We know there's a communication task force already at the federal level.

And what we're saying to the Secretary is that we want to make sure that blood interests through the blood community are represented there. We can tell ourselves to go out and make our own messages, but I don't think that's the federal government doing that at this point. I think what we want to say is we want to be at the table when you're crafting these messages.

I think there's a whole other set of issues that fall out of this committee meeting that really though fall on to the role of the blood organizations and not necessarily the Secretary. So everything we're doing in here is focused at what can the Secretary do.

CHAIRMAN BRACEY: Right. And on the order of the communications, for example, yesterday when Mr. Wolfson made his presentation, there was a committee and I can't recall the name of it, but in an earlier draft that specific entity was inserted.

However, that was really limiting and this actually is more broad in terms of suggesting that the blood--someone from the blood industry should be incorporated, and I think the message that at least I heard from Wolfson is that, you know, there will be singular message.

And so as long as we can get in there--or at least three messages--as long as we can get in there and make that point, if we're on that key committee, it should work.

Dr. Epstein.

DR. EPSTEIN: Well, my take on I guess it was Dr. Matyas' remark is that we ought to say something directly about adding messages regarding the blood system to the HHS message map. In other words, it's a very concrete thing that we want here, which is to be on the map.

MR. MATYAS: Sorry.

CHAIRMAN BRACEY: Mr. Matyas.

MR. MATYAS: Oh, and by the way, for clarification, I don't have a Ph.D. next to my name unfortunately, so you can just call me "hey, you."

I'm now in careful reading seeing maybe what you all were getting at by the fact that it says federal policy making and communication committees. So I guess by the inclusion of communication committees, you may be getting to the task of making sure that it's in at least an action item.

CHAIRMAN BRACEY: Dr. Bloche and then Dr. Ramsey.

DR. BLOCHE: I have some wordsmithing suggestions on just a couple of the "whereas's" and

then a substantive concern about item (4), which I could defer to later.

Maybe we do the "whereas's" first.

CHAIRMAN BRACEY: Can we go to the "whereas's" please?

DR. BLOCHE: Yeah. The first one is trivial but stylistic. Item (c) I would just stop with is a critical public health need. Get rid of central to the medical system. It's more punchy and less wordy that way.

That's what we law professors do for a living. And then--

DR. RAMSEY: They might have trouble hearing you on the tape because the people over there on that side are facing away from the microphones.

DR. BLOCHE: Okay. Changing, thanks a lot. New microphone which I did not pay for. For item (c) under the "whereas's," I suggest ending the sentence after is a critical public health need and deleting central to the medical system because it's redundant and less punchy.

And for (g), risk education and communication, I'd suggest after communication adding the words "to the public" just to clarify who we're communicating to, who we're calling for communication to.

And I'm happy to defer on my substantive thoughts on number (4) or I could do that now. Okay. Okay. Four under the recommendations, whether it's in four or whether it's in a new item, I do think it's important to make some reference to the importance of priorities, a priority scheme, a triage or rationing scheme in the event of crisis, in order to avoid unfairness of disparity, et cetera, what we were talking about before.

Because right now, as this says, it basically defers to the industry to handle, to be the central handler of this issue. We're saying nothing in this document about the question of prioritization.

CHAIRMAN BRACEY: Dr. Holmberg.

DR. HOLMBERG: I can't remember. If you go back to (2), recommendation two, we did talk

about collection and processing and--

DR. BLOCHE: Was it somewhere else?

CHAIRMAN BRACEY: It's not in two.

DR. HOLMBERG: --and use.

CHAIRMAN BRACEY: Let's pan up.

DR. HOLMBERG: There it is. One.

CHAIRMAN BRACEY: Yes, one.

DR. HOLMBERG: Establish national recognition of the blood and plasma systems, collection, process and use.

Okay. I was just thinking the use in there could be the utilization, but I think that what I hear you saying is that we really need a more definitive statement on that, and I agree with you. I think that this doesn't carry all the weight. I was thinking that this carried some more weight than it does so--

DR. BLOCHE: In capturing it, I certainly want to--I realize I want to defer to Dr. Lipton's concerns about the difficulty of practice guidelines, but some maybe language like principles for triage in the event of shortages.

MS. LIPTON: Can we go to principles of equitable distribution or something, you know, rather than--triage is a--I think if we--well, it's really an allocation of a scarce resource. Triage, though, I think has this emergency room--

DR. BLOCHE: But we're talking about an emergency.

CHAIRMAN BRACEY: But I think it would fit best in four because in four, we specifically address development of a strategy for blood shortages, so this is where we would consider some language that would incorporate developing a uniform supply, avoiding--what language would you prefer?

DR. BLOCHE: Well, four could be introduced in a different way because four, the way four is set up now, it says recognize the central role of the trade associations.

And it seems to me that certainly the Association of Blood Banks should have a large role, but stating that aside from that, there is a need for--and this can be left ambiguous who should

do it, but there's a need for a set of principles for the management of blood shortages in a fashion that--

CHAIRMAN BRACEY: Ensures an equitable distribution of--

DR. BLOCHE: --of equitable, fair and consistent amongst competing--

CHAIRMAN BRACEY: Okay. Let's--so principles--as number five, principles--

DR. BLOCHE: Establish principles.

CHAIRMAN BRACEY: Establish principles--

DR. BLOCHE: Develop principles. Develop principles for the fair and equitable distribution of blood in the event of local, regional or national shortfalls,--

CHAIRMAN BRACEY: Now, again that's something--the question is whether it would be at the level of the Secretary because--Karen?

MS. LIPTON: Well, no, I was going to say I'm concerned more about saying equitable distribution when you get to a national shortage because then we're right back into are we talking

about shipping stuff, you know, that we're asking the Secretary to set principles for shipping blood around the country? And I don't think that's what we're asking to do.

I think what we're asking them is to set principles for state and local authorities to set up--we want national principles that are to be used at the local level to make sure that there is a fair and adequate distribution of blood in the event of shortage to the community.

DR. BLOCHE: Can I just finish the sentence and then it can be wordsmithed and changed accordingly?

In the event of local, regional or national shortfalls, to minimize disparities in blood availability and use.

