NATIONAL INSTITUTES OF HEALTH

GENETIC TESTING REGISTRY

PUBLIC MEETING

November 2, 2010

Walter E. Washington Convention Center
Room 147
801 Mount Vernon Place, Northwest
Washington, DC

EBERLIN REPORTING SERVICE
576 Hooker Drive
Gettysburg, Pennsylvania 17325
(717) 334-8200

I N D E X

WELCOME AND OPENING REMARKS
Francis Collins, M.D., Ph.D.
Director, National Institutes of Health 5

OVERVIEW OF PUBLIC COMMENTS RECEIVED IN RESPONSE TO NIH'S REQUEST FOR INFORMATION ON THE GENETIC TESTING REGISTRY
Amy Patterson, M.D.
Acting Associate Director for Science Policy, NIH 15

PROTYPE DATA ELEMENTS FOR THE GENETIC TESTING REGISTRY
James Ostell, Ph.D.
Chief, Information Engineering Branch, NCBI, NLM, NIH 22

PUBLIC COMMENTS ON THE FOLLOWING QUESTIONS:

Question 1: Based on an analysis of RFI comments and other operational issues, NIH is considering a phased approach to developing the GTR in which some types of tests would be eligible for early entry in the GTR and other types of tests would be added later. If NIH adopts this approach, what criteria should be used to determine which genetic test should be included in the first phase of the GTR, and what types of tests would meet these criteria?

Question 2: Several RFI responders, who are potential data submitters, noted that it makes more sense for clinicians and genetics professionals to be the source of clinical utility evidence rather than test developers and/or test providers. Given that data submitters are unlikely to have clinical utility information, how is this data element best addressed in the GTR?

Question 3: Among respondents to the RFI question about including a data element for test cost, half were in favor of including cost information and half were opposed. What are the benefits, risks, and challenges of including cost information in the GTR?

Question 4: What safeguards can be put in place to prevent GTR users from misunderstanding, misinterpreting, or misusing the information in the Registry?

I N D E X (Continued)

PUBLIC COMMENTS ON THE FOLLOWING QUESTIONS: (continued)

Question 5: What mechanisms can be used to provide materials that explain the GTR's data elements to audiences with varying technical expertise?

REGISTERED PUBLIC COMMENTERS

Bruce Korf, M.D., Ph.D.
American College of Medical Genetics 31

Elaine Lyon, Ph.D.
Association for Molecular Pathology 35

W. Andrew Faucett, M.S.
Emory University School of Medicine 39

Sharon Terry, M.A.
Genetic Alliance 44

Misha Angrist, Ph.D.
Duke University 50

Sherri Bale, Ph.D.
GeneDX 55

Barbara Harrison, M.S.
Howard University 58

Jan Nowak, M.D., Ph.D.
College of American Pathologists 61

Jason DuBois
American Clinical Laboratory Association 66

David Ledbetter, Ph.D.
Geisinger Health System 69

Lisa Baumbach-Reardon, Ph.D.
Miller School of Medicine, University of Miami 74

Robert DiTullio
AdvaMed 77

Edward McCabe, M.D., Ph.D.
Past-President, American Society of Human Genetics 82

I N D E X (Continued)

PANEL DISCUSSION
Moderator:
Kathy Hudson, Ph.D.,
Deputy Director of Science, Outreach,
and Policy, NIH 84

Question 1:
Robert Nussbaum, M.D.
Chief, Division of Medical Genetics
University of California, San Francisco 87

Question 2:
Victoria Pratt, Ph.D.
Chief Director, Molecular Genetics
Quest Diagnostics Nichols Institute 102

Question 3:
Misha Angrist, Ph.D.
Assistant Professor
Institute for Genome Science and Policy
Duke University 106

David Mongillo
Vice President, Policy and Medical Affairs
American Clinical Laboratory Association 110

Question 4:
Myrl Weinberg, M.A.
President
National Health Council 119

Question 5:
Joanna Mountain, Ph.D.
Senior Director of Research
23 and Me 127

Concluding Remarks
Kathy Hudson, Ph.D.
Deputy Director of Science, Outreach,
and Policy, NIH 134

1 P R O C E E D I N G S

2 **WELCOME AND OPENING REMARKS**

3 DR. COLLINS: Good morning, everyone.

4 I'm Francis Collins, the Director of the
5 National Institutes of Health and I'd like to
6 welcome you to a public meeting on the Genetic
7 Testing Registry.

8 Engaging interested stakeholders has been
9 a central part of NIH's commitment to many things
10 and certainly to the development of this GTR and we
11 are delighted to have the chance to spend time here
12 this morning in the early days of the ASHG 60th
13 anniversary meeting and we thank you for your
14 interest in attending and for taking time to join in
15 what we hope will be a very positive and interactive
16 discussion.

17 I'd particularly like to thank Jo Boffman
18 (ph) and her staff for helping with the meeting
19 arrangements and making it possible for us to be
20 here in the convention center as part of a
21 conjunction with the ASHG.

22 This audience, many of whom I know quite
23 well, is well aware of the rapid growth in the
24 numbers and types of genetic tests and the
25 increasingly complex methodologies used in these

1 tests so many of you also recognize that GTR is
2 intended to fill what is currently a serious gap in
3 our understanding of that landscape and particularly
4 to provide a resource for providers.
5 There is no current centralized public
6 resource that provides comprehensive information for
7 a wide variety of tests quite like what is
8 envisioned in the GTR.
9 Discussions about the need for this have
10 played out over many years going back over many
11 years going back to the Secretary's Advisory
12 Committee on Genetic Testing where this was much
13 discussed and, as you know, SACGHS, the Secretary's
14 Advisory Committee on Genetics, Health and Society,
15 called for such a registry, as have other policy and
16 advocacy groups. These groups have all recommended
17 establishing such a registry to enhance transparency
18 by making it possible for information about
19 availability, scientific basis and usefulness of
20 genetic tests to be readily accessible. In the view
21 of those experts such a resource would assist
22 providers primarily but also patients and consumers
23 in making informed decisions about genetic testing
24 and assistance in understanding the limitations of
25 such tests, which may not always be apparent if the

