# SECRETARY'S ADVISORY COMMITTEE ON HERITABLE DISORDERS IN NEWBORNS AND CHILDREN

Thursday, September 16, 2010

8:30 a.m.

Washington Marriott at Metro Center

775 12th Street, N.W.

Washington, D.C. 20005

## COMMITTEE MEMBERS

Joseph A. Bocchini, Jr., M.D.

Jeffrey Botkin, M.D., M.P.H.

Rebecca H. Buckley, M.D.

Bruce Nedrow Calonge, M.D., M.P.H.

R. Rodney Howell, M.D.

Jana Monaco

Kwaku Ohene-Frempong, M.D.

Michael Skeels, Ph.D., M.P.H.

Tracy L. Trotter, M.D., F.A.A.P.

Gerard Vockley, M.D., Ph.D.

Coleen Boyle, Ph.D., M.S.

Denise Dougherty, Ph.D.

Alan E. Guttmacher, M.D.

Kellie B. Kelm, Ph.D.

Peter C. van Dyck, M.D., M.P.H., M.S.

Michele A. Lloyd-Puryear, M.D., Ph.D.

Frederick M. Chen, MD, MPH, FAAFP

Timothy A. Geleske, MD, FAAP

Michael S. Watson, Ph.D., FACMG

William A. Hogge, M.D.

Jane Getchell, Dr. PH.

COMMITTEE MEMBERS [Continued]

Christopher Kus, M.D., M.P.H.

Bennett Lavenstein, M.D.

Mary J.H. Willis, M.D., Ph.D.

Sharon F. Terry, M.A.

Alan R. Fleischman, M.D.

Barbara K. Burton, M.D.

P R O C E E D I N G S

Dr. Howell: Let me welcome you to the 22nd meeting of the Secretary's Advisory Committee on Heritable Disorders in Newborn and Children. We would like to welcome our newest members, Dr. Jeff Botkin and Dr. Joseph Bocchini. And while both of them have attended the meetings in the past, this is the first time

that they've been official and anointed and are sitting at the table and we welcome you both.

We'd also like to welcome Dr. William Hogge, who is the organizational representative for the American College of Obstetricians and Gynecologists. Dr. Hogge is currently the chair of the ACOG Committee on Genetics and he'll be joining us today by telephone.

Ms. Harris at the outset here has some housekeeping duties. Alaina.

Ms. Harris: Good morning, just a few housekeeping notes for the Committee and the audience. When you are exiting the general session the restrooms are down the hallway to the left. Altarum Staff, that's Maureen, Rebecca, and Tiffany they're at the registration desk and ready to assist you.

We do want to let you know that we were unable to provide wireless internet access while you're in this room but the hotel does offer complimentary wireless in the hotel lobby. The continental breakfast and lunch are available to Committee Members, representatives and presenters, and that's in the London Room which is also down the hall and to the left.

Tonight, we have not organized a fixed menu dinner for the Committee Members, representatives, and presenters but we are going to a restaurant. So if you'd like to sign up for that please do so at the registration desk before lunch. And what

we're going to do is meet in the hotel lobby at 6:30 this evening.

Our sub-Committee meetings will be this afternoon from 2:00 p.m. to 5:00 p.m. The Laboratory Standards and Procedures is going to be in Salon 1, which is on the second floor. Also on the second floor will be the Education and Training group. They'll be in Salon 3 on the second floor.

And then the Follow-up and Treatment group is going to meet in this room. So everybody exit quickly when we're done unless you're in the Follow-up and Treatment and then you can stay here. We're also going to have an HIT workgroup meeting from 5:15 to 6:30 today. That will be in Salon 1 on the second floor. And that meeting is open to the public.

If any of the presenters have changed their presentations after you've already submitted them to Altarum we ask that you please save a revised copy of the presentation on the laptop and let Altarum know.

Finally, Committee Members, organization reps, presenters you all should have received a thumb drive that contains a supplement to your briefing book. If you have not, please let us know or swing by the registration desk. That supplement was in a thumb drive.

Thank you.

Dr. Howell: Thank you very much Alaina. The first that

that we need to do is approve the minutes from the May 2010 meeting and those have been sent to the Committee some time ago and hopefully everybody's had a chance to read those. Can we have a motion? Are there any changes to the minutes as you've received them?

[No response.]

Dr. Howell: Hearing no changes that are recommended, can we have a motion to approve the minutes?

Dr. Trotter: So moved.

Dr. Howell: Second?

Dr. Buckley: Second.

Dr. Howell: Those favoring it, an aye.

[Chorus of Ayes.]

Dr. Howell: I hear no opposition so we'll move ahead. We have a lot of Committee correspondence that's in your book and I hope that you've had a chance to look at -- your book that I'm referring to is a PDF file which is a great paper saver and also a very, very convenient. I have a hard copy simply to make notes and so forth in.

But I think it's fair to say that if you look at all the correspondence we have, the most exciting letter that we have is he one dated May 21st, 2010 from the Secretary. And in her letter she announces the adoption of the recommendations of this Committee, re: the Uniform Screening Panel with 30 core

conditions and 26 secondary conditions.

I think it's very important to read that letter because she also says that this is now a national standard and we think that's very important in a formal letter from the Secretary to this Committee and we appreciate that.

She also has requested a report to be sent to her by May of 2011 on the status of the states' implementation of the recommendation to add SCID to the core condition and the related T-Cell Lymphocyte deficiencies, et cetera. And there have been a couple of meetings involving that, one of which was yesterday.

The Newborn Screening Translational Research Network held a workgroup meeting regarding the SCID trial. And in October of this year the CDC, APHL, HRSA and one of HRSA's centers are hosting a meeting entitled Newborn Screening for Severe Combined Immunodeficiency Implementation Challenges in upstate. We also have in your book the communications that have been provided by the California Department of Health concerning SCID.

I wonder, Tracy, would you like to comment about that? Where are you Tracy?

Dr. Trotter: Here.

Dr. Howell: Oh, you're right there.

Dr. Trotter: The pilot study in California started last month and the method is a specimen is taken after the mandated screen is completed and we are using TRECS followed-up with flow

cytometry. The positive screens will be reported to the primary care physician and referred to either Dr. Jennifer Puck or Dr. Sean McGhee depending on which part of California you're in.

Negative screens will not be reported during the pilot. It's expected to last 18 months and involve about 800,000 specimens. And it will become part of -- we expect to be come part of the mandated routine screen by 2011. And Fred Lorey is here today if you have any questions about it we're a month into it now.

Dr. Howell: Let me ask Mike Watson if he would briefly comment about the meeting that was at the American College of Medical Genetics that had most of the folks in the country involved in pilot studies and the ACMG under Newborn Screening Translational Research Network is coordinating some of those efforts, particularly as far as data acquisition and so forth.

Dr. Watson: Not much left to say. Yeah, it was a good meeting. It was all the states involved in both the NICHD funded pilots as well as the CDC funded pilots. Sorting through sort of the protocols for screening, looking at the follow-up issues, ensuring that there are networks of providers not just in the states where this -- the pilots are taking place but thinking more broadly about national networks since patients could appear from supplemental screening programs anywhere in the country independent of the pilots. So we just spent a lot

of time standardizing --

Dr. Howell: Mike, you might mention the states that are involved in these pilot studies since all the Committee may not be aware of that.

Dr. Watson: Sure, Wisconsin and Massachusetts have been funded for three year projects by the CDC. They're about in their -- I guess approaching the end of the second year. NICHD has funded a subcontract to New York State that is funding additional patients from Puerto Rico who will be screened in the Massachusetts lab. Patients from Louisiana that will be funding in -- or tested in the Wisconsin laboratory. Plus the California screening that Tracy alluded to.

Dr. Howell: And all those groups were well represented yesterday and so forth. Any questions or comments about that?

[No response.]

Dr. Howell: Those pilot studies seem to be ticking along. One of the -- I'd like to make is the Secretary's adoption in addition to the screening panel that the timing is fortuitous because the Patient Protection and Affordable Care Act was signed into law on March 30th.

And on July 14th, the Departments of Health and Human Services, Labor and Treasury issued a interim final regulation for the Patient Protection and Affordable Care Act. And the Committee's recommended screening panel is a service that is

covered under the interim final regulations as recommended as a preventive service.

So the timing of that was really very fortuitous to get that rolled into that effort. The interim final regulations require new plans and issues to cover certain preventive services without any cost sharing to the enrollee. So that was very interesting.

Plans and insurers are required to provide coverage without cost for our recommended screening panel in the first plan year that begins May 21, 2001. So that it would be a required preventive services without cost sharing. That's really a very timely recommendation in its adoption to get into this plan.

On March the 23rd -- and the Committee has all this correspondence in your material but let me review it with you. We sent a letter to the Secretary that forwarded our White Paper on health care reform. And the Secretary will either need to say yeah or nay by this coming Sunday which is September the 19th. As you know, the Newborn Screening Saves Lives Act has a time frame in which the Secretary must respond to our efforts. And that's been very -- she's been extremely timely.

Our briefing letter also contains letters from this Committee after the last meeting. The letter to the Secretary about insurance coverage, of medical foods, foods modified to be low in protein and pharmacologic doses of vitamins and amino

acids, etcetera.

In addition, the letter to the Secretary about Sickle Cell train and disease. About the NCAA recommendation concerning athletes. And as you know, we're going to hear -- Kwaku's going to report on that in some detail later. But we sent a letter actually before we had this final document because we thought this was a very timely issue.

