

1 responsible environment that poses innovation, where
2 resources are shared as part of the social network,
3 and where stakeholders have mutually agreed standards
4 of guidelines, and hope. This is no utopia. We hope
5 this is going to happen.

6 I'm going to tell you a little bit more
7 about or enumerate our priority areas. The priority,
8 number one is to develop and adopt standards and
9 guidelines for the different stages of the bench to
10 bedside continuum to insure that only biomarkers with
11 clinical utility make their way into routine clinical
12 practice.

13 And I will read the four recommendations
14 in that area. The first one is to incorporate the
15 best components of drug development, guide the
16 development and evaluation of biomarker assays.

17 The second is to expand and encourage the
18 adoption of guidelines for the publication of
19 biomarker study results, and we hear a lot about the
20 multiplicity and the studies that are published, but
21 there are no clear standards as to how and what should
22 be included in those publications. They are
23 guidelines now and they should be expanded in and
24 adopted.

25 We should maintain and update current

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1 guidelines for the clinical use of biomarkers and
2 insure their implementation.

3 And the fourth recommendation in that area
4 is to develop standards to encompass the clinical
5 methodologies for biomarker measurement and reporting.

6 The second priority talks about improving
7 access to biological specimens including associated
8 clinical data and research study information,
9 therefore, recommendations that you can read in the
10 report.

11 The third recommendation is very specific
12 and relevant to today's meeting, strengthening in some
13 sense, expanding the role of regulatory agencies,
14 particularly FDA and insuring the responsible and
15 evidence based clinical use of biomarkers.

16 Two of the recommendations I'm going to
17 highlight. Review of relevant (unintelligible)
18 pertaining to biomarker assay oversight and recommend
19 changes where needed, and this came because in the
20 discussion or in the meeting it wasn't clear really
21 whether FDA had the regulatory power to do this, and
22 so we felt that it was -- or whether an act of
23 Congress was required to give FDA that power.

24 So we recommended that this be done, and
25 also to establish rules and our recommendation to

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1 establish rules for post marketing surveillance, also
2 prove biomarker assays.

3 The four general priorities were to
4 promote the synergistic collaboration across research
5 disciplines and among industry, academia and consumer
6 advocates. One of the recommendations here is to
7 insure that the relevant biomarker assays be in tandem
8 with new therapies.

9 The fifth priority, educate all
10 stakeholders including clinicians and consumers in all
11 aspects of biomarker research and use.

12 And the sixth recommendation, to enact
13 legislation to protect patients against discrimination
14 on the basis of biomarker information.

15 Some of the comments and really the
16 rationale for the priority number three, which is
17 strengthening the role of regulatory agencies to
18 insure the responsible use of biomarkers, in the
19 report it stated that the current regulatory framework
20 for cancer biomarker oversight is insufficient to
21 serve the best interest of consumers. It permits the
22 clinical use of assays that are not reviewed by the
23 FDA and the widespread use of FDA reviewed assays for
24 nonapproved indications.

25 Further, there was concern that even in

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1 the case of FDA approved biomarker assays there's no
2 assurance that the biomarker has demonstrated clinical
3 utility as defined in the report.

4 The report states that the scope of FDA
5 review should be expanded to include clinical utility
6 as defined, the clinical potential process as well as
7 extended to tests currently under the authority of
8 CLEA.

9 Again, panelists expressed considerable
10 concern regarding the premature or inappropriate noted
11 basis of biomarker assays. Such use wastes welfare
12 dollars and can lead to negative physical and
13 psychological consequences and affect consumers.

14 The National Breast Cancer Coalition
15 believes that the draft guidance is a step in the
16 right direction as it intends to exercise more
17 significant regulation oversight of biomarker assays
18 to insure clinical relevance that should lead to
19 evidence use of these biomarker assays.

20 I would agree with other comments that we
21 really need a more comprehensive approach that creates
22 a clear path moving forward and in which criteria and
23 definitions clearly reflect the real and key issue,
24 the impact of this test on patient outcomes,
25 regardless of the technology that is being used.

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1 While business considerations are
2 important, they really should be secondary to the best
3 interest of our patients and consumers. We urge you
4 and invite you to take a look at this report. As I
5 said, we have copies here, and if we run out of them,
6 we will be happy to provide you a copy.

7 Thank you.

8 DR. KESSLER: Thank you, Carolina.

9 We're next to hear from Guido Brink from
10 Agendia.

11 MR. BRINK: Good afternoon. My name is
12 Guido Brink. It's a pleasure to be here, and I
13 appreciate the opportunity to bring forward our vision
14 on IVDMIAs.

