SECRETARY'S ADVISORY COMMITTEE ON

HERITABLE DISORDERS IN NEWBORNS AND CHILDREN

Thursday, May 17, 2012

AFTERNOON SESSION

1:00 p.m. — 1:55 p.m.

Hilton Alexandria Old Town Hotel

1767 King Street

Alexandria, Virginia 22314

APPEARANCES

COMMITTEE MEMBERS:

JOSEPH A. BOCCHINI, JR., M.D. - Chairman

DON BAILEY, PH.D., M.Ed

CHARLES HOMER, M.D., M.P.H.

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NATASHA BONHOMME, B.A.

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REPRESENTATIVES (continued)

JANE GETCHELL, DR.PH., MT (ASCP)

CAROL GREENE, M.D.

CHRISTOPHER KUS, M.D., M.P.H.

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C O N T E N T S

P R O C E E D I N G S

CHAIRMAN BOCCHINI: Let's go ahead and get the afternoon session started. Okay, thank you. Welcome back.

Next on the agenda is the second condition that was nominated for consideration for moving on to the Evidence Review Committee, was Pompe's disease. And so in this session we're going to have public comment for 15 minutes, and then follow that with presentation of the summary of data and recommendations of the Nomination and Prioritization Committee. And then we'll move towards a decision about a vote as to whether to move it forward to evidence review.

So let's start with public comment. On the list, first we have Sean Clark from the Genetic and Metabolic Disease Advisory Committee.

MR. CLARK: Good afternoon, ladies and gentlemen of the committee, and thank you for the opportunity to speak to you today. My name is Sean Clark, and with me today are my wife, Mary, and my son, Ryan. We traveled here from Chicago.

We wanted to let you know that our lives were really profoundly altered back in October of 2004 when Ryan was diagnosed with Pompe disease. He was nine months old at the time, and we were told by the diagnosing doctor don't have any expectations for your child. This was a devastating and seemingly uncaring remark, but as my wife and I began to research and understand Pompe more, we understood the reality behind it.

Thankfully Ryan was able to begin myozyme infusions at Duke under the care of Dr. Kishnani, but it was not until about a year after the diagnosis. And although the most dire prognosis for Ryan has not played out fortunately, our lives nonetheless have been profoundly altered by the disease.

Of course most significant and immediate was the impact on Ryan's health and the attendant need to adjust family schedules and priorities. Ryan cannot run, walk long distances, and has great difficulty climbing stairs. Every two weeks he has to go into the hospital for his infusions. These

take over eight hours, and Ryan is required to miss a full day of school each time. Additionally, there are frequent visits to specialists and trips back to Duke to monitor Ryan's health.

He also wears a brace for about 12 hours each day to combat the scoliosis that has twisted his spine. We also need to think about Ryan needing a scooter any time he might encounter a walk longer than a couple of blocks, such as on school field trips and cub scout outings.

Although he is a bright, young boy, Ryan is unable to participate in PE classes or other sports. As you can appreciate, such physical activity provides a basis for much social interaction and bonding among boys Ryan's age. Although he's developed good friendships at school, this is an area where he often feel excluded.

Perhaps most hurtful is when Ryan has to confront questions such as, why do you walk funny, or, why do you need a scooter? Such remarks can be difficult to cope for a young boy.

And the question that always haunts my

wife and me is, what if Ryan had gotten the drug sooner? How many of these difficulties might not we have to deal with? Ryan was born with Pompe, but did not begin the myozyme treatments until he was 20 months of age. We firmly believe that Ryan would now be a much healthier boy had he been diagnosed and begun treatments much earlier in life. Perhaps he'd be able to run freely with his classmates and enjoy life to the fullest.

Given the great potential benefit that newborn screening for Pompe offers, the ability to profoundly change young lives, we strongly urge you to approve the evidence review for Pompe and hope that you ultimately decide to add Pompe to the National Screening Panel. Thank you.

CHAIRMAN BOCCHINI: Thank you for your comments.

MR. CLARK: My son, Ryan, for just a couple of seconds here.

MR. RYAN CLARK: Hi. I'm Ryan Clark. I came from Chicago, and I think you should vote to do this.