The Committee has now got also the Sickle Cell Disease workgroup and the updated version. And later, we're going to discuss whether or not you would like to send that paper that you're going to hear about forwarded to the Secretary.

And the other thing is, we sent a letter to the Secretary about the National Contingency Plan for the Newborn Screening. And that was sent on August the 6th, 2010. So there's been lots of stuff going.

At your seats today we have the latest version of the NCC Collaborator which is hot off the press. It was just put down this morning. We also -- on your supplementary -- you have a supplementary little PDF -- you have a supplementary PDF series of files. And in that is also the draft of the Institute of Medicine's workshop that they had on handling the dried blood spots. And we appreciate the work that Adam Berger and IOM has done doing that.

Before we go forward with the rest of this meeting I would

like to recognize the outstanding work of three of the pillars of this Committee. And that's Jana Monaco, KOF, and Dr. Michael Skeels. This will be their last Committee meeting as Committee Members since their terms end in September.

However, they have agreed to stay on for additional 120 days until new members are appointed. Good luck in 120 days. I don't know whether your contract has a specific date in it, but I wouldn't bet on it. But I have certificates for all of this distinguished group that I would like to provide.

The first certificate is Kwaku Ohene Frempong, better known as KOF.

[Applause.]

Dr. Howell: We also recently saw some very nice material from KOF's recent outstanding efforts in Ghana where he was really working with the hoi paloi and he was shown with the First Lady and so forth honoring all of his fine work --

Dr. Frempong: Where did you see this?

Dr. Howell: Well I have --

[Laughter.]

Dr. Howell: If you do anything you can guarantee I'll know about it.

[Laughter.]

Dr. Howell: It's that same group that helps me quiet the audience. Maybe we can get those sent around because KOF in

addition to being honored was wearing extremely attractive garments. I think you should wear those to this meeting sometime, it would brighten this group up.

Dr. Frempong: Yes it would.

Dr. Howell: And Jana Monaco.

[Applause.]

Dr. Howell: And I'm sure that Jana being in the region and being so active, we will continue to see a great deal of you we hope Jana.

Ms. Monaco: Absolutely.

Dr. Howell: Thank you Jana.

Ms. Monaco: Thank you.

Dr. Howell: Great. And then finally we have Mike Skeels.

[Applause.]

Dr. Howell: And these are really very nice certificates. They're signed by the administrative person Mary Wakefield, and also Kathleen Sebelius.

Dr. Skeels: Thanks. I want to also thank you for doubling my rate of pay for the next 120 days.

[Laughter.]

Dr. Howell: Okay, good, good. Well I mean you're extremely well paid. But we, for the public record, we won't go on to the huge amount of funds that you get here.

[Laughter.]

Dr. Howell: We now move into our first area of activity which is a report on the briefing paper from the Sickle Cell Disease Carrier Screening Workgroup. And we'll have KOF to -- on that. I think that many of you saw a commentary that appeared in New England Journal that reviewed and outlined many of the things that we've discussed at length at this Committee that was authored by Vence Bonham and some of his colleagues. KOF.

Dr. Frempong: Thank you very much.

Dr. Howell: I think that while KOF's getting his things up, I think that you all will remember that we had at our January meeting we had a workshop, a report from the workshop about evidence for screening for Sickle Cell carriers.

And then a workgroup was formed by this Committee to really work on a paper that would be more extensive that we will hear about today. And each of you has a copy of this paper, it went out in your material. And the issue we will deal with is sending this forward.

Dr. Frempong: Okay, thank you very much. This is the second presentation that we've done on this work. And so I'll move really to read quickly through them. So it's more of an update of the work and hopefully this may be near final.

So the purpose of the briefing paper was to apprise the Secretary of new rules and practices concerning the screening of

college athletes for Sickle Cell Trait. And we'll define what is meant by Sickle Cell Trait in this context in a second. To also discuss the impact of these policies and practices on the public health system. And then to make appropriate recommendations and responses from the Secretary on this issue.

The working group members, you see here a distinguished group of experts and others have worked very hard through several drafts to do this and I'm really just the spokesperson more than the hard worker in the group. This is the general organization of the briefing book.

It has an introduction and a little background to the whole story. Then a summary of the findings that we know now on health outcomes of Sickle Cell Trait. Then the impact of the screening rule of NCAA on the population and public health systems, newborn screening systems and other stakeholders. And then finally, the actual recommendations that the Committee put together.

These are the areas that are covered sort of generally. National and global prevalence of Sickle Cell Trait, the effects of Sickle Cell Trait on health. The specific issue of unexpected deaths in athletes and military recruits with Sickle Cell Trait.

Then the recommendations made by the NCAA and specifically also the National Athletic Trainers Association backed by the

College of American Pathologies. And then general issues related to screening people for Sickle Cell Trait.

So just briefly, to update most of you and I'm sure some of you to whom this may be new, the Sickle Cell Trait is a very common genetic condition. It's part of a group of disorders called hemoglobinopathies that are supposed to be the most common genetic disease of humans.

It's estimated over 300 million people in the world with Sickle Cell Trait. The highest prevalence rates are in Sub-Saharan Africa where about 15 percent of the 800 million people have Sickle Cell Trait. They are very -- pockets of India with very high prevalence of Sickle Cell Trait also.

All the Middle Eastern countries have Sickle Cell Trait and all the Caribbean countries and many South American countries also have relatively high prevalances. For comparison, 1.31 percent of all newborns in the United States have Sickle Cell Trait also. And it's estimated therefore that about a little over 4 million people in the United States who have Sickle Cell Trait. These are some of the countries with the highest prevalances.

And the reason for showing this data is really to see that if you have this many people in your population with Sickle Cell Trait, and if there are any sort of serious health outcomes related to Sickle Cell Trait, these are the countries that are

likely to see and report many of these issues. And if we don't hear from them it's not because they're missing it, it may be because it's not as common as we may think as far as these complications go.

By definition, the bullet number three is really what we are talking about when we say a Sickle Cell Trait. It's the inheritance of normal Beta A hemoglobin gene from parent and the Beta S or the Sickle hemoglobin gene from the other. That is simply defined as Sickle Cell Trait.

Each red cell of the person with Sickle Cell Trait contains both hemoglobins A and S, but there is always more A than S. And that's important because that is really what makes the condition a benign condition is that there is more hemoglobin A then S. There's another type of Sickle Cell Disease in which both hemoglobins are present but there is more S than A.

And when there is more S you have a disease, if there is more A you do not have a disease. The excess hemoglobin A in the red cell inhibits hemoglobin S polymerization. And inhibit is probably not the best word it because hemoglobin A actually can participate in the polymerization of hemoglobin S in extreme conditions.

I'm going to skip through this really just to quickly, just mention in the summary form, that there is good reason, there is good biochemical reason why in a person with Sickle Cell Trait,

under some conditions, that the red cells can actually become Sickle Cells.

In vitro is easy to demonstrate but there in vivo it is possible for people with Sickle Cell Trait to have their cells Sickle. And the reason is because the way the hemoglobin is assembled within a red cell, a majority of the assembled hemoglobins actually can be induced easily to polymerize and therefore form Sickle Cells, just to mention that.

We all know that there are ways to test for Sickling by inducing red cells from people with Sickle Cell Trait to Sickle under conditions of low oxygen and high acidity or low PH, these cells that normally behave like normal cells, containing A and S hemoglobin, can actually be induced to Sickle.

That in may of the laboratory situations they do not behave exactly the name as normal cells. One of them is that blood banks have known for a long time that it's difficult to filter Sickle Cell Trait cells. Although now some manipulations have been made to make this possible. Sickle Cell Trait blood has increased whole blood viscosity. The red cells, a little bit more rigid than normal.

And an important feature that actually makes this condition what it is in terms of protecting humans from malaria is that when A/S cells are infected with malaria, there is increased splenic clearance. And that that may related to the fact that

the cells can Sickle and when they do so then the spleen clears them as a way to reduce the density of infection.

In vivo experimentally when people with Sickle Cell Trait are subjected to strenuous exercise under ambient conditions of high temperature and also under water depravation that Sickle Cells can actually be seen in the venous blood. The highest that's been reported is only about 8 percent of the cells. So there's not massive sickling.

People with Sickle Cell Trait do not have hemolysis normally so they're not anemic and their reticulocyte counts are in the normal range. Their cells look normal on blood smears and on peripheral smear one does not see Sickle Cells and Sickle Cell Trait individuals.

There is no pattern of the key risks or inclusive events that are typical of Sickle Cell Disease in people with Sickle Cell Trait. They don't get pain crisis although I'll tell you around the world there are many people, either because they're not properly diagnosed or because of what they've been told about Sickle Cell Trait, who report so-called crises even though they only have Sickle Cell Trait. But the general scientific information is that they really don't have that pattern.

What has been recognized for a very long time is that people with Sickle Cell Trait, starting at about maybe three or four years of age have inability to concentrate urine or

hyposthenuria. And this is thought to be caused by a loss of the renal concentrating ability in the renal medulla and this is maybe because they've lost some of the special vessels, the vasa recta, that make this renal concentrating ability possible.

So one presumes that in the environment of the renal medulla, where there is high osmolarity and low PH, that red cells in people with Sickle Cell Trait may actually be induced to sickle and cause this occlusion that may end up in the loss of these vessels. It hasn't been shown very clearly.

Perhaps the most important study that's ever been conducted on the health consequences on Sickle Cell Trait was a study done by Heller and colleagues reported in the New England Journal of Medicine in 1979. They looked at 65,000 consecutively admitted black male patients in 13 VA hospitals. And it is biased by the fact that this was only males and not females.