15 I'm the Director of Regulatory Affairs of
16 Agendia. You might have heard of our company. We're
17 a small, commercial, central laboratory located in
18 Amsterdam in the Netherlands.

19 Next slide.

20 The vision of Agendia is that complex
21 diagnostics are an integral part of health care
22 innovations that will expedite personalized medicine.

23 Next slide.

24 Agendia's first product required FDA
25 clearance as an IVDMIA is MammaPrint. MammaPrint is

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1 used in assessment of breast cancer recurrence risk
2 through microarray analysis of gene expression.

3 So why does Agendia think FDA oversight is
4 desirable? New technologies used in IVDMIAAs are
5 considered experimental by most physicians. It's hard
6 for physicians to understand and, therefore, trust new
7 complex gene tests and incorrect results can have
8 grave implications on morbidity and mortality and the
9 clinical acceptance and utility of IVDMIAAs will be
10 greatly accelerated by FDA oversight.

11 Next slide.

12 Why is it needed? The complexity of
13 IVDMIA test systems, indeed, warrants oversight
14 because experimental design of validation studies is
15 not straightforward and requires expert FDA agency
16 review. Algorithms employed require independent
17 review and validation by the FDA. Otherwise they are
18 just a black box, whereas clinical lab regulations,
19 such as CLEA are not focused on the complex text
20 systems, and within those systems no specific
21 regulatory standards exist that address IVDMIAAs.

22 Proficiency testing schemes often do not
23 exist and must be developed. Expertise for evaluating
24 validation studies do not exist.

25 To our opinion, the key differences

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1 between home brew and IVDMIAs are that home brew tests
2 can be independently validated. Technologies and
3 software exist that are readily available and allow
4 for independent confirmation of results.

5 For example, sequencing OLA, dHPLC, SSCP,
6 all get you to the same result and no complex, high
7 interpretive algorithm is needed to generate the
8 result.

9 However, IVDMIAs often cannot be
10 independently validated due to proprietary
11 algorithms. Therefore, FDA validation will add to the
12 validity of IVDMIAs.

13 Agendia is of the opinion that all IVDMIAs
14 must be held to the same standard. We strongly
15 believe that once the first IVDMIA has been cleared or
16 approved, all IVDMIAs must be regulated to create a
17 level playing field and to insure patient safety and
18 the device effectiveness.

19 I'd like to close acknowledging the people
20 that were instrumental in acquiring the appropriate
21 regulatory clearance for our MammaPrint product. From
22 Agendia, I would like to mention Dr. Laura van't Veer,
23 Chief Operating Officer, and Professor Rene Bernards,
24 Chief Scientific Officer of Agendia.

25 From FDA, I would like to thank Dr. Steve

1 Gutman, Dr. Robert Becker, Dr. Maria Chung, Dr.
2 Estelle Russell Cohen, and a special thanks to Dr.
3 Rena Phillip.

4 Thank you.

5 DR. KESSLER: You're welcome. Thank you.

6 I still don't think despite that very nice
7 praise that Dr. Gutman can do better than 30 days on
8 the next approval.

9 (Laughter.)

10 DR. KESSLER: Although if anyone can, it's
11 Dr. Gutman.

12 The next speaker is Judith Wilber. Dr.
13 Wilber is from Expression Diagnostic.

14 DR. WILBER: Thank you.

15 What I thought I would do today is to use
16 AlloMap testing as a specific example of CLEA
17 oversight of the laboratory developed test. I am the
18 lab director of the XDx Laboratory, meaning that it is
19 my feet that are to the fire on this, and I want to
20 give you some examples of how we take the CLEA rules
21 seriously, and exactly how we interpret the CLEA rules
22 in getting a complex test like this through.

23 The test itself is a service that's
24 provided to transplant cardiologists. It detects the
25 absence of acute cellular rejection in heart

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1 transplant patients. Currently heart transplant
2 patients are monitored by using heart biopsy, and
3 these are actually done quite frequently. In the
4 first year they're done about 14 times. So this is a
5 blood test that can substitute for that, and the hope
6 is to reduce the number of endomyocardial biopsies,
7 which, of course, can be traumatic to the patient.

8 This is performed entirely in the CLEA
9 certified Xdx Laboratory, and the laboratory besides
10 being CLEA certified has also been licensed by the
11 States of California and New York and the other states
12 that require individual licensing.