MR. WALSH: As a consumer from a community that depends on transplants here, it's almost prioritize utilization. What's fair and equitable? That means everybody gets the same amount? I mean we've got transplant issues. We've got other critical care needs.

And we're not going to get it with treatment guidelines. I totally agree with everybody else because the professional societies can't do that.

CHAIRMAN BRACEY: Right.

DR. BLOCHE: Well, separating this out from the treatment guidelines question, viewing this as a matter of triage, not good medical practice, I think gets, you know, protects us from that box of Pandora's.

CHAIRMAN BRACEY: I guess I'm still kind of stuck on the issue of the Secretary developing principles for the fair and equitable distribution because again what we talked about is encourage, you know, regional/state medical organizations to develop principles.

Dr. Epstein.

DR. EPSTEIN: Provide advocacy for and articulate general principles for the state, regional and local development of strategies to address distribution.

CHAIRMAN BRACEY: I like that.

DR. EPSTEIN: Yes.

CHAIRMAN BRACEY: Comments? Does that sound fair to the committee?

Mr. Walsh.

MR. WALSH: I'll always go along with Jay. He's the best one at the wordsmithing. I think that sounds good, and that addresses the prioritization and utilization.

CHAIRMAN BRACEY: Okay.

MR. MATYAS: What's done with respect to vaccines? I mean what does the Secretary do at the national level on vaccine prioritization down at the local level?

CHAIRMAN BRACEY: Executive Secretary Dr. Holmberg?

DR. HOLMBERG: Actually what we heard was that 90 percent of the vaccines are going to the state and that the state sets the priority then. So it has to be this is what we're trying to get to is that the state pushing, everything is being pushed down to the state and local government.

MR. MATYAS: But there are no guiding

principles that come down?

DR. HOLMBERG: Well, there is from the National Vaccine Program Office some of the priorities on the prioritization of these.

MR. MATYAS: Where is that office?

DR. HOLMBERG: That's at the Secretary's level.

MR. MATYAS: So why isn't it the same? That's, I guess that's the point. Why isn't it the same kind of--I'm not sure the vernacular you used in terms of principles coming down that go down the states to create the priorities, but there is something coming from the Secretary's Office in terms of--

CHAIRMAN BRACEY: I thought--maybe I was confused. I thought at the level of the Secretary, there was, in essence, the split of the percentages and then the critical infrastructure, et cetera, et cetera, were defined at the Secretary's level, and then the state was left up to its discretion for the rest. No?

DR. HOLMBERG: I'm not clear on that. But

I hear what you're saying and what we're trying to do--I mean with the National Vaccine Program, there is, I mean one could argue is that really the practice of medicine? Or is it the availability of a vaccine to the various high risk groups?

And I think what you're coming at is setting the utilization guidelines at the federal level and pushing it down to the state to implement that, if that's what I'm understanding?

MR. MATYAS: I'm not recommending it. I'm just seeing if there is an analogy to what's done with vaccine and whatever the principles, standards are that get pushed down in a similar kind of fashion.

DR. HOLMBERG: Well, I think this is what basically the UK has done in their utilization of blood products, and just as Dr. Roseff has mentioned, that in shortages, it's amazing how the physicians get away without transfusing as much as they do when there is availability of product.

And I think that that's okay for the UK situation where there is a nationalized blood

program, but I think that in the United States, we have a different aspect and trying to--nobody in the United States wants to take on the physician to be able to try to dictate the physician, even physicians don't want to tell other physicians what they should do as far as practicing medicine.

And so I think that, yes, there is an analogy there with vaccines, but in transfusion and also therapeutic products, that is a prescription, that is a medicine that is being prescribed, so there is analogies, but I think that there is definitely some gray areas.

CHAIRMAN BRACEY: It's new turf.

MS. LIPTON: I think we should reserve five percent of the blood to preserve the constitutional form of government that we have.

[Laughter.]

CHAIRMAN BRACEY: Excellent point. Dr. Bloche.

DR. BLOCHE: Just a wordsmithing suggestion that I think addresses, I believe it was Dr. Walsh and also Dr. Lipton's concerns. For

five, just saying, beginning it with the word "support," so it would say support the development of principles, et cetera.

CHAIRMAN BRACEY: That works. Committee comments on that recommendation? Thumbs up, thumbs down?

DR. BLOCHE: Beginning with "support." It's not really advocacy.

CHAIRMAN BRACEY: Okay. Dr. Epstein.

DR. EPSTEIN: Yes, first of all, I'm not a voting member, but I favor that modification, but let me suggest another, which is to convince us to say support the development of principles for state and local health authority to minimize disparities in blood availability and use during a shortfall.

CHAIRMAN BRACEY: Uh-huh.

DR. EPSTEIN: Because I think that this is a little bit too wordy for my taste and I think that it has the effect of blunting the focus which is that we want to charge the state and local government.

CHAIRMAN BRACEY: Right, right.

DR. EPSTEIN: So support development of principles for or under which state and local authorities--state and local authorities--if you want to say public health authorities--and then just zip right down to "to minimize." Delete everything else to "to minimize." And then add the words "during shortfalls."

CHAIRMAN BRACEY: And perhaps add public health in there to focus it on the appropriate.

DR. EPSTEIN: Public health authorities.

CHAIRMAN BRACEY: Dr. Bloche.

DR. BLOCHE: Yeah. I would at this point disagree with that. Because it does seem to me, and I'm open to--I'm personally open to leaving it more flexible. But the process of prioritizing, whether as part of normal medical practice or in the event of shortfalls, isn't just a local or state endeavor.

There are national medical organizations, and there are many national mechanisms, private as well as public, and this may well be too large a task to make a call on here, but to choose only

state and local rather than to acknowledge the reality that there is both private and public national policymaking when it comes to shortfalls I think would be a mistake.

CHAIRMAN BRACEY: That indeed is a reality in terms of the organizations, but I think on the other side, a reality in terms of what generally happens with the practice of medicine is that indeed the control usually rests at the state and local level.

DR. BLOCHE: Yeah, but as practical matter, every time there's a medical malpractice case, liability is based on a national standard of care. As a practical matter, boards that do certification are based on national standards of care.

There's a whole lot of private sources as well as public sources of national standards.

CHAIRMAN BRACEY: Dr. Bowman had a comment which I was holding.

