want to use the product, and the question is, well, what benefit will they obtain.

Luckily, we have the CUSTOM study where we got people who were inside the intended target range and outside of the target range. It was mentioned earlier today about an analysis done by Dr. Eric Brass where he took the actual distribution of Framingham risks in that cohort and tried to figure out how many events would be prevented.

So, if you could put slide up.

[Slide.1]

Let me guide you through this table which comes from his publication. You see in the first column the risk strata. So you have everything from very low risk, less than 5 percent, to people with pre-existing conditions.

The next column are the fraction of CUSTOM users in each of those stratum and, as you see at the bottom, it ends up to 100 percent. So, you see a distribution of risk all the way from very low to quite high.

If these people were not treated, that is the next column, how many events would they have had. We assumed a 25 percent risk reduction with OTC lovastatin and as you see there, the number of events prevented would be 33,000, and

this is over 10 years of treatment.

Now, people say okay, big number, but what is it, how can you bring that down to a smaller size. What that comes down to is a number needed to treat of 30. So, it is a very low number needed to treat, and these are events of MI, both fatal and non-fatal, and also angina.

I would posit that, you know, a mild MI is still not a minor deal. It means that you have had destruction of your myocardium and you are automatically now at a high risk. You are already now in secondary prevention. So, even a small heart attack is nothing to dismiss lightly.

DR. TINETTI: Can you just clarify for the people who are outside the risk, in the high range, you are comparing this with no treatment, not with optimal medical treatment; is this correct?

DR. ADAMSONS: Right, because a lot of people were not treated.

DR. TINETTI: I understand. I understand. Thank you.

DR. ADAMSONS: If you take into account there was some diversion within CUSTOM, so there were some people who were switched. And that took the events down from 33,000 to

23,000, still a very large number, and a number needed to treat of around 40, so still we are talking low numbers.

DR. TINETTI: From this, can we also say that 53 percent of the people who used the drugs were not in your target appropriateness?

DR. ADAMSONS: This is in CUSTOM, so this was with the CUSTOM label.

DR. TINETTI: Right. So, this is the only actual-use study that exists, correct?

DR. ADAMSONS: That is the only actual-use study that exists. So, we would expect, as you saw, there would be more people in the optimal range now, but we see a very good benefit, and we think it is a very real benefit that can be translated in a way that consumers can understand.

DR. TINETTI: Several people came up to me during the break to clarify the discussion about adverse consequences with pregnancy. Just to clarify, if I am correct, is that the FDA has established this as a Category X medication, and there are no plans to change that.

DR. LEONARD-SEGAL: Yes, that is true.

Questions

DR. TINETTI: I think we are ready to move on to

the questions. I think this is a big challenge in front of us, and we are going to give it a try to do electronic voting. I have been assured that if it doesn't work, we can go back to the old-fashioned way of raising our hands, but I think we are already to be in the 21st century and give this a try.

When it is time to vote, you will press--just like they do on TV--press 1 for Yes, No for abstain, and 3 for Clay Aikens. You can tell the generations who got that or didn't. 3 for abstain.

I guess once your light comes on, is this correct that you can change? You can change your vote until we call the end of the voting period, so you will have some time to change your vote. So, you will not be able to know what other people have voted until the end of the period, and the results will come up on the screen.

After the vote has closed, we will actually go around the table and have you then state what your vote was and name, so that while it is being tabulated, we will be able to do it, count as well.

DR. FLATAU: Is it 1 is Yes and 2 is No, is that right?

DR. TINETTI: 1 is Yes, 2 is No, 3 is abstain.

I think you all have your questions in front of you. Some of these are Yes/No and some of them are discussion questions. Make sure that before we vote, that if there are any questions to clarify the questions, we can certainly have a little discussion on that, as well.

The first question is: The ATP III guidelines use LDL as the basis for determining therapeutic targets and selecting the populations for drug treatment and ongoing management. The FDA advisory committee that convened in January of 2005 agreed that the population of subjects selected using the LDL-based paradigm was appropriate for drug treatment.

Given what we have heard today and given what previous committees have done, do you believe that a total cholesterol-based label paradigm is an appropriate approach to selecting patients for use of the nonprescription lovastatin and ongoing management? Please state the reasons for your position.

Perhaps we will have a little discussion about the pros and the cons before we actually do the voting. I think that may be the most efficient way to do that.

So, the question we are asking, given the fact that the guidelines are LDL, is it appropriate to do a cholesterol-based paradigm? Any discussion, pro or con?

DR. PICKERING: I think a question of clarification. Is the question using total cholesterol based versus LDL based?

DR. TINETTI: Yes.

DR. GLASSER: By "appropriate," do you mean would that be our preference, or is it just an option?

DR. TINETTI: I believe it would probably be is it an option. I mean I think we all agree that in the ideal world, if people could understand it and follow it, that we would follow an LDL paradigm. But, given everything we have heard about people understanding the cholesterol better, is it an appropriate alternative.

Is that an appropriate clarification of that question?

DR. CAPRIO: Yes.

DR. TINETTI: Sonia says yes.

What does the FDA say?

DR. LEONARD-SEGAL: Yes and no. I think that we want to focus on the concept. We also want to focus on the

paradigm as it was presented on this label, and the target population identified, since the target population for the LDL paradigm was looked at in 2005 and found to be an acceptable paradigm for a target population to be treated.

DR. TINETTI: So, you are asking not just the labeling, but the fact that the target population might be a little bit different, as well.

DR. LEONARD-SEGAL: Yes.

DR. TINETTI: So, taking all of that into account. Okay.

DR. TAYLOR: So, does that take into account the label, the sponsor's label that women have different criteria? Take that into account, as well.

DR. LEONARD-SEGAL: Yes.

DR. TAYLOR: The one risk factor versus none for men?

DR. LEONARD-SEGAL: Today, you have seen two labels for this application. They were both studied in the comprehension and in the SELECT study and we are interested in what you think of the total cholesterol paradigm.

We have discussed the LDL-C paradigm before this committee although not specifically all of you sitting at

the table today so we are not going there. But we are interested in what you think of this paradigm on this label and your views of using total cholesterol as a paradigm for an OTC statin.

DR. TAYLOR: Does that mean we have changed the question there? Should it be the LDL-C paradigm as proposed by the sponsor?

DR. LEONARD-SEGAL: No, we are just focusing on the total cholesterol paradigm for this question.