13 There was some talk earlier about the New
14 York regulations. It is true that all of the data,
15 validation data, including clinical validation data,
16 must be submitted to New York. However, they do
17 inspect as a laboratory. So they get clinical
18 validation data. They review it, and then they come
19 out and inspect the laboratory, but they inspect the
20 laboratory essentially the same way that CLEA does as
21 the laboratory service.

22 This test measures specific immune system
23 genes, and I'll get to a few of the details later, and
24 it was developed as a part of an Xdx initiated and
25 sponsored four-year study where we collected samples.

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1 The next slide, please.

2 This study was called CARGO for cardiac
3 allograft rejection gene expression observational
4 study. The sample collection was done at eight
5 transplant centers. It required 737 patients and
6 close to 6,000 samples in order to get enough
7 rejection samples in order to do the algorithm
8 development.

9 So I might point out here that there's
10 more than one reason why there might be only one
11 company doing this test, and that's because it would
12 be very difficult for somebody else to do a study such
13 as this at this point.

14 In addition to collecting blood samples
15 and clinical data, we also collected the biopsy slides
16 which were then reread by three centralized
17 pathologists. So we had four pathology readings on
18 all of the biopsy slides to go with.

19 And then we developed the technology first
20 looking at micro arrays, but once the genes were
21 selected all of the testing, current testing, and the
22 validation testing was done using quantitative real
23 time PCR on the exposed RNA.

24 The final set of markers were, of course
25 tested and validated on a separate set of samples.

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1 I just thought I'd pull out a little bit
2 of the CLEA language, and interestingly, I think we've
3 all seen the QSR regs also. It fits in a tiny, little
4 book, but there's an awful lot that needs to be done
5 as a result of that tiny, little book, and a lot of
6 things that need to be done for CLEA can fit on this
7 slide as well, but there's a lot of work that goes
8 into validating according to these rules.

9 But just to be really brief, you do need
10 to have accuracy measures, precision, analytic
11 sensitivity, analytical specificity, reportable range,
12 reference intervals, et cetera.

13 All of these things I would like to also
14 point out can be done not only on the individual
15 genes, but on the score itself so that while there may
16 be an algorithm that takes all of the information from
17 the individual genes into a single number, that
18 number can also be tested for reproducibility, et
19 cetera, and interference from other things.

20 May I have the next slide, please?

21 While CLEA doesn't specifically talk about
22 clinical verification, in order to get a test
23 instituted and used, you do need to determine what is
24 the clinical use of this and also some of the things
25 that are required by CLEA could be construed to be

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1 talking about clinical validation.

2 Accuracy, besides talking about analytical
3 sensitivity and specificity, you need to know clinical
4 sensitivity and specificity, and that can be done in
5 comparison with outcome measures, with other tests,
6 such as biopsy or other tests that might come to
7 similar conclusions, and then other clinical diagnoses
8 that have happened within the patient population.

9 Normal values also need to be established
10 actually even for FDA approved tests. Each laboratory
11 needs to establish normal values for their
12 populations, and then measures of positive predictive
13 value and negative predictive value are also needed.

14 Reference ranges also so that you know
15 what the range is of the scores that you might see.

16 Reproducibility studies, as I mentioned
17 earlier, can be done both on the individual genes and
18 on the score itself. The test that I'm talking about
19 has raw scores that can be tested, and then there's 11
20 different genes that are measured that go into the
21 algorithm, and there are nine other genes that are run
22 in order to control the assay.

23 Obviously, the rules of CLEA say you have
24 to establish the stability of every reagent that's
25 being used, all of your in process test materials.

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1 How long can the RNA sit out? All of those things
2 have to be validated.

3 You have to look at potential interfering
4 substances, and you also need to do guard band
5 studies, such as, you know, if you say it's supposed
6 to be incubated at 37 degrees, what happens if it's at
7 39 degrees, or is it 37 plus or minus what?

8 As an example, I thought I'd pull this one
9 out because it's looking at different genes in
10 relation to the preanalytical steps of the assay. If
11 we're looking at expression of RNA in white cells, you
12 need to have the test that we're doing to be on the
13 same sample at the same state as when it was taken
14 from the patient.

15 And so once we looked at the genes that we
16 had of interest, we went back and did a stability
17 study to determine the time to processing and whether
18 or not you kept the same signal from the time the
19 blood was drawn until it was put in the lysis buffer
20 and frozen.

21 If you can see, on the left there are some
22 that were quite stable from the time that the blood
23 was drawn. There were some others which were of
24 great interest to our scientists, but we had to drop
25 from the assay because they change from the time the

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1 blood was drawn until it was placed in the freeze.