The overall frequency of Sickle Cell Trait in that population was 7.8 percent. Not very different from the U.S. overall prevalence of Sickle Cell Trait. And they reviewed through the VA system the inpatient records of 24,000, almost 25,000 of these veterans. And about 18,000 had normal hemoglobins or no abnormal hemoglobins. About 5,000 had Sickle Cell Trait and about 1,400 were hemoglobin C traits, or AC.

The study concluded that Sickle Cell Trait had no effect on average age at hospitalization or death, had no effect on

overall mortality, length of hospitalization on medical or surgical wards or frequency of any of the common major diagnosis. But they found that Sickle Cell Trait was positively associated with essential hematuria, hematuria of otherwise unknown cause. And also an increased rate of pulmonary embolism. So this was back in 1979.

Some of the clinical manifestations have been mostly renal. And again, that may be related to the special environment of the tissues, deep tissues in the kidney. Venousthromboembolism has also been substantiated in a recent study.

It's been reported in several instances around the world of people with Sickle Cell Trait experiencing splenic infarction at high altitudes being reported here in the United States also. And then, there have been many reports, sporadic reports of exercise or heat related sudden death in people with Sickle Cell Trait. And that is the issue at hand.

The best record of these events or sudden unexpected deaths came from the military first reported by John Clark and associates in 1987. And they had reviewed retrospectively for five years between 1977 and 1981 records on 2.1 million enlisted recruits and their health during basic training. The deaths reported in this group were classified from autopsy and clinical records as either non-sudden, sudden explained or deaths unexplained by pre-existing disease.

Out of these 2.1 million people, there were 37,300 with Sickle Cell Trait classified as black. And another 1,300 with Sickle Cell Trait classified as non-black. And 429,000 blacks without Sickle Cell, with no hemoglobin S. And 1.6 million non-blacks with no hemoglobin S.

There were a total of 41 exercise related deaths in this group. 50 percent of the deaths were related to exertion or heat illness and 50 percent were classified as idiopathic sudden death.

Looking that the causes of death more carefully, within the black A/S group or Sickle Cell Trait group, there were 12 deaths among the 37,300 over the five year period. There was no death in the 1,300, a very small number of non-blacks with Sickle Cell Trait. Blacks without hemoglobin S, there were 5 deaths in the 429,000. And one death, I think actually it was 11, in the non-blacks with no hemoglobin S.

Just by statistics the relative risk of sudden death in Sickle Cell Trait recruits versus those without hemoglobin S was 27.6 in the black recruits. Meaning that blacks with Sickle Cell Trait had a 27.6 times more risk to have sudden unexplained death. And almost 40 times the risk for all the recruits put together who didn't have Sickle Cell Trait.

So this was a very alarming news. It was really the first carefully collected data on the subject. In the ensuing 10

years from 1982 to 1991, Kark was able to organize an intervention study through some of the recruitments and tests in the U.S. And the intervention that they adopted was for stricter rules for preventing exercise or heat related injury or illness. And also to directly observe the recruits drink prescribed amounts of water.

And for that 10 year period there were 2.3 million recruits. 40,000 among them were Sickle Cell Trait. And they had predicted that in the Sickle Cell Trait group they should see about 15 deaths, there was zero. There was no death. And they had predicted in the non-Sickle Cell Trait group that they would see 19 deaths and there were 11.

At the same time they collected data from centers that did not participate in the intervention program. And at that those centers the death rates were the same as had been reported previously. So it appeared as if this simple intervention of increased hydration and monitoring ambient temperature and humidity more carefully seemed to have solved this problem.

Since then there have been many single cases reported mostly in the mass media. And in many cases the basis for the hemoglobin diagnosis usually not clear since it was being made post-mortem and it wasn't always reported whether hemoglobin -- or another study to identify specifically what hemoglobins there may be in the person's tissues were actually done.

The association of sickling was usually based on autopsy findings of Sickle Cells in the tissues. And most cases suggested that this was either exercise related or heat related rhabdomyolysis similar to the cases that had been reported in the military recruits.

College football is the most common sport involved, but other sports had also seen this. And overwhelmingly more males then females. And that probably is just reflecting the participation in strenuous sports activity. Unlike the military though, there have been no large epidemiologic study of athletic deaths. And there's been no trial of simple intervention to reduce the risk of heat related illness.

An interesting discussion that was published in a series of papers in the Journal of Applied Physiology was topic; Point, Counterpoint Sickle Cell Trait Should or Should Not Be Considered Asymptomatic and as a Benign Condition During Physical Activity.

And these two references summarized what had been reported up to that point. Either warning about the dangers for people with Sickle Cell Trait engaged in strenuous physical activity or reporting on several teams in the U.S. and in the Caribbean and in Africa, the representation of Sickle Cell Trait at national level or college level athletics.

And in those live reports usually they found the same

representation, as it is expected of Sickle Cell Trait people in the general population. But in the counterpoint, these anecdotal cases of injury or deaths in people with Sickle Cell Trait.

The index case that brought the NCAA to their decision was the case of Dale Lloyd, II. A former football student athlete at Rice University who, at age 19, collapsed after 16 100 yard sprints in September 2006 and died one day later in the hospital. And the official autopsy listed the cause of death as acute exertional rhabdomyolysis, secondary to Sickle Cell Trait.

Lloyd, who had actually been screened as a newborn and found to have Sickle Cell Trait, himself did not know at that age that he had Sickle Cell Trait. The family sued Rice University, the football coach, and the NCAA and two nutritional supplement companies because he was taking some supplements for wrongful death.

As part of the resolution of the case, which was eventually settled out of court, the NCAA agreed to amend its Sports Medicine Handbook Guidelines, section 3C, to state that while Sickle Cell Trait screening is normally performed on all U.S. babies at birth, some student athletes may not know if they have the trait.

They also agreed to -- the family asked the NCAA to donate $50,000 to the Sickle Cell Disease Association of America in the

name of their son to provide awareness, education and screening for Sickle Cell Trait in the athletic population. The last I heard, I think the SCDAA had decided not to do anything with that money, at least not yet.

Also that NCAA should contribute $10,000 to a scholarship fund in the name of their son, to prepare an educational video about Sickle Cell Trait to appear on their website, which as been done, and to stress a point of emphasis in their handbook on regular preseason communication with the media prior to the 2009 football season. And that too has been done.

So the NCAA then went through a series of attempts to introduce new regulations regarding Sickle Cell Trait screening for their athletes. And the final and the current one was in April 2010 when for only Division I athletes, this was decided by the Division I Legislative Council, that Division I student athletes must be tested for Sickle Cell Trait, show proof of a prior test, or sign a waiver releasing an institution from liability if they decline to be tested.

The rule is taking effect as we speak for this 2010 to 2011 academic year. And the NCAA rules cited recommendations of the National Athletic Trainers Association that stated that institutions should carefully weigh the decision to screen. NATA, the Athletic Trainers Association, also made a set of recommendations on how to manage the athlete with Sickle Cell

Trait.

And it's a longer list but a little summary of it is here showing that the advice that the Sickle Cell Trait athletes build up the intensity of their training more slowly with pace, progression, longer periods of rest and recovery between repetitions. That preseason and year round they should undergo strength and conditioning so that they shouldn't decondition and come back into preseason.

That they should be excluding from mile runs or serious sprints. Something that I must say is a little surprising. They should cease activity on the onset of symptoms and set their own pace. In the recommendations of NATA also they do describe the symptoms that these athletes should look out for or trainers should look out for. They also talk about adjusting their work cycles and also educating the athletes with Sickle Cell Trait to report any symptoms.

So these issues were addressed in the briefing book. And this is a summary of some of the socio and ethical issues that the briefing discussed separate from just the technical part of doing the testing.

That we thought this would have an impact on the newborn screening programs as people went back to seek results of their newborn screening. And we're not sure whether all states screening programs are actually able to provide that

information. Also just how any sort of counseling may be provided with this retrieval of the information.

Another issue is the choice of screening tests that the NCAA recommends. Generally they recommend the simplest form of screening with is a solubility test or a sickling test, it's the cheapest. But it's not definitive in the sense that if one is positive it suggests that you have an appreciable amount of Hemoglobin S is the red cells but it's not specifically diagnostic of Sickle Cell Trait. And of course it misses other abnormal hemoglobin conditions that may exist. And they suggest that if the test is positive then it should be followed by a more definitive test.

There is a need for proper counseling for those who are going to be tested before testing and also after testing based on their results. There's a need to provide some privacy about this health information. And we're not sure whether athletic departments have the proper personnel or setting to provide this screening and counseling themselves. And there's concern expressed in the briefing book about discrimination based on genetic information.

So these are the specific recommendations. That all individuals should have the opportunity to find out their risk for various medical disorders including their Sickle Cell Trait status. That genetic testing should not be a prerequisite for

participation in sports. Evaluation and testing for Sickle Cell Disease and other genetic conditions should take place within the individual's medical home.

That evaluation should include counseling regarding the implications of the information for the individual and assurance of the privacy of genetic information. As part of the individual's medical evaluation for participation in organized sports, all potential athletes should be given education on safe practices for prevention of exercise and heat related illnesses.

Athletic programs should apply universally simple measures successfully used to prevent exercise and heat related deaths in military recruits. The Secretary of Health and Human Services should instruct this Committee to work with the Sickle Cell Disease Association of America, relevant Federal agencies including NIH, HRSA, CDC, the athletic associations, community based and health care professional organizations to develop guidelines and educational resources about screening for Sickle Cell Trait in all persons including athletes.