DR. PICKERING: I am still confused. The box we were given was highlighted earlier. Is our choice would we prefer an LDL-based or a total cholesterol based?

DR. LEONARD-SEGAL: Dr. Pickering, in the background packages, we were able to supply three labels for you. One was the CUSTOM study label, which is different than either of the two labels tested in the SELECT study. There is an LDL label and a total cholesterol label.

The boxes that were provided to you today were provided by the folks at Merck, and I guess that you must have chosen to just provide the LDL label today for the box for the committee.

DR. TINETTI: Do we have a slide of the

cholesterol label that we can put up, so people can see that? That would be helpful. Again, I think to clarify, we are not asking people to choose between the LDL and the cholesterol. It has already been established that the LDL is the appropriate.

What we are asked is given all the information we have available to us, the different labeling, the somewhat different population, the fact that may be somewhat better understood, is it a reasonable alternative. Is that--

DR. LEONARD-SEGAL: Yes. You heard in Dr. Craig's presentation about the population.

DR. TINETTI: Somewhat different.

DR. LEONARD-SEGAL: Label the target, so yes.

MR. LEVIN: I want to separate two different sort of thoughts. One is the understanding that total cholesterol may be an easier concept or better understood by the patient population. But, on the other hand, if we look at Slide 43, which is in the FDA review team hierarchies, after mitigation, there is hardly any difference in terms of looking at percent correct.

I guess what I am seeing is that while the concept of total cholesterol may be better understood in the general

population, it really doesn't seem to have an effect on communicating the hierarchy issues.

Does that gibe with what FDA showed us, which would be Slide 43?

DR. LEONARD-SEGAL: I think that what Dr. Hu is showing was that there were similar correct self-selection based on whatever the cholesterol parameters were in the slides.

We are interested in your discussion about the target population, that the total cholesterol label, the target--

DR. TINETTI: Can you show us?

DR. HEMWALL: Yes. Slide on, please.

I am going to show the decision tree part of the package, because that is where the difference is most evident. In the Drug Facts, all the materials are within the same spots in the Drug Facts.

The real difference, in what I showed earlier, there is a straight decision tree that all men and women fall together. In this one, the men and women split out in a different one, because women have to have a low good cholesterol to qualify, and men don't get a risk factor.

And it attracts roughly the same population when you do that.

What you were asking Dr. Leonard-Segal is yes, when the two labels are compared through that mitigation and hierarchy process, they ultimately perform about the same way. But, if you isolate out whether or not, how well they know their lipids, you do see improvement with the total cholesterol label.

DR. TINETTI: Thank you.

Does anybody want to comment on the FDA's question and concern for us that the target population might be a little different with the cholesterol versus LDL? I think that is the issue that they want to get at, so if anybody has any comment on that particular point.

DR. PICKERING: I would say that the total cholesterol is okay. So it is appropriate. But I would also prefer, given the choice, the LDL based thing, because I think that is the wave of the future and you showed us that obviously, there are going to be different people appropriately taking the Mevacor depending on one criteria. But I can't say I get too excited about that.

I think the important thing is if there is a

difference in the safety, which I would put at the top of the hierarchy, and I had the impression that it really didn't make much difference.

So, given the choice, I would vote for LDL because that is the way everybody is talking now, and it is sort of an accident of history that the Framingham risk score uses total cholesterol. But that is, I guess. because it was developed many, many years ago.

DR. TINETTI: Any other comments before we vote?

[No response.]

DR. TINETTI: We will take it to a vote then, try out our little machines.

The question is: Do you believe--this will be a Yes or No, 1 Yes, 2 No, 3 Abstain--do you believe that a cholesterol-based label paradigm is an appropriate approach to selecting patients for use of nonprescription lovastatin and ongoing management again taking into account all the aspects we discussed?

[Electronic voting.]

DR. TINETTI: I guess it takes a minute to tally, so while it is tallying, I believe that we can now raise our hands.

All the people who say Yes, it is appropriate, raise your hand.

[Show of hands.]

DR. TINETTI: So, you are voting Yes, that it is appropriate to do cholesterol based rather than LDL based. Okay.

DR. PICKERING: No.

DR. TINETTI: That was a Yes.

DR. PROSCHAN: Tom, did you vote for Pat Buchanan?

[Laughter.]

DR. TINETTI: That failure was not electronics. Okay. Perhaps it would help for FDA to really specify exactly what question you want, because it sounds like we are all answering different question.

DR. LEONARD-SEGAL: I will say something. Eric, if you have any other comments that you would like to make. The total cholesterol population--

DR. TINETTI: Let me reword it. Is it "acceptable" rather than "appropriate"? Is it acceptable, can we change the wording, so that people are answering all the same--we understand all the background. We want to know very specific what question you want us to answer.

DR. LEONARD-SEGAL: Let me just state that the total cholesterol population defined on this label targets a broader group of people with different--

DR. TINETTI: Is that your question, is it appropriate?

DR. LEONARD-SEGAL: Is it appropriate. Is this population defined by this total cholesterol label, it is a different one.

DR. TINETTI: We understand all of that. We are still not clear what question you want us to answer.

DR. LEONARD-SEGAL: The question that we wrote is do you believe that a total cholesterol-based label paradigm is an appropriate approach to selecting patients. I guess that maybe what we need to say, is this total cholesterol paradigm, that is one question. The other question would be is it appropriate to try to define a population based on total cholesterol that would be consistent with treatment guidelines, if you want to go there.

Where is your confusion specifically?

DR. GLASSER: What Dr. Pickering and I are grappling with is it sounds like we both believe that the LDL cholesterol is the way to go, but if we didn't have

that, could you use the other, and the answer is yes. But that is not what we want. So, that is the problem that we are grappling with.

DR. LEONARD-SEGAL: Let me try to state that we are going to take an action on this application at some point, and there are two labels under consideration.

I guess that we would like to know whether you think that this total cholesterol label would be appropriate--

DR. TINETTI: Is this premature? Perhaps we should go through the rest of the questions first to see if this is even--

DR. LEONARD-SEGAL: Dr. Tinetti, let's try it this way. What do you think of the population defined by the total cholesterol paradigm on this label? Eric, do you have views on that one?

DR. GANLEY: This is Charlie Ganley. Can I just clarify? I think in Dr. Craig's presentation, she was trying to establish that if you went by total cholesterol, you could end up with individuals who are at greater risk than this moderate risk population.