DR. BOWMAN: Yes, I'm not a voting member, but sometimes the term "promote" has more punch in

bureaucracies than "support," but I also notice that item (b) also has promote under (4) so there might be too many promotes there.

CHAIRMAN BRACEY: Dr. Epstein.

DR. EPSTEIN: Develop national principles. Let me just repeat what I said. What if we state "develop national principles"? Because I think that the dilemma that we're circling around is that we don't think that the federal government can actually come out with the treatment guidelines.

On the other hand, we do think that there's a need for a national statement on certain overarching principles. So perhaps the charge here is develop or development of national principles under which state and local public authorities can take steps or can take appropriate steps.

Because I understand that we haven't come to consensus on the core issue, which is how much of this should be national? But, and I think what we're trying to do here is strike the achievable balance in the present context? And I don't know where that lies in terms of the sense of the group,

but I think--

DR. BLOCHE: I think that's really helpful suggestion.

CHAIRMAN BRACEY: We did see a thumbs up from Dr. Sandler. But Dr. Sayers had a comment or question.

DR. SAYERS: [Inaudible.] I'm not going to repeat that.

[Laughter.]

DR. SAYERS: I would go with what Dr. Epstein has to say if we could consider national guidelines instead of national principles.

MR. WALSH: If there is an issue about, you know, who has the authority here, I mean you could, you could just say public health authorities. But then you lose the direction to state and local. That's the down side of that.

CHAIRMAN BRACEY: I would see that as, again, thinking about the reception, I would see that as a down side, again, thinking back to transplant issues, et cetera.

Mr. Walsh and then I'll come to the

Executive Secretary.

MR. WALSH: I'm not certain that minimize disparities covers prioritize, prioritization or prioritize utilization. I mean I'm really not certain what disparities means in the context of selecting or triaging one need as opposed the other.

And then just as a comment, guidelines to me are something that, you know, you have to have, you know, a specific authority and it takes a long time to establish, and you have to get everybody to embrace and then nobody follows them.

And to hear that, with all due respect to all the physicians at the table, I mean professional societies can't get their respective memberships to follow guidelines.

CHAIRMAN BRACEY: That's a good point. I mean principles are easier to espouse than guidelines are to enforce and generate enforcement.

DR. SAYERS: I suppose what worries me about principles is that they're pretty akin to something carved in stone.

CHAIRMAN BRACEY: Yeah. Dr. Sandler. I mean Dr. Holmberg.

DR. HOLMBERG: As the messenger that has to carry this back, I really struggle with the idea what do you mean by either principles or guidelines? Are you asking the Secretary to develop transfusion practices? Are you asking the Secretary to put on his agenda when he speaks to the states that the states need to look at the principles?

From what I just heard, it sounds like at the national level, you're asking for national principles or national guidelines.

CHAIRMAN BRACEY: Well, one of the things that I was thinking of, in a simplistic manner, would be that, for example, if blood shortages and access to blood components is discovered within a given region, that then that would trigger some--I mean it could be very general. It's not saying that the hemoglobin has to be eight prior to transfusion, but upon, at the state and local level, upon determining that indeed there are

patients who are being denied blood availability, that something would be triggered that would cause some sort of general review within the system of its availability.

I mean I don't think that we want to be prescriptive in the sense of, you know, recommending that 50,000 platelets is the magic number for transfusion, et cetera.

DR. HOLMBERG: If that's the interpretation from the committee, then I can live with it.

CHAIRMAN BRACEY: That's just from me. Dr. Epstein.

DR. EPSTEIN: Well, may I suggest that the word "policies" is a softer word? Because that can be translated into any number of mechanisms, and if we said, and it shouldn't be support development. I thought we had agreed it should state "develop national" something or others. Develop national policies under which state and local public health authorities.

And then coming back to Mr. Walsh's point,

what if we added the words before where it says "can minimize," "can prioritize allocation and minimize disparities"?

CHAIRMAN BRACEY: Yeah. That's a good point. Dr. Bloche.

DR. BLOCHE: I favor adding the words "prioritize allocation." I actually think--funny, different words have different meanings to different folks--but I think the term "policies" and the term "guidelines" both sound more official and more forceful than "principles."

Principles I think allows more flexibility. Certainly I think that's how both ethicists and lawyers would read the difference between the term "principles" and the words either "policy" or "guidelines." So I would urge going back to principles for that reason.

The other point I'd want to make is that we're talking not only about public health authorities. We're also talking about health care providers, especially doctors and hospitals, who are the ones who at the micro level are making

these allocations and who can make decisions, exercising their discretion, that generate disparities at the macro level.

So I would urge adding to state and local public health authorities health care providers. Yeah, I think that captures it. Health care as opposed to health providers.

CHAIRMAN BRACEY: General sense of the committee? Acceptable? Okay. General sense of the committee. Okay. Executive Secretary. Oh, sorry.

MR. MATYAS: Is blood sufficient or to be consistent throughout it's blood and blood products or--

CHAIRMAN BRACEY: Blood and blood products.

MR. MATYAS: Okay.

CHAIRMAN BRACEY: Thank you.

DR. BLOCHE: And this policies and guidelines thing versus principles, this, I suspect that many will read this doing exactly the things that some folks over on that side wanted to avoid

doing. That's just a kind of friendly wordsmithing suggestion. Flipping out the principles.

MS. LIPTON: And I would with that. First of all, guidelines is going to send us into federal advisory committee heaven. We'll never get them out. Maybe that's what we're all trying to accomplish, but I don't think so.

And I do think, yeah, I mean a policy has a very distinct definition. A principle is more like a stated goal, if you will, or an objective, and I think maybe that's a better, a safer word for us at this point.

CHAIRMAN BRACEY: Okay. So does the committee favor principles then?

DR. KUEHNERT: Maybe we've been through this, but recommendations is usually what we use in public health. I mean we're talking about public health, I mean they're going to develop recommendations.

DR. BLOCHE: That makes it too soft. Recommendations. Principles at least leaves ambiguity that reflects the differences of opinion

in this room.

DR. KUEHNERT: Well, I guess, but I mean you can't proscribe this sort of activity to clinicians. I mean if you talk about a public health department, you know, having the power to prescribe--I mean unless you're talking about a regulatory authority, I mean it's--well, from a federal standpoint, we can't do anything other than recommend, from that standpoint.