And then finally, the National Institutes of Health and the Center of Disease Control and Prevention conduct and support research to ascertain if some athletes with Sickle Cell Trait are at increased risk of exercise related sudden death.

Just some activities that have taken place around these issues. The NIH convened a special meeting in June to develop a

-- to explore research agenda for Sickle Cell Trait as related to these sudden death issues. And just currently in the New England Journal of Medicine there's a very interesting article by Vence Bonham, George Dover and Dr. Brody on screening student athletes for Sickle Cell Trait, a socio and clinical Experiment. And that discusses some of the ethical and socio issues related to this issue. The Sickle Cell Disease Association of America will devote a special session to Sickle Cell Trait at their annual convention which will be held here in the Washington area next week.

That's the report. Thank you.

Dr. Howell: Thank you very much for this very thoughtful report.

Dr. Puryear: Can I add one thing?

Dr. Howell: Michele has some wisdom.

Dr. Puryear: I just also want to say that NIH, the Genome Institute and HRSA have begun an evidence review of the literature around health outcomes for individuals with Sickle Cell Trait and should have at least the preliminary results of that evidence review at the next Committee meeting.

Dr. Howell: And what will you do with the evidence review?

Dr. Puryear: What will we do with it?

Dr. Howell: Yeah.

Dr. Puryear: Publish it.

Dr. Howell: Okay. Are there questions of KOF about his report?

[No response.]

Dr. Howell: I assume that you -- number one, I assume that your group plans to organize this and publish this report, is that correct?

Dr. Frempong: Well I think we'll take advice from the Committee because we did the work for the Committee.

Dr. Howell: Yeah.

Dr. Frempong: And if the Committee advises us that we should publish it then we will do so.

Dr. Howell: I think that there are two issues to consider with this report. Number one, this publication and recommendations. And the second thing is whether or not it should go forward as work of this Committee to the Secretary for her review.

Jeff.

Dr. Botkin: Yeah, this is an excellent report. I noticed some discrepancy though between the recommendations that were on your slide and the ones that are part of the letter to the Secretary and part of the report. So I wanted to see which ones were the active recommendations.

Dr. Puryear: The ones that are in the letter to the Secretary.

Dr. Botkin: Okay. Can we look at one of them then for a minute?

Dr. Puryear: Sure.

Dr. Botkin: I want to look at the first recommendation.

Dr. Puryear: And I can pull up -- I think.

Dr. Frempong: Should I try to bring it back up?

Dr. Botkin: That would be great.

Dr. Frempong: Okay.

Dr. Botkin: Okay, so the first bullet in the letter to the Secretary and the report that we have in the briefing book says, all individuals should know their medical risks for various disorders including their carrier status for various inherited genetic conditions such as Sickle Cell Disease. Whereas this one said all individuals should have the opportunity to find out their risk for various medical -- so from my perspective, as written on the slide is much preferable to how it's written in --

Dr. Puryear: The letter --

Dr. Botkin: -- the briefing book which tends to suggest that all of us ought to be getting Sickle Cell carrier screening.

Dr. Puryear: Do you mean the letter or the -- because I'm having trouble bringing up the --

Dr. Botkin: Both the letter and the briefing book.

Dr. Puryear: Well the letter's gone.

Dr. Botkin: Well okay. But the briefing -- the report as it's provided to us in the materials for the meeting again state, all individuals should know their medical risks for various disorders including their carrier status for various inherited genetic conditions such as Sickle Cell Disease. That just seems to me to be overly --

Dr. Puryear: This is what it --

Dr. Botkin: -- broad.

Dr. Puryear: Well this is what the Committee approved.

Dr. Frempong: Right, I think really the issue was to find out versus knowing. Knowing is sort of subjective. If somebody say you should know something it's not the same thing as I'll give you the opportunity to find out. You can teach somebody something but they will still not know it. And so I think the sense of that knowledge is that people should be given the opportunity to know, to find it out.

Dr. Botkin: Right, which sounds wonderful to me. I mean is this a moot point? Are we -- is the -- do we have an opportunity to talk about these recommendations or is it for informational purposes here?

Dr. Puryear: The Committee can refine the recommendations.

Dr. Frempong: Sure.

Dr. Botkin: Okay.

Dr. Trotter: So the recommendations we're going to in theory vote on today are these, is that correct?

Dr. Frempong: Yes.

Dr. Trotter: Okay.

Dr. Frempong: I think the Committee can make -- suggest any changes.

Dr. Howell: Of course.

Dr. Frempong: I mean we're not -- we're working for the Committee so please.

Dr. Howell: And so Jeff, tell me what you would like to do with number one as it's presented.

Dr. Botkin: Well one, as it's presented here I think is entirely appropriate.

Dr. Howell: Okay.

Dr. Botkin: As it's in the report itself I would have concerns that it is overly broad and seems to imply that all of us ought to be getting genetic testing for Sickle Cell Trait for example, when I don't think that's what is probably meant by the wording here or intended.

Am I making sense to folks here?

Unknown Male Speaker: Yes.

Dr. Howell: Yes, Fred.

Dr. Chen: Michele can I ask a point of clarification about the letter? I recall this conversation from our last meeting

and I don't recall sort of -- maybe I missed it, sort of discussion about the specific recommendations that went into the letter. And I'm not finding it in the minutes from the meeting. Can you remind sort of us about what that process was before that letter went out?

Dr. Puryear: We went back and forth between the Committee and the workgroup to refine the recommendations.

Dr. Chen: That was in the meeting, during the meeting?

Dr. Puryear: No, no.

Dr. Chen: It was after?

Dr. Puryear: Yeah.

Dr. Chen: Okay.

Dr. Puryear: Mainly because of the -- if you remember the original recommendation that came forward from the workgroup was felt to be to limiting and actually not definitive enough. So it took some time to work out what those recommendations should be. So we also worked with CDC and NIH since they were going to be part of the -- any implementation of these recommendations.

Dr. Howell: Is the Committee comfortable with the recommendations? And KOF's saying, this is obviously the first page, the first three. But would you go through the rest of them. Are there comments other than what Jeff has said about this page?

Dr. Boyle: I have a comment.

Dr. Howell: Yeah.

Dr. Boyle: Coleen. I'm looking at the NCAA recommendations relative to your Committee's recommendations. By the way, I think you've done a wonderful job and this is a very complex area. But the NCAA's really trying to avoid any liability issues.

And I'm wondering if in your discussions -- I mean obviously you must have thought about that issue relative to these recommendations and do you feel like that -- they -- I mean are we addressing that? Should we be addressing that in these recommendations?

Dr. Frempong: In terms of the liability issues?

Dr. Boyle: Yeah.

Dr. Frempong: I'm not -- I think the Committee and particularly if you read the New England Journal discussion with Bonham, and I think we all understood that NCAA did not take this action primarily because of concern about the athlete. They were -- this is part of their legal settlement to do it.

And so even though we felt that their lead may broaden beyond the Division I athlete, that we should address the issue more broadly then maybe the issue of legal responsibility of colleges or athletic associations in this. But that the overwhelming interest is to protect the health of people with Sickle Cell Trait in these circumstances, for them to learn

about it. So we did not -- I don't think the issue of the liability was an overwhelming consideration in what we did.

Dr. Howell: You know it may be worthwhile for the folks that sit -- let me read to you from the Board of Directors meeting of the NCAA when this was actually approved.

They said -- this has some word about proposal number whatever as amended whatever, which specifies that the required medical examination or evaluation that student athletes who are beginning their initial season of eligibility and students who are trying out for a team must undergo, prior to participation, in voluntary summer conditioning or voluntary individual workouts pursuant to the safety exception practice, competition or out of season conditioning activities, that shall include a Sickle Cell solubility test unless documented results of a prior test are provided to an institution or the individual declines the testing or sign a written thing.

So basically that was what was approved by the Board of Directors and then their various Committees have gone over it -- but their actual recommendations is a solubility which you point out is one of the recommendations about to be sure that the test used is this.

Yeah, Chris.

Dr. Kus: I guess the issue of addressing liability, because to me this report talks about good practice for all

athletes and you could say that that's probably a better thing to do. I don't think you can ever do anything that's going to say you're not going to get sued for something. And actually the direction of this, I strongly support because I think it's going to affect, it could affect all athletes and prevent deaths in that population.

Dr. Howell: I think the Committee recommendation should just be the very best practice or based on scientific information and not necessarily tie it to a legal settlement --

Dr. Kus: Absolutely.

Dr. Howell: -- that was crafted with the family. Are there further -- Mike.

Dr. Trotter: I agree and would say that if this becomes a recommendation from a Committee such as this and the Secretary adopts it, it will in fact, effect liability quite a lot.

Dr. Howell: Mike.

Dr. Skeels: I have a concern about number two although it's appealing. I think we would all agree that before participating in vigorous sports one should have a thorough medical exam. And some physicians might feel that genetic testing or testing for an underlying genetic disorder might be part of a thorough medical exam.

They might think that screening for Sickle Cell Trait or Cystic Fibrosis or pretty much anything else you could imagine,

in their medical judgement, as mentioned in number three, which is actually number one on the slide, they might think that that's appropriate.

So why would we be making a blanket general statement like this that sort of says if you, the physician, feel a genetic testing is appropriate you're wrong.

Dr. Howell: I don't read that that way.

Dr. Skeels: Well that's why -- that could not be more direct.

Dr. Howell: Yeah.

Dr. Skeels: Genetic testing should not be a prerequisite for participation in sports.

