

1 could actually see what changing their diet did if I
2 explain to them what happens after they eat, and
3 talked about post prandial. But more likely, I would
4 maybe use it if a patient wasn't coming in for four
5 months and maybe in between, they were going to test
6 it and call me. Again, it has to be really accurate
7 to be helpful there.

8 I would see it also as a way for people to
9 screen themselves on a one-time basis, to identify
10 themselves as needing follow-up. But I think, you
11 know, I would see it being used maybe a few times a
12 year.

13 DR. EVERETT: What about the inappropriate
14 use? That is, using it as a diagnostic tool. Do you
15 think it is acceptable for that purpose?

16 DR. GINSBERG: You mean for an individual
17 to test themselves?

18 DR. EVERETT: And determine that they have
19 elevated triglycerides, without seeing a physician.

20 DR. GINSBERG: Well, if they do that and
21 then they see a physician, obviously if they are a
22 false positive, then there is some inefficiency there.

1 But I would think -- I think screening is good. I
2 think the more screening you have, the better off you
3 are. So I would rather get a few false positives and
4 identify more people. That is my view.

5 DR. EVERETT: So you think it is
6 acceptable to use it as a screening tool?

7 DR. GINSBERG: I would be positive about
8 having the availability for someone who hasn't been to
9 a doctor to see this in a store, stick their finger,
10 and find out their triglyceride. Even if its fasting,
11 if they find the triglyceride of 300, that would get
12 them to go to their physician.

13 DR. EVERETT: Okay. Thanks.

14 CHAIRPERSON NIPPER: Dr. Manno, do you
15 have any questions?

16 DR. MANNO: I have no questions.

17 CHAIRPERSON NIPPER: Dr. Doumas?

18 DR. DOUMAS: I had a question, and I am
19 going to ask you, Dr. Ginsberg. When it comes to when
20 in the labels, around this test, two to three times a
21 year or at least monthly if you are diabetic or a
22 woman post-menopause. Do you agree with that

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 statement, that recommendation?

2 DR. GINSBERG: I can't see the reasoning
3 behind the monthly testing for post-menopausal women.
4 The majority of post-menopausal women don't have
5 dyslipodemia. Obviously women aren't as well off
6 lipid-wise or insulin sensitivity wise post-
7 menopausally, but that doesn't mean they become
8 diabetic or dylipidemia.

9 Every woman probably should have her
10 lipids measured post-menopausally if it hasn't been
11 done before or even if they have been done before,
12 because there are some changes. They do become much
13 more prone to hypertriglyceridemia. But I don't see
14 any reason if the first test is normal, to follow that
15 up on a monthly basis.

16 In terms of the diabetics, most diabetics
17 should be seen every three to four months, depending
18 on their complications. So I would possibly see maybe
19 two to three times a year, you know, somewhere in
20 between those visits as possibly being of value. Or
21 if I change the therapy and they went home and in two
22 weeks instead of coming to see me again, if I knew

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 they could test well and they had in that case maybe
2 precision, to tell them to try that and have them call
3 me rather than having them come into the lab. But I
4 don't think I would see it once a month.

5 DR. DOUMAS: Also for non-diabetics and
6 non-menopause, do you think that -- they are past
7 menopause, do you think that somebody should do it
8 three times a year?

9 DR. GINSBERG: No.

10 DR. DOUMAS: Thank you.

11 DR. GINSBERG: I think if the first one is
12 normal, I would follow NCEP guidelines there. At that
13 age, probably once a year people should get tested.
14 Now whether they should get tested at a lab which is
15 a wet bench or home is a separate issue.

16 DR. DOUMAS: That's another issue. Thank
17 you.

18 CHAIRPERSON NIPPER: Dr. Janosky? Dr.
19 Lewis?

20 DR. LEWIS: I have nothing.

21 CHAIRPERSON NIPPER: Ms. Kruger?

22 MS. KRUGER: I am just struggling with the

1 whole notion of acceptability, when to use an
2 accuracy. Most of the patients we -- we don't see
3 most of the Type 2 patients. The majority of us
4 specialists don't see those. Those are seen by the
5 internists. Even with the UK PDS studies, which are
6 hammering away tight control, tight control, control
7 the blood pressure, control the lipids, the fact is,
8 we still haven't been able to get that through for a
9 lot of reasons to the internists. They don't have the
10 time. I mean there's just a host of things.

11 One of the reasons they don't want to do
12 blood glucose or recommend to their patients to do
13 blood glucose is that it's more data they have to deal
14 with on the telephone, more data that they have to
15 deal with when the patient comes in, and the concern
16 of accuracy when they are manipulating medication.

17 So I guess I am struggling with -- I think
18 blood glucose monitoring today, the meters we see
19 today are accurate. I am not comfortable yet that we
20 are going to see reproducibility in this device. I am
21 concerned that while I believe in empowerment of the
22 patients, we still have to have buy-in by the

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 healthcare community. I am not convinced we are going
2 to get the internists buy in who, for the most part
3 are going to be -- in the way, in the global way we
4 are speaking about using this meter, would be using
5 this meter.

6 Those are things that are sort of catching
7 me up, is --

8 DR. GINSBERG: Let me just respond. I
9 think in the lipid field, we are so -- I mean there
10 has been such an abysmal participation by the general
11 health community in terms of treating hyperlipidemia
12 in the face of tremendous data. I mean if you want to
13 practice evidence-based medicine, there may not be a
14 better model than cholesterol-lowering trials and even
15 the triglyceride lowering trials. That if patients
16 find out they have a bad number, and they go to their
17 physician and ask them why they are not being treated,
18 to me maybe that's what we need to do. It's not
19 optimal.

20 Again, I don't see this as something that
21 people would be doing weekly or monthly to help manage
22 this. I would see it being done at much more

1 infrequent intervals as an adjunct.

2 MS. KRUGER: That would also raise my
3 eyebrows again, is if these people are not monitoring
4 blood, so they don't have the technique for that, and
5 they are doing it so sporadically, are we in fact
6 going to get accuracy and precision? I just throw
7 that out as a concern.

8 The other question I have, are there other
9 labs that need to be done at the same time, say every
10 four to six, eight, twelve weeks, like we do when we
11 do lipidtor, zocor, liver enzymes, or any of those
12 that need to be done, that we'll miss doing for making
13 sure that the drugs are safe if the patients aren't
14 coming in frequently enough for --

15 DR. GINSBERG: For the Stattons now, I
16 think the FDA actually, I think the package inserts
17 talk about twice a year for LFTs. So hopefully this
18 wouldn't replace the patient's visit to the doctor.

19 CHAIRPERSON NIPPER: Dr. Rosenbloom, did
20 you have anything?

21 DR. ROSENBLOOM: Yes. How many patients
22 have you seen in the last couple of years, the last

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 three or four years since the cholesterol testing has
2 been in existence, who have come to your attention
3 because they have gone out and gotten this test and
4 found it abnormal?

5 DR. GINSBERG: None.

6 DR. ROSENBLOOM: Okay. Secondly, have you
7 ever ordered a triglyceride by itself?

8 DR. GINSBERG: No. Possibly rarely in a
9 patient whose triglycerides in the thousands. But
10 otherwise, no.

11 CHAIRPERSON NIPPER: Dr. Clement?

12 DR. CLEMENT: Interesting. Have you been
13 concerned about the blank, the unblank issue with high
14 triglyceridemia, hypertriglyceridemia in folks with
15 diabetes? Is that a clinical and significant issue
16 that we should be concerned about?

17 DR. GINSBERG: So the issue of glycerol.
18 I think glycerol levels tend to be somewhat greater
19 proportion of triglyceride. Free glycerol tends to go
20 up as triglycerides go up. Post parandially, where I
21 was thinking this might have utility with all the
22 lipolysis going on, glycerol levels could be even a

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 little bit higher.

2 Usually there is still not more than maybe
3 I think 10 percent or 15 percent of value. So there
4 might be an overestimation of the triglycerides by
5 that level. Luckily, they turn over so fast that even
6 during lipolysis, they probably don't go up that much.
7 But it is another built-in error to the system that
8 doesn't have a blank.

9 MS. KIMBERLY: I don't have any questions.

10 DR. RIFAI: I don't either.

11 CHAIRPERSON NIPPER: Well, we thank you
12 very much, Dr. Ginsberg, and hope you make your
13 shuttle.

14 Thanks, Arleen. Were you going to go over
15 the questions?

16 MS. PINKOS: Yes.

17 CHAIRPERSON NIPPER: Okay.

18 DR. REJ: Is there time to ask questions
19 about the FDA presentation?

20 CHAIRPERSON NIPPER: Why don't we just go
21 over the questions. Then we'll just throw it open and
22 ask questions to the FDA persons and others that come

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 up. Is that all right with you? Is the panel okay on
2 that?

3 MS. PINKOS: Okay. I have 10 questions
4 that we would like you to discuss during your
5 deliberations this afternoon. The first one is, is
6 the Agency's requirement for comparison to a CDC
7 reference method reasonable when the device is
8 intended for over-the-counter use? Other options
9 include characterization of only the predicate device
10 by a CDC lab or no requirement at all for any
11 comparisons to a CDC reference lab and simply label
12 the device as not having been evaluated by a method
13 recommended by NCEP.

14 The other thing I want to say here is that
15 we realize that CDC reference laboratory studies are
16 undoubtedly more costly and labor intensive for the
17 sponsor. The Agency is committed to finding the least
18 burdensome path to market for industry. But at the
19 same time, we don't want to compromise safety or
20 effectiveness in the device. So we're asking here
21 what the minimum study should be for a device.

22 Okay. Should an over-the-counter device

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 be required to meet NCEP performance goals? If a
2 device does not meet NCEP performance goals, is it
3 acceptable to clear it for marketing with cautionary
4 labeling? Or if NCEP is not an appropriate minimum
5 threshold for performance, what criteria should be
6 applied?

7 Because it is difficult to convey the
8 performance limitations of a laboratory test to a lay
9 user, and because results are interpreted as a single
10 entity, FDA generally believes that over-the-counter
11 devices need to be pretty good. So should these NCEP
12 performance goals be the threshold? Or do you think
13 that there is another more appropriate yardstick?

14 I just want to make a couple extra points
15 on this, that the question was raised earlier whether
16 NCEP had specific performance goals for whole blood
17 assays. If you read their information, they don't
18 specifically address whole blood performance. But
19 they do make the statement, I believe it's on the
20 bottom of page 133, that the performance goals are
21 appropriate for all methods, depending on where they
22 are being performed. They go into a little bit of

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 discussion about that, if you are interested in
2 reading it.

3 But NCEP, we have to remember that NCEP is
4 not used to balancing performance requirements with
5 the claims that are associated with the device. We're
6 also considering the benefits that a device being run
7 at home might have. Sometimes there is a little bit
8 of a tradeoff there.

9 In the packet that was sent to you from
10 NCEP, there is also a discussion on total error and
11 why NCEP likes total error so much. That sort of ties
12 into a little bit of the discussion that we were
13 having earlier. The reason that they like total error
14 is it is give and take on accuracy and precision, so
15 that if a device is more accurate and less precise,
16 it's still going to meet a total error target or vice
17 versa. So it is a little bit forgiving in each
18 direction there.

19 Okay. What is the appropriate minimum
20 sample size for evaluating an over-the-counter lipid
21 test, and should there be a minimum requirement for
22 sample distribution? That was brought up in the

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 review of the product here today, that there was -- a
2 couple people agreed from both sides of the fence, if
3 you will, that they needed to get a few more samples
4 in that upper end. So if you have any recommendations
5 for us in general on lipid tests, we would appreciate
6 that.