If you're talking about, you know, states having regulatory authority, then I guess maybe you're right, but I'm thinking from a public health perspective.

DR. BLOCHE: We're talking about, I think, multiple levels here in the sense that there's a message from the national government, then there's also messages from state public health authorities. Then there is where the rubber hits the road which is actually in the hospitals where the decisions actually get made, and in reality it's going to be what those hospitals set as their own internal policies and what they require the docs to do

that's going to determine the question of disparity.

So just allowing--

DR. KUEHNERT: But the hospitals still can't--I mean they can't tell--I mean unless you get into reimbursement, you know, that you won't get reimbursed if you do it this way, I mean then it becomes more prescriptive, but I mean a hospital can't order a physician to operate in a certain way.

DR. BLOCHE: The word "principle" also has a moral force, I think, a moral authority that the word "recommendation" doesn't have.

CHAIRMAN BRACEY: I'll get to the Executive Secretary. Can I--

DR. HOLMBERG: My question was answered.

CHAIRMAN BRACEY: Oh, it's answered. Okay. Dr. Bianco.

DR. BIANCO: Dr. Bracey, I have one simple suggestion.

CHAIRMAN BRACEY: Yes.

DR. BIANCO: Instead of "shortfalls,"

"emergencies." These will only be really applied in cases of emergencies.

CHAIRMAN BRACEY: Excellent. Great point. Yeah, because we experience shortfalls not infrequently. Excellent.

DR. EPSTEIN: Well, is critical shortages better than that, though, Celso?

DR. BIANCO: Well, anything that expresses it as an exception, is not a rule. That is if 20 percent less blood is available, I don't think that that makes it something that the federal government will define principles.

The only thing that they will be able to do is to make recommendations, let's say, to restrict transfusions only to emergencies, for instance. It will be much more difficult to create allocation.

CHAIRMAN BRACEY: So I guess the consideration would be critical shortfalls as opposed to shortfalls versus emergencies?

DR. EPSTEIN: Critical shortages.

CHAIRMAN BRACEY: Critical shortages,

critical shortages. Dr. Epstein.

DR. EPSTEIN: Could I just repropose that we substitute "policies" for "principles"? There seemed to be a transient satisfaction with that term. The problem is that it said /guidelines, and then we got back to substituting for guidelines. So let me just ask the question whether the group is happier saying "policies" or happier saying "principles"? Those seeming to be the two viable competitors.

CHAIRMAN BRACEY: Dr. Sayers has a burning comment and question.

DR. SAYERS: Hardly. But I was going to say to get the sense of the group, can we put that to the vote? Who wants policies? Who wants principles?

CHAIRMAN BRACEY: Well, that's a good point. All right. Then, so, for number five then, we will get the sense of the committee. Strike "of."

Yes, Ms. Thomas.

MS. THOMAS: I just would like to ask Dr.

Lipton again--earlier, you had given us very specific definitions. If you would that one more time before the vote, I'd appreciate it.

MS. LIPTON: Well, I will, but I caution you two things. First of all, I should say I'm not a doctor either, but I love to play one on this committee.

[Laughter.]

MS. LIPTON: But to my mind, when you get into the regulatory environment, if you use the word "guidelines," it brings into play a whole series of processes that the government has to go through to set guidelines, and it's a very lengthy process and if we use that term, that would be a problem.

To me, the distinction between a policy and a principle, a policy is something that you must follow. A principle to me is aspirational in nature. This is the principle under which I would like you to operate, but it allows you the freedom to accomplish that goal in whatever way you want.

A policy to me means you must do it this

way. This is our policy to follow. So I don't know. I kind of--that's why I think about what are the principles of our government? It's a democracy and it's, you can state them very high level, and I think what we're trying to get out of this is a very high level statement of sort of I think what Dr. Bloche was saying, the moral, the high moral ground here.

And I think that's what we're trying to establish in the principles and saying when you set these, when you do this at the local level, we want to make sure that you treat the patients first who are the most critical, that everyone has access in the allocation, that it doesn't go just to one hospital who is a favored customer, but that's what I sort of think of as the principles that we're articulating.

CHAIRMAN BRACEY: So then are you willing to make that in the form of a motion?

MS. LIPTON: Principles. Well it's up there already so--

CHAIRMAN BRACEY: Second.

DR. BLOCHE: Second.

CHAIRMAN BRACEY: Okay. There's a motion and second.

[Motion made and seconded.]

CHAIRMAN BRACEY: So what we're voting on is whether we will leave the statement number five, as to develop national principles under which state and local public health authorities and health care providers can prioritize allocation and minimize disparities in blood and blood products availability and use during critical shortages. Allocation of, yes.

All in favor?

[Show of hands.]

CHAIRMAN BRACEY: Okay. We have a count.

DR. SAYERS: Are we going to have any discussion?

CHAIRMAN BRACEY: Well, we had plenty of discussion.

CHAIRMAN BRACEY: I guess I only vote in a tie-breaker. Okay. Opposed?

[Show of hands.]

CHAIRMAN BRACEY: All right. Then it stands approved. Okay. Let's go back.

Should we start at--yes? Dr. Pierce.

DR. PIERCE: Can I go back to my earlier comment on the "whereas's" because I don't think it was addressed here.

CHAIRMAN BRACEY: Okay. Let's go to the "whereas's," please.

DR. PIERCE: Well, the point is that I was trying to make is that this is very centric to H5N1 or to influenza pandemics, and I continue to see that as we go through the entire document. So should this be broadened out to say that this is a model of other potential pandemics that could strike the United States?

CHAIRMAN BRACEY: Okay. I see. Okay. So the point--

MR. MATYAS: I'm sorry. Actually reading it was, I thought it was based on the fact that we had this, the outbreak of H5N1 virus, we've gone through all of this as opposed to all of this only applies to H5N1.

CHAIRMAN BRACEY: Well, that was my sense, but we do in the body specifically repetitively address H5N1, and so I assume it's open for interpretation. Comments from other committee members?

Karen Lipton?

MS. LIPTON: I thought we referenced--I thought we referenced avian flu specifically because we had some specific opportunities that we wanted to take advantage of right now? Certain studies that we could do because those events were out there right now, and I think we tried to limit those.