Dr. Howell: I would think that an individual who --

Dr. Skeels: I mean we're saying it's --

Dr. Howell: Yeah.

Dr. Skeels: That's a medical judgement in my view --

Dr. Howell: Right.

Dr. Skeels: -- that I think is best left to the physician who's taking care of the patient. And in fact it even says in the next section that testing should take place within an individual's medical home.

Dr. Howell: Yes, and I think that would -- in my mind I thought that if you, as a physician, feel that a patient that you're seeing would benefit from certain things, I would think

that that would, that would not be a prerequisite but that would be based on your decision.

Dr. Skeels: Yeah, maybe there's something about number two that could just be -- the wording could be changed so it doesn't sound quite as --

Dr. Trotter: How about unless clinically indicated?

Dr. Skeels: Yeah, something like that yeah.

Dr. Frempong: I think probably maybe what we were trying to avoid, and I understand what you're saying is that this seems to be prohibiting even the physician as part of his or her regular medical evaluation from going genetic testing if the person was, in fact, getting a medical evaluation in order to participate --

Dr. Skeels: Thank you, you said that much better than I did.

Dr. Frempong: -- in sports.

Dr. Skeels: That's what I was trying to say.

Dr. Frempong: But I think the idea here, and it needs to be probably restated, is that we didn't want the athletic department to be the source of the requirement.

Dr. Howell: Jeff has a comment and then Michele.

Dr. Botkin: Perhaps what we mean here is, genetic screening should not be a prerequisite. Testing may be on an individual case, but screening --

Dr. Skeels: A physician may think that it's -- they may not draw the distinction between screening and testing.

Dr. Howell: Right.

Dr. Puryear: I think you have to remember that there's a whole history here with Sickle Cell Disease specifically and secondarily other diseases. But with Sickle Cell Disease there was a prerequisite in many states for Sickle Cell Disease screening before you got married and Sickle Cell Disease for jobs and insurance. So I think you can't take that history -- and that was actually prohibited. And then when various companies -- I think Burlington or Burlingame, I can't remember the name, but they were requiring a specific genetic test for their workers. That was outlawed and deemed illegal. So I think you can't single out Sickle Cell Disease. What we could do, and I think I understand what you're saying, is actually roll in number two into number three because what you're saying is it should take place -- I mean it should be part -- whether or not to do a genetic test should be part of the medical evaluation. And rolling that -- I mean it just could be another sentence within that third recommendation.

Dr. Skeels: Sure, that sounds fine. Thanks. Yeah, it's just the words on paper without that other context that you just mentioned Michele is a --

Dr. Howell: That seems like that's a word smithing thing

to roll that in.

Dr. Frempong: Yes.

Dr. Howell: So that it would testing and not be a thing. Are there further comments about this paper and its recommendation?

[No response.]

Dr. Howell: I think that the two issues for the Committee to decide and discuss -- and we're going to hear from her in just a bit, for us to decide number one, to recommended publication. And I personally would want to do that. And I personally would like to see it go forth to the Secretary because certain of the recommendations have to do with organizations and efforts under her aegis, i.e. some of the studies recommended so forth and etcetera. But let's hear from our distinguished lady at the microphone.

Ms. Green: Hi, thank you. Nancy Green. Can you hear me?

Dr. Howell: Yes, but you'll have to grow a little bit I think.

[Laughter.]

Dr. Howell: Wear high heels tomorrow.

Ms. Green: All right, thank you. So I mean I think it's understood and Bonham, et al. had pointed out very well that the NCAA rulings are not solely based in concerns about public health. But as a public health entity, I think it might be

helpful to make the statement that any such screenings, mass screenings would include a component of evaluation so that the outcomes of the screenings, the health of the individual screened, whether they're partitioned into screened positive, screened negative, that that would be a useful aspect of this. I mean sort of comparable to the military experiment right? Where as you described so well KOF that the implementation made a difference for outcomes. But under the current scheme there's no, there's nothing in position, there's nothing to assess outcomes both in terms of the health of the students and also more subtle aspects of the politics of Sickle Cell Trait.

Dr. Howell: Okay.

Ms. Green: So maybe the Committee would like -- so specifically I'm suggesting that the Committee make a recommendation about evaluation of outcomes of these kinds of programs.

Dr. Howell: Thank you very much. I think this is an excellent work that outlined a lot about Sickle Cell Disease, the incidents, the potential impact, etcetera. And has some recommendations that I think are thoughtful and sensible.

Are there further comments about that?

[No response.]

Dr. Howell: Let's hear first, is there a motion that this paper go forward as a publication that comes from the Committee.

Can we hear a comment about that?

Dr. Trotter: So moved.

Dr. Howell: Second?

Dr. Buckley: Second.

Dr. Howell: That's a motion that this be -- that word smithing take place there and obviously I'm sure there'll be a little editing or tweaking but that it go forth from the Committee. We've had a motion and a second. Those in favor of that raise your hand.

[Hands raised.]

Dr. Howell: Is there any opposition?

[No response.]

Dr. Howell: Is there anyone abstaining?

[No response.]

Dr. Howell: Unanimous. And what about the paper going forward from the Committee to the Secretary with these recommendations? Can we have a motion on that?

Dr. Trotter: Same motion.

Dr. Howell: Second?

Dr. Buckley: Second.

Dr. Howell: We have Tracy and Becky in a tag team today. But we have a motion and a second to go forth. Can we -- any discussion?

[No response.]

Dr. Howell: Let's see a hand on that favoring that.

[Hands raised.]

Dr. Howell: Any opposition?

[No response.]

Dr. Howell: Any abstentions?

[No response.]

Dr. Howell: So it goes forth. Thank you very much KOF.

Dr. Frempong: Thank you very much. Just a final point. In the military after the intervention studies proved successful the Secretary of the Defense Department issued a statement that in the military Sickle Cell Trait is no longer a required part of screening recruits for exception in the military.

Dr. Howell: It may be interesting, it's obviously not our work, but it might be interesting to send a copy of that comment along with our stuff to the Secretary just for some historical perspective. Michele has some wording I think.

Dr. Puryear: I just want to -- can you put the recommendation back up please. I just want to make that -- because you've already voted that you're also -- know what you're voting on.

[Laughter.]

Dr. Puryear: So we're going to remove number two and reword number three which is number one up there. Evaluation and testing for Sickle Cell Disease and other genetic conditions

should take place within the individual's medical home. Genetic testing or screening should not be a prerequisite for participation in sports or other activities unless deemed medically necessary. Is that okay?

Dr. Howell: That's I think the wording that the group was expecting and I think that the -- that would continue to include the evaluation could include counseling in regarding, etcetera. That should be --

Dr. Puryear: That would stay.

Dr. Howell: That would stay.

Dr. Puryear: The evaluation.

Dr. Howell: That would stay?

Dr. Puryear: Yeah.

Dr. Howell: I think that's what the Committee --

Dr. Puryear: We're just adding a middle --

Dr. Howell: That's what the Committee expected and I think that's what the Committee voted on.

Dr. Puryear: Okay.

Dr. Howell: Thank you very much KOF. Any further discussion?

[No response.]

Dr. Howell: Excellent. Next we're going to hear about the updates to the various divisions concerning health information exchange within the newborn screening system. And as you

recall, we established a Health Information Technology Workgroup that was co-chaired by Alan Zuckerman and Sharon Terry.

And today we're going to hear their work about quality measures for newborn screening that will call on the decision to send a letter to the National Quality Forum or NQF regarding measures from the CDC, HRSA, and NCQA.

So Sharon and Alan, you're on.

Ms. Terry: All right, thanks very much. We've been very busy. This is a very busy time and it's very timely that in fact the Committee decided to have this workgroup. We're going to talk today about the quality measures issue.

We've put a lot of information in your briefing book and we don't expect that you've poured through it and understood every single word of it. We're going to go through a lot of information quickly because we do want to get to the recommendations. But we also welcome you to ask whatever questions you have.

So a quick overview of what hi-tech incentives create for us in terms of an opportunity. And the HITECH, which is the Health Information Technology for Economic and Clinical Health Act, authorizes HHS to establish programs to improve health care quality, safety, and efficacy through the promotion of HIT, Health Information Technology. And under HITECH, and I think everybody's heard about this, eligible health care professionals

and hospitals will qualify for Medicare and Medicaid incentive payments when they adopt certified EHR technology and use it for specified objectives.

The incentives to use EHR to improve quality of care have captured the attention of providers and this Secretary's Advisory Committee can play a role in making newborn screening part of that program. Two regulations have been released.

The first, most people have known under the A.K.A., which is Meaningful Use Objectives. And that's issued by CMS and this is a final rule for a first phase that defines the minimum requirements that providers must meet through the use of their certified EHR technology in order to qualify for these bonus payments.

And the Standards and Certification Criteria for EHR were issued by ONC, the Office of the National Coordinator for Health Information Technology. And this rule certifies the technical capabilities required for a certified EHR technologies.

So the overview is that the CMS incentive program for health -- electronic health records will be organized in three phases. The first of which is 2011, the second 2013, and third 2015. And that they will report data, measure quality, and improve quality. They're very patient focused, very much concerned about care coordination. And that's heartening and good to see.

During phase one, and there's lots of other attributes of this that we're not going to talk about. But the population Health piece will be represented by three activities that will be sending immunization data to an immunization registry, reporting disease surveillance and sending lab data from hospitals to public health to monitor disease patterns such as influenza.

Newborn screening could be added in phase two if specific quality measures are available and tested. CMS has said that it's a prime candidate, in fact, for phase two and would be a good model.