So that is really what the issue is here, is you

will broaden the population, and is that acceptable.

DR. TINETTI: Let me try to restate that new question. Is the broader target population that will be appropriate for the cholesterol versus an LDL paradigm acceptable? All right.

So, now we get to vote again.

[Pause.]

DR. TINETTI: It is not letting us vote.

They are retyping that question. We will move on to the next question while they are doing that.

All right. We can vote now? Okay.

[Electronic voting.l]

DR. TINETTI: Has everybody voted? Okay.

While they are tallying, then, all the people saying Yes to this new question, raise your hand.

[Show of hands.l]

DR. TINETTI: That is two Yeses. We are supposed to state our names.

DR. PROSCHAN: I am Mike Proschan. Did you want me to say something more than my name?

DR. TINETTI: Let's just do the vote now. I am Mary Tinetti.

Noes? We will start over with William.

DR. SHRANK: Will Shrank. No.

DR. FLATAU: Art Flatau. No.

DR. PARKER: Ruth Parker. No.

DR. TAYLOR: Robert Taylor. No.

DR. NEILL: Richard Neill. No.

MR. LEVIN: Arthur Levin. No.

DR. GLASSER: Steve Glasser. No.

DR. ROSEN: Cliff Rosen. No.

DR. CAPRIO: Sonia Caprio. No.

DR. BURMAN: Ken Burman. No.

DR. TINETTI: Abstain?

DR. PICKERING: Yes. I just think it is a bad question.

DR. NGO: We have 2 Yes, 10 No, and 1 Abstain, a total of 13 votes.

DR. TINETTI: We thought that was a fun question. The next is the hierarchy. Before we even attempt this, I am going to suggest that we do not have enough information to vote on the various hierarchies, but I think it is appropriate to look at all of the different criteria to identify which ones definitely need to be included in the

decision and whether or not we think any of them are potentially optional.

Would people be willing to do that? Okay.

Do we have a list of those? So, we can just do Yes or No on each of the individual ones. Do you have a list of those?

DR. LEONARD-SEGAL: Yes, they should be on Linda's slide.

DR. TINETTI: As I understand it, and FDA can clarify this, the understanding is that there are many different criteria that have gone into identifying this optimal appropriate target group for over the counter.

The question is, because there are so many different components to it, are there any of these criteria that we think absolutely if people cannot make an informed decision, appropriate self-selection based on these criteria, it is I guess what they are calling a deal breaker, that if they can't understand and get these correct, that it is a deal breaker.

Are there others, on the other hand, that are optional even if people didn't quite understand it, didn't self-select correctly, that the benefit versus harm ratio

would still favor over-the-counter status? Is that clear?

Let's clarify it to make sure everybody understands that.

DR. SHRANK: Initial clarification might be, let's say, in the Benefits section, can we drop any of them, because if we do, we really lose our ability to risk stratify with according to NCEP guidelines.

Just saying that maybe we don't care as much about HDL, it might be true, but then we are no longer using NCEP guidelines. Maybe there is a factorial decision, can we get rid of anything, and if so, then--

DR. TINETTI: So, your question is just is there anything that is really expendable and can we get rid of, are they all part of the risk stratification? Fair enough.

DR. NEILL: I think I am the only person at the table that has been at every one of these meetings save staff and industry. I have to say I love what you each respectively have done with regard to this hierarchy thing.

Having said that, my answer to the question, as phrased, is yes, there is a hierarchy that has been presented today that is helpful, and it is helpful because my recollection of the conversation was that. if there were

deal breakers--and we have data from a label comprehension and self-selection study that indicated how well consumers could both comprehend and self-select based on, and stratified by, those kinds of deal breakers--then, we would have a better sense of whether we could judge the benefit of having this move into a market where those kind of decisions would happen.

Specifically, I believe that the kind of stratification that staff did, specifically Slide 41 in Dr. Hu's presentation where there were some groupings based on both safety and benefit--I don't know that it is necessary to change the slide, because each of us can look at this slide and look at and consider the NCEP criteria, age, pregnancy, breast-feeding. Pregnancy, breast-feeding clearly has nothing to do with benefit, everything to do with safety.

So, just going through each of those and parsing them into the safety and benefit, you can get the sense--and I am going to focus just on the LDL label--that considering only the safety metrics, you can get pretty good self-selection, looking at benefit maybe not so good, and safety and benefit not as good, and we knew that before we withdrew

the whole hierarchy conversation. That is why we had it, to see if there were some things that could be tossed out. And now we have this new information that suggests to me that, in fact, consumers have some difficulty assessing whether they would benefit.

What concerns me, not most, but does concern me about that inability, if you will, to appropriately self-select is the data that has been presented on both sides with regard to people already on statins who might substitute or go off, and to consider those at higher risk, already on statins, as benefitting from an OTC I think becomes a little disingenuous when you include those in the correct--you know, they need to be on a statin, this is good.

Having said that, it is a also true that there is a large undertreated population. That is why we are dealing with this, to begin with I think.

So, the answer to the next question here, if yes, there is data that is useful to me, that has been presented, then, which one? Here it is. Which one would I suggest for the purpose? This, but I have got to tell you that, you know, just based on this, given that data, I am not real

compelled.

So, the hierarchy data is useful. As a concept, it seems like it is helpful, maybe applicable in other kinds of circumstances. I am not sure that it has been as helpful in pushing this towards eventual approval status.

Does that make sense?

DR. TINETTI: I guess my question is, is that sufficient discussion for what you are interested in, and what I am hearing is if you are going to do a hierarchy, you want to start with safety, you want to add in safety and benefit, and perhaps that is as much as we can do in that question today.

DR. NEILL: I think that to the extent that it has been addressed actually earlier, one of the interesting points here is really we are asking, through the creation of a hierarchy, to parse the NCEP or Framingham criteria so that we can ask ourselves, okay, well, of those benefit characteristics that patients show they can appropriately self-select for, which ones are the biggest bang for the buck.

While that is very valid question, I think it really begs the question of whether or not FDA or sponsor is

anxious to redefine what are already extant evidence-based guidelines for managing this through what amounts to drug label in an OTC setting, and that is very iffy.

It is not directly speaking to the question at hand, but I do think that it is relevant in the marketplace.

DR. PROSCHAN: You mentioned the switching a prescription drug for this, switch the other way around, and I actually was kind of relieved to hear that the price was not going to go way down because that is what I would worry about most in that situation. I mean if I can get an over the counter--

DR. TINETTI: I would like to stay focused on the question here at hand. It is already quarter after 4:00, and we really need to move on. That may be an appropriate point in another question.