I think what we're looking at and trying to get our arms around here is pandemic influenza, and that's what we're trying to prepare for, and the rest of the committee who are newer members don't know this, but we already have a system in place to respond to disasters and acts of terrorism that might cause shortages or other issues.

And it's actually I think getting better and better. We've gone through a number of

nationwide exercises with HHS and DHS and so I--

CHAIRMAN BRACEY: That's a good point.

MS. LIPTON: --I want to be very careful that we don't suddenly take this and then change things that are already actually incorporated into HHS policy that have been functioning fairly well.

CHAIRMAN BRACEY: That's a good point, a good point. Dr. Ramsey.

DR. RAMSEY: Yeah. And just to add to that in number four, if we leave the reference to AABB Interorganizational Task Force in there, which I have a few doubts about, we should specific which task force it is because I think we're all thinking the pandemic task force, but just to make sure there's no confusion out there in people reading this that we don't mean the disaster task force.

CHAIRMAN BRACEY: Good point.

MS. LIPTON: Well, actually we do mean the disaster task force.

DR. RAMSEY: Okay. So what do we mean?

MS. LIPTON: Well, because what we're talking about is strategy to address massive blood

shortages and that is exactly--once we make some recommendations, the implementation of this on that level goes to the task force.

CHAIRMAN BRACEY: Dr. Holmberg.

DR. RAMSEY: So which task force I guess is--we just need to be clear about who we are talking about.

DR. HOLMBERG: And I think that it's okay the way it is because in ESF 8, which is the emergency support function, it clearly refers to that HHS will liaison with the AABB task force and it identifies this.

I have another comment, but I'll defer.

CHAIRMAN BRACEY: Okay. Dr. Epstein.

DR. EPSTEIN: Shouldn't we just give it the full name, Interorganizational Task Force on, you know, Domestic Disaster--

DR. HOLMBERG: I agree with that, because it needs to be consistent with what is in ESF 8.

CHAIRMAN BRACEY: Okay.

DR. EPSTEIN: So, Karen, can you give us the correct full name?

MS. LIPTON: If I remember. Interorganizational Task Force on Disasters and Acts--help me out, Kay. Domestic Disasters and Acts of Terrorism.

CHAIRMAN BRACEY: Okay. All right. So named. Dr. Holmberg.

DR. HOLMBERG: I should have voiced my concern about (a) earlier, and I was really struggling with this, but I really think that this is not going to go very far if it is presented in the way that it is worded at the present time, primarily because there are some committees--first of all, they're not necessarily committees, but they're working groups within HHS, and they're inherent government operations.

And so I would say that I would prefer that the committee consider maybe the wording "assuring blood and plasma systems are recognized in federal policymaking and communication."

CHAIRMAN BRACEY: Well, so, again, one of the issues that we were concerned about, I thought I heard various members of the committee state was

the absence of involvement of members. I mean there's input but to be certain that the message is right, the feeling was that there should be someone there.

DR. HOLMBERG: Well, I think that it carries that message because it is a sub-bullet underneath four.

CHAIRMAN BRACEY: Uh-huh. Comments from the committee? Dr. Epstein.

DR. EPSTEIN: Well, two points, Jerry. One is that one can use SGEs. You have to decide to, but short of that, if we reworded it to say "assure blood organization input" instead of representation, it's softer, it's lesser, but it gets at the point that there shouldn't be blind-siding or lack of attention to the views.

DR. HOLMBERG: Well, and I think that we already have this mechanism in place as far as communication, that making sure that we have a consistent unified message, and that is handled through the task force.

So I mean I was taking the position that

we already identify the AABB task force in four and that what is does is it assures that there is going to be--the message goes out there, and that we constantly are pinging this. We don't necessarily, you know, it may not be appropriate for a non-government person to be part of this.

And the blood organizations are representatives and not special government employees.

CHAIRMAN BRACEY: Dr. Epstein.

DR. EPSTEIN: Well, what if we shifted the focus away from committees, just to the policymaking and communication, assuring blood organization input into key federal policymaking and communication? And sort of finesse the issue of the mechanism being representation on committees?

Again, it is softer, but I understand the point. It's going to be very hard in practice.

MS. BIRKHOFER: Blood and plasma--

CHAIRMAN BRACEY: So, again, it's been softened by taking committees out? Ms. Birkhofer,

you would say blood and blood plasma.

DR. HOLMBERG: And that's what I was referring to with the blood and plasma systems.

CHAIRMAN BRACEY: Blood and plasma. Okay. Dr. Bloche.

DR. BLOCHE: Just a brief pitch for Dr. Holmberg's way of phrasing it before. I do think that the intro to item four pretty clearly underscores the importance of the blood organizations' input and I think you're right on target. So I forget what your language was, but maybe the vote--I don't know the process, the procedures of the committee since I'm new to all this, but maybe the voting mechanism is the way to do this.

CHAIRMAN BRACEY: Well, yeah, we're losing members. First of all, does the committee feel--do we need a vote or is there consensus with this statement as 4(a) is reasonable?

MS. LIPTON: I just have a question. The committee we were all talking about was sort of a joint--was a committee that deals primarily--

DR. HOLMBERG: Ms. Thomas, excuse me.

MS. LIPTON: I'm sorry.

DR. HOLMBERG: Ms. Thomas, could you just hold on for just a second? We're trying to vote. We're trying to see if we have a quorum. Okay. We don't have a quorum?

Dr. Sayers has given me the proxy that he was in favor of this.

CAPT McMURTY: It works for me. Hold your hand up. Okay. We have a--

CHAIRMAN BRACEY: Of 4(a). Okay. All right. We have your proxy. Did you count me?

MS. LIPTON: So my only question was I thought there was some key committee communication that everyone was concerned that--

CHAIRMAN BRACEY: Right. There is one.

MS. LIPTON: And so I think that was what started this whole conversation.

DR. HOLMBERG: It's not a committee. It's a working group, and I think what Dr. Epstein had mentioned earlier as far as making sure that we have in our communication mapping that the message

gets there. And I think this, the way the committee has worded it now, I think that this message gets across and will be acceptable.

CHAIRMAN BRACEY: Okay. Dr. Sandler.