(Laughter.)

CHAIRMAN BOCCHINI: Thank you very much.

(Applause.)

CHAIRMAN BOCCHINI: Next we have Crystal Hayes, a parent.

MS. HAYES: Hello. I'm Crystal Hayes. This is my husband, David, and our daughter, Haley. We also have another daughter, Brittany, who could not be with us today.

When Haley was six months old, she was admitted to the hospital for failure to thrive. Within the first week, we were told that her heart was severely enlarged, barely functioning, and that she was in congestive heart failure. It took a few weeks to get a diagnosis, and then we were told she had Pompe disease.

Even being a nurse, I had never heard of Pompe disease before, but we quickly learned all we could about it. Initially we were devastated because we were told that children didn't live to be one, but we were given some hope when they told us that a treatment was just approved by the FDA just

two months prior.

Soon after the diagnosis, Haley was started on enzyme replacement therapy, or ERT. These infusions of myozyme replaced the enzyme her body was missing causing the glycogen buildup in her muscles and heart. Because Haley was so sick and weak at the time, we didn't notice immediate improvement, but fortunately within the first year or treatment, her heart function was improving. By the age of three, Haley's heart was basically normal. She also began to make other advancements, like eating on her own and moving around by scooting.

Now Haley is six years old. She attends kindergarten, and loves doing homework. She enjoys other activities, like playing on the computer, Skyping, and doing things outdoors like swimming. She continues to get ERT infusions of myozyme weekly and uses equipment, like standers, walkers, and her electric and manual wheelchairs, to get around since her legs are weak. She also has had several surgeries, one of them on her legs, to help loosen

the tight muscles with the thought that it will help her one day if she gets strong enough to stand. While Haley has done extremely well since starting infusions, she is also very weak.

We know that the treatment she started at six and a half months of age reversed her heart damage and has basically kept her alive the last six years. But we also know that if she was started on ERT earlier in life, that her physical disabilities would not be as severe as they are now.

For instance, Haley does infusions with a six-year-old friend, also with Pompe disease, that was diagnosed before birth due to an older brother passing away from the disease. His treatment was started within two weeks of birth, and if you were to see him, physically you would know that he had Pompe disease. This stresses the importance of early testing such, such as newborn screening for diseases such as these.

Also another mom that has recently reached out to me lost her daughter at four months of age, and wishes more than anything in life that screening

was done at birth so that her daughter had a chance at life.

Speaking for myself and all families of children with Pompe disease, these are a few of the reasons that Pompe disease should be added to newborn screening. If a child not being able to walk because of late diagnosis or a family not able to see their child grow up isn't reason enough, then what is? Thank you.

MS. HALEY HAYES: Hello. I'm Haley. I'm six. Please add newborn screening to Pompe disease. And you have a nice day.

(Applause.)

CHAIRMAN BOCCHINI: Thank you very much.

Next we have Priya Kishnani from Duke University.

UNIDENTIFIED SPEAKER: No, Marsha Zimmerman.

CHAIRMAN BOCCHINI: Oh, I'm sorry, Marsha Zimmerman. I apologize. Acid Maltase Deficiency Association. Sorry.

MS. ZIMMERMAN: Hello. My name is Marsha

Zimmerman, and I'm the Patient Advocate for the AMDA. The AMDA is the patient organization here in the United States, and we service 450 patients, both late onset and infantile.

I'm here to represent the late onset patient. Tiffany House is the President of the AMDA, and she is a severely affected Pompe patient. She is wheelchair bound. She cannot raise her hands above her shoulders. She needs total care from another caregiver. However, she's an amazing young woman.

She was diagnosed in 1995 after about 13, 12 years, somewhere around there, of looking for answers. When she was diagnosed, she was started on treatment four years later. By the time she started on treatment, her lung function was 20 percent of normal, and they were afraid she was going to die.