I guess I am going to take the prerogative here and ask us to vote on the proposal here, that basically, what I am hearing here is that everything we know right now, these were the appropriate characteristics that went into the decision, and that the hierarchy that has been proposed takes all of those into account and to help guide FDA in the future, is that the approach that we feel that they should

be taking rather than trying to vote on each of the individual hierarchies or characteristics.

I don't think we are going to get too much other helpful information.

DR. GANLEY: Right. I think that was important, and that is why we invited Dr. Neill back, because he is the only person who has been at all three meetings now.

But it gets to the point that even for any OTC drug product, if we applied, you know, 15 criteria to it, very few are going to get it right, and so I think Dr. Neill was right on target there is we have to identify what are the important ones here that really we have to focus on. I think that is very helpful in his discussion, and I am not sure we need a vote on it, if others agree.

DR. TINETTI: Thank you.

In the spirit of time--I know some people in our group are probably going to have to be taking off to get transportation-- FDA, are there specific questions you want to make sure we get to in the next 40 minutes we may jump ahead and get to, if there is any particular question you want to make sure we address? Other than, of course, No. 6, we could just jump right ahead. Barring No. 6, any?

I do want to be able to vote on No. 6 before people leave, but before we get to that, are there other ones that you want us to make sure we get to?

DR. LEONARD-SEGAL: We definitely need comments on No. 3. We are very interested in your comments on safety.

Eric, do you want to weigh in on any of these? I mean we thought that all of these were important when we wrote them. I realize that there is an interest of time here.

Dr. Ganley is thinking that No. 5 is not essential, and that probably is true.

DR. CAPRIO: We don't have 5 on this sheet.

DR. LEONARD-SEGAL: Maybe that was on purpose.

DR. TINETTI: It's on page 3.

Let's have some discussion on Question 3 and we will see how time goes at that point.

I think the way that FDA has set these out, I think are pretty reasonable. The overall question is: Do the results of the SELECT self-selection study demonstrate that OTC consumers could make an appropriate self-selection decision?

Before we get to that vote, I think we want to

have some discussion on these particular components. The first one is those who receive little benefit because they are at lower risk for coronary heart disease.

Any particular discussion? Is that something that needs to be, is that an important part of the decision of interpreting the SELECT study, any particular discussion on those at low benefit?

Remember that about 29 percent of the people who took this medication were at low risk, probably a little bit higher if you take the 10 percent rather than a 5 percent risk cutoff.

DR. FLATAU: So, is the question whether these people benefited, or is the question, is this like another hierarchy, do we think it is important enough--

DR. TINETTI: This is not a specific question, this is a discussion. As you go into the decision, whether it is appropriate for over the counter, how do you factor in that a relatively high percent of the users were in this lower risk group.

DR. PICKERING: I am not too bothered by this one. I was at a meeting last week where a very well-known expert in hypertension said that every hypertensive patient should

have an LDL below 100, which is not, of course, what the guidelines say.

I think this is an incredibly safe group of drugs and I am really not that bothered about the safety issues. We hear a lot about the liver effects, but it is mostly symptomless changes in enzymes. The muscle effects are mostly very nonspecific muscles aches and pains, which is hard to distinguish from placebo effects, whereas, the benefits are very well established.

I have patients with LDLs of 120 who want to get them lowered.

DR. TINETTI: I will take that counterpoint to that one. I think if there was a drug that was without any adverse consequences, then, certainly we would not worry about that group at low benefit as long as they got any benefit, but I think there is still a lot we don't know about the harms of some of these medications.

I think certainly depending upon what literature you read, and certainly Dr. Golomb has spoken out eloquently about this, that there probably is more muscle in neuropathy than we presently know. Unfortunately, we don't really know in this low risk group of people, because they haven't been

exposed to this drug.

A lot more people are going to be taking this over the counter as we have heard and, again, there are other things that hopefully are still under study, things like the hemorrhagic stroke where it is the people with the low LDL, and as we are hearing about, these are the people that will have the least likelihood of benefit, and any kind of risk I think is really important to consider, so I think they do need to go into our equation.

The second one, is there any discussion on the suboptimal benefit because those people are at higher risk for coronary heart disease than the population identified on the label. So, presumably, these are the people who either are taking statins who will now switch to over the counter or those who are not being treated that will go to over the counter rather than get treated with prescription drugs? Any discussion on the consequences of that?

DR. GLASSER: Yes. I would have less of a problem even with this group than the low-risk group, because particularly that latter group you described would probably not get treatment at all, and at least these will now get some treatment albeit not optimal treatment.

I think that is valid, so I would have less of an issue with that than the low-risk group.

DR. PROSCHAN: I renew my previous comment that wasn't appropriate in the last question.

DR. TINETTI: Would you remind us what that was?

DR. PROSCHAN: The switching issue is the one that is troubling. If you switch a stronger prescription medicine and you use this instead, to me, that would be much more likely to happen if this over-the-counter drug were very cheap. Then, I would say, hey, I will take two of these instead of one of my prescription meds.

DR. SHRANK: I think there is two questions here. One is if somebody is at high risk and is untreated, I bet many of us would feel comfortable that they get something rather than nothing, but if the patient is high risk and is receiving an appropriate medication and then gets switched to a less effective medication that is over the counter, and probably more expensive, then, maybe we would feel differently. I don't know if it's actually two different questions.

DR. BURMAN: I am concerned with Dr. Craig's Slide No. 14, which summarizes how many people would take the

medication, and not be in the goal category that we want, and it is about 60 to 67 percent of people, of which 20 percent would be taking it when they had a higher risk, and I think that is not good.

That does bother me that they are not getting monitored, they are not getting other medications, and they are not getting counseling.

DR. PICKERING: I am not too concerned about this high-risk group. Presumably, pretty much by definition, they are people who are regularly seeing physicians since these are a health-conscious group, they are high risk, they are already on a statin.

It seems to me rather unlikely that they are going to just take the over the counter and quit contact with their physicians who presumably would not agree with the switch.

DR. TINETTI: There is one concern I have with this untreated group is we are making the assumption that they will remain untreated unless they have the over-the-counter option, and is this going to further absolve the public health community, the pharmaceuticals, and physicians from really pushing maximum optimal treatment, and that is a

concern that I would have with this untreated group. We are making the assumption that it is no treatment or OTC, and I am not convinced that a greater push towards optimum treatment isn't better.