2 And the next slide shows how we then can
3 look at that with the score itself. So this is
4 looking at all of the genes that are in the final
5 assay, and you can see they're quite stable over a
6 period of eight hours, and we actually require that
7 the samples be placed in the freezer within two hours.

8 Next slide.

9 This is our final gene set. This is
10 published, and what the genes represent is also
11 published.

12 Can I have the next slide, please?

13 We look at the sensitivity, specificity,
14 NPV, PPV, et cetera, in comparison with the biopsy.
15 Now, the biopsy is not a gold, gold standard, and
16 that's actually a challenge with any test
17 manufacturer, is figuring out what exactly is a gold
18 standard and what is truth. But that's the reason for
19 having so many readings of the same slide, so that we
20 could come to a consensus of whether this was a
21 rejection or not.

22 Next slide.

23 The final test procedure is 60 real time
24 PCRs, quantitative real time PCRs. There's 20 genes
25 that are tested, and they're all done in duplicate,

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1 and they're all separate PCR reactions.

2 The next slide, please.

3 The next couple of slides I was just
4 pointing out that this is a lab process. We have not
5 put it in -- it's fairly complicated. It's not in a
6 kit, and we probably are not going to put it in a kit,
7 but this is the way we look at it as a lab process,
8 and this is very standard, according to CLEA rules,
9 looking at preanalytic, analytic, and post analytic
10 phases of the testing.

11 So the next slide, I know you can't read
12 this, but these are the flow charts that we go through
13 and figure out what QC needs to be done at each step,
14 whether something goes wrong, where we can loop back
15 and retest, things like that. This is preanalytic
16 process detail.

17 The next slide is the analytic and post
18 analytic process detail.

19 The next slide is some of the QC we go
20 through, and if you can see, the next slide is not
21 only the QC but the whole QA procedure, quality
22 assurance, which is what the CLEA also requires.

23 This is our test report. It gives some
24 information to the physician on how to interpret the
25 results, and the final is the references, which

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1 include the first reference up there, which is the
2 clinical experience using this test from several
3 different prominent heart transplant centers.

4 Thank you for your time.

5 DR. KESSLER: Thank you very much.

6 In a minute I'll introduce our last
7 speaker. Following that, we'll have the microphones
8 open again as we have the last two times, and then at
9 the end of that I'll ask Dr. Schultz, our Center
10 Director, and Dr. Gutman to make a couple of comments,
11 and we'll close the day out. So if you have anything
12 to say after Carolyn Jones from AdvaMed speaks, the
13 mics will be open.

14 Carolyn.

15 MS. JONES: Good afternoon. I'm Carolyn
16 Jones. I'm with the Technology and Regulatory Affairs
17 Department at AdvaMed.

18 And AdvaMed is a trade association
19 representing medical device manufacturers, diagnostic
20 products, and medical information systems.

21 We want to join the other participants
22 here today in thanking FDA leadership for holding this
23 public meeting to allow stakeholders' input on this
24 important subject.

25 We at AdvaMed support the goal identified

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1 in FDA's draft guidance document and applaud your
2 efforts to dispel confusion that has resulted in the
3 way FDA turn -- derives in part from FDA's approach to
4 the regulation of laboratory developed tests that use
5 FDA regulated components and, I guess, most
6 specifically ASRs.

7 From an IVD perspective, AdvaMed
8 represents a diverse group of interest, from
9 manufacturers of IVDs that are clearly approved by
10 FDA, companies that make ASRs that are used in
11 laboratory developed tests, companies that provide
12 laboratory services, and some combinations thereof.

13 The breadth of AdvaMed's membership makes
14 us a good sounding board for diagnostic policies. The
15 vast majority of AdvaMed's membership, IVD membership,
16 has concluded that laboratory developed tests,
17 including IVDMIA's, used for clinical diagnostic
18 purposes meets the definition of a medical device and
19 should be subject to a reasonable risk-based
20 regulatory approach.

21 They believe that the laboratory developed
22 tests should be subject to the same regulatory
23 standard as other IVDs.

24 A few members have concluded that an
25 IVDMIA is not a medical device, but a test system

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1 regulated by CMS under the CLEA regulations.

2 The views of our members almost certainly
3 reflect the discussions taking place among other
4 stakeholders, which is why this public meeting and
5 additional explanation from FDA are very important.

6 All parties agree that patients need
7 timely access to safe and effective diagnostics.
8 Although the FDA IVD clearance process provides for
9 safe and effective tests, it is still too burdensome
10 and too slow moving for some new, novel technologies.
11 It needs further streamlining to meet patient care and
12 public health needs in a timely way.