So this Committee made comments on the Meaningful Use Notice Proposed Rule Making and they were submitted in May and they were very well received by CMS. And there is a commitment therefore from CMS to attempt to add pediatric measures and to include newborn screening, as I said, as a prime candidate in phase two. And that adding these newborn screening measure to the future regulations will require that we have available specifically endorsed and tested quality measures that will be a requirement to get newborn screening into the meaningful use requirements.

So there's three components. The final regulation has been issued for the first of the three phases but the details are continuing to evolve. There's lots of -- you know as I'm on the

Standard Committee and as they've said, it's a document written by Committee which means there's a lot of issues to resolve and harmonize throughout.

The definition of certified EHR is based on certification criteria that included specific standards and coding that's expected to be in a vendor's product and can be tested. Measures of meaningful use are data that an end user of a system must collect and report to receive these incentives. They depend on properly coded data stored in the EHR. And the State Medicaid programs can receive funds for HIT to implement the EHR incentive programs. In fact, they can also add in other core or additional curriculum.

So basically it's impossible for newborn screening to be completely left out of meaningful use. It's going to be part of it. And several meaningful use functions will have the potential to benefit the newborn screening programs if providers choose to use them for that purpose.

Do you want to jump in now?

Dr. Zuckerman: You can continue.

Ms. Terry: So meaningful use objectives that are relevant to newborn screening that are in the code essentially say that we need to maintain an up to date problem list of current and active diagnoses, incorporate clinical laboratory test results into the EHR as structured data, report clinical quality

measures to CMS and the states. And we have that in red today because that's the specific piece that we're going to speak to.

Generate lists of patients by specific conditions for quality improvement, send reminders to patients for preventative and follow-up care, and then provide patients with timely electronic access to their health information. And again, there's a lot of objectives but these are ones that are very relevant to newborn screening.

So quality measures are a strategy for improving compliance with newborn screening and legislative mandates create an opportunity for this Committee to play new roles by endorsing quality measures. And Alan's going to talk about those.

Dr. Zuckerman: Today we're going to continue talking about the Recovery Act process. But in the briefing book we have an excellent presentation from AHRQ. And of course we have Denise Dougherty here, Ed Lomenten in the office about progress under the CHIPRA Legislation. And there will many other pieces of legislation that will call for specific quality actions.

But it's important to keep in mind that when we talk about quality measures, some people are developing the measures for others to use and some are using them. And one important role is expert panels such as the Joint Committee on Infant Hearing that define what the standard of care might be.

Others like the National Committee on Quality Assurance try

to translate standards of care into actual data measures that would be collected. Groups like the National Quality Forum are playing a review role to develop the eligible candidates of approved measures that can then go on to other organizations like ONC and CMS, who can select them for use in incentive programs and other types of regulations.

And on the other side there are many people who are tying to use these measures, put them in place. Some of them may apply to the states newborn screening program, others apply to the providers of care in hospitals, ambulatory practices and specialty clinics.

Some organizations are receiving the measures such as reports come in on hearing screening. Some now require the use of quality measures as a condition of licensure and certification. And there may be some interesting opportunities through JCAHO through with hospital certification and maintenance of certification under many specialty societies require active participation in quality. So giving people the options to deliver on this is helpful.

Again, they're also part of various incentive programs such as pay for performance, not just this EHR funds. And then of course, for any of these things to really be in use we need to have data on how they work in the real world and CMS is going to be setting off a group of specific pilot projects to test

various child health measures.

So while the process in the past hasn't been very orderly, it's impossible to have quality measures if you don't have a standard of care to base them on, you don't have someone actually develop the tools, you need to evaluate them in the real world. Someone has to play the role of reviewing what others have done to put measures forward.

And then someone has to select which measures will be used in different legislative programs. And then it becomes the responsibility of the providers and the health departments to collect data. And there are others who need to receive and use these reports such as state Medicaid programs.

At the present time, the National Quality Forum is conducting a special initiative on child health quality measures and 11 measures dealing with newborn screening were submitted by the August 31st deadline. And these are some listed in the briefing book.

Evaluation is now underway in fact, it's probably going to take place in November. So before your next meeting in January they'll be opportunities to review these measures to submit individual public comments and to encourage getting these on the list of candidate measures.

To qualify under NQF, there are many preconditions to be considered. And of course they want things that are entirely in

the public domain. Someone has to take ownership or stewardship to maintain and update the measures.

And they're very concerned that these measures play a role in quality improvement and that they're not just there as a report card or for public reporting. And one has to document the intended improvement in health care that they can produce. And they also want these measures to be tested and submitted, but at the present time they're making exemptions to give people 12 or sometimes even 24 months to prove that people can use and apply the measures.

They begin by asking, is this something that's important to report. And they want to see demonstration and we've tried to pull together evidence that there are quality problems in newborn screening, that there are opportunities for improvement.

Today, under the EHR meaningful use almost all of the measures deal with the process of care which is documented in the record. But there are very exciting opportunities to expand this, to look at outcomes, to look at patient experience. In the case of newborn screening, it may even be appropriate to look at structure of programs and services provided as a indicator of quality.

They have detailed criteria on scientific acceptability that the measures are being used have some validity and reproducibility. And of course, we need to gather data on this

when we go to compare birth certificate data to screening lab or hearing testing data as measures of the completeness of screening.

And finally, they want documentation of usability and feasability that the proposed measures actually give a complete condition and describe quality and that people can understand them. They also are particularly seeking to move into the electronic world, to have electronic quality measures which don't add to the cost of care and which may be based on data that's generated as a bi-product of care and already available in existing sources.

The early hearing detection programs have singled out eight specific measures, some applying to hospitals in terms of both doing the hearing testing and what they're referral rates might be. Some on the ambulatory side that people are identifying risk factors and continuing to do hearing screening after the newborn period. And some apply to the completion of diagnostic and referral evaluations.

HRSA is attempting to add measurement of the percentage of children that fully comply with all of the state mandates and critical to that is being able to define the denominator and be able to define any exclusions in the numerator of why some children might not be tested.

The National Committee on Quality Assurance is introducing

a very new set of measures based on the medical home. Attempting to go to the charts of six month old infants, clearly well past the normal recommended time for screening to look for documentation both the metabolic and hearing screening in the chart along with documentation of additional testing and referral.

This may be too late to intervene and make up for things that are missed, but the purpose of quality measures is to detect problems and come up with strategies for solutions. So by reviewing at a six month interval, it may indicate problems that we need to be fixing within the first two weeks.

And again, we do have Sara Copeland here from HRSA and John Ikewall from CDC who can speak to their measures. The NCQA staff is involved in certain HEDIS measure reviews today. We'll be in touch with them tonight if you have questions or comments. We do have copies of the complete submissions that we can share with anyone who's interested.

The final area that we want to turn to is what is the appropriate role for this Committee in this process of introducing quality measures. And of course, the HIT workgroup is here to bring these factors to your attention and to look for methods for implementing electronic measures. But it's up to the Committee to define what it's role will be in selecting and recommending.

Ms. Terry: So the Committee could recommend use of specific measures for newborn screening. This Committee could recommend that NQF endorse specific newborn screening measures. EHDI measures currently under review, the HRSA and NCQA measures for completing the screening process that are currently under review.

This Committee could recommended that the meaningful use incentive programs include specific newborn screening measures as requirements or options in the future and send these recommendations to the HIT Policy Committee on including newborn screening as a part of the Population Health Meaningful Use Measures for 2013.

The Advisory Committee could encourage develop of the follow-up and treatment subCommittees already involved in quality measures as part of long term follow-up. Other organizations could be encouraged to make newborn screening as part of their quality improvement agenda. JCAHO, as Alan said, has great potential to influence the role of hospitals in short term follow-up.

Also, this Committee could encourage filling data gaps about newborn screening quality. So what is the evidence that there are variations in the quality of newborn screening and room for improvement? We've seen some papers recently. What is the evidence that there are health disparities in newborn

screening? What's the evidence that risk adjustments in clinical exclusions are needed to measure the quality of newborn screening? And how soon can we add outcome measures to the current process and structure measures?

This Committee could also facilitate implementation of quality measures by addressing certain barriers. The ONC HIT Policy Committee is evaluating barriers to using HIT in population health raised by the state health departments. Pooling funds from different federal agencies and different categorical disease programs may speed the adoption of HIT.

Privacy regulations have been identified as a problem for EHDI data collection and sharing. Integration of child health programs such as immunization registries, lead screening and newborn screening may facilitate quality improvement.

So the action items that should be before this Committee today are; should the Advisory Committee take on new roles of recommending specific quality measures. Should the Advisory Committee make specific recommendations to NQF at this time. And should the Advisory Committee encourage the Follow-up and Treatment SubCommittee to continue developing quality measures and filling data gaps.

So let me just put those back up. And that is what is before you.

Dr. Howell: Thank you very much Sharon and Alan. Are

there questions and comments of our presenters?

[No response.]

Dr. Howell: Let me make the following suggestion. It seems to me that this Committee is certainly interested in quality measures and I think would be very supportive of implementing them. And you're going to be -- your Committee is going to be meeting and you're going to be speaking again tomorrow.

And what I would like you to do, if you could, would be to come up with a very specific list of concrete things that you would like this Committee to do and outline exactly how we might help. Because I think the Committee -- you've covered a huge number of groups and efforts and so forth.

But if you could be very concrete tomorrow about what we should do and tying in about how these might be funded. For example, I was just asking Michele, does HRSA have the money to do what they're planning to do, and the answer is yeah.