DR. SANDLER: If it's their input they needed an apostrophe after the "s."

CHAIRMAN BRACEY: Okay. All right. Shall we go back through four? Okay. So number four, item four: recognize the central role of AABB Interorganizational Task Force on Domestic Disasters and Acts of Terrorism in the development and implementation of a national strategy to address potentially massive blood and blood product shortages during a pandemic of influenza by (a) assuring blood and plasma systems' input into key federal policymaking and communication;

(b) promoting cooperation amongst state and local public health authorities and appropriate blood collection organizations, hospitals, medical professional organization, and patient advocacy organizations.

So that's where we left item four.

DR. RAMSEY: How about communication and cooperation or is there too many communications. Maybe we don't need to worry about style so much, but promoting communication and cooperation?

CHAIRMAN BRACEY: Where were you now?

DR. RAMSEY: Sorry.

CHAIRMAN BRACEY: Cooperation. Okay. Communication. Okay.

MS. BIRKHOFER: Mr. Chairman.

CHAIRMAN BRACEY: Communication. Yes.

MS. BIRKHOFER: Just as a matter of course as staff edits this, can we just be consistent that blood and blood products throughout the document?

CHAIRMAN BRACEY: That's fine. Yes. Good recommendation.

Okay. So, Mr. Secretary, Dr. Holmberg, at this point, we have the document. The question is can we--we have proxies, two proxies.

DR. HOLMBERG: We have two proxies and we're seeing if we have a third proxy.

CHAIRMAN BRACEY: Okay. Dr. Epstein.

DR. EPSTEIN: I would like to raise two

points. The first is I think we need to say something about model building back up in the research item. I think that was bullet three. You know we only heard about that today, and I think there is something warranted to be said about supporting the development and validation of predictive models.

Item two. Okay.

CHAIRMAN BRACEY: Yeah.

DR. EPSTEIN: Yeah. Okay. So I think we need to add a subpoint (d) on support development and validation of predictive--of quantitative models and validation of quantitative models for blood availability and utilization in an influenza pandemic and the potential value of candidate interventions against shortages.

CHAIRMAN BRACEY: Okay. So support development and validation of quantitative models for blood availability and utilization in an influenza pandemic and the potential value of candidate interventions against shortages--to prevent shortages.

DR. EPSTEIN: Yeah, sure. It can be fixed. Spinning if off here after a couple of cups of coffee.

CHAIRMAN BRACEY: All right.

MR. MATYAS: Sorry.

CHAIRMAN BRACEY: Yes.

MR. MATYAS: The potential value of candidate interventions. Candidate interventions, what does that mean?

DR. EPSTEIN: Well, there are a whole variety of things one can think of doing. You know there's vaccinating, there's reducing use for non-emergencies.

CHAIRMAN BRACEY: Well, maybe if we just said interventions.

MR. MATYAS: No, no, no. Now, I understand what you mean. I was thinking of candidate as an individual in the interventions. I'm sorry. I understand what you're saying.

DR. EPSTEIN: You could say alternative interventions or--

CHAIRMAN BRACEY: Okay. All right.

DR. EPSTEIN: We may want to discuss this more, but the second point I wanted to make is that I don't think we quite resolved Glenn Pierce's issue which is whether we want to flag the development of strategies for pandemic influenza for the blood system as contributory to the need for strategic improvement in the blood system in general?

We talked about it, but we sort of didn't figure out whether it belonged in a "whereas" and we didn't figure out whether we wanted it in an action item.

I personally think that it's worth flagging the "whereas" section.

CHAIRMAN BRACEY: I thought one of the things that Karen mentioned and tied to other efforts that we have, i.e., the strategic plan, which is forthcoming, that will be addressed, but not specifically in this--

MS. LIPTON: That's what I was thinking. I mean I think, you know, once we start putting together the strategic plan, remember we had issues

of research. We had sort of all of these things as the elements of a strategic plan, and I think this naturally will show up there, so I'm not--

DR. EPSTEIN: I'm in complete agreement. I think the question is whether we want to add under the "whereas" section a statement to the effect that preparedness for pandemic influenza in the blood system will contribute generally to disaster preparedness for the blood system.

I'm not wedded to that point, but I don't think we ever sort of put to the vote whether we wanted to incorporate Glenn's suggestion or not.

I don't think it's in dispute that this naturally falls into the broader picture.

CHAIRMAN BRACEY: Actually, that's I think an easy enough point to put in. There's no point of action. It doesn't detract. It only adds. The committee's favor on that?

DR. EPSTEIN: Unless it's gratuitous, you know.

CHAIRMAN BRACEY: So can we go to the "whereas's"? Okay. So this would be under (h) and

this would be what--the development of a--

DR. EPSTEIN: Preparedness of the blood system to address pandemic influenza would contribute generally to preparedness of the blood system for disasters, something along those lines.

CHAIRMAN BRACEY: You got that? Oh. Preparedness of the blood system for--

DR. EPSTEIN: Pandemic influenza.

CHAIRMAN BRACEY: --pandemic influenza would contribute to the general--

DR. EPSTEIN: Disaster preparedness.

CHAIRMAN BRACEY: Yes. Dr. Holmberg?

DR. HOLMBERG: To be consistent, does the committee want to put blood and plasma systems?

CHAIRMAN BRACEY: Yes, yes, yes. Yeah. I think that--Dr. Sandler?

DR. SANDLER: Dr. Roseff asked me to make a suggestion for her regarding item number one, and she would like to add the word "distribution" as follows:

Establish national recognition of the blood and plasma systems (collection processing,

distribution and use).

CHAIRMAN BRACEY: That's fine. Used to be there. Yeah. We took it out.

[Laughter.]

MS. LIPTON: 30 words.

CHAIRMAN BRACEY: There you are. Okay.

MS. LIPTON: Put us over the top.

CHAIRMAN BRACEY: All right. Are we getting--is the general sense of the committee that we would like to go through it again? Are we close? Are we not quite there? What's the general consensus of the committee? Yeah, Dr. Epstein.

DR. EPSTEIN: I sort of had my checklist of new items that came up in today's discussion, and there is one more on my list, which is whether we want to say anything about surge capacity as a strategy? This is--this is the idea that building surge capacity would serve to underpin both influenza preparedness as well as create a more robust system in the face of staff and donor losses.