13 That being said, the IVDMIA guidance
14 document introduces new FDA policy to actively
15 regulate some laboratory developed tests as medical
16 devices, and the clinical laboratories that offer
17 these testing services as manufacturers. This is a
18 significant change in FDA policy and practice.

19 AdvaMed is here today because the IVDMIA
20 guidance document raises important policy questions
21 that require further clarification and to raise some
22 concerns regarding the process FDA employed to
23 announce this new policy.

24 Because the new IVDMIA policy guidance
25 announces the significant change in policy, we

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1 believe the public would be better served by going
2 through a guidance process that allows earlier empiric
3 so that all stakeholders can participate and present
4 their opinions on how such changes in policy will
5 impact public health and the operations of the health
6 care sector most affected, in this instance the
7 clinical laboratories.

8 The involvement of stakeholders earlier in
9 the process provides all potentially affected parties,
10 including industry, a better understanding of the
11 purpose of this change and FDA a better understanding
12 of the potential impact of the new policy. We are
13 glad for the hearing today, but because this guidance
14 raises new questions for the laboratory community, we
15 believe the process would have been better served if
16 FDA had issued a concept paper and held this public
17 meeting before issuing the guidance.

18 We believe the guidance as issued also
19 needs some clarification. Because of the new
20 requirements, AdvaMed believes it is important that
21 its scope be clear and unambiguous. For example,
22 based on discussions with stakeholders, it is clear to
23 us that the clinical laboratory community does not
24 understand the types of medical algorithms that FDA
25 intends to regulate. They believe a guidance may

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1 include medical algorithms that have been longstanding
2 truths of medical practice, and I think Elissa alluded
3 to that in her presentation as well.

4 Therefore, we believe that FDA should
5 provide more detailed information regarding which
6 products will be subject to regulation.

7 In addition, we believe that if FDA goes
8 forward with the initiative as drafted, fairness
9 requires a substantial transition time from the point
10 FDA publishes any final policy to the date the new
11 policy is in force.

12 Laboratories will not fully understand
13 which tests are or are not considered IVDMIA by FDA or
14 how to come into compliance with the new regulations
15 unless FDA takes the time to educate these entities
16 and answer their questions.

17 Finally, we hope and expect that the new
18 FDA thinking and transparency called for in today's
19 meeting will extend to all of our members'
20 enterprises, including those companies currently
21 regulated by FDA that are investing heavily in
22 delivering new know-how into the worldwide advances in
23 medicine.

24 To meet the continuing needs of hospitals,
25 physicians, and their patients and public health, and

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1 to address the disease challenges of all
2 constituencies, including our companies, we should be
3 invited to work with FDA to continue to develop more
4 streamlined, cost effective approaches to insure these
5 essential assays are safe and effective for worldwide
6 use.

7 Again, we commend FDA's efforts, and we
8 intend to continue to work with FDA and the laboratory
9 organizations to achieve our shared goal of insuring
10 timely patient access to safe and effective diagnostic
11 tests wherever they are made.

12 Thank you for the opportunity to present
13 here today, and we will be offering more extensive
14 recommendations in our submission on this matter
15 before the comment part closes on March 5th.

16 Thank you.

17 DR. KESSLER: Thank you, Carolyn.

18 I'd like to spend a moment and thank all
19 of the speakers today for not only being on time, but
20 for their thoughtful and careful consideration of the
21 issues that we face and for the generally constructive
22 tone and nature of the comments.

23 Microphones are open. We're here to
24 listen. That's okay. You had one shot. You can take
25 another. Go ahead. State your name again, please.

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1 MS. CARACHE: I'm Patricia Carache. I
2 represent the AMA, but I'm going to comment on a
3 couple of other issues that have become forward this
4 afternoon very briefly.

5 As I had commented earlier on the need for
6 some type of clear-cut oversight, particularly in a
7 setting in which the clinicians are not in a position
8 to assess the quality of the tests that they are
9 currently very excited about because it meets their
10 clinical needs, as well as the consumer associated
11 marketing. But there are three things I'd like to
12 comment on of increasing importance, in my view.

13 The first is the concept of the orphan
14 test, the need to regulate or not regulate rare
15 diseases, and I point out there and my experience
16 there is from discussions on this in which I was in
17 working groups associated with the original SACGT, the
18 Secretary's Committee on Genetic Testing.