I met her in 2001 as her research nurse. I didn't know much about Pompe. I didn't know it was glycogen storage. I knew that myozyme was supposed to clear the glycogen from the muscles. So I expected Tiffany to walk again, even though I'm a

nurse and I should know better. But anyway, after having her as my patient for about six months, I talked to the medical monitor saying, when are we going to see her moving her legs? When are we going to expect her to walk? And I was told by the medical monitor, Marsha, she is never going to walk again. Her damage is still so severe. What we're hoping for is to save her life.

And I can just remember that day. I just sat and I just cried. I thought, oh, my god. I thought the treatment was going to make her walk again. She will never walk again. So it is so very important to diagnose these people.

Late onset patients, even though there is an effective treatment right now, still takes five to 10 years to get diagnosed. And in those five to 10 years, the muscle damage is irreversible. And it's just so sad to know that we could stop that. We could start treatment early for these patients and let them have a healthy, normal life.

So I ask, please, please, consider putting this on the newborn screening. It is so, so

important. Thank you.

CHAIRMAN BOCCHINI: Thank you very much for your comments.

Now Dr. Kishnani.

DR. KISHNANI: Good afternoon. I'm Priya Kishnani. I'm a clinical and biochemical geneticist at Duke University Medical Center. And I've been involved in the care and management of children with Pompe disease for the last 21 years, so I've seen the difference from when there was no therapy to now with the treatment that is clearly very life-saving.

Also I've had the privilege of following many of these children and adults with Pompe disease. And I think whilst we've made a difference with the advent of the therapy, we've not done the complete service in the sense that because of a delay in diagnosis.

I'm following children who are unable to walk. I'm following children who will never walk. And I'm following children who are on a ventilator because of a delay in their diagnosis, and, hence, the treatment for Pompe disease.

We had submitted this in 2006 for consideration for newborn screening for Pompe disease, and I think we had some very useful comments that was provided by the committee. I think from 2006 to 2012, we've tried to make progress, and I think we've achieved a lot of progress and tried to answer the unanswered questions that had been raised at the time.

So one of them I think at the time was the evidence of data from a newborn screening program, and at that time Taiwan was in its infancy stages in the newborn screening program. We now have data of over six years from Taiwan showing that the false positive rate is very acceptable, and also that the difference, most importantly, is that these children who were picked up clinically in the island versus those who were treated through newborn screening, there's a significant difference in the outcome with those picked up by newborn screening who are now walking, not on a ventilator, not in a wheelchair as compared to those who were picked up clinically.

I think the second question that was

raised was about CRU-negative and what do we do with them. And I took that as a very personal situation that I had to try and fix having lost so many babies to Pompe disease because of the rising antibody titles.

We've made a lot of strides there both in terms of making a diagnosis of CRU-negative in a very timely fashion after a diagnosis of Pompe is made. And most importantly now, we can abrogate the immune response with simple immunomodulation. And those children, our oldest cohort now is over five years of age, and those children are doing very well.

So I think we've tried to bring that to the attention of the committee. Also we have the package that was submitted.

I think the third point I want to make is about late-onset Pompe disease. And whilst they don't die within the first year of life, there is very significant morbidity and very early mortality, even for those individuals. And there's supporting data for it. And as was brought about earlier,

Tiffany House is an example of such a situation.

And so I think identifying those patients, once again evidence from the Taiwan group is earlier treatment for those individuals has been helpful and has prevented the diagnostic odyssey of over 10 plus years for those who do not have a diagnosis and are trying to search for one at this current time.

I want to close with one statement about early -- the need for early intervention as a treating clinician. I think the difference is not just life and death. I think it's the quality of life that we can afford to these children and to these adults. Having a child being able to walk freely, and run, and do the things that a typical child does versus being in a wheelchair or on a ventilator. And similarly for the adults with Pompe disease, having an adequate quality of life versus not being able to fly. This is an example of why Tiffany House is not able to come here today is because of her ventilator needs.

And so I do hope that we've tried to address everything, and I do hope that the committee

finds this information useful. Thank you.

CHAIRMAN BOCCHINI: Thank you. And thank all of you who made public comments, adults and children.

We're now going to go to presentation of the deliberations, sort of an overview, and then deliberations and conclusions of the Nomination and Prioritization Committee. And again, Nancy Green is going to make the presentation. Nancy?