1 only source of information is from the test
2 provider.
3 NIH has been seen as a natural home for
4 the GTR given our role in advancing public health
5 through science, our mandate to disseminate
6 scientific and health information, and our expertise
7 and experience in developing databases particularly
8 at the National Center for Biotechnology
9 Information, part of the National Library of
10 Medicine.
11 But before deciding to move forward with
12 the GTR we consulted extensively with FDA and with
13 CMS since these are the agencies with a leading role
14 in the oversight of genetic testing, and we were
15 encouraged by their enthusiasm for going forward.
16 We have been keeping our colleagues updated on this
17 program and have been attuned to relevant policy
18 developments.
19 As an aside, last Thursday Peggy Hamburg
20 and I chaired the very first meeting of the NIH-FDA
21 Leadership Council, which involves the center
22 directors at FDA and a series of senior institute
23 directors at NIH. And I would say that the dynamics
24 of that conversation were extremely positive and
25 provides yet another very high level opportunity to

1 be sure that we're working effectively together on
2 this issue and many others as well.
3 I'm pleased a number of our FDA colleagues
4 are here today.
5 So the primary function of the GTR is to
6 enhance transparency about test availability and
7 utility. And as mentioned a minute ago but let me
8 say it again, I think, it's being designed primarily
9 to serve the information needs of healthcare
10 providers but, of course, many individuals in the
11 general public are also getting quite sophisticated
12 about such tests and while that is not the intended
13 primary audience we recognize that well informed
14 patients and consumers will likely also use the GTR
15 as a resource and that's fine. It's a public
16 database.
17 The GTR also has a public health goal
18 because not only does it list what's available but
19 may also reveal knowledge gaps, and we hope that
20 will then help focus research efforts that will
21 further our understanding of the genetic basis of
22 health and disease. This should also provide
23 opportunities for linkages to information in other
24 NIH genetic, scientific and medical databases, which
25 will assist those who want to use this to help make

1 discoveries such as genotype-phenotype correlations
2 that ultimately lead to science advances.
3 So we have been thinking about this and
4 talking to many people about it, and obviously we
5 want to move carefully here not to build this
6 registry in a vacuum but to consult widely and
7 gather information and perspectives from
8 stakeholders, and that's what this morning is about.
9 But already we have created a website with
10 information about the GTR development process and
11 encouraged feedback from the moment the process was
12 launched. We created a listserv for GTR to
13 communicate with interested stakeholders and are
14 using that to reach out proactively.
15 In May we issued a request for
16 information, generally known as an RFI, to gather
17 input more formally and systematically. That was
18 posted on the GTR website, disseminated on the GTR
19 listserv and published in the *Federal Register*, and
20 in a few moments Dr. Amy Patterson will review what
21 we learned from those RFI comments.
22 And we've also been meeting with other
23 stakeholder groups to understand their concerns and
24 hear their ideas about critical and feasible data
25 elements that should be included in the registry and

1 mechanisms that ease submitting data to the GTR and
2 minimize redundancy with requirements of other
3 federal agencies and accrediting organizations.
4 I would certainly like to thank Jim Ostell
5 of NCBI for his very flexible approach to receiving
6 that kind of input and making sure that the way in
7 which this GTR is put together is responsive to the
8 needs.
9 So we have worked hard to be transparent
10 and to be open to your input and are grateful to all
11 those who have shared those thoughts and expertise
12 but before closing and introducing Dr. Patterson I
13 want to take a moment to address a couple of the
14 concerns that have been repeatedly expressed in RFI
15 comments or that we've heard or read about in news
16 articles or blogs. There has obviously been a great
17 deal of interest in this process.
18 So first of all the GTR is a voluntary
19 registry. We will not ask for trade secrets or
20 confidential commercial information.
21 Second, the GTR will not include test
22 results from patients or consumers and, therefore,
23 will not pose a threat to patient privacy.
24 Third, and I know this has been a source
25 of confusion perhaps in the medical genetics

1 community, in relating to existing databases the GTR
2 will not--let me repeat that--will not gene reviews,
3 which will continue to go forward as a very valuable
4 resource that all of us medical geneticists use. It
5 will eventually replace only the laboratory
6 directory component of GeneTests.org and there will
7 be a sufficient period of overlap when the GTR and
8 gene test lab directory will coexist so that there's
9 an orderly transition and an opportunity for
10 everyone to get used to the shift.
11 There has also been the question about our
12 decision to start a new registry rather than build
13 on to the existing GeneTests registry. It turns
14 out, and Jim could give you much more of the
15 technical details, it is just not practical from
16 either a technical or an economic perspective to
17 expand GeneTests. Its underlying infrastructure
18 cannot support the GTR's expanded scope and
19 additional data, which we believe is timely to add
20 to this resource and which really, therefore,
21 becomes a strong mandate for a new database with a
22 new structure.
23 Some have expressed concerns about whether
24 clinical experts are sufficiently involved in the
25 GTR. In fact, two groups will be engaged with that

1 expertise. First, we tap expertise within NIH,
2 which has a vigorous medical genetics community, and
3 formed a group of clinical advisors with backgrounds
4 and portfolios in a wide range of genetic
5 conditions. But we will also receive outside
6 advice through the Board of Scientific Counselors of
7 the NCBI, which has formed a Medical Genetics
8 Working Group. In addition to those groups, staff
9 working on the implementation of GTR will include
10 many other individuals with experience in health
11 care, clinical genetics and genetic testing. So we
12 do believe that we have adequate advice about the
13 construction and design of this effort from people
14 with personal and intimate familiarity with medical
15 genetics.
16 Another concern has been the accuracy of
17 the information in the GTR. How can people be
18 confident that what they see there is trustworthy?
19 Well, we can verify information such as CLIA
20 certification numbers and FDA premarket approval
21 numbers, and also quality control submissions to
22 detect the internal inconsistencies in the data.
23 But, to be honest, it will take resources beyond our
24 means and authority, and I think that would be true
25 of any such registry, to validate primary