MS. LIPTON: I think we already have surge

capacity built in and we use it all the time. I think it's just a question of in the blood centers recognizing it.

What I don't think we can do easily is go out and hire a bunch of new employees and train them in advance of doing something. I mean we found that was the hardest thing to do.

DR. EPSTEIN: But that's just the point that is troubling me, Karen, because, you know, if you have a 30 percent donor loss and a 30 percent staff loss, and you don't have people you can call in to be the recruiters, to be the phlebotomists, to be the processors, then you're in a much worse situation than if you have created that infrastructure.

MS. LIPTON: But I think we don't know that from our level and I think from an operational standpoint, that's something a blood center needs to look at.

I mean is Celso still here? I mean I think one of the things that's very important is to not try to dictate to a blood center how to deal

with that, and I'm just very concerned that when we start talking about telling people to develop surge capacity, the worst people we had coming into those centers were people who hadn't been trained, and training, as you know, is just a tremendously huge issue in keeping people trained out there who we're not going to bring in and use everyday is really critical.

DR. EPSTEIN: Well, I agree with you, Karen, but there are other models. For example, there is cross-training. One of the biggest problems that we had in 9/11 was when the managers started being the phlebotomists and didn't know the procedures for phlebotomy or using nurses as surge staff, you know, but I think we need to learn from that experience and do better.

And it isn't necessarily a question of teaching new people who can come in ad hoc; it's potentially also an issue of cross-training with the staff you already have and can regularly train.

I'm just saying that one thing I learned from Steve Anderson's presentation is that

potentially extremely valuable strategy is to over collect in anticipation of the crisis, and that additionally we have to anticipate that second bump which is when all the delayed elective procedures start to happen because they've become more urgent.

And I'm just saying don't we need to think about that in some way? Now, it doesn't necessarily have to be a dictate, and I didn't mean it to be a dictate, but should there be some exploration of that issue?

MS. LIPTON: I think it will naturally happen in the pandemic influenza working group that we're working with now. I mean I think we have to go back and model and see if it even works for us.

CHAIRMAN BRACEY: Yeah, my thought was that as long as we have the piece in there for the development of the models, that should sort of foster the consideration of these possibilities.

DR. BIANCO: I just want to say, so Jay can sleep tonight, is that it is being considered by the task force, and that they actually considering adding some HR people to the task

people to review those issues.

And if we talk about surge capacity, you are really talking about something that we have to try to discuss in this committee many times. That is the emergency reserve, and which we have not been able to create.

CHAIRMAN BRACEY: Okay. So additional thoughts, considerations? Dr. Ramsey.

DR. RAMSEY: Can you just show the rest of number two for a second?

CHAIRMAN BRACEY: Yes.

DR. RAMSEY: I was just concerned that we might be a little bit too specific about some of these scientific studies that we're recommending. Just to make sure for the scientists here, which doesn't include me, that we're not being too restrictive in terms of the recommendations?

For example, support studies of avian influenza virus? Maybe might be instead of specifying H5N1 in number (b), in (b).

CHAIRMAN BRACEY: Take away H5N1.

DR. EPSTEIN: Well, wait, I don't quite

agree.

DR. RAMSEY: Okay. That's--I'm just--

CHAIRMAN BRACEY: Okay.

DR. EPSTEIN: Right now we have a problem with H5N1. We don't know that it's going to become pandemic, but it's got a 50 percent mortality rate. There have been some cases of human-to-human transmission, and I think part of preparedness really is to study H5N1.

I think the point that you're making is that it shouldn't be to the level of disregarding other candidate pandemic strains like H9. So I agree with that, but I would hate to see us drop an emphasis to support studies on H5N1. I think that's the immediate problem.

CHAIRMAN BRACEY: Mr. Matyas.

MR. MATYAS: I'd actually then say influenza viruses including but not limited to H5N1, and then you get to the point which is that's the immediate issue, but we're not limiting it to just this.

DR. EPSTEIN: Well, what if we did it in

reverse order? Studies of H5N1 and other potential pandemic strains.

CHAIRMAN BRACEY: Yeah, that's good. That's good. We have a pressing issue and that is that we're approaching five. We need to make a decision as to whether this is close to being acceptable and something that we could vote on or whether we would want to delay? I would favor a vote personally. Is that the consensus of the group?

All right. So should we go through it once again to make sure--no. Okay. All right. All members then who are in favor of the resolution to the Secretary as we have drafted throughout this afternoon, please indicate by raising your hand.

[Show of hands.]

CHAIRMAN BRACEY: I guess I'll raise my hand on this one, too. Voting members?

CAPT McMURTY: Dr. Bracey, Ms. Thomas did say for you to vote her proxy.

CHAIRMAN BRACEY: Okay. Then count me twice. Okay. Okay. Then all opposed?

[No response.]

CHAIRMAN BRACEY: Sounds like the work was worth it. Unanimous vote. Thank you for your contributions. Dr. Holmberg.

DR. HOLMBERG: Yes, just a quick, and I can follow up this by an e-mail, but in looking through the strategic plan that we talked about at the last meeting, I identified six different groups, policy, economics, clinical practice, research, disaster planning, donor retention, as areas of work groups that we will be working or trying to put together the strategic plan.

And so what I would like to do is get some input on what group you would like to be part of, if you'd be willing to volunteer to be part of the work group, the government work group on that.

MR. WALSH: Excuse me. Are you going to include a reimbursement?

DR. HOLMBERG: The reimbursement is actually under the economics.

MR. WALSH: Okay.

DR. HOLMBERG: Okay.

MR. WALSH: Sign me up.

DR. EPSTEIN: Jerry can you read them again more slowly?

DR. HOLMBERG: Yes, I'm sorry. Policy, economics, clinical practice, research, disaster planning and donor retention. Yes?

DR. BLOCHE: Could you clarify the distinction between the policy group and the economics group?

DR. HOLMBERG: Well, the policy is basically how do we establish our policy, what is the process for establishing the policy?

DR. BLOCHE: Processes. Whereas economics is more the substance.

DR. HOLMBERG: Exactly.

DR. KUEHNERT: Is surveillance included under research?

DR. HOLMBERG: Yes, I did put that under--right, we have a seventh group, surveillance.