DR. GREEN: Thank you. Thank you very much, and again thanks to the leadership of the committee, and to the Nomination and Prioritization Group, and for the public comments to frame this presentation.

So I'm tempted to kind of say ditto, but I won't. I think we have to consider each disorder separately and the strengths and weaknesses, if any, of the nomination. So that's what I'm going to present. And, again, I certainly invite the other members of the Nomination and Prioritization Group to correct me if I've made a mistake or supplement the presentation.

So as Priya Kishnani mentioned, this is a re-review. I guess this our first -- right -- that had been previously nominated, deemed not ready for addition to the panel. And now this is the re-review. And the understanding was that we would focus on what's new for this nomination.

But I would like to just, if I could, describe the disorder just for those of you who are not -- had not dug into the nomination the first time around.

So like MPS I, this is another lysosomal storage disorder. It's a different enzyme involved and different manifestations, some of which we heard eloquently just now by the public comments. This is alpha -- GAA, acid alpha-gluocosidase, which hydrolyzes lysosomal glycogen. And so with the deficiency of that enzyme, there's accumulation in muscle.

As you heard from some of the families, there are progressive muscle disease, skeletal, and in some forms cardiac. About a third of the diagnosed cases have the infant form, which, like

MPS I, means early symptoms, aggressive symptoms, cardiac involvement as well, with symptoms presenting on average clinically at age two months, but as you heard, with considerable and variable delays in diagnosis. And there's 100 percent mortality in the first year of life. The estimated incidents of this disorder is 1 in 40,000, and that includes the whole spectrum that we understand for clinical presentation of the disorder.

So I'm not going to use the word "attenuated" anymore. I'm going to use "early onset" and "late onset" because I think that's very important.

Okay. So, again, the infantile versus the later onset. Again, the timing of onset is more variable, and its impact on health and treatment issues. I would just say that given the spectrum of the disorder, I don't know since I'm not a clinician who takes care of these patients. And we didn't discuss this in the Nomination Group. I don't know if four people were with the later onset how early they could be detected if they had newborn screening

and early diagnosis. So what I'm going to talk about is really clinical presentation.

So distinguishing the infantile from the later onset is challenging. There's also a pseudo deficiency, which, again, I don't have the expertise to address, and maybe, Dieter, you want to comment on. It's prevalent among Asian populations, and that would need to be discerned from those with real disease.

Okay. Here, too, the screening algorithm has been defined by this ASMG Workgroup on LSD diagnostic confirmation, and the reference is there from 2011. But like the MPS I that we heard about earlier today, the pre-lunch presentation, this is also an enzyme-based screening and can be done by fluorometry or by tandem mass spectrometry. And apparently the two versions, when done in anonymous pilot testing at the State level, have performed similarly.

Also like the MPS I, the enzyme levels differ by the tissue tested. So, again, whether you do a muscle biopsy or lymphocytes -- perfo

lymphocytes. So there, too, like the MPS I, there's then a need for DNA evaluation, and I'm sure Dr. Greene -- the other Dr. Greene will tell you about the clinical part of diagnosis, which I'm sure is important, too.

But for the algorithm that was established for Pompe is, again, first tier is the enzyme level screening, and then there's a -- from what I understand is a second tier, which is leukocyte activity. So that would be not from the dried blood spot. That would have to be a clinical testing, and then followed again by DNA sequencing of the GAA gene.

Like we heard before, there are mutations that are recognized as abrogating enzyme activity, and there will inevitably be, and have been reported as enzymes with uncertain impact. Here, too, there are going to be issues that need to be addressed around the ability of States -- State labs to handle the technical aspects of this. But, again, New York has, I think, set a very fine example, and New York is here, for Krabbe in terms of molecular diagnosis.

And then there's the issue of the CRIM status, and I can't remember right now what CRIM stands. Somebody can help me. I'm sorry?

UNIDENTIFIED SPEAKER: Cross reactive material.