1 performance characteristics data. Regulators,
2 laboratory accrediting organizations and third party
3 reviewers will have access to date in the GTR and
4 the registry will link to any publications or
5 assessments of these data in order to provide that
6 connection.
7 So those are a few of the issues that have
8 been raised and I suspect may well be talked about
9 further this morning, and again I appreciate your
10 attendance to be part of that conversation.
11 I just want to say as NIH Director I have
12 made GTR a priority because of its potential to
13 enhance transparency, advance science and improve
14 public health. It is very much part of the Obama
15 Administration's philosophy of this attitude of
16 openness and data access, and GTR fits within that
17 and so NIH has dedicated resources to the
18 development of this and made its development a
19 priority and a key goal for NIH in the next year or
20 two.
21 I very much want to thank staff in the
22 Office of the Director and at NCBI, and that
23 includes Kathy Hudson, Amy Patterson and others in
24 the Director's office, and Jim Ostell and his team
25 at NCBI for their commitment and dedication to

1 bringing this to fruition.
2 So this morning you're going to hear two
3 presentations from NIH.
4 First, Dr. Patterson will provide an
5 overview of the public comments that we've received
6 in response to the RFI.
7 Then Jim Ostell will share registry
8 prototypes for three different types of genetic
9 tests to see where this is going.
10 And then following those presentations
11 there will be time for public comments and then a
12 panel discussion with the individuals whose names
13 you see here.
14 So, personally I'm delighted to be here.
15 We look forward to advancing the development of the
16 GTR with the comments we hear today and with
17 continued engagement with interested stakeholders.
18 We want this to be a success for everyone and so
19 thank you for being here and for sharing your
20 insights and perspectives.
21 And now I would just like to introduce Dr.
22 Amy Patterson, who is the Acting Director of the
23 Office of Science Policy at NIH.
24 Thank you very much.
25 (Applause.)

1 **OVERVIEW OF PUBLIC COMMENTS RECEIVED IN RESPONSE**
2 **TO NIH'S REQUEST FOR INFORMATION ON THE GENETIC**
3 **TESTING REGISTRY**
4 DR. PATTERSON: Good morning, everyone.
5 (Slide.)
6 As Dr. Collins said, I will give you a
7 brief bird's eye view of the comments that we
8 received in response to NIH's request for
9 information on the Genetic Testing Registry. The
10 RFI was issued through multiple channels in May and
11 as you may recall it set forth a number of fairly
12 straight forward questions that we wanted your input
13 on.
14 One was what should be the scope of the
15 registry? What do you envision as the potential
16 uses of such a registry? What are critical data
17 elements that should be considered for inclusion to
18 satisfy the needs of various stakeholder groups?
19 What potential benefits and risks of wide access to
20 information about the availability, validity and
21 utility of genetic tests do you foresee? And what's
22 the best way to distinguish between data fields that
23 are left blank simply because there's no known data
24 versus the submitting not actually providing the
25 information? And what's the value of specific data

1 elements that were proposed? And is there
2 information that would be particularly difficult for
3 submitters to provide?
4 (Slide.)
5 What are the advantages and disadvantages
6 of capturing the molecular basis of the tests? What
7 information resources should be provided to help put
8 the test performance characteristics into context,
9 for example, and to enhance understanding of the
10 information presented? Is there any way that the
11 NIH in hosting this registry could put in place
12 processes that would facilitate data submission?
13 And what are the potential benefits and risks to
14 posting the information that might affect data
15 submission decisions? A very important question is
16 how can we continue to ensure stakeholder input as
17 the development of the registry will be an iterative
18 process and has to be informed by how well its
19 meeting the needs of its various users and how do
20 you intend on using the Genetic Testing Registry,
21 and anything else you wanted to tell us.
22 (Slide.)
23 So this pie chart shows you the
24 distribution of the 68 responses that we received.
25 The majority of them came from health care

1 providers. A fair number from industry,
2 professional organizations, academia and laboratory
3 or laboratory professionals.
4 (Slide.)
5 I want to sketch out a couple of the
6 general themes and then take a little bit of a
7 deeper dive in terms of the specific comments that
8 we received. Overall, the comments were pretty
9 supportive of the GTR concept. There was general
10 agreement with most of the proposed data elements
11 that were set forth. However, a number of people
12 pointed out the need to provide educational
13 materials or other information context to help
14 define and explain each data element.
15 In terms of the potential uses of the
16 registry, commenters pointed out providing
17 information about test availability, identifying
18 laboratories that could confirm research results,
19 learning about specimen requirements and test
20 benefits and limitations, and finally GTR providing
21 a venue to facilitate research, for example, by
22 providing contact information of potential
23 collaborators.
24 (Slide.)
25 In terms of the concerns--I should note

1 that the next two slides list the concerns roughly
2 in order of the number of people that noted these as
3 issues that were on their mind. The most common
4 concern cited was the notion that it would be
5 critical to ensure the accuracy of the information
6 in the GTR. And Dr. Collins touched on this issue
7 in his remarks. The fear was expressed that users
8 logging on to the registry will assume that the test
9 information on an NIH sponsored website is accurate
10 and valid.
11 The second most frequently cited concern
12 was the notion that there could be potential harm to
13 patients if information in the registry is
14 inaccurate or incomplete or is misunderstood or
15 misinterpreted. And some of the results of that
16 could be inappropriate testing or denial of
17 insurance coverage.
18 The third most frequently cited concern
19 was that data elements--for example, clinical
20 utility or price--will be difficult to provide
21 particularly for rare diseases.
22 People also noted that the need for the
23 GTR--and again Dr. Collins touched on this concern--
24 is not obvious when a voluntary registry is already
25 hosted at NCBI, GeneTests.

1 (Slide.)

2 People also raised the issue that the GTR
3 could contribute to increased demand on the health
4 care system and health care spending, people being
5 more aware of the availability of certain genetic
6 tests and, therefore, ordering them.

7 People also noted that the GTR should
8 include, in their minds, only those tests with high
9 sensitivity and specificity and well-established
10 clinical validity. This comment harkens back to an
11 earlier concern about the potential misuse or
12 misinterpretation or misunderstanding of the
13 information.

14 And, finally, people noted that in their
15 minds data submission would be a time consuming
16 endeavor, especially for small niche laboratories it
17 will be challenging to keep the data up to date.

18 (Slide.)