But if we could do that. Maybe the other group has other questions about this that you would like them to do in the morning. I don't think we're adequately informed at this point to make sensible recommendations. Others may disagree. Are others adequately informed to make recommendations now?

[No response.]

Dr. Howell: I don't see -- I hear people that seem to

agree with me. So come up with some concrete areas. There are many acronyms, there are many abbreviations and so forth of the groups that are new to us, some are not and so forth. Ned.

Dr. Calonge: I think the only thing I would add that we should make a decision on is whether or not this is an area we should be involved in. And maybe we can't be -- we can't make that decision until we see some measures. But I guess proactively saying we can see our role in recommending quality metrics around newborn screening. Something we can yep, we should take that on and we should figure out how to develop those metrics before we make recommendations.

Dr. Howell: I think that's my sense. In other words, I'm sure this Committee is interested in quality measures for newborn screening and there are a lot of things we can do. And I think trying to figure out how to focus on those would be I think the thing. Coleen.

Dr. Boyle: I was just going to say on the second recommendation there I do feel like there's a time window of urgency and I do think that the Committee urging the you know, adoption or whatever NQF will do with the hearing the newborn screening measures, I do think we should take some action on that. So maybe being very explicit tomorrow in terms of what those measures are and maybe how we can move forward on that.

Ms. Terry: Okay.

Dr. Zuckerman: Yes, that would be appreciated and in the briefing book we do have a one page summary of the hearing measures and the other measures.

Dr. Puryear: But you didn't present them in the slides and if you could actually present exactly what the hearing screening measures -- detail what the hearing screening measures are, what the NCQA measures are that have been submitted. So then the Committee knows if they can vote on those or not.

Dr. Howell: I agree with Coleen that we should be active in this area and so forth. But I think that if we do this tomorrow, that will provide adequate timing. Thank you very much. Excellent presentation.

We now have a presentation on the development of coding standards for newborn screening tests. And we would like to welcome Dr. Carla Cuthbert from the Centers -- from the CDC. Carla is Chief of the Newborn Screening and Molecular Biology branch at the National Center for Environmental Health at the CDC.

And we also have on the program Clem McDonald. I haven't seen him, but I assume that he's here somewhere. He's Director of the Lister Hill National Center for Biomedical Communications at the National Library of Medicine.

Carla.

Dr. Cuthbert: Thank you. I'm here to talk about -- I'm

actually representing the Vocabulary and Coding team, giving you an update about what we've been doing. And I'm going to be talking about the development of new codes for newborn screening conditions. Specifically, I'm going to be talking about developing new codes for Severe Combined Immune Deficiency, Lysosomal storage disorders. And then looking at some codes for the hemoglobinopathies.

So the team goal is to identify requirements to expand the newborn screening coding and terminology guide to include new requirements for data coding and language standardization. The initial project, as I've just indicated, is to request new LOINC variable codes for newborn screening methods that are currently available for SCID for Severe Combined Immune Deficiency and also for Lysosomal storage disorders. And also, we want to request new LOINC, newborn screening answer codes for the hemoglobinopathies.

Now in terms of -- and again, this presentation is really to help you to demystify what is actually required for the request or the submission of request for new LOINC codes. And as part of that process, the information that is required and that should be submitted by anyone who's interested in getting these LOINC codes are the name, what the submitter wants to call that particular condition or that test, a brief description of the condition or test and its use.

And this is very important again because we're working not alone just trying to understand what the test is involved with and so on. The clinical significance and the clinical significance of the disease, the significance of use of the test. The usual units of measure and the typical normal range for that particular test.

The bits of information that are also very critical and the formal name of the LOINC code includes the component, the property, the timing, the sample, the scale, and the method. And all of this information is actually included on the LOINC website. And there is a LOINC users guide that you can make your way through. But again, this is going to walk you through some of the formal name parts that are very critical for the submission.

So in terms of the name of the component or the analyte that's measured, this is the analyte name that is being measured. So for example, for t-cell receptor excision circles, TREC would be the component that you would submit.

There are other components to this particular part of the component. And that's also a challenge test if it's relevant. So if you're doing say an oral glucose test, this is not relevant to newborn screening. But that's another part of the component as it's defined.

And also, any other standardization that you might include

say if you're adjusting a value to a certain PH. Again, this does not necessarily -- this does not apply to any of the newborn screening tests. So really the part that we're considering is the analyte name that is actually being measured.

The second part of the formal name that you need to be aware of is the property. The kind of property or the quantity that's being observed. Whether or not it's actually a mass, i.e. whether or not it's -- what you're measuring is reported in mass units.

Is it reported in milimoles or miliequivalents in which case it would be a substance. Whether or not it's reported as a in somatic activity, in which case it would be a catalytic activity. Are arbitrary units being present in the numerator or is it just a number. So are you looking just at a number of say TRECS per unit volume. So that has to be indicated and submitted as part of the submission.

The timing of the measurement, whether or not it's just a random time point or if it's a specific time point. The duration of the study, duration of the encounter, duration of the particular episode. For most of our newborn screening tests the timing will be PT.

The type of sample measured, in our case that's going to easy although they do give serum, blood, urine and so on. Our sample type would be a blood dot or a blood filter paper. And

the scale of measurement. And this just goes through whether or not you're looking at qualitative measurements. Whether or not it's ordinal or order categorical responses, say it's plus 1, plus 2, positive, negative and so on.

Is it a combination of the quantitative or the ordinal. Is it nominal meaning is it just a name of bacteria. Is it color. Something that doesn't have a natural ordering. Is there a narrative associated with that measurement. A text per se when you're describing some entity. Or is it multi, having many separate results structured as one test.

And then finally the method. The method is expressed as a part of the name only when it provides a distinction between two or more tests that measure the same component. And this is used to distinguish methods that may have a different clinical significance or a different clinical reference range.

And examples that currently exist right now that are defined are say, molecular genetics the abbreviation is molgen. Coagulation assays, chromogenic or enzymatic assays and enzyme immunoassays. So you can select from what is existing. Or again, we can work with a team to decide what the appropriate abbreviation is if there is no definition.

So given that overview I'm just going to describe what we've been doing and what we are planning on presenting for the SCID. And this is just a description of the condition which I

know that you are all very much familiar with.

And what we would submit with our package is the fact that SCID, of course is characterized by the absence of both humoral and cellular immunity. At least 15 different genes are known to cause SCID when they're mutated. And patients with SCID have very profound defects in T lymphocyte differentiation and function.

And as maternal antibodies decrease during the first few months of life, the affected infants will develop infections due to common and opportunistic pathogens. Treatment and prevention of infections can prolong life. And the best hope for these patients are hematopoietic stem cell transplantation before the onset of infections.

A brief overview of the TREC assay, and this is just a very brief overview. TREC again stands for T cell receptor excision circles. And these are bi-products of the rearrangement of t cell receptor genes during thymocyte maturation in the thymus. TRECS are episomal and don't replicate during mitosis.

So peripheral blood TREC levels reflect t lymphocyte production in the thymus. The assay that's used is real time PCR. And there are variations in the TREC assay procedures and this is mostly based on primer selection and probes and on DNA extraction procedures.

And this just goes through a very schematic. You can

puncture samples into tubes, take them through two different washes and dilute. And then in one particular variation of the TREC assay the washed blood spot is incubated with a master mix and the PCR reaction is run as is and you are able to collect your data.

The proposed coding information therefore of when you are taking a look at the test for SCID using the TREC assay, the component, as defined, is TREC and that stands for the t cell receptor excision circle.

The property, as defined by the table that already exists in our users guide, is a number concentration because the TRECS are always reported as the number of TREC copies per microlitre. Timing of course is PT defined as a sample taken at a specific moment in time. Blood filter paper is used, it's a quantitative assay, and the method is PCR.

Considering the lysosomal storage disorders, there are two main approaches for evaluation of newborn screening for lysosomal storage disorders and they both include mass spectometry and fluorometry. For mass spec evaluation, substrates have been provided for five diseases and they include Fabry, Gaucher, Krabbe, Neimann-Pick A/B, and Pompe. And fluorometric evaluation involves four -- based substrates which are also available.

In terms of the mass spec assay, there are separate

incubations of for each of the reactions for the different diseases. And it's incubated at 37 degrees for about an hour depending on the assay that's being used. Oh, I'm sorry. They are incubated in terms of the assay for 20 hours and then combined, undergoes liquid liquid extraction, solid phase extraction, elution, drying and then placing on the mass spec.

And the proposed coding information that we would have for this, and this just -- instead of showing you five slides with similar information, the component would be an acronym for the different diseases. The property is that of catalytic concentration because they're reported in milimoles per litre per hour, PT for timing, blood filter paper, quantitative assay.

And of course at this point in time we do not have a code for mass spec for this particular method so there's no appropriate method name and that's something that we have to work with to determine.

For the lysosomal storage assay by enzyme assay by fluorometry. Again, this is an assay in which the blood spots are incubated and there's a stop buffer which increases the PH and stops it. And that is evaluated by fluorometry. Again in a very similar way.

We've got three of the enzymes listed here according to their acronyms. The property is a catalytic concentration reported in milimoles per litre per hour, the timing is PT,

sample is a blood filter paper, it's a quantitative assay. And again, at this point in time there's no appropriate method name for this assay.

Switching gears to the hemoglobinopathies. We do already have method codes for the hemoglobinopathies and what we need now are the new -- are new answer codes. And earlier this year in May in Oakland, there was a harmonization meeting.