DR. GREEN: Cross reactive material, thank you. So that's done by western blotting. And if your CRIM negative, it means you have no activity. And so that is a poor prognostic future for new diagnosis and also, as Dr. Kishnani mentioned, for people who have enzyme replacement, that they are either at increased risk for developing antibodies to the enzyme replacement or, in fact, have developed the antibodies. So being CRIM negative is another way to discern -- another level of prognostic significantly for therapy.

So the analytic validity experience for Pompe is the following: again, there's different methods that have been tested, that appear to be comparable in terms of detecting lower absent activity of the enzyme. And hereto this has been multiplexed with other lysosomal disorders.

So, again, looking at the data from Washington State where there's piloted -- again, I believe that was anonymous, yes, and with a false positive rate that was .01 percent reported, so not able to be clinically validated.

And from Illinois, there actually was a letter submitted with the nomination from Barbara Burton, who used to serve on this committee, in February where they had screened 8,000 infants with two false positives. And not surprisingly, given the incident of the disorder, no true positive has been found yet.

We have also experienced from Taiwan, which is pilot data beyond the anonymous testing. So this is really a live program in Taiwan now where about 130,000 infants have been screened, and four have been diagnosed with Pompe. And the metrics as far as repeat blood testing and clinical recall rate are as listed.

And then in Austria also, 35,000 babies have been screened with a false positive rate. That's actually quite a bit lower than what the

others have reported. So certainly with respect to the maturity of pilot screening, that's certainly the Taiwan data for Pompe as much because it's a real program has gone beyond really what the data were for MPS I.

Okay. So, as I said, with the clinical utility, so the Taiwanese experience was that there were four children who were diagnosed by newborn screening within the first month of life. And then I don't know if this is -- I couldn't tell from the publication if this is a separate group or a concomitant cohort, so I don't know. But three were diagnosed clinically of that same group between three and six months. So certainly the diagnosis was later for those who were presented and diagnosed clinically versus by newborn screening. And I can't comment on the difference between four and three.

But, again, the impact of diagnosis on therapy I think depends on the form of Pompe. And the slide here says that a third of those identified would benefit, but I'm not sure that that's true because my guess is that the older -- those who

present at an older age would also benefit from the enzyme replacement. And so I think the one-third refers to focusing on the newborn screening aspect of diagnosis and therapy.

And, in fact, the clinical utility of children who have been diagnosed by newborn screening who have the later onset, that has not been -- that was not addressed by the nominator. And so we did not review that literature, so I'm not aware of it.

You know, in terms of sort of the charge of the committee that we spoke about earlier today and going beyond the newborn period, just something to think about for the committee that since the charge does go beyond newborn screening, that those disorders, like Pompe or MPS I that have an infantile form and a later form, this might be a window to look at the impact of newborn screening on later onset disorders. So just something to think about. It does not bear directly on what we're talking about, I think, right now, which is the nomination for newborn screening.

So the treatments are defined protocols. As you heard using enzyme replacement therapy with -- and certainly with earlier diagnosis and treatment that have been shown to improve clinical outcomes. And there was a European consensus document from 2011 that supported the benefit of early diagnosis and therapy.

So there are some open issues around this cross-reactive immunologic material or CRIM. Again, those who are CRIM negative, I guess they're about 20 or 30 percent of those who are -- the infantile form, and those have a more complex response to therapy. There's data on immunologic modification, et cetera, but that has to be kept in mind as far as response to therapy.

And also there was a report of African-Americans who are particularly susceptible to CRIM negative, and then, as I mentioned, the sensitization. So those who are absent enzyme and then get replaced can develop the antibodies to -- sort of anti-CRIM antibodies analogous to other disorders where there's absent protein and the

development of inhibitors in the hemophilia world.

So the open issues, I think, for Pompe are what to do with the identification of later onset cases. And, again, that's about two-thirds of those anticipated to be detected by newborn screening. The challenges inherent in DNA sequencing about the clinical predictive value of that sequencing and the technical challenges, and the potential for needing to sequence family members to understand the impact of particular variants on enzyme function. And, again, the enzyme replacement sensitization issue.