19 So for today's meeting what we've done is
20 to try to comb through those comments and also
21 consider other inputs through our inbox and through
22 various blogs to try to cull out five key questions
23 and these five questions will be the focus of the
24 panel discussion and, hopefully, the focus of many
25 of your comments today during the public session.

1 I'll just briefly run through these. These are also
2 included on your agenda and we'll post this slide
3 throughout the discussion so you can refer to it.
4 So question one: If NIH adopts a phased
5 approach to build the GTR, what criteria should be
6 used to determine which genetic tests should be
7 included in the first phase and what types of tests
8 would meet those criteria?
9 Question two: Given that data submitters
10 are unlikely to have clinical utility information,
11 how is this data element best addressed in the
12 registry?
13 What are the benefits, risks and
14 challenges of including price information in the
15 registry?
16 And what safeguards could be put in place
17 to prevent GTR users from misunderstanding,
18 misinterpreting or even misusing information in the
19 registry?
20 And, finally, what mechanisms can be used
21 to provide materials that explain the data elements
22 to audiences with varying technical expertise?
23 (Slide.)
24 Today is not your last chance to voice
25 your concerns or comments. The comment period

1 closes on November 12th, 2010, but I should say we
2 are always glad to hear from you and we really want
3 to ensure that this registry meets your needs and
4 the needs of a wider community.
5 Please submit your written comments if you
6 haven't already done so to the attention of Cathy
7 Fomous and we'll take it any way you can get it to
8 us as shown on this slide, email, fax or snail mail.
9
10 In terms of next steps we're certainly
11 going to listen carefully today. We're taking notes
12 and we'll analyze what you tell us. We'll continue
13 to engage our federal siblings, CMS, CDC, FDA and
14 AHRQ, and we'll continue to have meetings with
15 stakeholder groups similar to this. We also intend
16 on convening some focus groups to provide feedback
17 on the registry prototypes as it gets developed and
18 Jim will speak to this in greater detail but we
19 expect the GTR to be launched. We're targeting the
20 spring of 2011 and we will certainly look at usage
21 patterns and feedback we get on that and continue to
22 develop and fine tune it based on the input that you
23 give us.
24 And with that I'll hand the podium over to
25 Jim Ostell.

1 (Applause.)

2 **PROTYPE DATA ELEMENTS FOR THE**

3 **GENETIC TESTING REGISTRY**

4 DR. OSTELL: Thank you, Amy.

5 (Slide.)

6 So the main change in the GTR design is
7 that each record is an actual specific, orderable
8 test from a specific laboratory. It's not sort of a
9 general statement that a laboratory test for a
10 disease by some set of techniques. It's literally a
11 series of tests. A number of laboratories may offer
12 several tests or different types of tests for the
13 same disease. They may combine things into packages
14 and so this is--the registry is meant to directly
15 correlate with the ordering directory of a
16 laboratory.

17 Each record has a stable, trackable
18 accession and version. That means that it is
19 citable, the same way that you could cite an OMIM
20 number or a PubMed ID or a GenBank accession number,
21 and they are versioned so that when a test is
22 updated and more information is provided it's clear
23 that it has been changed and it's also possible to
24 go back and look at older versions that we'll keep.
25 The reason for that is what Dr. Collins alluded to,

1 which is part of the idea behind the registry is
2 that this is something that people can look at and
3 analyze and write reports about in a way that's
4 citable forward in time.
5 Because of this a record can be explicitly
6 linked to one or more diseases and one or more
7 specific genome regions. It doesn't need to be just
8 a gene name. It can be coordinates on a genome.
9 This means that it's natural to support large panels
10 and arrays. It also means that the tests can be
11 linked to specific mutations, not just in the body
12 of the text but actually connected to the genome and
13 defined genomic positions, not just gene names.
14 And, in addition, a record can point at
15 another record. So one example would be that an FDA
16 approved test can be entered into the database once,
17 the information about its analytical validity and
18 clinical validity put down once, and then a lab
19 which uses that test can just refer to it rather
20 than recreate that. If they have a modified version
21 of that test they can put their modification into
22 their test record and then for the rest of it refer
23 back to the FDA approved test. And over time there
24 may be other classes of tests or test platforms that
25 are used more broadly in multiple laboratories, and

1 we're trying to avoid people having to reproduce the
2 entry.
3 (Slide.)
4 Under this one section is basically the
5 last six months of conversation. We've had detailed
6 discussions of schemas, of course, with GeneTests,
7 which is at NCBI now and we know it intimately, but
8 also with the proposed HL7 electronic directory of
9 services, the AMP Test Directory, several commercial
10 enterprises that have registries of tests that are
11 used for payers. Of course, the FDA Registry and
12 Listing Service, the CLIA Database, other commercial
13 groups which are involved in claims payment for CMS,
14 American College of Medical Genetics. And through
15 all of these conversations there has been a lot of
16 give and take about trying to find the right balance
17 to collecting enough information to be useful while
18 at the same time managing reporting burden and
19 keeping it to some reasonable level and information
20 that can be connected.
21 We're also trying very hard to be
22 compatible with these resources in order to open the
23 possibility of exchanging data back and forth with
24 other services.
25 We've also correlated the GTR data items

1 with other proposals. In particular, the CAP
2 Molecular Pathology Checklist which is used to
3 assess laboratories that do genetic tests so that
4 items that we're asking for in the registry we can
5 say corresponds to the type of information you
6 prepare for the CAP inspector. We have talked to
7 CAP about this, as well as other recommendations.
8 Along with these discussions we're trying
9 to open the opportunity for bulk upload. That is
10 big laboratories with large sets of tests, if they
11 already have the data in a database in some
12 electronic form we don't want to have you have to
13 type into forms for all of this and so we'd like to
14 be able to sort of dump from your database directly
15 into the GTR and not have to enter it twice.
16 And, of course, we also have--because
17 GeneTests is at NCBI--set up a system to
18 automatically populate the information from
19 GeneTests into GTR so that you don't--if you've
20 already put your information into GeneTest you don't
21 have to reenter it. GeneTests, of course, isn't
22 really tracking specific tests, specific orderable
23 tests but we can move a large amount of that
24 information automatically.
25 (Slide.)