And one of the presentations by Dr. Roger Eaton described the work of about 15 states that participated in this activity that looked at harmonizing laboratory reporting. And what they will be doing is to request new answer codes for differences in reporting newborn screening results in the hemoglobinopathies. Later on they will be looking at differences in confirmatory and diagnostic or second tier testing.

What is the outcome of this particular meeting? Well we plan to assemble a workgroup to address harmonization of the hemoglobinopathy answer list. And this is aimed -- we plan on building on the very strong foundation set out by Dr. Eaton and his colleagues. And we know that several of the Oakland meeting participants have already indicated a strong interest in participating.

Also, we want a task group to be developed to develop a draft White Paper. And this will serve as a working document for circulation to address harmonization of electronic reporting

in the hemoglobinopathies. This workgroup will report to the HIT workgroup on its progress.

And that's it. Thank you and thank you for the team and all of the support of the people who are participating.

Dr. Howell: Thank you very much Carla. Now we're going to hear from Dr. McDonald.

Dr. McDonald: I was promised that the slides are on but I don't know what magic wand to waive to make them be on. I was asked if I was going to throw pigs today and I'm not, because there's not enough time. But I'm going to give Carla one because she's become such a LOINC expert so quickly and been so helpful. It's a talking pig which is why I don't throw it. It'll take too long, people start making it talk.

And I have -- what I'm going to talk about basically is the progress and success with the HRSA/NLM guidance for messages about newborn screening. And for those of you who want it, I have everything you want to know and more -- I mean what's actually in the package our paper that got published or will be published in November describing the process and some other stuff with real examples.

So I don't know, I mean I don't think we -- we are not going to go over that now. They're there but they're not here. How'd we do that. So will I see them here after awhile?

Dr. Puryear: He will forward them.

Dr. McDonald: I don't know that sign language. Well I can't see on the screen if I talk to you this way it'll be hard. So I guess I should just forward and it'll happen? I'm sorry, I've been in computers for 30 years but you know, you kind of screw up.

Dr. Howell: Well whatever you did just moved the slides.

Dr. McDonald: Oh, okay.

Dr. Howell: And if you want to, your microphone is portable and it'll come out of that holder and you're set then.

Dr. McDonald: Where did I get to? All right, sorry. I don't know what I've done now. I think I killed it. There are four buttons and I picked the wrong one.

Dr. Howell: Fabulous.

Dr. McDonald: So really what this -- to emphasize what this, what the effort is, it's to go from what's largely non-structured reports, narrative reports in many cases for newborn screening to structured reports. To go to structures that are standardized so that everybody's will be interpretable by whatever state the same way and to increase the use of quantitative reporting. And so those are sort of the three threads.

And the standards for structures are HL7v2.5.1 with some specificity added to it. For codes, you saw some being proposed for the new conditions, LOINC for the questions or the variable

and SNOMED CT for the answers. And this is in keeping with all the national standards.

The details I just talked about, for those who want them and I don't know where they went.

Ms. Harris: We'll put them at their desks.

Dr. McDonald: Oh, okay. I mentioned that already. And then we are working very well and actively with PHII to integrate order, specifications and some of that work they've already done. So this is going to come to pass fairly fast.

So the successes I want to emphasize. We've actually got some progress to report. The three major vendors and I'm -- I apologize if there are five or six, but the ones that I were able to poll quickly have all adopted it and can show, actually show examples of the real messages coming or going; Perkin Elmer, Natus/Neometrics and Oz Systems.

And what I understand is they cover about 65 percent of the labs which makes me optimistic that it will be easy to kind of pass this into the industry. They all can show sample messages. We actually got like 150 pages of sample -- we identified messages from one that could convince me this is really, really happening.

Pennsylvania's sending standard messages with standard LOINC codes to a web server by Oz Systems from two separate newborn screening labs and that's -- is in pilot stage right

now. Kentucky is sending standard messages with standard LOINC codes from Perkin Elmer Systems to their health information exchange system. It's in testing mode. It's in -- they actually set a final go live November 1. And that will tie to immunization and many other public health things.

There are other active efforts. New York State is actively going in two directions trying to connect to HIE and to individual hospitals and have had some success. I don't think anything's up and live yet. Iowa and Texas have legacy electronic interfaces for newborn screening to individual hospitals. And that is planned to be updated to the more standard form in the near term.

Other active efforts, Indiana University has an interaction between the lab and the public health system. It's a two step transfer to the HIE. And they got their first message Tuesday. So the things are happening there. Colorado, Ohio and Utah all have activities going on. And I don't -- I apologize, I'm sure there are other activities beyond these.

There's also delivery to regional systems. So actively and on the basis of an older system they've been sending from all Region IV newborn screening labs and a number of other labs to the Region IV center. The actual quantitative details on those are encoded as the LOINC codes at the Region IV center. So that we consider sort of a win as well.

There are challenges. So there's sort of differences in the different use cases as we read it and talking to people and seeing how they're progressing. And the least difficult we believe is the newborn screening to lab or a newborn screening programs to health information exchanges or other equivalent web services and to regional centers. It's because there's not as many communications is one of the reasons. And these systems are designed to take in.

The more difficult, but not impossible are newborn screening to hospitals and newborn screening to direct individual practitioners. That's not supposed to say hospitals. And the reasons for that is that the -- well for the hospitals, I think that comes next.

For the physicians the problem is that the name is not always known at the time the specimen is sent to the lab. And there's a lot of complexities in that but the two changes -- we're going to make a change in the standard to explicitly ask for those variables. Although some cards do ask for that kind of information. The patient may or may not know for sure who's going to be taken. But that's a big problem.

And then codes and messages -- I left out that the hospital linkage has a number of complexities. One of them, there's lots of them so you have a lot of places to negotiate with.

Secondly, the hospitals are now kind of drowning in new

work because of the standards and the requirements that are just coming out, ICD9, ICD10. And it's sometimes difficult, at least a lot of times difficult with larger hospitals to figure out who you really have to talk to to get them going at it. And we're working with New York State to sort of try a couple of examples to see if we can give guidance as to that.

The second thing is there's the orders and resulting which makes it best when you can do them both. It adds another layer of complexity. And it also puts additional work on the hospitals which they may be reluctant. They have to now -- what used to be sort of standing orders, boom the card just went off. Now they have to figure out a work process, work flow and change their computers a little bit.

But we're still optimistic that can and will happen. I think what we really need to do is to figure out the processes and the incentives including getting it part of the meaningful use. So then this is something to Committee.

That if newborn screening reporting back to the individuals and hospitals was part of meaningful use, it would be very, very quickly you know get attention. And I talked last night with Brad about some other strategies for getting incentives. But we won't get into that today.

I think I must be done.

[Laughter.]

Dr. McDonald: But going forward we've got -- we've got some new codes to build for the new conditions, that's part of the job. We've got work to clarify what are the follow-up and the diagnostic tests. What exactly are they. We've got a lot of them are probably already in LOINC. But to create those terms that are needed for further diagnostic testing and then move on to follow-up testing.

But I want to emphasize, we really have to get this reporting done a little better so there is the place to know who has to be followed-up. There's a lot of activity on developing follow-up variables which you may hear about later day.

So thank you.

Dr. Howell: Clem and Carla, thank you very much. Are there questions from the Committee?

[No response.]

Dr. Howell: This was very informative and I guess the question that I have is that is there something that the Committee could or should do that would help you in your work here?

Dr. McDonald: Well I think the main thing is to politically get newborn screening's priority raised on the national scene especially in ONC and in terms of the next round of meaningful use. That would be the single most effective thing that would ever happen.

And I think many are worried and working on that topic. Sharon I know is very interested in that. That if we get newborn screening being part of the meaningful use reporting, it would ice it, it would just happen. So you may have the ability, this Committee may have some influence in that direction.

Dr. Howell: Sharon, do you have any comments about that particular?

Ms. Terry: No, I think Clem said that well. And I think that we are really poised and tomorrow we'll be very clear about what exactly this Committee can do. And I think that we're also copying some of the recommendations etcetera to hand out.

Dr. Howell: Right, because --

Dr. Puryear: I have a question.

Dr. Howell: Michele has a question.

Dr. Puryear: You reported on what you're doing around blood spot screening, what about point of care or point of service screening like hearing screening or other things that may be coming along?

Dr. McDonald: Thank you. The hearing screening is also part of this package. And with much collaboration with CDC and it's only -- it's fewer questions so I didn't emphasize, and it seems easier but I may be wrong about that. So yeah, hearing screening is definitely all part of it and a very, very

important part of it. And it's -- when we talk about the meaningful use, that's the package, it includes both of those.

Dr. Howell: Why is it easier? I'm interested in that comment.

Dr. McDonald: Well maybe I'm -- there's only two or three variables, that makes one thing. I think the audiology community and how they capture it is very tuned to this. It happens you know, at a different phase -- there's not a specimen that has to be sent off anywhere. So I may be wrong. I'd be happy to hear that I'm wrong but I have the -- that's been my impression.

Dr. Howell: I think that this is important because some of the conditions that this Committee will be considering are point of care which is -- and the only example we have today of that of course is hearing.

Dr. McDonald: Well I can't say all point of care will be easy. We'll face them one at a time. But we can certainly define the codes and the message and it can all -- and a way to communicate them back and forth.

Dr. Howell: Right.

Dr. McDonald: There will be different players depending upon the special subject.

Dr. Howell: Any further comments or questions? Thank you very much. It's now time for a break and we will return at

10:45.

[Whereupon, at 10:24 a.m., a brief recess was taken.]