So the workgroup recommendation is here. This one, I think, was clearer for the workgroup. So the recommendation to the committee is to move forward for evidence review for Pompe, and in particular consider the list of issues here which have been improved since the previous nomination -- improved screening tests, specificity for infantile form, standardized method of diagnosing, pre-symptomatic infants.

So that gets to the issue raised in the MPS I discussion about the need to have clinical

input for diagnosis, and certainly probably a clinical algorithm for diagnosis, in addition to the enzyme assays and the DNA sequencing.

The benefit and harm of diagnosing late onset Pompe during infancy and then issues around cost or cost effectiveness, public health impact, impact on public health departments and newborn screening programs.

So I open this up. Thank you. Thank you very much.

CHAIRMAN BOCCHINI: Nancy, thank you for another good presentation.

So this now is open for discussion by the committee. Are there any questions or comments?

(No response.)

CHAIRMAN BOCCHINI: If none from the committee, let's go to Carol.

DR. GREENE: So, great presentation, thank you. And you asked if I had anything to add clinically.

I would say that there are definitely clinical criteria that we use to determine when

somebody should be treated. And I think it was very clear that there are some ongoing research and questions about DNA genotype/phenotype correlation. But, again, this is a condition in which physical examination, looking at cardiac echo, looking at the heart -- we don't actually need a clear, clear answer in the DNA to help us determine whether and when to treat a child. So there's certainly research still ongoing, but there's clear -- I think you said it, and I just want to emphasize there's clear clinical criteria.

And very similar to the whole cog story and cancer story, people trying to make the treatments better, I actually pay a little more attention to this than some things because mine is one of the CRIM negative -- presumably CRIM negative patients who died in infancy, and we also treat some adults. So it's really an amazing therapy, and they're working on desensitization.

So I think a small majority of the infants respond beautifully to treatment, and then the CRIM negative ones get worse, but there are already

protocols to try to prevent that that are showing a lot of promise. So I think clinically this has come a long way.

CHAIRMAN BOCCHINI: Thank you. Questions? Comments? All right. Oh, I'm sorry. Coleen and then Dieter.

DR. BOYLE: So maybe just thinking about the two conditions that we discussed, and maybe where were previously with Pompe. The committee clearly asked for more evidence, particularly around the integration of the screening within the context of newborn screening program, similar to what was done in Taiwan.

And then getting back to my question that I left with the last condition. You know, I guess this demonstrates that, you know, now there is data in place. I'm not sure it's clinical utility per se, but clearly short-term follow-up for these children, unless there's more in the paper that wasn't provided here.

But I guess I think as a committee we still need to wrestle with that issue, what needs to

be in place before we move a condition on, because I feel like we are treating conditions a little bit differently.

CHAIRMAN BOCCHINI: I think that's an important question, and I think that, you know, clearly we want each condition to meet whatever the minimum requirements that the committee has set. Obviously there's going to be some differences in the condition and in all of the parameters that might balance that out. But I think you're right. That certainly deserves a specific discussion in terms of what would be the minimum standard that must be met.

So I think that's a good point, and we need to discuss that further. I think we can do that in the context of additional -- you know, outside of these specific nominations. But I think that's important. We need to do it.

Dieter?

DR. MATERN: Yeah. I had a question actually. I don't know if someone if someone from Washington State is here or whether Priya can answer

it.

In Dr. Scott's support letter, he indicates the issue of pseudo deficiency in their population in Washington, which appears to be an Asian mutation. Priya or someone else, do you think we need a second tier molecular test to do newborn screening for Pompe disease?

DR. KISHNANI: Dieter, to your point, I think as part of screening, if there is a deficiency that's identified, I think as Carol Greene pointed out, separating a true infantile from some other pseudo deficiency is very easy. For infantile Pompe, even an EKG shows it is an echocardiogram where it confirms it.

So I think in the scheme of this disease, the classic infantile form of the disease, it actually presents right at birth. I mean, we have data to show that. And so the presence of the deficiency can easily be validated by looking at the patient, but if one needs to do a second layer or a second tier, one can go ahead and look for the pseudo deficiency.

The second part that I want to clarify is that the mutations are very clear for those with infantile. They're deleterious or, you know, they're nonsense or they're pretty well characterized. And you can separate late onset from infantile, classic infantile, even by notation analysis and where this one followed the pseudo deficiency.