7 Has the sponsor done the appropriate
8 precision and interference studies? What is the
9 appropriate claim for this device? Has the claim
10 encapsulated in the labeling? Is performance adequate
11 to support the intended use or claims for this device?
12 Again, this just means to make the point that the
13 performance required is very much linked to the
14 intended use of the device or how it is going to be
15 used. That question of course relates to the last
16 question, what should be the intended use of the
17 device.

18 The last four questions that I have all
19 have to do with the labeling. Is it an acceptable
20 approach to refer lay users to a second professional
21 use package insert for additional information such as
22 quality control instructions. The sponsor is taking

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 this rather unique approach to labeling. Do you think
2 this is an acceptable way of transmitting that
3 information?

4 Does the labeling adequately address
5 quality control instructions, recommendations, and
6 interpretation? Is performance of the device properly
7 conveyed in the labeling? You'll notice that the
8 performance is currently -- and we already discussed
9 this a little bit, the performance is currently
10 presented as being accurate in 95 percent of the time.
11 Precision is described in terms of mean, standard
12 deviation, and coefficient of variation. Sometimes
13 that's not the easiest way to convey information to
14 lay users. So if you have got some guidance for us
15 and the sponsor, we would appreciate that.

16 Finally, do the benefits of this device
17 outweigh the risks? This is almost a rhetorical
18 question by the time you answer the rest of the
19 questions, but it is one that we always ask for over-
20 the-counter products because it is such a fundamental
21 review issue, not just for over-the-counter, but for
22 all products. You would have to consider all parts of

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 the device and what it brings.

2 Considering the performance of the device
3 and its intended use, can it be labeled in such a way
4 so that the information is more beneficial than
5 harmful to the consumer?

6 That's it.

7 CHAIRPERSON NIPPER: Okay. Thanks. Now
8 just to get us back on track here, since Dr. Ginsberg
9 had to kind of scoot, we did the Q&A period for him
10 after the FDA presentation. There may be some
11 questions that the panel has of the three presenters
12 from the FDA, Arleen Pinkos, Carol Benson, or Telba
13 Irony, the statistician.

14 I think we can go ahead and go around the
15 room and try to get FDA questions, specific questions
16 about their presentations, any clarifications that you
17 need to make for that. Then the agenda calls for an
18 open public hearing. We'll do that. Then we will
19 devolve into open committee discussion, where I will
20 try to answer the questions that Ms. Pinkos has
21 discussed with us now.

22 We will try to get as many of these

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 questions answered by panel members as possible, and
2 final recommendations made as soon as possible. But
3 we would like to get a thorough job done here before
4 we lose our panel.

5 So Bob, did you have questions for any of
6 the three FDA presenters?

7 DR. REJ: I do have one question that's
8 related to the FDA statistician's presentation, but
9 maybe it can be clarified from the sponsor. It has to
10 do with the study on precision. If you can put those
11 data on the screen, I don't know how hard that is to
12 do. But this was a case where there were three
13 consumers, the precision, inter-consumer precision was
14 estimated. Perhaps the sponsor could explain exactly
15 what was done for that study.

16 DR. IRONY: I'm trying to get the
17 presentation.

18 CHAIRPERSON NIPPER: Bob, that's the one,
19 the slide that says whole blood, three consumers, two
20 levels each?

21 DR. REJ: Yes. Two levels each, and
22 consumer one, consumer two. It has standard deviation

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 CV. So perhaps the sponsor could --

2 CHAIRPERSON NIPPER: I think that's in the
3 packet too.

4 DR. IRONY: Yes. Maybe you can ask the
5 question.

6 DR. REJ: Give me a little information
7 about the specimen used in those studies, how that
8 study was done.

9 MS. PINKOS: That's the three consumers
10 with the whole blood?

11 DR. REJ: Yes.

12 MS. PINKOS: It was an EDTA whole blood
13 sample.

14 DR. REJ: Right. And across consumers,
15 was it the same sample?

16 DR. IRONY: No. Each consumer had a
17 different sample.

18 DR. REJ: A different sample?

19 DR. IRONY: Actually they had two
20 different samples each.

21 DR. REJ: Each. So that the two samples
22 that were given to consumer one are different samples

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 than those given to consumer two?

2 DR. IRONY: Right.

3 DR. REJ: Thank you.

4 DR. EVERETT: Questions for the
5 statistician. In the slides you showed where the
6 levels of triglyceride was labeled 100 percent, 200,
7 and 400 --

8 DR. IRONY: Let me just try to find it.

9 DR. EVERETT: And you gave the total
10 percent of.

11 DR. IRONY: Which one? The precision
12 study? This one?

13 DR. EVERETT: No. It was a summary slide
14 where you had the levels of triglyceride measured
15 compared to the total percent error.

16 DR. IRONY: I have to go through the whole
17 thing?

18 DR. EVERETT: You may be able to answer my
19 question without the slide.

20 DR. IRONY: Okay.

21 DR. EVERETT: My question is, is the total
22 percent error at each one of those sub-categories, is

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 the total percent error significantly different
2 between any of the two levels?

3 DR. IRONY: Let me just clarify here.
4 Here is not the total percent error. What it shows in
5 this slide is actually the difference, what will be
6 the bias. The difference between the measurement
7 taken by the BioScanner and the measurement taken by
8 the reference lab. What I'm showing here is just like
9 a descriptive analysis. These red bars, they
10 represent the 15 percent. Of course 15 percent of 400
11 is a lot more than 15 percent of 100. So that's why
12 these intervals are larger.

13 The points of the actual measurements, so
14 you can see, for instance, around 100 you have more
15 points outside the bars. Whereas in 400, well we
16 don't have enough, but let's say at 300, we have more
17 points in between the bars because the percentage is
18 higher there.

19 DR. EVERETT: Can I realistically say the
20 total percent area is greater at one level than
21 another?

22 DR. IRONY: No. We can say from here.

1 No, what we can say is that the tolerance limits are
2 different. That's what we can say here. The
3 tolerance limits at the level 400 here will be greater
4 than at a level 100. We can say they are greater --
5 I mean the actual measurements are greater because we
6 don't have enough points. You can see at 400, we lost
7 some points.

8 DR. EVERETT: Okay. Then my other
9 question is, do you think the target population that
10 they used to generate the data resembles the
11 population at large? When I asked the question, they
12 said there was no limit on who could use this
13 particular test. I assume it's for the general
14 population. In the study, the population that they
15 use in the study, in my opinion, doesn't represent the
16 general population.

17 DR. IRONY: Yes, I guess the physicians,
18 the clinicians will be able to tell better than
19 myself. You know, this is a small sample of 220. I
20 don't know if it represents the target population or
21 not. Then the sample has to be analyzed and see how
22 many diabetic people are in this population and we

1 don't have this data.

2 DR. EVERETT: So how do you decide then
3 who is recommended to use this particular test?

4 MS. PINKOS: The sponsor hasn't in their
5 claims of their intended use specifically targeted any
6 particular group. I think they have said, and they
7 can chime in if they would like, that probably who was
8 going to end up using it are diabetics, just because
9 of the way their device is packaged with glucose and
10 cholesterol. They are also trying to get some other
11 tests that are probably typically used by diabetics.

12 So whether they shot themselves in the
13 foot or did themselves a favor by having a non-
14 diabetic population doing the study, I don't know. I
15 mean they made the argument, and there is certainly
16 some truth to it, that if you have a diabetic
17 population that are used to doing finger sticks more
18 often, but then we also have to consider that it is
19 being put on the market and anybody can buy it, and
20 anybody can use it. So because they are not limiting
21 their claims for use, the target population that they
22 did use is probably okay.

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 DR. EVERETT: Okay. Then my last question
2 is, are there any statistically strong points about
3 this study that support the intended use of this
4 particular instrument?

5 DR. IRONY: What would be the statistical
6 strong points?

7 DR. EVERETT: Well that's what I'm asking.

8 DR. IRONY: What would you desire from
9 such an instrument?

10 DR. EVERETT: Well, something better
11 precision-wise, as well as accuracy so that when I
12 look at total error, it's better than what's being
13 presented here.

14 DR. IRONY: Well, I guess that is the data
15 we have got. I can't tell from what I haven't seen,
16 so I guess that's the data we have got and that's what
17 is happening.

18 DR. EVERETT: That, I understand. But my
19 question is what do you think are particular strong
20 points?

21 MR. GUTMAN: Actually, that is why we
22 asked you folks to come together. I think that Dr.

1 Cooper sort of captured I think the issue that we deal
2 with. There is no question that there is a
3 performance deterioration on this assay. There is no
4 question that there is a change in access which might
5 be good or might not be good. As you are
6 deliberating, that should be a light motif behind the
7 thing. Is the compromise from performance outweighed
8 by the access or is it not? We don't know. We're
9 confused. We don't have the expertise that this group
10 has. We are honestly asking you to tell us, does this
11 performance match either this intended use or other
12 intended uses that might make this reasonable to put
13 on the market?

14 DR. EVERETT: Sure. That, I understand.
15 My question is one about statistics, not about all the
16 parameters of the study. She is a statistician. She
17 is an expert in that area. I think she is qualified
18 to answer the question.

19 DR. IRONY: But I still don't understand
20 your question. If you want me to tell what is the
21 good side about the instrument, I don't know.

22 DR. EVERETT: Only about the statistics

1 and as it relates to the data that they presented.

2 DR. IRONY: Right. That is exactly what
3 I gave you, was just analyze the data and interpret
4 the data as it came. I guess so the clinician is to
5 decide whether the error both in precision-wise and
6 bias-wise will be tolerable or not.

7 DR. EVERETT: This could go on forever.

8 CHAIRPERSON NIPPER: It won't, Dr.
9 Everett. That's why they hired me.

10 (Laughter.)

11 CHAIRPERSON NIPPER: Dr. Rej wanted to
12 jump in for a minute.

13 DR. REJ: One follow-up question which I
14 forgot to ask about the Bland Altman plot that's up
15 here. Again, because of the way you have these red
16 bars that show the NCEP guidelines of plus or minus 15
17 percent, is it safe to say that there are more data
18 points outside of the NCEP guidelines than there are
19 within in this set?

20 DR. IRONY: Well, you are seeing the same
21 data as I'm seeing. Right.

22 DR. REJ: Again, because those bars are

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS

1323 RHODE ISLAND AVE., N.W.

WASHINGTON, D.C. 20005-3701

1 not linear, I mean we're not following -- we have
2 these sort of segmented set. Are there more points?
3 I can't count them, especially from this angle. You
4 know more intimately.

5 DR. IRONY: You can see. You can see in
6 the neighborhood of 100, okay, there are lots, lots of
7 points. The further analysis was then when I did the
8 distribution of the frequency. For the 400 level, we
9 can tell not because there are many, but there aren't
10 enough observations to support --

11 DR. REJ: And of course the NCEP
12 guidelines are more forgiving as you get to higher
13 concentrations of triglyceride.

14 DR. IRONY: In this case, it is, yes.
15 However, 400 is a decision point.

16 DR. REJ: Yes, I'm aware of that. But to
17 my eye, it looks to me like from this data set of
18 comparison with the reference method, more points
19 exceed the NCEP guidelines than are within it.

20 CHAIRPERSON NIPPER: Let's see if Dr.
21 Manno wants to try to catch a hummingbird with a net
22 or wants to try to nail a statistician down to

1 something concrete.

2 DR. MANNO: I'm happy. I have no
3 questions. I'm waiting until later.

4 CHAIRPERSON NIPPER: Dr. Doumas?

5 DR. DOUMAS: I'm referring to a table
6 where you talk about the random error, upper limit.
7 You take your confidence interval. You have, for
8 example, 35 -- or 86, 38, 73. What is the probability
9 of having this kind of error statistically?