19 We found that when we used the criteria
20 for rare diseases that's currently used for
21 antibiotics and other drugs, 90 percent of genetic
22 diseases would be ignored because they would all fall
23 below that threshold, and this actually would apply
24 particularly to many of the particular analytes and
25 microarrays and what have you that are being developed

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1 for cancer diseases and even some cancer diseases
2 would fall below the threshold.

3 So even though a given disease may be in
4 small numbers, the total population of those affected
5 by genetic diseases and by many forms of cancer is
6 grave, and it was decided that one should have
7 criteria that could apply to all in a given category
8 as a function of risk.

9 The second comment has to do with the
10 current CLEA regulations, that if a test is not
11 cleared by the FDA, it's the responsibility of the
12 laboratory director that offers the test -- and we've
13 heard just now perhaps the normal ranges in terms of
14 gene expression -- to validate the test before he
15 offers it.

16 I think the fallacy in this is extremely
17 clear when you realize immediately that no individual
18 laboratory directors, even if they had the money and
19 the time required to do this, has the patient
20 population available to him or her for the kinds of
21 diseases we've heard discussed today. They can't
22 validate it.

23 This also, I might add, applies to ASRs
24 where there are analyte specific tests out for anthrax
25 and for meningitis due to diseases that no laboratory

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1 -- even our own had to spend three years to develop a
2 patient base at Johns Hopkins to diagnose some of the
3 viral diseases that are out and in use. The
4 laboratory directors rarely can do this. It has an
5 Alice in Wonderland kind of component to it. So it
6 almost has to be done through a premarket type of
7 review that makes sense.

8 And finally, my comment pertains to a
9 recurrent theme that has come up in many different
10 formats today of the need to have CLEA participate in
11 clinical validation, as well as in what they're doing
12 now, which is a very limited form of analyte
13 validation, and it was just pointed out that although
14 we heard that we have a wonderful model here in New
15 York State, in fact, it combines the activities of
16 CLEA and the FDA

17 So New York State has had available
18 something that we don't have nationally, where the
19 policies of moving together, the FDA and CLEA, has
20 seemed to me almost like trying to make the North Rim
21 and the South Rim join at the Grand Canyon.

22 And I think that we do have enough smarts
23 in this room and enough support from agencies that
24 concede the value of smoothing out the entire system
25 to see what can be done to coordinate as New York

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1 State has coordinated the regulatory activities
2 pertaining to laboratory testing.

3 Thank you.

4 DR. KESSLER: Thank you very much.

5 Other comments from the floor? Don't be
6 shy.

7 Well, I have to thank the speakers. They
8 must have said everything there is to say.

9 (Laughter.)

10 DR. SHIMASAKI: Craig Shimasaki. I spoke
11 earlier for InterGenetics.

12 I think it is clear from everyone that
13 spoke that there was no disagreement that it is
14 important that we find better ways to insure safety
15 and efficacy for patients in welfare. I think it's
16 clear that we want to make sure that innovation is not
17 hampered as a result.

18 So, therefore, the question is how do you
19 go about it. I've taken five products from a previous
20 company through Dr. Gutman's office, and we've been
21 very pleased with the candid interaction and the
22 capabilities of the staff.

23 And so it was quite surprising and a
24 little uncharacteristic to be in sort of a confusing
25 situation that actually resulted in something that is

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1 detrimental to the organization. So none of us would
2 want to be in your position because we know that
3 that's a difficult thing to have to regulate an entire
4 industry and try to target a moving target here as it
5 moves.

6 But we do realize that that's important.
7 So one of my questions would be: what is the process
8 going forward after hearing the comments? And then
9 what's the time frame that you may anticipate that
10 things may be done or maybe actions might be taken
11 such that we might have a better idea of what to
12 expect as companies that are developing or companies
13 that are already in the market for products that
14 people do use now.

15 DR. KESSLER: We'll try to address some of
16 that in our final comments.

17 We've been fortunate today to have Dr.
18 Daniel Schultz, who is the Director of the Center for
19 Device and Radiological Health, spend the day with
20 us, and I'm going to turn to Dan to make a few
21 comments about some of the things he's heard, and next
22 we'll turn to Steve Gutman.

23 DR. SCHULTZ: Thank you very much, Larry,
24 and thanks for running what I think is a great
25 meeting.

1 I think it's certainly clear to me based
2 on the size of this group that there's a lot of
3 interest in this area, and very frankly, there should
4 be. I think a number of speakers today have made
5 comments about how we really are on the cusp of a
6 fundamental change in the way medicine is practiced in
7 this country and around the world, and a lot of that
8 will be based on the types of diagnostic tests that
9 have been discussed here today.