1 In terms of taking into account the design
2 we do have a lot of experience supporting GeneTests.
3 We've done analysis of the GeneTests usage patterns
4 that affects the user interface design and we've had
5 lots of discussion with the potential submitters and
6 users. These are people that have sort of
7 voluntarily come forward and offered to collaborate
8 on this project. We really appreciate it. Those
9 people are still actively involved and if there's
10 anybody else in the audience that would like to jump
11 in we're happy to have as many active inputs as
12 possible.
13 (Slide.)
14 This is sort of our prototype screen for
15 what the search would look like. We have set this
16 up so that you can search all of Genetics Testing
17 Registry but you can also sort of look at it from
18 different points of view. So you come in looking at
19 it from the point of view of diseases or genes or
20 specific tests or labs or the clinics or other
21 resources, and that's what I'm going to show you
22 now.
23 (Slide.)
24 So I am clicking on labs.
25 (Slide.)

1 I'm going to the advanced search to show
2 you that there are specialized fields you can have
3 that change for which point of view that you look at
4 but our hope is that you don't really have to do
5 that and most work can be done with a simple one
6 query box, a query more like Google. In this case
7 we're going to look up for cardiomyopathy in the
8 disease section.
9 (Slide.)
10 We can see there are actually a large
11 number of cardiomyopathies so you get an extended
12 list. We show you the genes associated. Resources
13 are available over here, including OMIM and gene
14 reviews and a number of other resources.
15 (Slide.)
16 If you click on the gene review section,
17 for example, it will take you right to it to try to
18 sort of keep that connection alive as much as
19 possible. That can be expanded, of course.
20 (Slide.)
21 This is the disease-centered view. So, on
22 the disease page there's a little summary of the
23 disease, more information about it, related
24 diseases, related genes, and then a panel of tests
25 for this.

1 (Slide.)
2 We're going to look at a panel with--this
3 is actually at Partners.
4 (Slide.)
5 This is the CardioChip panel with a large
6 number of characters. There's detailed sections
7 about each one of these tests. In this case we can
8 look in a little more detail at the methodology
9 section where it breaks down a little further into
10 the pieces, the limitations of the test and so on.
11 (Slide.)
12 From another point of view we can look at
13 a pharmacogenomic test. In this case we're going to
14 take a look at Warfarin sensitivity.
15 (Slide.)
16 In this case there is only one condition
17 for Warfarin sensitivity so we don't need a list.
18 We can take you right there and have a variety of
19 labs that offer tests for it.
20 (Slide.)
21 In this case it's a targeted mutation
22 panel.
23 (Slide.)
24 If we take a look at the test page for
25 that there is some overview of what the test is

1 about, the mutations that are tested for, for this
2 particular test, including the specific mutations
3 that are being tested up here.
4 The point of this particular example as we
5 go to the credentials, this is based on an FDA
6 approved test and this is one of those examples I
7 gave where we're actually pointing at information
8 that came from the FDA test and didn't have to be
9 re-entered by this particular group, as well as the
10 credentials for the laboratory itself.
11 (Slide.)
12 Then in sort of the last quick example
13 here, this is one that's coming in from now the gene
14 point of view. In this case we're looking for genes
15 involved in Rett Syndrome. Pick the MECP2.
16 (Slide.)
17 This is the gene page, a summary of the
18 gene, other diseases that are derived from it, a
19 view of the gene region with clinically important
20 SNPs marked where we know where they are. And then
21 this is information from the Locus-specific database
22 for Rett Syndrome and then other resources for
23 RETTs.
24 (Slide.)
25 On those pages, of course, we hope that

1 over time as more and more biological information is
2 obtained about these diseases we can array out
3 what's known against those sort of displays, as well
4 as what's being tested by the particular test that
5 you're looking at.
6 So that's the quick overview.
7 Thank you.
8 (Applause.)
9 DR. FOMOUS: Good morning.
10 I'm Cathy Fomous by the way.
11 I'm delighted to have emailed with many of
12 you, especially those who are going to be making
13 public comment shortly. It will be nice to meet you
14 in person.
15 As Dr. Collins mentioned in his opening
16 remarks this morning, engaging with stakeholders is
17 a critical element in developing the GTR. We
18 welcome and appreciate the views that the commenters
19 will share with us today.
20 We have requested that the public
21 commenters address one or more of the focus
22 questions that you see up on the screen. And in the
23 interest of keeping to our time frame we've asked
24 the commenters to limit their remarks to six
25 minutes.

1 We will put copies of the public comments
2 on our website sometime this month and then
3 following public comments today we'll have a
4 moderated panel discussion.
5 So I'd like to introduce our first speaker
6 who is Dr. Bruce Korf, who will provide comments on
7 behalf of the American College of Medical Genetics.
8 **BRUCE KORF, M.D., Ph.D.**
9 **AMERICAN COLLEGE OF MEDICAL GENETICS**
10 DR. KORF: I appreciate this opportunity.
11 I'm a little disadvantaged because our
12 board is meeting as we speak and that means, Number
13 1, I didn't hear the comments that preceded and,
14 Number 2, I've only had a few moments to vet all of
15 this through the board. So I apologize for the fact
16 that I'll read but I think it would be a way to make
17 this done more quickly.
18 So, the American College of Medical
19 Genetics as a professional society representing
20 clinical and lab geneticists and genetic counselors
21 we recognize that genetic testing is playing an
22 increasing role in the delivery of medical care for
23 both rare and common disorders. Genetic tests
24 differ widely in terms of clinical validity and
25 utility. There are some instances, especially in

1 tests for rare disorders, where the validity of a
2 genetic test is obvious, as in the case for a
3 chromosome abnormality.
4 Another instance is the interpretation of
5 some variants are substantially more challenging and
6 in some cases, in fact, a particular variant might
7 only be pathogenic in a specific circumstance
8 determined by genetic background or environmental
9 exposure making it difficult or impossible to
10 ascribe a definitive phenotype to the variant.
11 The challenges are even more complex in
12 studying the genetics of common disorders where
13 clinical validity and utility may be less clear,
14 knowledge of genetic contributions to health and
15 disease are far more incomplete, and where the
16 information is likely to be used by practitioners
17 and the public with little experience in working
18 with genetic test data.
19 The medical genetics community, including
20 clinicians, counselors and lab geneticists, are
21 accustomed to working together to provide up-to-date
22 information on the interpretation of tests related
23 to rare Mendelian and chromosomal disorders.
24 Substantial progress has been made in making genetic
25 tests available for diagnosis of rare disorders and