10 DR. IRONY: Are you talking about this
11 table?

12 DR. DOUMAS: No. I think it's the
13 previous. Yes, those. What is the probability of
14 having random errors of this size? I mean this is the
15 upper limit. The maximum error in other words is 35
16 milligrams. How many times out of 100, those values
17 will be obtained, these kind of errors?

18 DR. IRONY: Well, it will depend on the
19 viability of the population you are analyzing. You
20 have to make several assumptions.

21 If the instrument will vary precise.
22 Let's say you have it perfect, you never have any

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 variability. Every time you measure it, you get that
2 value. So I can't tell. That's exactly what we are
3 trying to make inferences based on these samples to
4 say what will be the precision of this particular
5 instrument that we are analyzing.

6 The problem I see in this particular study
7 is that we have only three consumers.

8 DR. DOUMAS: I see.

9 DR. IRONY: You see? So as you can see,
10 that for consumer three, for instance, you know there
11 is low variability either because the person was good
12 in measurement or something we can't control. For
13 consumer two, for the same kind of level, which had a
14 lot more variability.

15 What we will need to characterize this
16 instrument, in my opinion, would be much more
17 consumers.

18 DR. DOUMAS: Another question unrelated.
19 Would you define, please, for an ignoramus, what you
20 mean by goodness of fit? How do you evaluate the
21 thing? Somewhere I have seen in the materials here
22 from the FDA "goodness of fit."

1 DR. IRONY: Well, these basically will
2 tell when you are fitting a line or any curve to
3 points. We have to see how well you fit.

4 When I did the analysis of residuals, I
5 would say the perfect fit will be all residuals will
6 be zero. Let me go back.

7 What is a perfect fit? All points --

8 DR. DOUMAS: Everything on the line.

9 DR. IRONY: On the line. The further the
10 points are from the line, the worse the fit.

11 DR. DOUMAS: Okay.

12 DR. IRONY: There are statistical tests
13 that will measure how good the fit is and how bad the
14 fit is. But intuitively, you know, the closer the
15 points are from the line, the better the fit is.

16 DR. DOUMAS: The better the fit.

17 DR. IRONY: Right.

18 DR. DOUMAS: Thank you.

19 CHAIRPERSON NIPPER: We're going to have
20 dueling statisticians.

21 (Laughter.)

22 DR. JANOSKY: I have been waiting. I have

1 a series of questions. Two of them are ones that I
2 had asked the sponsor this morning, so I wanted to
3 address them also to FDA and the reviewers. The other
4 one is sort of a take-off on some of the discussion
5 that we have had here. So why don't I start with that
6 take-off one.

7 At the University of Pittsburgh, we call
8 what was presented this morning Syndrome X. Syndrome
9 X is this syndrome that seems to be associated with
10 obesity, diabetes, high blood pressure, et cetera,
11 which the sponsor had presented and they called it
12 something else.

13 Trying to tease apart whether the
14 population that was studied in the consumer study was
15 appropriate or not. So does anybody have an estimate
16 or can someone please tell me what would be the
17 relationship within a group of diabetics for the
18 triglycerides? What would be the expected value?
19 Because it seems to me that you want to, if the
20 intended use is specifically within diabetics, you
21 want to map your sample group to that particular group
22 of patients.

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 I tried to look it up. I couldn't find
2 anything for triglycerides average in that group of
3 population. Is there some data I'm missing?

4 DR. CLEMENT: I can answer.

5 CHAIRPERSON NIPPER: Steve?

6 DR. CLEMENT: As a clinician, one of the
7 several clinicians in the group, if someone has well
8 controlled diabetes, their triglycerides can range
9 from 100 to 150, still to as high as 500. Many of
10 these folks that have lipoprotein, lipase
11 hypermenalese as well, even if they are well
12 controlled. So they can meet the whole spectrum even
13 higher.

14 DR. JANOSKY: So within that, you would
15 expect a larger percentage to be within this 300 to
16 400 range than what we would consider an undiabetic
17 population, a normal population without diabetes?

18 DR. CLEMENT: Yes. I mean there would be
19 a higher percentage depending on how well controlled
20 the population is. So I think it is useful to have
21 accurate data.

22 DR. JANOSKY: So now going back to this

1 question as to whether the appropriate population was
2 used or not used, given that piece of information, can
3 you help me sort of get an assessment as to whether
4 the population that was used for the consumer study
5 would be very similar to the population of the
6 consumers that would be using this instrument or this
7 device?

8 MS. PINKOS: I would ask you, Dr. Clement,
9 since you were the clinician, to look at for instance,
10 the CRMLN plot, and see where most of the points fell.
11 I mean they predominantly fell promptly.

12 DR. CLEMENT: Just a handful, about 400.
13 That is concerning. I think that gets to one of your
14 questions of how many should be the end in different
15 levels, and should there be a certain minimum number
16 within a certain level. I think that is a very valid
17 question.

18 DR. JANOSKY: That is actually the issue
19 that I'm grappling with, which is the issue that I
20 asked the sponsor this morning, as to what do I do
21 with those values of say 350 and above, where there
22 are very few samples taken there, and you might have

1 the expectation of getting a lot of measurements in
2 that area.

3 DR. CLEMENT: In clinical practice you
4 would.

5 DR. JANOSKY: You would, right. That is
6 what I am especially thinking about with an individual
7 who has diabetes, or a group of individuals that have
8 diabetes.

9 So going along that vein, in terms of that
10 upper end, it seems to me that it would be very
11 reasonable to -- and again, we could hedge our bet and
12 we can find the type of patient or find the type of
13 population that most likely would have those values
14 before you finger stick and actually take a look at
15 them. That would probably be the way that I would
16 advocate that you look at that upper end.

17 Is there something that you know that I
18 don't know that doesn't make sense in that respect?

19 DR. IRONY: No. I agree.

20 DR. JANOSKY: Okay. Then also talk about
21 that bias or under estimation that you had presented
22 and I had asked the sponsor about this morning. That

1 coupled with what we had just talked about a few
2 seconds ago was also telling me that then you have the
3 probability of a mis-diagnosis, diagnosis being a high
4 triglyceride value.

5 You were talking about an estimate of I
6 think within there about 51 point differences.

7 DR. IRONY: At the level 400?

8 DR. JANOSKY: Right. Exactly.

9 DR. IRONY: Yes, around that.

10 DR. JANOSKY: So then you have a large
11 percentage that are anywhere from let's say 380 and
12 above, that might be --

13 DR. IRONY: Different.

14 DR. JANOSKY: That's right. Exactly. So
15 you are talking about missing a percentage of those
16 that we would consider within, refer to a physician.

17 Do you have an estimate as to how many
18 those would actually be in the population? What
19 percentage would be missed?

20 DR. IRONY: I guess we will need more data
21 in that region to estimate that. As I said, we have
22 so few in that region, that it's difficult to estimate

1 from the points we have.

2 DR. JANOSKY: But you didn't do any
3 calculations to see how many would be missed in terms
4 of saying 390, 400, and above, refer on?

5 DR. IRONY: No.

6 DR. JANOSKY: Okay. I didn't have the
7 data, so I would have played around with it to just
8 see. I think for now that probably would be the
9 questions.

10 CHAIRPERSON NIPPER: Thank you.

11 Dr. Lewis, do you have any questions for
12 the FDA?

13 DR. LEWIS: Just one quick one. Not so
14 much one for the statistician. But how typical is it
15 for FDA to have a statement in the users instructions
16 or information that says, and I'm just quoting from
17 this one, "The instrument can be run by a consumer,
18 (lay person), in their own home." I'm not questioning
19 the grammatics there. "With accurate results 95
20 percent of the time."

21 Is that typical to have that kind of a
22 statement in one of these inserts? If so, how do you

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 anticipate that the lay user interprets that kind of
2 a statement?

3 MS. PINKOS: Characterizing the
4 performance in a lay user package insert is very
5 challenging. There are several documents that have
6 been written describing how to characterize that
7 performance, but I think saying something like 95
8 percent of the time it's accurate, if that were the
9 case, you know, having something that's general like
10 that might be acceptable for a lay user labeling.

11 We try to, for instance, stay away from
12 regression analysis or anything like that because a
13 lay user is just not going to understand that. So
14 it's always challenging, based on the performance, to
15 try to capture an easy user-friendly way of telling a
16 consumer what kind of performance they can expect.

17 I mean sometimes people will say 95
18 percent of the time I agreed within 10 percent of a
19 professional device, or something like that, because
20 people might be able to understand something like
21 that.

22 I don't know whether that answers your

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 question or not.

2 DR. LEWIS: Probably not completely
3 because I am thinking of myself as that lay user and
4 say without having any statistics understanding.

5 MS. PINKOS: Right. To say 95 percent of
6 the time you are going to get an accurate result, you
7 would still have to have some kind of measure of what
8 accurate meant.

9 DR. LEWIS: Or as the lay user, I might
10 say well, if I do this once more and there again have
11 a 95 percent accurate chance, I have done it twice.
12 So that brings me pretty darn -- and is that the
13 appropriate interpretation of that? Obviously not.
14 I don't know what you would better do, but it just
15 seems that that leaves a lot to be desired.

16 MR. GUTMAN: Let me interject, because
17 it's a real challenge. Again, in the course of the
18 discussion of this product, if you have suggestions,
19 we would be grateful.

20 We key off of an NCCLS document for
21 labeling of home use. That document uses the Galin
22 and Gambino context. Actually it's not for continuous

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE, N.W.
WASHINGTON, D.C. 20005-3701

1 stat. It's for nominal data. But it uses essentially
2 their term "efficiency." Then it converts that into
3 accuracy and uses it for lay use so that it's
4 essentially the positive and negative agreement. We
5 have been using that, I mean that NCCLS document has
6 been out for a decade.

7 We actually have it in the context of an
8 existing guidance we were thinking about issuing. We
9 are kind of hung up about it and wondering if that's
10 the best we can do in 1999, because efficiency isn't
11 accuracy. But the trick is, how do you couch in an
12 intelligent way for consumers how reliable a product
13 is. I don't know that we have come up with something
14 better than that. Certainly we don't like to get too
15 embroiled in accuracy and precision data because it
16 goes right over most people's heads.

17 So if you don't have suggestions today,
18 but would like to throw something at us post-panel, as
19 you are riding home and thinking about this, we
20 probably could use some help in this area, not just
21 for this submission, but for other akin submissions.

22 DR. LEWIS: Thank you.

1 CHAIRPERSON NIPPER: Ms. Kruger, do you
2 have any questions for the FDA?

3 MS. KRUGER: Yes. I have one for Ms.
4 Pinkos. You had said that there were still some
5 issues with short sampling technique and in terms of
6 accuracy. When I went back and looked at the
7 materials that we were handed, it basically says that
8 if you have a volume of 15 to 30 microliters, that
9 it's statistically and clinically indistinguishable,
10 and they used a 200 milligram per deciliter
11 triglyceride, and basically those would be okay. When
12 you look at the data and you go down to 9 or even 11,
13 it's 103 to 104, is what you are going to get.

14 My question is, and I know there are some
15 backups that patients may or may not do, but my
16 question is, at some point the meter will not start if
17 there is not enough volume. I am not sure what that
18 is, and I think that would be important to know, given
19 that at 9 microliters, a 200 specimen is only reading
20 103.

21 MS. PINKOS: I agree. Can you bring some
22 clarification that? I was assuming that -- I can't

1 recall the data set exactly, but at that lowest point
2 that was presented in that study, was that the point
3 at which the instrument read a short sample and
4 wouldn't get a readout? Do you remember that, Margo?

5 CHAIRPERSON NIPPER: Come to the
6 microphone, please, Mr. Connolly.

7 MR. CONNOLLY: The fellow that could
8 answer that question the best is no longer with the
9 company, so the five of us are sitting here
10 struggling, trying to figure out how they measure
11 short samples right now. I don't think we can come up
12 -- we could come up with a guess, but I don't think we
13 have the correct answer.