DR. PROSCHAN: The one thing I would worry about, though, is the possibility of interactions with other cholesterol-lowering drugs and the issue of more side effects with more medication.

DR. CAPRIO: As a pediatrician, I treat children, you know, who have lipidemia myself, so I have not heard that at all in today's presentation. There is some chance, a slight chance that a parent will treat the child with high cholesterol on an OTC medication, so that should be in our mind when we are considering it.

DR. TINETTI: Before we go to the vote, any other comments? I think basically, some of our comments have addressed (c) and (d). Are there other issues related to the self-select study demonstrating that consumers can make an appropriate self-selection decision, any other discussion before we go to a vote?

DR. NEILL: Just speaking strictly from the data on benefit that industry provided, I think the strict answer

to this question must be No. Having said that, I tend to concur with my colleagues on the panel that, gosh, it doesn't make much difference, it is better to be on something than nothing even if they have been appropriately self-selected.

DR. PARKER: The only other thought I have is just for the consumer, when there is some uncertainty about the particular issues, these four that you raised, all of which I think are very specific and make all of us take pause, for the consumer, many of whom if the language for the regulation for OTC has to do with the average consumer, and sort of grasping this, going through it, and then making a good choice on the other side.

A lot of this will have to do with how it is presented to you and how persuasive the--I will use the word "advertising" is, the education, the information, whatever it is that you receive and, given that the FDA does not have jurisdiction over that component, which does influence how you read a label and what you understand from a label.

That is one area that I think, you know, for me gives pause, because I think whatever a consumer takes in, is taken in, in a broader context of all the information

that they receive that encourages or discourages them to self-select correctly.

The regulatory status as it currently exists over who has jurisdiction over the content that frames gives me pause.

DR. ROSEN: One final comment about self-selection is the component of registering drug use either with a pharmacy or with a physician, and we have heard very little about how often, in a self-select situation, they would fill out the form, hand it back to the pharmacist and make sure that that pharmacist knows, because future prescriptions will depend on what the history of their drug use is.

I have heard nothing about that. That is another layer of complexity for the individual consumer when he or she obtains the medication.

DR. SHRANK: Ultimately, that would be very hard to track because patients use more than one pharmacy.

DR. ROSEN: So, that is a big problem. I mean both for the physician, who doesn't know for sure what their patient is taking, and obviously, for the pharmacist who is going to interact or try to determine drug interactions.

DR. PARKER: One other thing. We did hear about

the sale of this being limited to stores where there is a pharmacy. I assume that would mean the pharmacy would have to be open 24 hours even though that wasn't specified, but having a pharmacy doesn't always mean that it's open, and we might, if that is a point of clarity, having this person that you could go to for your questions, want to make sure that they are actually there.

DR. TINETTI: I think one other point with the self-selection is how much we are putting on the label to have to do all the informing, and I think they have done a wonderful job getting as much information as they possibly can. But, for somebody who reads at above 8th grade level slightly, it is sort of an overwhelming sort of thing, and that is just once they make a decision to take it the first time, much less sort of on an ongoing basis.

One of the concerns that I would have already for the number of people who self-selected even at the baseline that were not appropriate is it is just going to get compounded over time.

At the present time, there is no method for sort of monitoring appropriateness over time, and I think that is certainly something the FDA is going to have to deal with,

with these long-term over-the-counter, but it certainly is a gap that presently exists.

Any other discussion on this question? Are we ready to come to a vote?

The question is: Do the results from this SELECT self-selection study demonstrate that OTC consumers could make an appropriate self-selection decision?

Does everybody understand and agree to what that question is? Does everybody understand that question before we go to vote? Okay.

Again, 1 is Yes, 2 is No, 3 is abstain.

[Electronic voting.]

All the Yeses raise your hand.

[Show of hands.]

DR. TINETTI: We will start over here.

DR. PROSCHAN: Mike Proschan.

DR. PICKERING: Tom Pickering.

DR. TINETTI: Okay. Noes?

DR. SHRANK: Will Shrank.

DR. TINETTI: You need to keep your hand up.

DR. FLATAU: Art Flatau.

DR. PARKER: Ruth Parker.

DR. TAYLOR: Robert Taylor.

DR. NEILL: Richard Neill.

MR. LEVIN: Arthur Levin.

DR. TINETTI: Mary Tinetti.

DR. GLASSER: Steve Glasser.

DR. ROSEN: Cliff Rosen.

DR. CAPRIO: Sonia Caprio.

DR. BURMAN: Ken Burman.

DR. NGO: We have a total of 2 Yes, 11 No, and 0 abstain for a total of 13 votes.

DR. TINETTI: I think the safety questions, I presume you want us to address those safety questions before we go on to the final vote. I think that is probably an important question.

These are all a series of Yes and No, so perhaps if there is any brief comments, please go ahead and make the brief comments, otherwise we can go vote on these one at a time.

To address the safety of lovastatin in the nonprescription setting:

First of all, do the data support adequate consumer understanding of the warning concerning pregnancy

and appropriate self-selection by women of childbearing potential? If not, what further data would be needed?

Any brief discussion on that?

DR. NEILL: I am actually going to give a brief discussion to all four elements of this.

DR. TINETTI: All at once?

DR. NEILL: All at one time.

DR. TINETTI: Oh, that is beautiful, go ahead.

DR. NEILL: Lovastatin is a safe medicine and I have heard nothing to suggest otherwise today. The wording of these questions in terms of pregnancy and the patients need to understand yes, it's safe--but it's pregnancy, you know, I don't want to go there. It's a safe medication.

DR. TINETTI: Does anybody else have a comment? Otherwise, we will just go Yes or No.

Would it be helpful to do a vote on each of these? Okay. So, we will go ahead to the vote.

The first one is on pregnancy, do we feel that their understanding of the warning is appropriate? So, Yes or No or--can we tally all of these and do them all at once, or do we have to go through each of them individually? Okay.

The second one. Do the data support adequate consumer understanding of muscle pain, and I will add weakness, warning? If not, what further data would be needed? Please consider self-selection responses of those who are already on statins and chose to switch.

So, the question is--we will see if there is yeses, and if there are many noes, we will have a discussion at that point--so do the data support consumer understanding of the muscle pain and weakness warning? Yes/No.