1 providing expert advice on interpretation of genetic
2 changes that may be unique to an individual.
3 Conducting clinical trials to establish the clinical
4 validity of some of these variants will be daunting
5 and often will be impossible. Any system that
6 requires this level of evidence on clinical validity
7 for genetic test data on rare disorders is more
8 likely to impede than to promote the responsible use
9 of genetic testing in patient care.
10 Imposing a regulatory system on genetic
11 testing for rare Mendelian and chromosomal disorders
12 will likely have serious unintended detrimental
13 consequences. Interpretation of genetic test data
14 for these rare disorders is the core of medical
15 genetics practice and we believe it should be
16 recognized as such.
17 Genetics of common disorders presents a
18 different set of issues. Here a large scale
19 population-based approach is necessary and the
20 potential for misinterpretation and even misuse of
21 data is greater than for rare disorders. There is
22 also less of an existing infrastructure to vet the
23 validity and utility of genetic test data related to
24 multi-factorial disorders and hence a greater need
25 to bring order to the process, answering or at least

1 commenting on the first question. If the registry
2 were to stage its efforts to approach genetic test
3 data ACMG would suggest beginning here.
4 Inclusion of information about costs of
5 testing, addressing another point, might well be
6 useful for the consumer but could be a difficult and
7 even misleading form of data to obtain. Testing
8 laboratories often have contracts with specific
9 providers or insurance companies making it difficult
10 to know the true cost of a test. Cost of testing
11 will also be a moving target in the years to come
12 converging on whole genome approaches where the cost
13 of interpretation is likely to far exceed the
14 incremental cost of performing a test.
15 So, in summary, ACMG suggests that if GTR
16 employs a phased approach that it begin with the
17 genetics of common complex disorders.
18 ACMG is eager to work with its membership
19 and with the larger medical community to integrate
20 new knowledge of genetics and genomics into medical
21 practice.
22 We appreciate this opportunity to comment
23 on the GTR and look forward to working with the NIH
24 to use our expertise to ensure that the best quality
25 data on genetic tests are available to the

1 professional and public communities.
2 Thank you.
3 (Applause.)
4 DR. FOMOUS: Thank you, Dr. Korf.
5 Our next speaker is Dr. Elaine Lyon, who
6 will provide comments on behalf of the Association
7 of Molecular Pathology.
8 **ELAINE LYON, Ph.D.**
9 **ASSOCIATION FOR MOLECULAR PATHOLOGY**
10 DR. LYON: The Association for Molecular
11 Pathology appreciates the opportunity for further
12 discussions of elements for the GTR.
13 We provided written comments previously
14 based on a survey from AMP membership and we will
15 refer to them here.
16 In response to Question Number 1 regarding
17 which genetic tests should be included in the first
18 phase, as an intent of the GTR is to facilitate
19 research, AMP believes that the GTR should address
20 those tests that are most likely to achieve this
21 goal, namely new clinical tests translated from the
22 genome-wide association studies, pharmacogenomics or
23 tests that are offered from sole source providers.
24 In response to Question Number 2 regarding
25 clinical utility information, individual

1 laboratories are responsible for understanding the
2 clinical utility of their tests as a care
3 requirement. However, for tests for which the
4 majority of providers generate the same or similar
5 results, the clinical utility can be addressed most
6 efficiently in a centralized manner rather than
7 having each laboratory submit clinical utility data.
8 We recommend that clinical utility be provided by
9 experts in the field, as well as professional
10 societies, such as AMP, ACMG, ASCO, and the CDC's
11 EGAP and AHRQ reviews. A format similar to the
12 existing gene reviews is easily accessed and
13 readable. Other reviews are available in Europe,
14 such as Orphanet that includes clinical utility
15 summary reports.
16 In response to Question Number 3 regarding
17 cost information in the GTR, AMP notes that cost and
18 price are two different issues and we will address
19 them separately.
20 Laboratory costs are based on price of
21 reagents from manufacturers, labor, which can vary
22 based on location of the laboratory, and other costs
23 such as royalties, equipment, depreciation, overhead
24 and other expenses. Based on our survey, only 23
25 percent of respondents were willing to provide the

1 cost of the testing. Most respondents consider cost
2 to be confidential information.
3 With respect to the price of the test,
4 contracts with various payers reflect a negotiated
5 price that is often quite different than the list
6 price. Thus there is no one price the respondent
7 can list easily. In addition, most tests are
8 currently paid by federal payers in accordance with
9 a fee schedule of method based staffing codes.
10 Based on our survey, only 52 percent of respondents
11 were willing to provide CPT codes.
12 As part of academic, hospital or
13 institutional settings, some laboratories may not
14 know the actual costs, billing prices or
15 reimbursement of the tests they produce. These may
16 be managed by administrative units.
17 We believe that the NIH should respect the
18 user's right not to disclose cost and price
19 information. This is essential to the GTR's
20 credibility.
21 In response to Question Number 4 regarding
22 misinterpreting information in the registry,
23 sections containing definitions and hyperlinks to
24 other sources of relevant information will encourage
25 and facilitate proper understanding of the

1 information provided but as any information can be
2 misunderstood, misinterpreted or misused, AMP
3 recommends that proprietary information not be
4 included in the GTR. The GTR will be most useful if
5 it remains a scientific resource.
6 In response to Question Number 5 regarding
7 audiences with varying technical expertise, a
8 majority, 88 percent, of survey respondents
9 indicated that the genetic test registry would be
10 most relevant for healthcare providers and other
11 laboratories. Notably only half of the respondents
12 felt that the current content of the GTR would be
13 relevant for genetic research. Other elements,
14 approach and format in the registry designed for
15 diagnostic or treatment oriented information will be
16 very different than a registry intended for genetic
17 research or for public education.
18 The GTR must differentiate between the
19 goals of each potential audience. We question
20 whether this can be achieved by a single product.
21 This dichotomy is evident in the NIH's own disease
22 information website wherein the data available is
23 different for the general public and the medical
24 community and differentiated upfront in the menu
25 selection. Effort to distinguish the intended