14 There is software and there is methods in
15 place via one of the other wavelengths to measure and
16 distinguish between whole blood and controls for QC
17 purposes. Those same algorithms can be used to
18 determine sample volumes, but I can't tell you if they
19 are in use or how they work.

20 MS. PINKOS: We consider the critical
21 element of that study, the fact that the short sample
22 mechanism did not keep the device from giving you an

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 incorrect result if a short sample was added to it.
2 That is somewhat disturbing. That is why they tried
3 to counteract that by having them turn the strip over.
4 But that is a little bit of a concern, is well,
5 because to turn the strip over and say does the color
6 look even, you know, that's somewhat subjective too.

7 MS. KRUGER: When there is already a blood
8 glucose monitor on the market that does the same
9 thing, and patients just don't do it or they reapply
10 samples. It does truly affect the validity of the
11 answer, the accuracy of the answer you are getting.
12 If the meter won't start because the volume is too low
13 or the meter won't start until you have adequate
14 volume, that's okay. So that would be where my
15 concern lies.

16 CHAIRPERSON NIPPER: Dr. Floyd?

17 DR. FLOYD: I have got a couple of
18 questions about the package inserts, which I went back
19 and took another look at after thinking about this
20 over lunch. One of the things that occurs to me as
21 we're talking about a test here that is intended,
22 recommended in worst case scenario to be used 12 times

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 a year in a post-menopausal female, but in reality as
2 I'm understanding the discussion, we're thinking may
3 be used three to one time a year, depending upon who
4 you are listening to around the discussion.

5 So my question is very simple. What is
6 the number of strips in a package? What is their
7 shelf life? There are instructions in the package
8 insert as to storage conditions, but it doesn't tell
9 me what the shelf life is.

10 So the question is, are they going to
11 still be good if you have got 12 in a package and you
12 don't get to them for four years down the road?

13 MR. CONNOLLY: You have to make money
14 somehow. There are six test strips in a package, and
15 the dating gets longer as the product gets more
16 mature. Right now, we would like to have a goal of 12
17 to 15 months. We have seen stability in excess of 24
18 months.

19 DR. PASQUA: Right now, we have stability
20 of six months, but we need to get more data. That's
21 all I am willing to go. These are ongoing. Right
22 now, I can just say six months.

1 CHAIRPERSON NIPPER: Are there any
2 questions? Dr. Rosenbloom, do you have any questions
3 specifically for the FDA about their presentation? We
4 can ask the sponsor questions after we get around the
5 table once, and we can go to open public hearing.
6 Then we can throw it open to anybody.

7 DR. ROSENBLOOM: Yes. The presentation on
8 performance goals.

9 CHAIRPERSON NIPPER: How about getting to
10 the microphone?

11 DR. ROSENBLOOM: Oh, I'm sorry.

12 CHAIRPERSON NIPPER: That's okay.

13 DR. ROSENBLOOM: On the performance goals,
14 the slide on interference, the discussion on
15 interference only talked about ascorbic acid, elevated
16 hematocrit levels and cholesterol. What happened to
17 the drugs?

18 MS. PINKOS: They just didn't make it onto
19 the slide. That wasn't to slight them.

20 DR. ROSENBLOOM: Okay. I was wondering
21 why, if that had been forgotten.

22 CHAIRPERSON NIPPER: Thanks. Any others?

1 Dr. Clement?

2 DR. CLEMENT: I'm confused about the
3 precision testing. I am going over this document over
4 and over. This is the one that was given to us, TZI-
5 2. It talks about precision testing. The precision
6 study says, "precision testing should be done under
7 reasonable conditions of use, i.e. conditions under
8 which the regular patient will use the device."

9 Then we are presented with the data where
10 we get a "consumer" we're basically testing their
11 pipet technique. You don't teach patients to draw
12 their blood at home, and then pipet it in to see how
13 good they are in pipeting to get the same results on
14 the device.

15 So is this a valid test of precision?

16 MS. PINKOS: This is a question that we
17 grapple with for whole blood devices because there is
18 no way, for instance, to characterize day to day usage
19 on a device like this because of the problem with the
20 matrix. When you have a test strip such as this, the
21 reproducibility is really -- it's not like you have a
22 reagent system where the reagents are deteriorating or

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 the calibration is drifting out of place. Those are
2 pretty much set.

3 So what we are really looking for is
4 characterization of the technique as you described it,
5 captured it. The technique for the patient getting a
6 finger stick and pipetting it on. Not pipetting it
7 on, but getting a finger stick and analyzing it. But
8 you can't do a finger stick blood and get precision.
9 So the closest thing that we can get is having whole
10 blood samples by a group of consumers repeatedly run.

11 If you have got any suggestions, because
12 we grapple with this with glucose meters as well.
13 It's difficult to characterize precision for whole
14 blood analyzers. You have to get it -- you know, the
15 best thing to do, we think, is perhaps just having a
16 lot of users do the test, because day-to-day has no
17 meaning, and you can't do it.

18 DR. CLEMENT: But even, I'm thinking like
19 for a YSI machine, if you are doing whole blood,
20 there's even techniques to get accurate precision with
21 that. You have to mix it, make sure it's air rated.
22 If it's not air rated, then your numbers can drift

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 considerably. We are having "consumers" who are never
2 trained to do this that may be taking samples over
3 time that this data may be falsely high.

4 For example, compared to if they did a
5 multiple serial fingerstick test very frequently over
6 10 minutes during the fasting state when they are
7 fasting triglycerides. In theory would be the same,
8 or you could check a fasting triglyceride at the
9 beginning of the series of tests at the end of the
10 series of tests and make sure it is steady, and then
11 average those two out and make sure it hasn't drifted
12 upwards and downwards during the start of the
13 beginning of the test.

14 I mean potentially you can measure
15 precision that way directly from a patient's finger to
16 the test. It just seems kind of crazy, actually,
17 because there's techniques on pipetting it out if it's
18 not mixed and all these other things that may actually
19 make these numbers higher than they potentially really
20 are.

21 MS. PINKOS: You're right. It's a
22 tradeoff.

1 CHAIRPERSON NIPPER: Dr. Kimberly?

2 MS. KIMBERLY: I don't have any questions.

3 CHAIRPERSON NIPPER: Dr. Rifai, did you
4 have a question for the FDA?

5 DR. RIFAI: I just want to add to the
6 interference study that you showed. We were told this
7 morning -- when I read the information here, I thought
8 that usually the red cells lyse, and there's a way to
9 capture the hemoglobin prevented from going down to
10 the reaction. But we were told this morning that
11 actually capture the cells to prevent them from going
12 down to the reaction.

13 Is hemoglobin or checking for interference
14 from hemoglobin was on the list?

15 MS. PINKOS: I think that was on the list,
16 wasn't it?

17 DR. RIFAI: Because it was not on the list
18 that we got.

19 MS. PINKOS: I believe it was done.

20 CHAIRPERSON NIPPER: I appreciate the
21 FDA's forbearance while we ask all sorts of questions.
22 Thank you very much. Why don't you all step back and

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 let me open the meeting as an open public hearing this
2 afternoon. We still have some time allotted for
3 interested persons who may address the panel and
4 present information relevant to the agenda. Speakers
5 are asked to state whether or not they have any
6 financial involvement with the manufacturer of the
7 product being discussed or with their competitors.

8 Okay. Hearing none, seeing no one ask for
9 recognition --

10 DR. DOUMAS: May I ask for recognition?

11 CHAIRPERSON NIPPER: I think it's meant
12 for people outside the panel. I'll get back to you,
13 Basil.

14 DR. DOUMAS: I just looked at something
15 which could explain something.

16 CHAIRPERSON NIPPER: Okay. We will get
17 back to that in an open committee discussion in just
18 a minute.

19 Why don't we use the open committee
20 discussion meeting to try to get some consensus on the
21 review questions. Then if comments that are
22 appropriate come up as we go around the room or

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 questions come up that we need to call on the FDA or
2 the sponsor, we can do that, because we don't want
3 time to get away from us and we would like very much
4 to have this panel reach consensus as much as possible
5 on the review questions.

6 Therefore, if we go around the room and
7 ask for questions, ask for answers to questions, let's
8 be as concise as possible, and stick to the question.
9 Or if you have something that just can't wait, go
10 ahead and ask it when the floor is yours.

11 To take Dr. Rej off the hook, we are going
12 to go around the room this way this time, with
13 question number one. Question number one is, is the
14 Agency's requirement for comparison to a CDC reference
15 laboratory reasonable when the device is for over-the-
16 counter use? We might want to display these questions
17 while we're thinking about it. I apologize for not
18 alerting you to the fact we were going to go to the
19 questions right away. I'll give you a couple of
20 seconds to put them up.

21 What do you think? Is the Agency's
22 requirement for comparison to a CDC reference

1 laboratory reasonable in the devices for OTC use?

2 DR. RIFAI: I think so. I believe so. I
3 don't see why you should have different standards if
4 the test is going to be done OTC versus as a test that
5 is going to be in the laboratory.

6 Unfortunately, the issue for triglyceride
7 is a little bit more complex than let's say if you are
8 measuring cholesterol because triglyceride, as done by
9 the CDC method, as we alluded to earlier this morning,
10 is with correction for endogenous glycerol, and the
11 great majority of labs around the country do not
12 correct for endogenous glycerol.

13 Here, although you are sending the samples
14 to a CDC certified laboratory, from the data that's
15 used in the comparison study, is the one that included
16 the endogenous glycerol. So it's not so-called
17 traceable to the CDC method.

18 One would argue that at least if you go to
19 a CDC-certified lab, they will have tighter measure or
20 small measure of variability than you go to other lab,
21 where you set it up yourself.

22 CHAIRPERSON NIPPER: Thank you.

1 Dr. Kimberly, do you have a -- you are
2 from a CDC laboratory.

3 MS. KIMBERLY: I certainly do have an
4 opinion. I believe absolutely that an OTC device
5 should be compared to the CDC reference method. I
6 would like to point out though that the method that
7 was used at Pacific Biometrics is an enzymatic method
8 that is a method that is monitored monthly by CDC
9 because we do that for all of the cholesterol method
10 lab network participants.

11 While we are evaluating them on their
12 glycerol blank method, we at CDC have a method in-
13 house, where we can determine the free glycerol in the
14 reference materials that we're using so that we can
15 get an idea of how these CDC standardized labs are
16 doing on their total triglyceride methods.

17 Another thing, concern I have about this
18 particular device is that they are calibrating against
19 their predicate device. I think that it would be
20 important to calibrate with the reference method or by
21 a standardized method. I think that's something that
22 the sponsor should take into consideration as they

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 proceed with this.

2 CHAIRPERSON NIPPER: Dr. Clement, what do
3 you think about question one?

4 DR. CLEMENT: I will defer to my expert
5 analytical colleague. So I would say yes.

6 CHAIRPERSON NIPPER: Dr. Rosenbloom, how
7 about you?

8 DR. ROSENBLOOM: I said yes.

9 CHAIRPERSON NIPPER: Okay. How about you,
10 Dr. Floyd?

11 DR. FLOYD: I would say yes. I bring it
12 up from a different issue. In this case, over-the-
13 counter use, when I see that term, it's for tests that
14 in general we have sort of assumed the consumer
15 interprets for themselves.

16 As I interpret the remarks we have heard
17 today, what we are really talking about in this test
18 is a number that the consumer collects and then
19 reports to their attending physician, we hope. If in
20 point of fact the number doesn't correspond to
21 anything the physician is used to hearing, how can
22 they interpret it? So I would say yes, it has to be

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 pegged to some kind of reference.