DR. MATERN: But in newborn screening you would have an abnormal enzyme activity, which is low. And then we don't know, is it just looking at that result. We don't know whether it's infantile, late onset, or pseudo deficiency. And my concern is always that I would hate to inform a family about a possibility of Pompe disease. Yes, we can do an EKG and we can tell them, okay, you don't have the infantile form, but it will still take a week or more to verify whether you have the pseudo deficiency or whether you're fine or not.

DR. KISHNANI: So your point is well taken. I think one can go ahead and then look for the pseudo deficiency as a second tier if there's no

enzyme activity.

DR. MATERN: I know one can, but should one?

DR. KISHNANI: I think, yes.

DR. MATERN: Because that comes back to the issue of the impact on public health and the cost of the screening.

DR. KISHNANI: Yes. And, in fact, that's what's going on in Taiwan. And I wanted to add one more comment for the later onset forms of the disease. There is data from Taiwan where early treatment has been initiated that were picked by newborn screening. There are publications for that.

CHAIRMAN BOCCHINI: Other comments? All right. If not, I would entertain a motion from the committee to either accept the Nomination and Prioritization Committee recommendations in preparation for a vote or not.

DR. HOMER: So moved.

CHAIRMAN BOCCHINI: All right. Moved by Dr. Homer. Is there a second?

DR. MCDONOUGH: Second.

CHAIRMAN BOCCHINI: Dr. McDonough. So it's been moved and seconded to accept the recommendations of the Nomination and Prioritization Committee to move this to evidence review. And so now, is there any further discussion?

(No response.)

CHAIRMAN BOCCHINI: If not, then we will now move to a vote. So this time we'll start on the opposite side of the alphabet and give Dr. Bailey a break.

So first we need to know if there's anybody who will abstain with this vote.

DR. MATERN: I'm not sure, but I think I will abstain given that we do the study that includes Pompe screening.

CHAIRMAN BOCCHINI: Okay. All right. All right. So we have one abstain. Any others?

(No response.)

CHAIRMAN BOCCHINI: Okay. Andrea Williams?

MS. WILLIAMS: Yes.

CHAIRMAN BOCCHINI: Alexis Thompson?

DR. THOMPSON: Yes.
CHAIRMAN BOCCHINI: Melissa Parisi?
DR. PARISI: Yes.
CHAIRMAN BOCCHINI: Steven McDonough?
DR. MCDONOUGH: Aye.
CHAIRMAN BOCCHINI: Kellie Kelm?
DR. KELM: Yes.
CHAIRMAN BOCCHINI: Oh, Michael Lu. He's in dark here. I always assume that that means he doesn't vote. I'm sorry. Michael Lu?
DR. LU: Yes.
CHAIRMAN BOCCHINI: Thank you. Charles Homer?
DR. HOMER: Yes.
CHAIRMAN BOCCHINI: Denise Dougherty?
DR. DOUGHERTY: Yes.
CHAIRMAN BOCCHINI: Coleen Boyle?
DR. BOYLE: Yep.
CHAIRMAN BOCCHINI: I will vote yes. Don Bailey?
DR. BAILEY: Yes.
CHAIRMAN BOCCHINI: All right. Thank you

all very much.

Now the committee now has an additional task. Thank you, Nancy.

DR. GREEN: Thank you.

CHAIRMAN BOCCHINI: Since we have approved the report to add -- to send to -- nominated conditions to the evidence review committee, we now have to decide which one they should look at first. So I'll entertain discussion concerning which of these two conditions should we consider first. And I would assume that we could consider which we feel based on the evidence review or the nomination presentations as perhaps the most data at the present time. That would lend itself to evidence review and a conclusion, so that the second condition additional data may evolve while the first one is being studied. But with that, I'll open this to discussion. Michael?

DR. LU: So Pompe seems to have the best pilot studies available at the current time, both for follow-up -- length of follow-up after treatment and for population-based studies.