10 So I think the interest is warranted, and
11 I think that the need for these types of discussions
12 is extremely important. Certainly there are a lot of
13 issues that were brought up today that I listened to
14 very, very carefully. I think there were a lot of
15 divergent opinions regarding the scope of the guidance
16 and our activities in this area. Clearly that scope
17 will have to be defined, and to me one of the main
18 things that we need to do is pay careful attention for
19 the need for us to be able to define things as clearly
20 as possible.

21 We may not in the end be able to satisfy
22 everyone with exactly whatever policy we finally come
23 up with, but at the very least we should be able to
24 make that policy as clear as possible, and I think
25 that that's certainly a message that I took out of

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1 today's discussion.

2 Another couple of issues that I think were
3 very clear to me is that we need to do a better job
4 associating technology and risk. I think that there
5 were some comments today about how we were regulating
6 things based on technology as opposed to using a risk
7 based approach. If that was the message in the
8 guidance, from the guidance or some message that
9 people think they heard, frankly, in terms of our own
10 internal discussions and knowing the people that
11 actually have formulated this policy, I think that
12 that, in fact, couldn't be further from the truth.

13 I think at the end of the day what we are
14 very, very interested in is providing a regulatory
15 oversight framework that does, in fact, reflect the
16 risk of the product. And I would say that to some
17 extent and perhaps, again, we need to do a little bit
18 better job explaining and defining this, but to some
19 extent there is a link between the changes in
20 technology and the level of risk, and I think that we
21 need to be able to explain that because if people
22 don't understand it, then we haven't succeeded the way
23 we need to.

24 There were also a number of comments about
25 how we move forward, and I think the last speaker

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1 certainly asked what is the plan for moving forward.
2 And I guess what I would say to that is there is a
3 plan for moving forward, and I think that the idea
4 that we can simply go back to where we were several
5 months ago, I guess that to me is the one notion that
6 would be unacceptable.

7 The field is moving very quickly. The
8 technology is moving very quickly. Expectations both
9 in this room and, I think, throughout the country are
10 moving very quickly in terms of us being able to get
11 a handle on this type of technology and to be able to,
12 as many people said, do it right, and I think we need
13 to continue moving forward based on today's
14 discussion.

15 In terms of the time frame, I think we
16 will move with deliberate speed. I think we're going
17 to take the time required once the comments come in to
18 digest the comments that were made here today and the
19 written comments that we get to the docket, and then
20 we'll move forward as quickly as we possibly can.

21 I don't think that this guidance will be
22 the last piece of this discussion, just as today's
23 meeting will not be the last meeting, but I do think
24 that we need to take deliberate but concrete steps in
25 order to be able to move this area forward and we

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1 fully intend to do that.

2 So anyway, I would just like to close,
3 again, with an acknowledgement of the fact that your
4 interest and participation in this meeting and in
5 future meetings and discussions is very, very much
6 appreciated. We certainly believe that we can do a
7 better job when we listen, and we're trying to do more
8 listening.

9 But again, I think at the end of the day
10 we all need to understand that this process needs to
11 proceed and will proceed.

12 So thank you very much.

13 DR. KESSLER: Thank you, Dan.

14 Dr. Gutman.

15 DR. GUTMAN: Yes, I also want to thank
16 everyone. It really was a very rich day. I'm very
17 close to our work group and very close to this
18 document. So being able to actually hear people with
19 their particular passions provide their perspectives
20 was just very valuable to me. So thank you.

21 We always expected that the document was
22 not perfect, and I guess you have suggested the same.
23 So I thank you for that.

24 We, actually as we were interacting with
25 people early in the life of the document, actually

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1 thought that people either over reading or misreading
2 the document, sort of blaming you and not us. But
3 I'll take part of the blame perhaps for not having
4 crafted language with the clarity that SEC does, and
5 we'll try and go to the SEC Website and be more
6 attuned or I'll look at mutual fund reports and try
7 and be more attuned to clarity in language.

8 We didn't think this was going to be easy.
9 I think you've reinforce that, and I can assure you
10 that from where I sit, and I'm not perfect and my work
11 group isn't perfect, but from where I sit
12 unfortunately I'm getting older. People in my family
13 are getting older. I actually do understand the
14 opportunity cost of the delayed lab test. So I don't
15 want anyone to walk away from this room and not
16 understand that I appreciate the value and importance
17 of this new technology. It would be in no one's best
18 interest to put up artificial hurdles that didn't
19 contribute in some positive way to that new
20 technology.