2 CHAIRPERSON NIPPER: Ms. Kruger?

3 MS. KIMBERLY: Yes.

4 CHAIRPERSON NIPPER: Dr. Lewis?

5 DR. LEWIS: Yes.

6 CHAIRPERSON NIPPER: Let the record show
7 that Dr. Janosky is nodding yes.

8 DR. JANOSKY: I did say yes also.

9 CHAIRPERSON NIPPER: Dr. Doumas?

10 DR. DOUMAS: Yes.

11 CHAIRPERSON NIPPER: Dr. Manno?

12 DR. MANNO: Yes.

13 CHAIRPERSON NIPPER: Dr. Everett?

14 DR. EVERETT: Yes.

15 CHAIRPERSON NIPPER: Dr. Rej?

16 DR. REJ: Yes. I think there must be
17 traceability to the system somehow. I think direct
18 comparison of the whole blood device with a reference
19 method has some problems because you are actually
20 using a different physical sample even if they are
21 taken at nearly identical times. So the comparison is
22 not quite as easy as if you have a plasma or serum

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 versus serum measurement. So I think that this system
2 that's in place has done a lot of good.

3 I know that most of you know that my
4 laboratory is one of the CDC reference laboratories.
5 I pointed out this to the FDA. We're not accepting
6 any samples from manufacturers. We're not doing
7 certification for triglyceride. So there is no
8 conflict of interest. But I think it is a very
9 important system. Our involvement is mainly for an
10 accuracy base for our proficiency testing program. So
11 I think the whole system is worthwhile. I think that
12 OTC devices should not be exempt from it.

13 But again, I am not sure that direct
14 comparison of the OTC device with a plasma sample done
15 by the CDC certified laboratories is absolutely
16 necessary. There has to be some traceability.

17 CHAIRPERSON NIPPER: My opinion is that
18 the answer to question one should be yes. The
19 question says requirement for comparison. It does not
20 say requirement for equivalency or it doesn't imply
21 stringency, but it implies traceability. I think it
22 is very important, as Dr. Rej says. I know Dr. Rej

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 and Dr. Doumas and others in the room, including
2 myself, who have served on standards committees for
3 the AECC in times past and we have seen a history of
4 improvement if we can trace to a benchmark. I think
5 that serves us well as a profession.

6 Question number two is should an over-the-
7 counter device be required to meet NCEP performance
8 goals, which is approaching the next issue. The
9 question is should the performance be in line with
10 other analytical systems. So let's go back around the
11 room.

12 Dr. Rej, what do you think about that?

13 DR. REJ: Yes, with the caveat that was
14 mentioned I think by Ms. Pinkos, is that you could
15 trade off accuracy for precision, I think, especially
16 in an over-the-counter device. But meeting the NCEP
17 goal for total error of less than 15 percent is
18 particularly important. But I think one could trade
19 off some precision for accuracy in such a device.

20 CHAIRPERSON NIPPER: Now there is an
21 inherent second question in here, is if it doesn't
22 meet the goals, can you clear it for marketing with

1 cautionary labeling?

2 DR. REJ: I don't believe so. I think the
3 goals -- you have to meet the NCEP goals for an
4 analytical technique.

5 CHAIRPERSON NIPPER: How about you, Dr.
6 Everett?

7 DR. EVERETT: My answer is yes, that it
8 should meet the goals.

9 CHAIRPERSON NIPPER: Okay.

10 DR. MANNO: It should meet the goals.

11 DR. DOUMAS: I tend to differ a little
12 bit. I will go with Dr. Ginsberg. If it doesn't meet
13 exactly, it should be close. So I will leave a little
14 bit of window. Maybe 15 percent over the goals. That
15 doesn't mean another 15 percent, 15 of the 15.
16 Probably you can go to 17.5. That's my opinion.

17 CHAIRPERSON NIPPER: Thank you, Dr.
18 Doumas.

19 Dr. Janosky?

20 DR. JANOSKY: Yes, to meeting the goals.

21 CHAIRPERSON NIPPER: Dr. Lewis?

22 DR. LEWIS: I am inclined to agree with

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 Dr. Doumas. In fact, before he made his comment, I
2 was thinking of something of that sort, whether it's
3 17.5 percent or whatever. But that there might be
4 some opportunity for a slight movement from that 15
5 percent based on everything I have heard about the
6 system and its performance characteristics in this
7 case.

8 CHAIRPERSON NIPPER: Ms. Kruger?

9 MS. KRUGER: I think it should meet its
10 goals.

11 CHAIRPERSON NIPPER: Okay.

12 DR. FLOYD: Yes.

13 CHAIRPERSON NIPPER: Dr. Rosenbloom?

14 DR. ROSENBLUM: I have said that I
15 thought that I was concerned that false security might
16 arise from an inappropriately low reading, and that
17 that would be more harmful than not testing, and that
18 inappropriately high readings would create needless
19 anxiety or misguided treatment changes. So the answer
20 is yes, it should meet the NCEP performance goals or
21 some modest modification of them.

22 CHAIRPERSON NIPPER: Dr. Clement?

1 DR. CLEMENT: Well, I'll be different from
2 the group. I'll say no, because I think this device
3 could be clinically useful if the labeling is
4 appropriately made.

5 Obviously I had issues in terms of the
6 precision testing, but I think -- I mean it sounds
7 like a major, an industry problem, and how do you
8 measure precision on whole blood. Obviously if that
9 can be shown to be reduced just by testing it a little
10 bit differently, then it may help narrow some of the
11 total system error.

12 I mean I think labeling could be modified.
13 I even wrote out some labeling, which we can talk
14 about a little bit later. I think possibly a total
15 system error of plus or minus 20 percent would be
16 clinically useful.

17 CHAIRPERSON NIPPER: Okay..

18 MS. KIMBERLY: I'll say yes, they should
19 meet the goals.

20 CHAIRPERSON NIPPER: Did you need to say
21 something, Mr. Connolly?

22 MR. CONNOLLY: No. I'm just making some

1 notes.

2 CHAIRPERSON NIPPER: Okay. I'm not sure
3 why, but I think that we need to step back from the
4 table. I don't know why we need to do that, but that
5 is kind of a rule at these things. Thank you.

6 Dr. Kimberly, did you have an opinion
7 about question two?

8 MS. KIMBERLY: Yes. I said that they
9 should meet the goals.

10 CHAIRPERSON NIPPER: Okay. I'm sorry. I
11 was preoccupied.

12 Dr. Rifai?

13 DR. RIFAI: Yes. I think they should meet
14 the goal. I have some concern about reaching by
15 consensus how much extra error you will allow a
16 particular device to exceed. I think if a particular
17 device will have different utility than the laboratory
18 test in a different setting, then you have to
19 demonstrate somehow by a study, not -- by consensus
20 how much error you can tolerate.

21 I think for the general public, if you add
22 a label, cautionary label about the error, I am not

1 sure really it's going to be -- the public is going to
2 understand it.

3 CHAIRPERSON NIPPER: Thank you.

4 Dr. Rifai took the words out of my mouth.
5 My problem with asking this group to deviate or to
6 move away from the NCEP goals is that I would like to
7 see some evidence that good medicine will result by
8 moving away from those goals. Not necessarily that
9 the goals are too stringent or that someone else got
10 a product in that somehow didn't meet the goals five
11 years ago, or that -- I would just like to see the
12 fact that the claims for improved public health can be
13 met by this device. I don't see that study.

14 So that is why I think that if you are not
15 going to come in and make a compelling case for
16 marketing the device without meeting the goals, then
17 I think you should meet the goals.

18 Okay. Question three. Do we know what
19 the appropriate minimum sample size for evaluating an
20 OTC lipid test is. Should there be minimum
21 requirements for sample distribution?

22 You took my answer away from me, so you

1 get on the hot seat again.

2 DR. RIFAI: I don't know about the
3 appropriate minimum sample size, but for the
4 distribution, I think it must encompass everything you
5 are going to be seeing clinically, with the special
6 emphasis on the area where the cutpoints for clinical
7 decision making usually are.

8 CHAIRPERSON NIPPER: Thank you.

9 MS. KIMBERLY: I think that statisticians
10 could probably adequately answer the question about a
11 minimum sample size. That would depend on the
12 difference to detect and the precision of the
13 instrument. But ideally, I would think that the
14 difference to detect would be based on the MCEP bias
15 recommendations. So I think that giving a number
16 there would depend on the statistics and the math
17 there.

18 As far as minimum requirements for sample
19 distribution, the NCCOS has recommended sample
20 distribution guidelines in their EP9, which is a
21 method comparison and bias estimation protocol. I
22 think there are some guidelines out there that could

1 be used. But certainly you definitely want to cover
2 the medical decision points that are relevant to the
3 particular analyte.

4 CHAIRPERSON NIPPER: Dr. Clement?

5 DR. CLEMENT: I agree with the previous.
6 Clearly, it needs more numbers in the 400 to 500. I
7 would say at least 20 within the 400-500 end, if we
8 had to come up with a number for measuring accuracy.

9 CHAIRPERSON NIPPER: Is the 20 an
10 arbitrary guess or did you base that on anything other
11 than seat of the pants?

12 DR. CLEMENT: Pure arbitrary guess, that
13 could be validated by the statisticians.

14 CHAIRPERSON NIPPER: Okay.

15 Dr. Rosenbloom?

16 DR. ROSENBLOOM: Yes. I agree. I would
17 certainly like to see more values in the range of
18 clinical utility that we live in.

19 DR. FLOYD: I agree with the previous
20 comments.

21 CHAIRPERSON NIPPER: Okay. Ms. Kruger?

22 MS. KRUGER: Same.

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 CHAIRPERSON NIPPER: Dr. Lewis?

2 DR. LEWIS: I agree.

3 CHAIRPERSON NIPPER: Dr. Janosky?

4 DR. JANOSKY: I agree, but I would add
5 that it should actually be powered within each of
6 those ranges of clinical decision making. My major
7 concern, as I have voiced today, was the 400 and
8 above. But also, there's other clinical decision
9 points along the way. So I would categorize the range
10 and then power within each of those categorizations.

11 CHAIRPERSON NIPPER: Dr. Doumas?

12 DR. DOUMAS: Oh yes. I think they can
13 consult an NCCLS document. It specifies there.

14 CHAIRPERSON NIPPER: Dr. Manno?

15 DR. MANNO: I agree.

16 CHAIRPERSON NIPPER: Dr. Everett?

17 DR. EVERETT: I agree. There are a number
18 of biostatistical calculations to determine sample
19 size based on the study and how the study is to be
20 done. I would recommend they select one of those and
21 follow it through as opposed to what appears here, is
22 that the studies are done backwards. The studies are

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 done first, and then the statistical tests are picked
2 at the end. That's inappropriate. I suggest they
3 just follow one of those and continue it all the way
4 through.

5 CHAIRPERSON NIPPER: Thank you.

6 Dr. Rej?

7 DR. REJ: I agree with Drs. Kimberly and
8 Janosky regarding both points, especially at least
9 some guidance can be given by the NCCLS guideline in
10 terms of distribution of samples for this particular
11 case.

12 CHAIRPERSON NIPPER: I like the NCCLS
13 approach too.

14 The follow-up question to this, which many
15 of you have already answered both before this round of
16 questioning as well as during this round of
17 questioning, is has the sponsor done the appropriate
18 precision and interference studies? If anyone would
19 like to elaborate on that, we can go around the room
20 again, starting with Dr. Rej, if you want to nail down
21 any addition information.

22 DR. REJ: I think the points made by Dr.

1 Doumas are relevant, that whole blood devices are not
2 exactly the same as traditional chemistry device.
3 Even the sponsor alluded to that. And that
4 interference studies done in highly diluted samples
5 don't necessarily turn out the same way with neat
6 samples, even though the basic chemistry for
7 measurement is similar.