DR. PROSCHAN: So, it is just a matter of if they read the label, do they understand it, not will they remember it six weeks later?

DR. TINETTI: Correct.

DR. PROSCHAN: Okay.

DR. TINETTI: That was the point I was making is that the label is one thing, but yes, exactly right, this is a label question.

We have just been told we have to do the tally for (a) before we can go on to (b).

For (a) Yes, is the warning sufficient?

[Show of hands.]

DR. PROSCHAN: Mike Proschan.

DR. SHRANK: Will Shrank.

DR. TINETTI: We have to go back to the pregnancy.

DR. FLATAU: Arthur Flatau.

DR. NEILL: Richard Neill.

DR. TINETTI: Mary Tinetti.

DR. PICKERING: Tom Pickering.

DR. ROSEN: Cliff Rosen.

DR. CAPRIO: Sonia Caprio.

DR. TINETTI: Noes?

[Show of hands.]

DR. PARKER: Ruth Parker.

MR. LEVIN: Arthur Levin.

DR. GLASSER: Steve Glasser.

DR. BURMAN: Ken Burman.

DR. TINETTI: Any abstains?

[No response.]

DR. TINETTI: Two votes are missing.

DR. NGO: Dr. Shrank and Dr. Taylor.

DR. TAYLOR: Robert Taylor, Yes.

DR. NGO: That was 9 Yes and 4 No and 0 abstentions for 13 votes.

DR. TINETTI: So, now for (b). Do the data

support adequate consumer understanding of the muscle pain and weakness warning on the label?

1 Yes, 2 No, 3 Abstain.

[Electronic voting.]

DR. TINETTI: All yeses?

[Show of hands.]

DR. SHRANK: Will Shrank.

DR. PROSCHAN: Mike Proschan.

DR. FLATAU: Arthur Flatau.

DR. PARKER: Ruth Parker.

DR. TAYLOR: Robert Taylor.

DR. NEILL: Richard Neill.

DR. TINETTI: Mary Tinetti.

DR. PICKERING: Tom Pickering.

DR. GLASSER: Steve Glasser.

DR. ROSEN: Cliff Rosen.

DR. CAPRIO: Sonia Caprio.

DR. BURMAN: Ken Burman.

DR. TINETTI: No?

MR. LEVIN: Arthur Levin, No.

DR. TINETTI: Abstain?

[No response.]

DR. NGO: That was 12 Yes, 1 No, 0 abstentions for 13 votes.

DR. TINETTI: 4(c). Do the data demonstrate that consumers with common asymptomatic liver disease can safely use lovastatin 20 mg without liver function monitoring? If there are noes, then, if no, could labeling minimize this risk?

DR. PROSCHAN: I would like to know what level of evidence you mean when you say "demonstrate." Are you saying, you know, does it have to be just a preponderance of evidence, or does it have to be, you know, strong, beyond a reasonable doubt? I don't know what "demonstrate" is.

DR. TINETTI: My guess is us, as the experts, have to make their own decision. There are those that have to have 100 percent, and those, if it's 0.5 percent. So I would presume that that is what you will be asking us, that is what they are trying to do, from a group of experts, how much evidence is enough?

Yes, No, or Abstain?

[Electronic voting.]

DR. TINETTI: All Yes, raise your hand.

[Show of hands.]

DR. TINETTI: I will start over this side this time.

DR. BURMAN: Ken Burman. Yes.

DR. CAPRIO: Sonia Caprio. Yes.

DR. GLASSER: Steve Glasser Yes.

DR. PICKERING: Tom Pickering.

DR. TINETTI: Mary Tinetti.

DR. TAYLOR: Robert Taylor.

DR. PARKER: Ruth Parker.

DR. FLATAU: Arthur Flatau.

DR. SHRANK: Will Shrank.

DR. TINETTI: Noes?

DR. PROSCHAN: Mike Proschan.

DR. NEILL: Richard Neill.

DR. ROSEN: Cliff Rosen.

MR. LEVIN: Arthur Levin. Abstain.

DR. NGO: That was 9 Yes, 3 No, 1 Abstain for 13 votes.

DR. TINETTI: The next question has to do with the data mining signal for ALS. Basically, we heard that the retrospective analyses from the primary and secondary prevention trials revealed similar incidences in the control

and intervention groups.

There is an ongoing case-control study examining the question of whether there is an increased risk, and this is expected to be out in mid-to-late 2008.

The question to us is: Considering the self-selection data and risk versus benefit of taking a statin for coronary heart disease, does the ALS mining signal impact on the OTC availability of statins?

I presume that question is until the results of the case-control study are out.

DR. LEONARD-SEGAL: No. Actually, we were interested in your discussion on this. We were interested in your thinking about how it would impact your views or how it would not impact your views, what you think about waiting until 2008, whether you aren't concerned about waiting until 2008. We want to hear something from you.

DR. TINETTI: So, this is a discussion, not a yes/no question.

Any discussion on that point?

DR. NEILL: As a chemical moiety already exists in OTC form, and in terms of the data that we have heard so far from FDA specifically, I think that there is insufficient

data to warrant a change in whatever other deliberations we might have going forward.

Certainly the signal does not seem to be specifically with request to this NDA, to be sufficiently strong to warrant action. It sounds like from the data that I saw for other statins not related, that it is of interest and it is being studied, but it would not otherwise change where things go.

The fascinating thing for me to consider is when this comes down the pike, if it turns into a positive signal, then, what happens to this chemical moiety that already exists OTC, and I am not looking for an answer.

DR. TINETTI: Any other discussion?

DR. LEONARD-SEGAL: Can I just ask you, which chemical moiety are you thinking about?

DR. NEILL: Mevalonic acid as Red Rice Yeast extract specifically.

DR. TINETTI: I presume it's not in this dosage.

Any other discussion on that question?

DR. ROSEN: It just seems to me we just don't have enough data, and I don't think you can throw out of choice. We have no randomized trials. We have got observational

data, and we have got the placebo-controlled trials, but that is three years maximum, and we just really don't have enough information to make an informed decision on it.

DR. TINETTI: I think one of their questions may be if we are lacking that information, and the information is coming down the pike, is it premature to make a decision OTC now, or would it make sense to wait.

I think when we weigh the risk and benefit, I think that is their question they want us to discuss.

DR. SHRANK: So, this is the biggest selling class of drugs in the world. You know, nothing is getting pulled from the market, and there hasn't been any other additional changes. It is hard to imagine that this signal should influence this decision, which corresponds to a medicine that is identical to something you can get by prescription.