1 audience seems warranted.
2 Thank you for the opportunity to respond
3 in this public meeting and for consideration of our
4 comments. AMP respectfully offers our assistance in
5 designing a practical, useful genetic test registry
6 that will be beneficial to all stakeholders.
7 Thank you.
8 (Applause.)
9 DR. FOMOUS: Thank you, Dr. Lyon.
10 Our next speaker is Mr. Andrew Faucett
11 from Emory School--Emory University School of
12 Medicine.
13 **W. ANDREW FAUCETT, M.S.**
14 **EMORY UNIVERSITY SCHOOL OF MEDICINE**
15 MR. FAUCETT: I would like to thank Dr.
16 Fomous, Patterson and Ostell for the opportunity to
17 share my thoughts about the Genetic Testing Registry
18 and how to make it an effective tool for health care
19 providers and consumers.
20 These comments come from my personal
21 experience in genetic test translation, quality
22 assessment and healthcare provider education over
23 the past ten years. Today I am not speaking for any
24 government agency or professional society.
25 From 2005 until this summer I was one of

1 the leaders in a program funded by the NIH Office of
2 Rare Disease Research to increase the translation of
3 genetic tests from research to clinical care. The
4 Collaboration, Education and Test Translation or
5 CETT program was created by NIH/ORDR and multiple
6 partners, including the American Society of Human
7 Genetics, the American College of Medical Genetics,
8 the Center for Disease Control and Prevention,
9 Genetic Alliance, and others. The primary goal of
10 the program was to facilitate the development of
11 clinical tests for rare genetic conditions. An
12 important secondary goal was to develop a
13 transparent way to ensure that these tests were
14 ready for the clinical arena and to work with the
15 research and laboratory communities to develop the
16 best tests that would meet the needs of the clinical
17 and patient communities.
18 I believe there are two components of the
19 CETT program that could be adapted by the Genetic
20 Testing Registry and would benefit the registry. In
21 the CETT program each test was evaluated by an
22 external review board comprised of medical
23 geneticists, nongenetic health care providers,
24 researchers, laboratory experts and patient
25 advocates. Each member provided an important

1 viewpoint in this review process. The group
2 reviewed each proposed test for its scientific merit
3 and potential impact on the patient. In almost all
4 reviews the submitting laboratory was provided
5 feedback that improved the test. Some of the labor
6 directors were initially unsure of this process but
7 the majority of them commented that the process was
8 very helpful and the feedback provided was
9 important. If done in the correct educational
10 spirit this process works well.
11 The Genetic Testing Registry should
12 consider developing an operational test review
13 process utilizing a similar panel of experts. Once
14 the laboratory community becomes familiar with the
15 process they will likely find it helpful. As a
16 health care provider and potential patient using
17 genetic testing, I would like to know that a genetic
18 test has been reviewed by an independent group. If
19 a test has not been reviewed that does not mean I
20 would not use the test, I would probably want more
21 information from the laboratory before ordering the
22 test. I know the FDA is developing a review process
23 and if that happens in a timely fashion I would
24 encourage the FDA to use a similar process and
25 include the research, medical, laboratory and

1 patient communities in the test assessment process.
2 The second lesson from the CETT program is
3 a process to determine potential clinical utility.
4 Almost all genetic tests offered today lack data to
5 confirm clinical utility. If we require clinical
6 utility before a test is released, many important
7 genetic tests may never be developed. Also having a
8 checkbox in the registry about clinical utility
9 would rarely be informative because it would be
10 blank most of the time.
11 It is possible to ask about potential
12 clinical utility. In the CETT program we asked the
13 applicants to develop two diagnostic and treatment
14 pathways, one without the test and one with the
15 test. Did the test change the diagnostic or
16 treatment pathway? The development of these
17 pathways was discussed with the researchers and
18 often the researchers could provide information to
19 reinforce the impact of the test on a pathway. In
20 some cases the test meant that the patient could
21 avoid invasive risky procedures. In other cases the
22 test provided additional information which could
23 help with prognosis. And at a minimum, the test
24 often reduced the time to diagnosis or the
25 diagnostic odyssey, thus reduced the number of

1 clinical visits and often reduced the total cost of
2 diagnosis.
3 The GTR should consider developing
4 categories of potential clinical utility which could
5 be applied to tests in the registry based on an
6 assessment of diagnostic and treatment pathways.
7 Examples might include avoidance of invasive
8 testing, improved disease description, shortened
9 diagnostic timeline, recurrence risk information.
10 By engaging the research and laboratory
11 communities in this discussion, the ability to
12 collect additional information to prove clinical
13 utility will likely occur. We found in the CETT
14 program that researchers often did not understand
15 the type of information that was needed--that needed
16 to be collected to support clinical utility. When
17 involved in the discussion researchers were
18 sometimes able to provide information or adapt their
19 research to collect some of the needed information.
20 Collecting the information to support
21 clinical utility will require the input of the
22 research, laboratory, clinical and patient
23 communities. It is not possible for the
24 laboratories to do this independently.
25 In closing, I believe the Genetic Testing

1 Registry should consider creating review boards
2 including researchers, geneticists, general health
3 care providers and the patient community, and it
4 should consider using a model of potential clinical
5 utility based on diagnostic and treatment pathways.
6 Thank you.
7 (Applause.)
8 DR. FOMOUS: Thank you, Mr. Faucett.
9 Our next speaker is Ms. Sharon Terry who
10 will provide comments from the Genetic Alliance.
11 **SHARON TERRY, M.A.**
12 **GENETIC ALLIANCE**
13 MS. TERRY: Thanks very much.
14 For Question 1, a phased approach,
15 priority should be given to tests that have the
16 highest impact for the public's health. Certainly
17 diagnostic tests for single gene disorders are low
18 hanging fruit for testing the robustness of the
19 system and we would look to the system to handle
20 this immediately and with competence. Following
21 this pilot, we would recommend NIH tool the registry
22 to meet the emerging regulatory needs, as well as
23 those developers, providers and consumers. FDA will
24 likely proceed with a risk-based schema for
25 oversight and so tests associated with diagnosis