8 I think that since this is intended for
9 over-the-counter use and uses individual disposable
10 devices for each measurement, three persons is nowhere
11 near adequate to demonstrate precision of the test in
12 the hands of the consumer.

13 CHAIRPERSON NIPPER: How about
14 interferences?

15 DR. REJ: Again, I agree with Dr. Doumas.
16 In terms of specific interferences, again, it depends
17 on the intended use. It was alluded to that this
18 would be used largely by diabetics as an adjunct to
19 their treatment for diabetes. But that's not spelled
20 out in the package insert, that it's really for
21 anybody. So limiting it to the drugs either lipid
22 lowering drugs or other drugs taken by diabetics, I

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 don't think is -- that's certainly the minimal list
2 for drug interference.

3 Again, I think there are some general
4 recommendations on the types of drugs, at least
5 certain classes of drugs that can be used. You don't
6 have to check each and every one, but that certain
7 generic classes certainly. They did some studies with
8 reducing agents like ascorbate, but I think other
9 drugs need to be considered.

10 Just falling back on the literature to
11 more traditional wet chemistry may not apply in this
12 case.

13 CHAIRPERSON NIPPER: Dr. Everett?

14 DR. EVERETT: Yes. I agree. Those were my
15 points exactly.

16 CHAIRPERSON NIPPER: Okay.

17 DR. EVERETT: They just have to do the
18 rest of the work.

19 CHAIRPERSON NIPPER: Dr. Manno?

20 DR. MANNO: I would like to add something
21 to the two previous comments, that if any more work is
22 done, and it should be done on the interference

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 studies with relation to the drugs, but if you are
2 using whole blood from people who are taking drugs,
3 you are not only going to be finding parent drug, in
4 many instances, you are going to be finding a variety
5 of metabolites. So you are going to have to have some
6 feel for interference there, perhaps.

7 I am still not clear in my own mind. This
8 goes a little bit to what I asked this morning in
9 terms of interference in the response that I got about
10 looking at pore size. When I was told that there are
11 fragments of red cells that get through and the like,
12 I would like to ask the sponsor if they used any other
13 pore size for their strip. Have they looked at that
14 to get the optimum pore size?

15 Because my experience with doing things
16 like this is such that you can go lower and get rid of
17 some of the cellular components by going to a smaller
18 pore size. So if you could address that for me, I
19 would appreciate it.

20 MR. CONNOLLY: We said the right thing
21 this morning, but it was the wrong answer. The pore
22 size of the reaction membrane has nothing to do with

1 exclusion of the red blood cells.

2 DR. MANNO: But that's what is provided to
3 us, because this goes back to my original question
4 this morning. Are you really testing whole blood or
5 are you testing the aqueous component?

6 MR. CONNOLLY: We are testing the aqueous
7 component, mostly.

8 DR. MANNO: Then we have got some
9 definitions here that need to be clarified in my mind
10 in describing the reactions that are taking place and
11 the intended use. It also may present us with, in
12 truth, we're talking about the same matrix when we're
13 talking about serum as a matrix for the comparison
14 here. So in terms of those studies, I think that that
15 needs to be clarified.

16 MR. CONNOLLY: That's your opinion. I'm
17 just answering the pore size issue. That had nothing
18 to do with exclusion of red blood cells.

19 CHAIRPERSON NIPPER: Okay.

20 DR. MANNO: I have no more questions.
21 Thank you.

22 CHAIRPERSON NIPPER: Dr. Dumas?

1 DR. DOUMAS: I agree with the others about
2 omission of drugs that are taken. However, we missed
3 something. I apologize that I missed this. If you
4 look at interference by ascorbic acid even at the
5 lowest level, that's a 10 percent inaccuracy, negative
6 bias, when only allow five percent.

7 Now .75 milligrams per deciliter of
8 ascorbic acid, you will not find it in people who do
9 not get extra vitamin C. But those who follow the
10 recommendations of the late Dr. Linus Pauling, they
11 may easily get to that level or even higher. So you
12 want 1.5, that's a 20 percent bias already.

13 I want to emphasize again what I said in
14 the morning, that samples here are not diluted like in
15 wet chemistry. So interference, concentration that
16 will interfere is much higher for the same level in
17 this type of chemistry, dry chemistry, as it is in the
18 wet chemistry. So .75 milligrams may not have the
19 same effect in any other instant, I mean non-dry
20 chemistry. Probably this is the reason, you see 11
21 percent bias with a 0.75.

22 I would suggest or maybe this can explain

1 all the negative bias that we have seen, because a lot
2 of people swallow ascorbic acid, 500 milligrams or a
3 gram daily to protect themselves against some cold.

4 CHAIRPERSON NIPPER: Thank you. Dr.
5 Janosky?

6 DR. JANOSKY: I have nothing to add.

7 CHAIRPERSON NIPPER: Dr. Lewis?

8 DR. LEWIS: Nor I.

9 CHAIRPERSON NIPPER: Have they done
10 appropriate precision in interference studies?

11 DR. JANOSKY: I have nothing to add. I
12 defer to my colleague.

13 CHAIRPERSON NIPPER: Okay.

14 DR. LEWIS: I thought I had nothing to
15 add, but to answer the question as posed, I would have
16 to say no.

17 CHAIRPERSON NIPPER: Okay, thank you.

18 Ms. Kruger?

19 MS. KRUGER: I would agree.

20 CHAIRPERSON NIPPER: Okay. Dr. Floyd?

21 DR. FLOYD: I would agree with the
22 previous comments.

1 CHAIRPERSON NIPPER: Thank you.

2 Dr. Rosenbloom?

3 DR. ROSENBLOOM: Yes. I am also concerned
4 about the real life situation with people with these
5 drugs circulating.

6 CHAIRPERSON NIPPER: Thank you.

7 DR. CLEMENT: I was going to mention on
8 the precision data, I think it's unfair to measure
9 precision and putting so much weight on it, on having
10 untrained "consumers" whoever they are, doing this.
11 If we are going to measure in that way, we should have
12 trained people measuring samples using oxygenated
13 whole blood.

14 CHAIRPERSON NIPPER: Thank you.

15 Dr. Kimberly?

16 MS. KIMBERLY: I defer to my colleagues
17 who have already spoken.

18 CHAIRPERSON NIPPER: Okay. Dr. Rifai?

19 DR. RIFAI: I just want to add one thing
20 about the other interference studies that were
21 suggested by others like checking for interference
22 from fibrate, stattons, even diuretics, whatever type

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 of drugs that patient will be taking.

2 I think Dr. Manno suggested that taken
3 from patients who are taking these medications because
4 you want to not look at the effect of the parent
5 drugs, but you want to look at the effect of the
6 metabolites. Unfortunately, in these particular
7 drugs, the drugs affect the levels of triglyceride.
8 So it would be very difficult to determine if that's
9 the effect of the drug or that's the effect of the
10 interference. Probably the only way to check for
11 these drugs is just by spiking experiment, and that
12 would be the best way to do it because I can not see
13 any other way.

14 CHAIRPERSON NIPPER: Dr. Gutman?

15 MR. GUTMAN: Yes. I would like to
16 actually raise that because there is a side issue that
17 Ms. Pinkos raised that's relevant, frankly, to the
18 issue of spiking, which is a traditional way of doing
19 things, again, building off of an NCCLS document.
20 That is, the sponsors propose that cholesterol
21 interference be done by looking at regression testing,
22 comparing triglycerides with cholesterol levels. We

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 have not seen that either ever or certainly not seen
2 that very often. I was wondering if anyone on the
3 panel would like to comment as to whether that is an
4 insightful approach or whether in fact we should ask
5 the sponsor to go back and do more standard NCCLS type
6 spiking experiments with lipids.

7 CHAIRPERSON NIPPER: Does anybody on the
8 panel want to tackle that question?

9 DR. REJ: It's not so easy to do spiking
10 experiments with cholesterol. It may be unusual, but
11 it seemed a reasonable way to do it. I didn't find
12 any fault with that. Although I did notice that there
13 was a bias in the actual cholesterol measurement that
14 exceeded NCEP guidelines.

15 CHAIRPERSON NIPPER: Does anyone on the
16 panel have anything to add to what Dr. Rej said?

17 Thank you. I agree with that.

18 I had a question that may not be an
19 interference study, but I had a question for the
20 sponsor. I am curious to know whether the actual
21 signal is taken as a reaction rate or whether it's
22 taken as what we analytical chemists called an

1 endpoint, whether you waited for a maximum color to
2 develop and then you measured say a single
3 measurement, or whether you measured a series of
4 points as the reaction occurred.

5 MR. CONNOLLY: They are all endpoint
6 values.

7 CHAIRPERSON NIPPER: Okay. That reassures
8 me a little bit about maybe a substrate depletion
9 turning out to be a very low triglyceride measurement.

10 Question number five, please. What's the
11 appropriate claim for this device, and has that claim
12 been captured in the label?

13 I can't remember where I started last
14 time. Did I zing you, Dr. Rifai? Why don't we mix it
15 all up, and we'll start with Dr. Floyd.

16 DR. FLOYD: I would have to say that I'm
17 not sure in my own mind, and maybe it's because I
18 missed it as I read the thing. But in my mind, I am
19 not sure if the appropriate claim has been captured in
20 the labeling for this device.

21 CHAIRPERSON NIPPER: We're talking about
22 intended use here. I checked with my co-colleague

1 here. Intended use, according to the document I have
2 is this test measures triglycerides in fingerstick
3 blood. Then it goes on to say why. Then this test
4 can be run by any person -- who -- this test can be
5 run by any person at home as easily as in the doctor's
6 office or a hospital. When, run this test two to
7 three times a year or at least monthly if you are
8 diabetic or a woman past menopause.

9 Did I get it right?

10 DR. FLOYD: I'll stick by my comments.
11 It's not clear to me that the average consumer is
12 going to understand what that means.

13 MS. KRUGER: I think they have got part of
14 that in the claim. I think we have discussed at
15 length the issue of post-menopausal women, that
16 probably that needs to be rethought.

17 As far as the claim, I think that we have
18 made a lot of comments that it appears that the
19 sponsor is comfortable taking back and going back and
20 looking at their labeling. So I guess I would say
21 that not really to the first, and no to the second.
22 But that there has been a lot of discussion today,

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 very positive discussion that could be incorporated,
2 that the labeling could be made appropriate.

3 CHAIRPERSON NIPPER: Dr. Lewis?

4 DR. LEWIS: I'm inclined to agree that
5 with all the discussion that's taken place regarding
6 the intended purpose, if the sponsor were to
7 incorporate that to some good measure, I would say
8 yes. Has it been captured in the labeling? When
9 that's done and the labeling then reflects it, I would
10 say yes.

11 CHAIRPERSON NIPPER: Thank you.

12 DR. JANOSKY: The labeling as it stands,
13 the answer is no. But with the flavor of the
14 intention of what I believe the panel has presented
15 today, then yes.

16 CHAIRPERSON NIPPER: Thank you.

17 Dr. Doumas? How about appropriate claims
18 and has that claim been captured in the labeling?

19 DR. DOUMAS: I would say no in general
20 because I found the statements on procedure and
21 accuracy very vague and maybe not correct. I think
22 the intended use, I strongly disagree with what, as

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 it's written right now.

2 CHAIRPERSON NIPPER: What would you think
3 the appropriate claim should be or do you have an
4 opinion about that?

5 DR. DOUMAS: I think as far as when to
6 use, I think the patient should consult his doctor
7 when to use that test. Second, about procedure and
8 accuracy, I think they should follow recommendation of
9 the statistician, who presented a very good case about
10 what is the total error.

11 CHAIRPERSON NIPPER: So to follow up that,
12 not to nail you to the floor on it, but if you believe
13 the patient should consult the doctor before they use
14 the test, it sounds to me like you are not comfortable
15 with this being over the counter, or am I putting
16 words? You would like it to just be prescription
17 only? Or do you think that over-the-counter is okay
18 on this?