DR. NEILL: I am sorry. It is also important to consider that given--if the effect size is so small as to be requiring further study, you know, no sufficient data right now to make any statements about it. You have to consider the competing comorbidity of actions that would make these medicines unavailable or, you know, continue to restrict the availability of medications in terms of deaths that happen.

If you don't live long enough because you died of a heart attack, is it better to die of a heart attack, so you don't get the ALS that you would get because you are able to live 15 more years and be on a statin, and that is data that is way down the pike.

DR. TINETTI: I am going to add one comment and then I will summarize the discussion. I guess if I was going to ask something that they would look at the signal, I would rather have them look at the signal for hemorrhagic stroke. I think that is probably a more compelling issue and some biologic plausibility particularly as we are aiming towards a lower risk population who are going to have low LDLs.

I have been hearing time after time that the lower you get, the better, and I think there may be at least some not great data, but at least emerging data, to suggest that might not be the case. So, I think I would suggest you take the effort that you are devoting to ALS and devote that to hemorrhagic stroke.

In addition to that, I think the comments that there is insufficient data to warrant action at this time, that it is not going to be pulled from the market, and as we

get further data, certainly action will need to be taken. But there is no compelling reason to hold up OTC on that basis from what we presently know.

Moving on to Question 5, was there a question that you said you did not need us to address in Question 5?

DR. LEONARD-SEGAL: We would love you to address them all, but if you don't have time, we would rather see you go to 6. Obviously, we wrote 5 because we thought it was worth asking, but the time is late. We do understand that.

DR. TINETTI: What I am suggesting, let's move on to 6, because part of your question is why or why not, and there may be responses relevant to 5 that come up, so we can get everybody in before they have to leave. Is that a reasonable point? Okay.

Question 6 is: Should the FDA approve nonprescription lovastatin based on the data presented at this meeting? Why or why not? What additional data is needed?

What I am going to suggest here is we do the Yes, No, and Abstain, and for those, if you could, perhaps do a very succinct reason for your answer if you could, and if it

is something that somebody else has said, we don't need to be repetitive. I think that might be a way to go, because I think this is important to get the rationale as well as the decision.

DR. NELSON: Madam Chairman, I don't have a vote, I don't have a clicker, so could I just make a brief comment?

I have been coming to this committee for approximately 15 to 20 years, and this committee has had an opportunity over the years to really make major public health impacts, we heard about smoking and things, and if I was able to vote, I would vote Yes to make this available over the counter, because I think it will have a significant public impact.

I know there was discussion a little bit about the price and cost, but what wasn't considered was the cost of the visits to the doctor, all that type of thing, which really impact cost, as well as the cost of the actual consumer purchase.

But if I had the chance to push my clicker, I would vote Yes. Thank you.

DR. TINETTI: Thank you. As long as we are

addressing that point of cost, you have to remember that about 70 percent of people said they would still discuss this with their doctor, so it is not clear that we are saving any of those costs, I think we need if we are going to be talking costs.

Are we ready for a vote?

DR. GLASSER: Could I have one clarification?

DR. TINETTI: Yes.

DR. GLASSER: Is the question nonprescription or specifically OTC?

DR. LEONARD-SEGAL: The question is OTC, because that is what we have now.

DR. TINETTI: We do not have a behind the counter, so it is only over the counter. This country does not have a behind the counter.

Any other questions before we go to the vote?

Okay. So, should the FDA approve nonprescription lovastatin based on the data presented at this meeting? Then, we will have a brief discussion why or why not. So, vote.

[Electronic voting.]

DR. TINETTI: Yeses?

[Show of hands.]

DR. TINETTI: We will start over here. Dr. Taylor.

DR. TAYLOR: I was involved in the 2005 submission, as well, and I think we have got a safe drug. I think the label has been improved, still needs more work. I think the LDL paradigm can allow people to select. I am a bit worried about the folks that might be at high risk, but I think we have got a major problem with this, with elevated cholesterol, and I am willing to take a chance.

DR. PICKERING: Well, we heard very little about the benefits, but I think we have heard that there is a huge unmet need of people who should be taking statins and who are not, and this offers a plausible way of getting people to take them.

I have patients who take all sorts of things including Red Rice Yeast that they assume is safe because it is, quote "natural," whereas they will not take a statin because it's a synthetic drug and they think it will damage their liver and their muscles.

I think there is no question that these drugs really do lower risk. On the safety side, we have heard a

lot about pregnancy, and it is not clear that there really is a big risk there. My impression is very few pregnant women are actually going to want to start on a cholesterol-lowering medication.

The liver, we heard about Hy's Law, and there is really no indication that I heard that they cause irreversible liver damage. On the muscle side, rhabdomyolysis is certainly a consideration, but is extremely rare on the doses that we are talking about. So, in my view, the benefits greatly outweigh the risk.

DR. TINETTI: Thank you. Any other yeses? Noes?

Okay. We will start with you.

DR. SHRANK: Will Shrank. It just seemed to me the patients couldn't figure out whether the drug was for them, and certainly the ones who chose to use the drug frequently it wasn't right for them.

I didn't really buy the whole idea that doctors could serve as a useful mitigating factor considering that one of the reasons that over-the-counter statins improve access is that it is for patients who can't see their doctor, and I think it will be hard for patients to contact their doctors while they are at the pharmacy to try to make

it happen.

So, it is a selection problem and unclear role of the physician.

DR. TINETTI: Sonia, can you just give your vote before you leave?

DR. CAPRIO: No.

DR. TINETTI: No? Okay.

DR. CAPRIO: I am concerned that we are going to have excess people that do not need the medication will be taking--you know, there is going to be abuse of it.

DR. TINETTI: Thank you.

Other noes?

DR. FLATAU: Arthur Flatau. I agree with what Dr. Pickering said. It is not clear to me that the benefits to patients of it being over the counter outweigh the risk, although they are small. Clearly, there are a lot of people who are not on statins and should be on statins. I just don't believe that making it over the counter will increase the number of patients who would take it.

And the cost, you know, I find it hard to believe that they will go every six weeks and spend 50 or so dollars to get their new, safe, natural, over-the-counter statin

drug, and then they won't discontinue it.

DR. PARKER: I had concern about the--first of all, I commend you all. I think you did a lot of work on the label and indeed, there are some incredible improvements over the one that came forward last time. So I commend you on the progress that I think really was made on that.