MS. LIPTON: And where is risk communication?

DR. HOLMBERG: Risk communication is under

disaster planning. Yes?

DR. EPSTEIN: I'm concerned that the committee, if it's now being charged with sort of bringing forward the plan hasn't had a discussion about how it wishes to structure itself to do so.

And should that process be restricted to the committee or should it involve outside parties and is this being conceptualized initially as a government activity with the extension of SGEs? In other words, I just think that there's a lacking antecedent discussion here.

DR. HOLMBERG: Well, I thought that the recommendation that took place at the last meeting was a recommendation to the Secretary to move forward on this. So with that recommendation was the burden of the government putting together the strategic plan with the input from the various working people on this committee.

So I mean to what extent do you think that we need to have discussion on this?

DR. EPSTEIN: Well, for example, the categories of the working groups don't exactly

correspond to the categories of the plan as proposed by the committee so how did that happen, for example?

DR. HOLMBERG: Well, basically I'm a lumper and I was lumping things together to try to minimize the number of working groups that we would have. I mean if it's the wish of the committee, we can keep each one separate, but, for instance, risk communication, you know, I felt very--I felt that it logically went under disaster planning such as in the economics, the idea of the cost of blood products, the reimbursement, the funding of promising new technologies which were all key elements really falls under the economics part on how do we move forward on this.

CHAIRMAN BRACEY: Mr. Secretary, Executive Secretary, can we perhaps have a follow-up conference call of the subcommittee to address the implementation plan?

DR. HOLMBERG: Absolutely. If that's the wish of the committee.

CHAIRMAN BRACEY: Would that be the wish

of the committee?

MS. LIPTON: I think that makes the most sense.

MR. MATYAS: Yes.

MS. LIPTON: I mean even in putting risk communication, which I thought was more along the lines of not just about disasters, but really to the public about the risks and benefits of blood transfusion so maybe it would make sense to--of course, our chair of that committee is no longer on the committee, but--

CHAIRMAN BRACEY: Yeah.

MS. LIPTON: It was Jean Linden [ph]. But maybe that makes sense is to get it back together and talk about a proposed process that comes from the committee more.

CHAIRMAN BRACEY: Would you be willing to serve as the newly appointed chair of that subcommittee? Ms. Lipton?

[Laughter.]

CHAIRMAN BRACEY: All in favor?

[Laughter.]

MS. LIPTON: That will teach me--I'm going to be colorful on this committee, though, I just want you to know.

CHAIRMAN BRACEY: Okay.

[Laughter.]

CHAIRMAN BRACEY: The colorful corner over there.

MR. MATYAS: The document that lays out that, was that in the materials? Is that on the Web site?

DR. HOLMBERG: It's on the Web site under the recommendations from the last meeting.

MR. MATYAS: From the last meeting.

DR. HOLMBERG: And I can make sure that you get a copy of it also.

MR. MATYAS: No, no. I can go to the Web. That's fine.

DR. HOLMBERG: Okay.

MS. LIPTON: We'll need some more members on the committee because a number of them have graduated, so to speak.

DR. HOLMBERG: Well, let me send an e-mail

out and we'll get solicitation by e-mail.

CHAIRMAN BRACEY: Are we at the close? Dr. Kuehnert.

DR. KUEHNERT: I assume we sort of established this, but just that we talked about how the recommendations passed are relevant to the strategic plan, but that are we going to spend time at the next meeting determining how the recommendations are relevant to the strategic plan. Is that the objective?

DR. HOLMBERG: Well, to be honest with you, I don't think that we will have a final draft, not until maybe August. But I think that we can have a very, maybe bullets together for discussion, and I think that one of the problems that we have to be very cognizant of, and that is that any time we have subgroups, it is not a decision of the committee, that has to be reported back to the full committee.

So we--

DR. KUEHNERT: I meant at the next meeting, next time we meet--

DR. HOLMBERG: Right.

DR. KUEHNERT: --that we would discuss whatever progress is made on the strategic plan, but also how these recommendations fit into the strategic plan. Just the recommendations that we made don't get sort of put into the ether and then we don't really talk about them again.

DR. HOLMBERG: Right. Okay.

CHAIRMAN BRACEY: Dr. Epstein.

DR. EPSTEIN: Yeah. Thank you. Well, I guess what's troubling me is sort of a legal nuance. I guess I can wait till Jerry is done.

CHAIRMAN BRACEY: Dr. Holmberg.

DR. EPSTEIN: Jerry, I'm a little troubled by kind of a legal nuance about what's being asked. On the one hand, the department is now establishing a work plan to develop a strategic plan for blood for the 21st century. That of course is the prerogative of the department.

And if you're simply asking for participation from some of the SGEs, that's a simple matter. You just go forward. If on the

other hand, what you're asking is for this committee to establish subgroups to develop, then that's a different thing, and I think that we're into different procedures in those two different pathways.

DR. HOLMBERG: And I'm sorry if there was misclarification on that. What I was trying to communicate was the fact that the department is already moving forward on the recommendation that was made back in September, and so what we're--my goal now is to solicit comments from different SGEs and representatives from this committee and not let the committee go back and rehash it.

What I'd like to do, not until there's a final draft, and I think at that point in time bring it back to the committee. So, yes, that's, I was trying to keep it as simple as possible, and the fact that I wanted to have the government moving forward on this, but to also have input from the committee.

DR. EPSTEIN: Okay. So then you're soliciting participation by individual SGEs.

DR. HOLMBERG: Absolutely.

DR. EPSTEIN: And that's quite different than forming subgroups in these working group areas.

DR. HOLMBERG: Right.

CHAIRMAN BRACEY: Do we have any more business?

MS. LIPTON: No, we can just talk. Then I guess we don't need to have a committee call?

CHAIRMAN BRACEY: Yeah.

DR. EPSTEIN: That's right. Jerry is just looking for volunteers.

DR. HOLMBERG: Let me send out an e-mail and I need volunteers to help the government work on the various aspects of the strategic plan.

CHAIRMAN BRACEY: All right. Do we-- motion for adjournment.

[Motion made.]

CHAIRMAN BRACEY: All right. All in favor, aye. We're adjourned.

[Whereupon, at 5:01 p.m., the Advisory Committee was adjourned.]