19 DR. DOUMAS: I am not going to express an
20 opinion there. There is a difference when measuring
21 glucose and measuring triglyceride. Glucose, the
22 patient can take action or must take action sometimes

1 if it's too low or it's too high.

2 CHAIRPERSON NIPPER: Yes.

3 DR. DOUMAS: This one, what action the
4 patient is going to take? None. He has to go to the
5 doctor. I think if he needs to be tested, I think his
6 physician should tell him if and when.

7 CHAIRPERSON NIPPER: Okay. Thank you.

8 Dr. Manno?

9 DR. MANNO: I agree with Dr. Doumas.

10 CHAIRPERSON NIPPER: Dr. Everett?

11 DR. EVERETT: Well I think the claim is
12 appropriate, but I don't think it's really captured in
13 the labeling at all. I think it is too ambiguous and
14 misleading for someone with a seventh grade reading
15 level.

16 CHAIRPERSON NIPPER: Okay. Dr. Rej?

17 DR. REJ: In terms of the what, I think
18 not, because it fails by a long shot to meet NCEP
19 guidelines. Therefore, it does not measure
20 triglycerides accurately or precisely. The why,
21 probably correct. The who, that hasn't been
22 demonstrated with only three individuals. The when,

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 there's been a lot of criticism from my clinical
2 colleagues. I'll defer to them.

3 CHAIRPERSON NIPPER: Thank you.

4 Dr. Rifai, are you ready?

5 DR. RIFAI: Yes. I am in total agreement
6 with what Dr. Rej said. Also, I don't know if you
7 want to even clarify under who, run by any person at
8 home. I mean you have five-year-olds at home. We
9 don't want them to run that test. So I wonder if you
10 want to say any person above a certain age or any
11 adult. I don't know if that needs to be specified or
12 not.

13 CHAIRPERSON NIPPER: Dr. Kimberly?

14 MS. KIMBERLY: I agree with Dr. Rej.

15 CHAIRPERSON NIPPER: Dr. Clement?

16 DR. CLEMENT: I think the labeling could
17 be changed. In fact, I wrote out something. Is it
18 appropriate to just read it on here?

19 CHAIRPERSON NIPPER: I believe so.

20 DR. CLEMENT: In terms of the accuracy
21 issue, this is just a suggestion. It could possibly
22 put the results of the triglycerides measure can be

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 plus or minus X, whatever that is actually found to
2 be, of the reference method. Due to this variability
3 in accuracy, the device does not replace the
4 lipoprotein profile as measured by your healthcare
5 provider. The results should be used as a guide
6 between visits to your healthcare provider for
7 monitoring the management of your condition. This
8 management could include diet, exercise, or the
9 efficacy of medication.

10 CHAIRPERSON NIPPER: Thank you.

11 Dr. Rosenbloom?

12 DR. ROSENBLOOM: I agree with the previous
13 comments from the laboratory experts. I think that
14 that wording is excellent.

15 The who is rather an ambiguous and strange
16 statement. This test can be run by any person at home
17 as easily in the doctor's office or hospital. Well
18 any person at home doesn't run tests in the doctor's
19 office or hospital, which is what this sentence says.
20 So the grammar is bad, as well as being ambiguous. Of
21 course it is a very different as the recommended
22 wording indicates, it is a very different issue than

1 what's done in the doctor's office or the hospital.
2 So I think that whole thing of who is strange.

3 Then the when, of course, we have
4 addressed the inappropriateness. I think the when
5 should be entirely consistent, unless they can come up
6 with expertise, to suggest otherwise that the when
7 should be consistent with ADA guidelines for those
8 people with diabetes, and for the general public,
9 should be consistent with the NCEP guidelines. Of
10 course the ADA guidelines are based on NCEP
11 guidelines. But I see no reason why the availability
12 of this device changes those recommendations.

13 CHAIRPERSON NIPPER: Thank you, Dr.
14 Rosenbloom.

15 I believe that the claim is too broad. I
16 believe that the accuracy and precision of the device
17 needs to be improved. The sponsor made a statement
18 this morning as he began, that his company's goal was
19 hospital quality results in a dry phase. I think I
20 captured that quote. I do not believe these are
21 hospital-quality results. I have no problem with dry
22 phase. I would like to see people in the field be

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 able to get hospital quality results, because I
2 believe those have the chance of misleading results
3 fewer than we have with this device as it currently
4 stands.

5 I see no problem in targeting this device
6 once it's improved to the diabetic population or to
7 people who suspect they may have a lipoprotein
8 abnormality or hyperlipidemia or a cardiac risk. I
9 believe it ought to be tied much closer to physician's
10 visits. So I think the claims need to be really
11 nailed down in the labeling and really tightened up
12 before this device is marketed.

13 Is the performance adequate to support the
14 intended use? Many of us have already begun to
15 comment on this. You want to tackle that one, Bob?
16 I think you have already --

17 DR. REJ: I think clearly, at least in my
18 mind, the answer is no. More than half the results
19 from the device relative to the reference lab are
20 outside of the NCEP guidelines.

21 CHAIRPERSON NIPPER: Dr. Everett?

22 DR. EVERETT: I agree. Clearly not.

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 CHAIRPERSON NIPPER: Dr. Manno?
2 DR. MANNO: I concur.
3 CHAIRPERSON NIPPER: Dr. Doumas?
4 DR. DOUMAS: No, it is not.
5 CHAIRPERSON NIPPER: Dr. Janosky?
6 DR. JANOSKY: I agree that it is not.
7 CHAIRPERSON NIPPER: Dr. Lewis?
8 DR. LEWIS: I also agree that it's not.
9 CHAIRPERSON NIPPER: Ms. Kruger?
10 MS. KRUGER: It's not.
11 CHAIRPERSON NIPPER: Dr. Floyd?
12 DR. FLOYD: I agree.
13 CHAIRPERSON NIPPER: Thank you.
14 Dr. Rifai?
15 DR. RIFAI: Yes.
16 CHAIRPERSON NIPPER: You agree, okay.
17 Dr. Kimberly?
18 MS. KIMBERLY: When you say you agree, you
19 agree that it's not, okay. All right.
20 Yes. I agree. I have a lot of trouble
21 with that 95 percent accuracy claim. I don't really
22 know what that means or where that number came from.

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 CHAIRPERSON NIPPER: Dr. Clement?

2 DR. CLEMENT: It is obviously not an NCEP
3 guideline criteria. It is much too loose. But as I
4 mentioned before, I think for clinical purposes for a
5 home-use device that's used in comparison, as an
6 adjunct to an analytical measurement done at a
7 physician's office, that the total error could
8 possibly be monitored to as much as 20 percent.

9 CHAIRPERSON NIPPER: Dr. Rosenbloom?

10 DR. ROSENBLOOM: I concur with the
11 criticism.

12 CHAIRPERSON NIPPER: As the device stands
13 with the intended use, the intended use that's in the
14 documentation, I have questions about whether the
15 performance is adequate to support that intended use.
16 Unlike our esteemed consultant, Dr. Ginsberg, I do not
17 support widespread screening for the purposes of
18 screening. I think it has tremendous unintended use
19 in lots of false positives, lots of false negatives.
20 It causes people to chase their tails, so to speak,
21 diagnostically, and go off in all sorts of paths that
22 take them on the geolyses type journeys that they

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 shouldn't be down.

2 I think that if we put a device in the
3 field that's for measurement of triglycerides, it
4 ought to measure it accurately. So therefore, I am
5 assuming that the intended use is what we say it
6 should be. Then the performance needs to be adequate
7 to support it.

8 Okay. We have a specific question about
9 labeling. Is it an acceptable approach to refer lay
10 users to a second professional use package insert for
11 additional information, TG, quality control
12 instructions?

13 What do you think, Dr. Rifai?

14 DR. RIFAI: I have a lot of problems with
15 not including the QC material and everything you need
16 in one package. I think most likely for the general
17 public, that strip that I put in to check for if
18 electronically the device is working properly will
19 suffice. I don't think they are going to go and buy
20 the quality control material.

21 I think if you want to sell something as
22 an OTC device, it has to contain everything that the

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 person needs.

2 CHAIRPERSON NIPPER: Is it my
3 understanding that the quality control material is
4 with the strips? This is directed at the sponsor. In
5 other words, or do you need to buy a separate quality
6 control material?

7 MS. ENRIGHT: We don't package it with the
8 strips, mainly because there is an issue, a use issue.
9 There is not a good balance between the quality
10 control material and the strips. So logistically,
11 what happens with the customer, the consumer, is they
12 end up having a balance -- an imbalance between the
13 strips and the material. So from a logistical
14 standpoint. They have one that expires on them. So
15 based on that, we don't package them together because
16 they will have different expiration dates. So just to
17 be customer friendly to the consumer we do that. We
18 do have the material available.

19 DR. RIFAI: That would further support the
20 argument that they will not buy it.

21 MS. ENRIGHT: That's always an issue. The
22 way the strips are packaged, if they run a package of

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 six strips, if they run it twice a year, we have two
2 quality control materials. If we have even six months
3 dating, six months dating, there is no reason not to
4 run the quality control material because of the dating
5 of the strips. So you have two quality control
6 materials in one test, and run it twice a year. But
7 if you have other suggestions for our packaging, we'll
8 certainly listen to those. But that's our rationale.

9 CHAIRPERSON NIPPER: Thank you. I'm not
10 sure I interpreted that question the same way Dr.
11 Rifai did.

12 I interpreted that question, Dr. Rifai, as
13 referring to the fact that there were two package
14 inserts in with the strips. The first package insert
15 was the one you have on your lap there with your hands
16 on it. Then if you flip forward, there is a
17 professional package insert that has more information
18 on it, two more pages. There's two pages for the
19 over-the-counter package insert, and then right after
20 that is the professional package insert.

21 What the question was referring to was is
22 it acceptable to have two different package inserts

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 and then expect the lay consumer to read the
2 professional package insert for quality control
3 instructions.

4 Did I interpret that question correctly?

5 MR. GUTMAN: Yes. Actually, you have
6 combined, you have sort of combined question seven and
7 eight. If you wish to in fact combine seven and eight
8 and run through the panel looking at those as joint
9 questions, that might be an appropriate thing to do.

10 CHAIRPERSON NIPPER: That would be fine
11 with me, because the time is rolling here.

12 Nader, did you have anything to add to
13 your previous answer?

14 DR. RIFAI: Yes. I mean I prefer to have
15 them the same, on the same sheet, just small paragraph
16 about the quality control. First, how you do it to
17 check for electronic. Second, how to do it to check
18 if the whole system is working.

19 CHAIRPERSON NIPPER: Yes.

20 DR. RIFAI: Not to have two separate
21 sheets.

22 CHAIRPERSON NIPPER: Okay. Dr. Kimberly?

1 MS. KIMBERLY: Regarding the question
2 about referring to a professional package insert, I
3 don't think that's really acceptable for a lay user.
4 I think the lay user needs to have everything right
5 there in front of them, in language that they can
6 understand.

7 As far as question number eight, I thought
8 that the QC instructions -- is that the question? I
9 thought the QC instructions were a little confusing,
10 especially about how often they should be run. In the
11 same section, they instruct the user to run QC at
12 least once a month, and in another sentence two lines
13 down, it says at the beginning of each day.

14 Also, they instruct the user to take care
15 not to contaminate the dropper tip, but give the lay
16 user no concept of where contamination can occur and
17 how is somebody who has never worked in a laboratory
18 before supposed to understand that kind of thing.