21 I loved Carolyn's idea about dialogue.
22 Other people suggested it as well, and we would like
23 to seek dialogue. It certainly isn't in our best
24 interest to surprise or confuse people. It just makes
25 for extra work for us and for people. That's not the

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1 way we want to operate. That's not the way we've
2 historically operated, and I am certainly committed to
3 try and do my imperfect best to do that in the future.

4 And the one thing that you can do to help
5 make sure we move forward fast is please respect the
6 March 5th deadline. Get us good comments, concrete
7 comments. Some of you actually -- many of you
8 provided power points, but some actually have already
9 provided written comments, but please be attentive to
10 that document so you can help us start the hard work
11 of figuring out where we're going to go.

12 Thank you.

13 DR. KESSLER: So I'm going to make a few
14 closing comments.

15 The first thing I'd like to do is send a
16 special thank you to my left to Dr. Susan Altaie. She
17 helped arrange a lot of this meeting and the fact
18 that we were able to conduct the meeting and hear from
19 everybody in such a timely fashion is credit to her.

20 I'd like to thank Steve and his Office of
21 In Vitro Diagnostics for not only doing the work, but
22 providing the support for this, and our conference
23 people there in Murray Williams and Shirley Meeks are
24 always wonderfully helpful. So I appreciate that.

25 Susan says that we will in the very near

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1 future hope to post a transcript that we're doing, as
2 well as the slides that you saw today. They're part
3 of the public record. So if you wish to get slides,
4 we will put them on the Website at the FDA site so
5 that you can draw them down.

6 A few substantive comments from today.
7 I'm going to echo some of the things that Dan and
8 Steve just said just to make sure that we're all on
9 the same page, and I want to echo one of the comments
10 from one of our speakers from this afternoon. We do
11 this for ourselves because it's important for medicine
12 today.

13 More importantly, we do this for medicine
14 for future generations. It's important to all of us
15 to make sure that we're setting the ground work for
16 the way medicine, public health, and the regulated
17 products that we deal with will work in the future.

18 We do find ourselves in an exciting time.
19 For lab science it's very obvious for medicine and
20 public health, and here are a couple of things that we
21 heard.

22 You want us to be clear about making our
23 public health case for why this is important. I think
24 the interest in the room shows why it's important, but
25 I think we certainly can make the case why we've

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1 chosen the regulatory path that we have.

2 Dan said it again. I'm going to repeat it
3 in a different way. It's like the old adage in real
4 estate. What's important? Location, location,
5 location.

6 For us in this guidance, clearly clarify,
7 clarify, and again clarify, and we will endeavor to do
8 that as we move forward, and in doing so we hope to
9 provide both scientific and regulatory certainty in
10 terms of how we move forward because we recognize that
11 that's going to be important for the laboratories who
12 are involved with these tests, as well sa for the
13 companies and the scientists that are trying to
14 manufacture and create and innovate in this important
15 product area.

16 One of the things we also heard is that
17 you want us to work closely with our federal partners.
18 That would include the Center for Medicare and
19 Medicaid Services, CDC, FTC, and NCI was here in force
20 as was other parts of NIH, and we certainly do plan to
21 work with them. We have closely, and we continue to
22 do that.

23 We have heard contrasting things today.
24 Dan said it's going to be hard to fix this and make
25 everybody happy. We heard some people say we should

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1 be very narrow in what we try to do and others say we
2 should be both broad and comprehensive. It's hard to
3 do both, but we're going to try and look at the full
4 gamut of the possibilities and try and think about
5 thoughtful regulation in that.

6 Finally, it is clear we find ourselves at
7 the bring of a revolution in personalized medicine,
8 but just as previous dramatic advances in science have
9 delivered health benefits, they also sometimes
10 unexpectedly bring new risks. As a science based
11 public health agency, we seek to find the optimal
12 balance between risk and benefit and between rapid
13 access to market and careful deliberative product
14 review. That's a very difficult balance. Steve does
15 it every day. The people in the Office of Device
16 Evaluation do it every day. We do it in the post
17 market side every day.

18 We've listened to your concerns. We will
19 take your ideas into serious consideration and help us
20 chart the path to the future.

21 Thank you. We're adjourned.

22 (Whereupon, at 2:39 p.m., the public
23 meeting in the above-entitled matter was concluded.)

CERTIFICATE

This is to certify that the foregoing transcript
in the matter of: IVDMIA Public Meeting

Before: Dr. Larry Kessler

Date: February 8, 2007

Place: Gaithersburg, Maryland

represents the full and complete proceedings of the
aforementioned matter, as reported and reduced to
typewriting.


James Salandro