CHAIRMAN BOCCHINI: That's a good point, and plus this was one that this Advisory Committee had gone back and asked for additional data, which we now felt has been provided so that we can enable it to be moved to evidence review. So that's a good point. Additional comments?

So would the general consensus be to move Pompe first? Do we need to make that formal? No? So by consensus, would there be agreement to move Pompe first? Okay. Then that is done. Okay, thank you.

Well, that will conclude this session. Now shall we just review -- oh, I'm sorry. Steve?

DR. MCDONOUGH: I just have an observation. One of the discussions that we had today was a study in another country that was very helpful information for us. And I would like some, I guess, maybe discussion about how this committee can accelerate the process, help prioritize the process, get feedback on how pilot studies are done in this country, what is the mechanism.

If we are going to not approve anything

until we have prospective studies done and there's no funding for studies or studies aren't going to be done in this country, then we'll be relying on other countries to do them, or we won't have a lot to do, and we'll get involved in issues outside them. I'm not sure what the -- I need to be educated because I'm new to the committee, about it.

But it seems to me that it's something I'd like to have some dialogue on. I mean, how does that work? Is it happenstance? Is it who you know and which State -- yeah. How does that work?

CHAIRMAN BOCCHINI: Well, I think that dovetails very nicely into Coleen's question earlier about how much of that -- whether we should have very specific guides in terms of how much pilot data or what kind of pilot data needs to be available. So I think that fits very well in terms of would we accept on a regular basis or how data from other countries and how to look at that. So I think that's a good set of discussion.

We'll determine whether that becomes something that would be of value in a subcommittee

first, or to develop an ad hoc subcommittee to look at that, or whether that would just come forward as a discussion of the entire committee. So I think that's a good -- we need to go forward with that.

But it fits very well with what Coleen had suggested earlier. So we'll definitely look at how the best way to do that would be.

Any other comments? Carol?

DR. GREENE: This is possibly out of order, but what the committee might want to -- before we all go into the subcommittee meetings, there was some discussion this morning in each of the presentations about -- a lot of looking like nods of heads do we want to stay restricted to newborn screening, or do we want the subcommittees to think about looking at things beyond newborn screening. And it would be helpful to have some guidance before we head into our afternoon meetings and spend a lot of time fine-tuning priorities where there was a lot of -- anyway. Can we discuss it, or is that out of order?

CHAIRMAN BOCCHINI: It's certainly not out

of order. We can discuss that.

I think it would be good for us to take that more in a formal way and sort of think about that, and bring it forward with some background materials and other things, and potential impact of moving ahead. And so maybe it would be better to sort of schedule that in a way that we could have a more complete discussion.

I certainly have no problem with, as the subcommittees meet to sort of add that to their agendas in terms of what that mean, and sort of get that started. But then I think coming back with that, we can then go forward to sort of look at a more definitive plan. Sound reasonable? Okay, all right.

Other comments?

(No response.)

CHAIRMAN BOCCHINI: Okay. So just to remind everybody, the subcommittees will meet beginning at 2:00. Laboratory Standards and Procedures will meet in the Madison Room on the second floor. Follow-up and Treatment meets here in

the main ballroom. And the Education and Training Committee meets in the -- I guess they combined the Washington and Jefferson Room up on the second floor. And so they'll meet from 2:00 to 5:00.

And then those of you who have signed up for dinner tonight, it's at 6:30 at the Charterhouse. And it's about a mile walk if anybody wants to walk. So I think for those who wish to walk, maybe we could meet at about 5:45 or, I guess, 6:00 in the lobby? And then if not, those who don't wish to walk, we could just meet the rest of the group at the restaurant.

And then two more announcements?

DR. COPELAND: So, first off, the subcommittee meetings are open to the public. So if there's one that strikes your fancy, feel free to attend.

And the second thing is, for the chairs and the HRSA staff, your charge is to come up with a slide for Joe tomorrow that has your top three priorities and possible concrete projects that your subcommittee would like to work on over the course

of this next year. So you've got homework.

CHAIRMAN BOCCHINI: Okay. And that'll conclude the session. Thank you all very much.

(Whereupon, at 1:55 p.m., the meeting was adjourned.)