19 CHAIRPERSON NIPPER: Thank you very much.

20 Dr. Clement, do you have comments about
21 question seven and eight?

22 DR. CLEMENT: Yes. I agree with the

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 previous comments that working with patients, Murphy's
2 Law gets a new meaning, because they find even more
3 creative ways to abuse things. All the current table
4 top or home devices that I know of now, the modern
5 ones, have the control solutions in it, which makes it
6 very convenient with the patient.

7 If it's not physically packaged with the
8 control solution in some type of box, then the patient
9 is not going to do it.

10 CHAIRPERSON NIPPER: Dr. Rosenbloom?

11 DR. ROSENBLOOM: Yes. Since I am going to
12 be leaving, I'll address everything I have got in the
13 label highlighted. First, there is under the intended
14 use, triglycerides is a fat. There is a verb number
15 mismatch there.

16 Then under item six, after reading the
17 result down at the bottom, it says "discard result and
18 retest." People will use the same strip and put more
19 blood on it. So it needs to say discard result and
20 strip, and retest, or just discard strip and retest.
21 It isn't a matter of discarding the result. You have
22 got to discard the strip.

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 Then under precautions, it says "This test
2 system is designed for in vitro testing only, i.e.
3 outside the body testing." That is another strange
4 statement. Would people eat this stuff or use it to -
5 - I don't know what the purpose of that statement is.
6 Is there any reason why something like that has to be
7 in there? I think it's just confusing. It confused
8 me, and I have had a little more than a seventh grade
9 education.

10 The term "prior to" should be replaced by
11 "before" which is English. "Prior to" is jargon.
12 "Data generated" is another jargon term under
13 limitations in the procedure. Then there's some typos
14 like many of all of the lipids under expected values.

15 Then with the issue of quality control, I
16 agree whole heartedly that people have to know what a
17 value means. It can be put in seventh grade English.
18 For example, when you have a value of such and such,
19 it could be anywhere between such and such. That is
20 plain English, and people would understand that.

21 We have that problem with blood glucose
22 meters. People think because they get a number, that

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 that's gospel. They have to be reminded that those
2 things can be off.

3 CHAIRPERSON NIPPER: Thank you, Dr.
4 Rosenbloom. Have a safe journey.

5 Dr. Floyd?

6 DR. FLOYD: I think the issue of two
7 separate package inserts is a problem, particularly
8 since a lot of emphasis has been made on the fact that
9 the customer, the consumer insert is supposed to be
10 written at a seventh grade level. Does that imply
11 that the professional one will be also? I think the
12 package insert needs to be rewritten embodying the
13 comments that have been made before so that everything
14 the customer needs to know is in the one sheet and
15 tells them exactly what to do and why to do it.

16 CHAIRPERSON NIPPER: Thank you.

17 MS. KRUGER: I agree. No further
18 comments.

19 CHAIRPERSON NIPPER: Thank you. Dr.
20 Lewis?

21 DR. LEWIS: Likewise. I agree, with no
22 further comment.

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 CHAIRPERSON NIPPER: Dr. Janosky?

2 DR. JANOSKY: I am in agreement.

3 DR. DOUMAS: Same.

4 CHAIRPERSON NIPPER: Thank you, Dr.
5 Dumas.

6 DR. MANNO: Same.

7 CHAIRPERSON NIPPER: Thank you.

8 DR. EVERETT: I agree.

9 CHAIRPERSON NIPPER: Thank you, Dr.
10 Everett.

11 DR. REJ: I think as a general rule, all
12 OTC instructions should be stand-alone and not refer
13 to any other document, professional or otherwise. I
14 found the OTC version very, very difficult, with lots
15 of ambiguities. I think that the professional version
16 is woefully inadequate, particularly the measurement
17 and calibration on quality control.

18 CHAIRPERSON NIPPER: Do you think the
19 performance of the device is properly conveyed in the
20 labeling? That's question number nine.

21 DR. REJ: I asked the sponsor earlier what
22 the definition. Dr. Lewis asked too, and I think Dr.

1 Kimberly, about what the results of this device are.
2 I haven't gotten an answer yet.

3 Did you find that?

4 MS. ENRIGHT: I don't have the
5 calculation. I think based on the input of the
6 statistician, the format that we used was exactly what
7 was requested by the FDA.

8 DR. REJ: But you can't tell me what was
9 done?

10 MS. ENRIGHT: The 95 percent number. I
11 don't have the calculation with me. I will defer to
12 the FDA statistician to help us make that calculation.

13 DR. REJ: I am still just curious how you
14 came up with that number for this publication, and you
15 don't know.

16 The answer is no.

17 DR. EVERETT: My answer is no. I mean I
18 tried to get it from the statistician, but to no
19 avail.

20 CHAIRPERSON NIPPER: Okay. Dr. Manno?

21 DR. MANNO: No.

22 CHAIRPERSON NIPPER: Dr. Doumas?

1 DR. DOUMAS: No.

2 CHAIRPERSON NIPPER: Dr. Janosky?

3 DR. JANOSKY: Absolutely not.

4 CHAIRPERSON NIPPER: Dr. Lewis?

5 DR. LEWIS: No.

6 CHAIRPERSON NIPPER: Ms. Kruger?

7 MS. KRUGER: No.

8 CHAIRPERSON NIPPER: Dr. Floyd?

9 DR. FLOYD: No.

10 CHAIRPERSON NIPPER: And Dr. Rosenbloom's
11 answer is -- I'm sorry. Give me a second to find it.
12 He didn't answer that question, so we'll skip that
13 one.

14 Dr. Clement?

15 DR. CLEMENT: Not with the present
16 labeling, no.

17 CHAIRPERSON NIPPER: Okay.

18 DR. KIMBERLY: No.

19 CHAIRPERSON NIPPER: Dr. Rifai?

20 DR. RIFAI: No.

21 DR. NIPPER: And I don't understand the 95
22 percent of the time statement either. I believe that

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 the manufacturer can struggle a little bit and come up
2 with something that's very innovative and useful here.
3 But I think they have the work to do to get the
4 performance into the NCEP guidelines first.

5 Number 10. Do you benefits of this device
6 outweigh the risks? That's an interesting question.

7 Dr. Gutman, maybe you could help me with
8 this question because there are some of us who would
9 like to see this device perform a lot better. Should
10 we do an if-then statement or should we do an as-is
11 statement, or should we do both?

12 MR. GUTMAN: You can do both. With the
13 question on the table, is as-is. But you are welcome
14 to make recommendations for what we could do to help
15 the sponsor move forward, if the question is --

16 CHAIRPERSON NIPPER: It's more of an open-
17 ended question than it looks. Does anybody want to
18 start off and tackle this, or do I be a villain and
19 pick somebody? Dr. Rej?

20 DR. REJ: I believe Mr. Connolly closed
21 his presentation with saying that he couldn't imagine
22 any device where the benefit didn't outweigh the

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 risks. I think the risks of an erroneous result are
2 self-evident. Any test worth doing is worth doing
3 right. The NCEP have made some guidelines. From the
4 current data that we have seen, I think that the risks
5 outweigh the benefits.

6 DR. EVERETT: I tend to agree. I mean if
7 this instrument worked, I would have a different
8 opinion. But trying to decide if it really works, and
9 then if it's risky to use in its current status, I
10 would say it's very risky. So again, the risks
11 outweigh the benefit in its current position.

12 CHAIRPERSON NIPPER: Dr. Manno?

13 DR. MANNO: I concur.

14 CHAIRPERSON NIPPER: Dr. Doumas?

15 DR. DOUMAS: Yes, as is. If it's improved
16 in accuracy and procedure. Actually if the
17 reliability of the paper is improved, and is directed
18 to the right people for use, then it will be a
19 different thing. At this point, I see very little
20 benefit and a lot more risk.

21 CHAIRPERSON NIPPER: Dr. Janosky?

22 DR. JANOSKY: As presented to us today, I

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 see more risk than benefit.

2 CHAIRPERSON NIPPER: Dr. Lewis?

3 DR. LEWIS: I agree with Dr. Doumas'
4 statement, and would make the same statement myself
5 had he not.

6 CHAIRPERSON NIPPER: Ms. Kruger?

7 MS. KRUGER: I agree.

8 CHAIRPERSON NIPPER: Dr. Floyd?

9 DR. FLOYD: I agree. It's more risky than
10 beneficial as it stands today.

11 CHAIRPERSON NIPPER: Dr. Rosenbloom said
12 given the need for triglyceride to be interpreted in
13 the context of a lipid profile and the possibility of
14 inappropriate decision making with self testing that
15 is not medically supervised, potential risks far
16 outweigh the benefits.

17 Dr. Clement?

18 DR. CLEMENT: I agree with the current
19 accuracy and precision. It is risky. I think with
20 tightening up the accuracy and precision, it could be
21 quite useful. We know that Type 2 diabetes is as much
22 a problem of lipid disorders as it is glucose

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 disorders, and could be very, very useful.

2 We would all have a learning curve with
3 this, but I see a future for it if the accuracy and
4 precision can improve.

5 CHAIRPERSON NIPPER: Dr. Kimberly?

6 DR. KIMBERLY: Not in its present form.
7 However, I believe that if the accuracy could be tied
8 closer to the accepted accuracy base, and if the
9 precision was improved, it would be a better device.

10 CHAIRPERSON NIPPER: Thank you.

11 Dr. Rifai?

12 DR. RIFAI: I agree with what Dr. Clement
13 said.

14 CHAIRPERSON NIPPER: Thank you. I think
15 the onus is on the manufacturer, that if he claims
16 benefits, the manufacturer needs to show that in a
17 well-designed clinical study with the present device.
18 That would demonstrate that the benefits far outweigh
19 the risks. We do not have a clinical study.
20 Therefore, I think if you want to say it's equivalent
21 to the predicate device, and therefore it can be used
22 along side any of the other appropriate lab tests,

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 then you don't have to show that the benefits outweigh
2 the risks. It's the same as.

3 I think we have a conundrum that we
4 haven't done either thing appropriately. We haven't
5 shown it is equivalent to the predicate device in
6 precision and accuracy, and we haven't done the
7 clinical study to show that as-is, you can make hay
8 with this machine. So I have a lot of reservations as
9 well about this particular situation.

10 Okay. We have reached the end of the
11 questions. Dr. Kroll was not able to be here today.
12 Do I need to read his statement into the record?
13 Okay. I would ask the panel to bear with me. It's
14 only a page.

15 "Dear Ms. Calvin: Here are my responses
16 to Polymer Technology Systems Incorporated's over-the-
17 counter triglyceride system. In reviewing the
18 documentation of their device, I find the sponsor has
19 failed to adequately characterize its performance.
20 Further, the device fails to meet NHLBI lipid
21 standardization program criteria, which are for the
22 most part, are easy to meet. This requirement not

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701

1 only is reasonable, but also necessary. An error of
2 30 milligrams per deciliter of triglycerides
3 translates into an error of six milligrams per
4 deciliter of LDL. That's a critical value of 100
5 milligrams per deciliter for LDL. That error of six
6 milligrams per deciliter represents six percent, which
7 is fairly large."

8 "Adding the other allowable biases in,
9 gives us three percent from cholesterol and five
10 percent from HDL for a total of 14 percent bias. A
11 diabetic patient with an LDL cholesterol of 115
12 milligrams per deciliter (a treatable category), could
13 easily be read as 99 milligrams per DL, which is the
14 goal for treatment."

15 "The imprecision is too high for their
16 device. There is no control near 200 milligrams per
17 DL, the typical value for triglycerides. They did not
18 evaluate turbidity, nor glucose as sources of
19 interference. For the over-the-counter claim, they
20 did not have people with limited vision, coordination,
21 nor older diabetics use the device. Varying humidity
22 and storage conditions of the reagent strips was not

NEAL R. GROSS

COURT REPORTERS AND TRANSCRIBERS
1323 RHODE ISLAND AVE., N.W.
WASHINGTON, D.C. 20005-3701