But I can't make a cognitively between a label comprehension and an actual use on a different label. I think that from a methodologic standpoint we need to see actual use studies that are done with the actual label, not actual use studies that are done with another label that is not the one that we would be using, by the way.

I think that we need to be clear on that. I appreciate that CUSTOM had some merits and was done in the past, but I think our actual use and the data we get on it needs to follow from the label comprehension of the product as it goes forward for approval.

The other concern that I have has to do with the consumer in the broader context of making good judgments for self-selection, which is a major criterion that cuts out the learned intermediary and the role of the physician in counseling and in helping someone make a good self-selection

about going on a chronic medication.

The fact that there is no FDA input into the advertising that frames the broader context, that really to me presents a major concern and I think, as manufacturers move forward, I would encourage them to be a part of trying to creatively find a way to partner with some oversight that would give more confidence to the information that frames being more in an educational frame than in an advertising one. It is just one about buy it, buy it.

DR. NEILL: Richard Neill. Also, a No. Primarily, I think this is safe and effective actually. I don't think this is an OTC indication despite what the sponsor brings with regard to osteoporosis and aspirin use for MI prevention.

In both of those instances, those are monograph, not NDA drugs, and an Rx to OTC switch for an NDA drug to me is qualitatively different especially when the condition is one where there is difficulty making appropriate self-diagnosis and in which the presumption is that the patient is going to be on treatment whether lifestyle change or medication for life.

A wise professor of mine taught me that when your

patient asks, "How long am I going to be on this medicine," the answer is never, for the rest of your life. It is either until we know better or until something better comes along, and something better always comes along.

What NDAC time and this third meeting has taught me is that when it comes along, that better thing, it is going to be prescription, not OTC, until the patent runs out, and then somebody is going to bring an OTC switch application for the NDA. And when that happens, there needs to be some compelling data related to the indication that suggests that patients with those chronic illnesses are going to do better.

You gave great data to suggest that that broad target swath of folk that would select may do better and. within that data, some signal that there might be people who are less than optimally treated or even optimally treated now, whose treatment would decline a bit.

We don't have any data about how the overall switch process would influence overall public health. It is my belief not informed by data presented here that generic lovastatin would exist without the same education program, without the restrictions that bind sponsor to the agreement

that FDA has, just by virtue of this existing OTC, and I respect all of the work that you guys are doing, to do this the right way. I wish that others in industry would do it as well as Merck does.

The last point I would make is that lovastatin is just the first and there will, of course, potentially be many others. And, if lovastatin is the first for this kind of indication, it is very clear to me that asthma, high blood pressure, diabetes, this is a huge can of worms.

We talked about this a lot at the first of these three meetings, and it seems like we have never gotten to that central issue of the OTCness of the condition, and to me, that is prime, sorry it wasn't succinct.

DR. TINETTI: It was not succinct, but it was eloquent.

MR. LEVIN: Arthur Levin. No, and the only thing I will add is the point that the Chair brought up earlier today about we haven't learned how to present information in a way that really allows consumers to make an informed decision for themselves, for each individual decisionmaker.

I think until we get to that point, I don't feel comfortable with this kind of switch.

DR. TINETTI: Thank you. Mary Tinetti. No, and for many of the reasons that were presented, that there were subgroups that potentially will have less benefit than presently, and the major reason, as Mr. Levin just said, is that we really haven't learned how to provide that information, so that people can make an informed decision. Such a high percentage of people were inappropriate in their initial selection.

We still don't know sort of the long term monitoring. That is a whole sort of black box that we have to understand before we move forward with OTCs for chronic conditions.

I was also concerned about the reasons why people decided they would rather than an OTC, things like not only was it more convenient, they didn't need their physician although many of them said that they would rely on their physician to help them make the right decision, but that it was safer and more natural, and obviously, that is not the case. It just tells us that at this point, we are not in a situation where people can make that safe informed decision.

DR. GLASSER: Steve Glasser. No, and since I am not eloquent, I will make it brief. I will summarize it

with my dilemma. I am actually for it being nonprescription, but not in the present form.

DR. ROSEN: Rosen. No. I think there is an unmet need, as Dr. Taylor said, but this is not the way to do it. I think we overtreat low risk and undertreat high risk, and until we understand how to get that group of people that are most appropriate, we are not ready for this.

DR. BURMAN: Ken Burman. No. To be succinct, I agree with the comments that have been made, but to expand on them very quickly, and that is, the benefits and adverse effects have not been tested in a large population and real life situation where I think the results will be different than we have seen in these preliminary results.

In these large-scale studies that I propose, at least in the studies that have been done, there is no LDL goal met, there is no complication criteria, number of complications, following these people for a year or two or more, so a real life situation is lacking.

The 64 percent, at least 60 percent of the people didn't make the right decision as to whether they should be on the drug or not, which is quite disturbing to me. Then, the issue of follow-up and registry that was brought up

before, and the complexity all weighed in my decision.

DR. TINETTI: Are you suggesting that you would like to see real world randomized control trial data in an over-the-counter environment?

DR. BURMAN: I think what I am suggesting is the one thing that bothers me the most is that the preliminary studies that were presented are only preliminary studies showing that people could pick rightly or wrongly whether to use the medication or not, but really don't show, over the long term, over a two-year, three-year study, what have they done, how long did they stay with the drug, what are the complication rates, and do they actually get monitored.

DR. TINETTI: Thank you.

Any abstentions?

DR. PROSCHAN: Mike Proschan. I abstained because I do think it could have a lot of benefit. What I am worried about, though, is that what we have seen here in terms of selection is a best-case scenario, because you tell these people read the label, I will come back in a few minutes.

In reality, people are going to go in, they are not going to be told read the label and I will come back in

a few minutes to see if you want to buy it, and it is an open book test.

You know, when they are asked the questions, they are able to look at the label, and I just don't think that is what is going to happen in the real world, and I would worry about someone remembering it later also if they develop symptoms.

DR. NGO: We have a total of 2 Yes, 10 No, and 1 abstention, a total of 13 votes.

DR. LEONARD-SEGAL: Thank you. We appreciate all the hard work and all the discussion. It has been very interesting for us, informative, and we will think about everything that we have heard today, and we appreciate it.

DR. TINETTI: Thank you, thank the panel, thank the industry and the FDA. Thank you all.

[Whereupon, at 5:05 p.m., the proceedings were adjourned.]