1 and/or treatment related decisions should be in the
2 registry early on.
3 To Question Number 2, clinical utility:
4 This data element should be as objective as possible
5 obviously but every source has its limitations and
6 biases. These limitations should be as transparent
7 as possible. It's not simply a matter of clinicians
8 providing this information since they don't have
9 technical evidence or haven't done the necessary
10 reviews in some cases. The most obvious source for
11 clinical utility evidence is the published
12 literature.
13 Commercial providers of tests should be
14 required to indicate available peer reviewed
15 literature associated with the test. Beyond that,
16 professional societies that engage in an assessment
17 of tests to create guidelines, test developers, both
18 academic and industry, and payers are all possible
19 sources of evidence. Commercial developers, anyone
20 selling a test or a testing service, are sometimes
21 the only source of clinical utility, and they may be
22 running registries and amassing data. It is
23 probable that Phase IV monitoring and adverse event
24 reporting will be the responsibility of test
25 manufacturers and so GTR will want to amass this

1 data from them as well.
2 The GAPPNet initiative is preparing to
3 support the GTR by generating evidence reviews and
4 data that can link to the registry and create a more
5 robust data-source for genetic tests.
6 Patients often look for informational
7 utility, which is a more multifaceted usefulness
8 that is sometimes not reflected in a test clinical
9 utility determination alone.
10 Question 3 to cost: Defining cost will be
11 very important. Does this mean cost of goods,
12 commercial cost, gross cost, net cost, et cetera,
13 and how will those be measured to ensure some
14 comparability? We believe it will be very
15 beneficial to capture costs in some agreed upon
16 manner since the issues of coverage and cost are
17 important to the entire ecosystem of genetic
18 testing.
19 The benefits would be transparency,
20 leveling effect, price control pressures and
21 consumer pressures. The risks could be profit
22 margins for the companies, discordant information
23 access. The bigger companies could compete and
24 attempt pure market access, which could trigger
25 antitrust or monopoly issues.

1 The challenges: This will be the most
2 transient information, since it can change at any
3 time in response to many pressures. This will be a
4 unique data element to monitor and manage. The
5 turnover and life cycle will eclipse anything else
6 in the registry. One way to alleviate some of this
7 is to create pricing bans that could put tests into
8 buckets. Categorizing the information would be
9 useful for navigating past antitrust and monopoly
10 issues, and for provider and consumer comparisons.
11 From the patient and provider perspective,
12 providing cost information can help in determining
13 whether a patient can afford tests out of pocket
14 that may not be covered by their insurance. It
15 allows them to weigh the cost of different methods
16 and different laboratories so they can choose a
17 service that might be more affordable.
18 To Question Number 4, the safeguards for
19 misunderstanding, the registry is not going to
20 create marketplace stupidity. That already exists.
21 (Laughter.)
22 In fact, there will be less
23 misunderstanding, misinterpreting and misuse with a
24 transparent registry. The registry--further, the
25 test developer's attorneys, both the academic and

1 industry, will be conservative about making claims
2 about treatment decision making. The registries
3 existence does not mean consumers can choose a test
4 and order it; a medical professional is still
5 required for the practice of medicine. In fact, the
6 transparency that the GTR will provide will mitigate
7 to some extent the risk of harm.
8 The registry is ultimately organizing the
9 long tail and providing access to informational
10 utility, demonstrating, disclosing, compiling.
11 Informational management is clearly a challenge, and
12 the education must be a part of the endeavor for
13 both providers and consumers. The NIH has an
14 opportunity to bring order to a health care
15 marketplace and empower providers and consumers in
16 the process. This may set a precedent for the
17 cottage industry that is medicine today.
18 To Number 5, explaining the GTR to various
19 audiences: This will be an interesting and exciting
20 challenge. It may be a good pathway to improving
21 the public's health literacy level. Pilot testing
22 of the registry in various communities could help to
23 pinpoint in the registry the data that may be at
24 risk for misinterpretation or misunderstanding.
25 Forecasting these problems is possible for a few of

1 these items such as cost, clinical utility and the
2 reason for certain data fields being empty.
3 It's also important that this information
4 be tailored to reach audiences with varying levels
5 of experience and genetic literacy levels. There
6 are many partners for the NIH to engage: Health
7 professional societies; consumer and disease
8 advocacy organizations; regulatory and oversight
9 bodies; umbrella coalitions of the labs; and direct
10 to consumer testing companies that have spent
11 millions of dollars on understanding how to explain
12 these tests to the public.
13 Surveillance of the use of the GTR will
14 also be critical for understanding its impact on
15 test ordering and decision-making. Careful tracking
16 of GTR use will be necessary to determine the impact
17 of its use.
18 \ It will be important to provide users with
19 additional resources to help them interpret and
20 understand the data provided in the GTR. NCBI has
21 the capacity to provide link outs for data elements
22 that have additional resources and descriptions to
23 increase the value of the information for those who
24 may not be able to interpret it at face value.
25 From a patient perspective we appreciate

1 that the aggregation of the data in the GTR might be
2 considered onerous by both the laboratories and
3 perhaps by NIH itself but we also know how onerous
4 it is to live and die with these diseases and so we
5 appreciate the NIH's efforts on our behalf.
6 Thank you.
7 (Applause.)
8 DR. FOMOUS: Thank you, Ms. Terry.
9 Our next speaker is Dr. Misha Angrist, who
10 will provide comments from Duke University.
11 **Misha Angrist, Ph.D.**
12 **Duke University**
13 DR. ANGRIST: Thank you.
14 I want to make two points that come out of
15 my experience preparing a case study in 2008-2009 on
16 the effects of gene patents on diagnostic testing.
17 The case I prepared was on long QT syndrome, a rare
18 but significant cause of sudden cardiac death,
19 susceptibility to which can be inherited in either
20 autosomal dominant or autosomal recessive fashion.
21 This work was done for the late great Secretary's
22 Advisory Committee on Genetics, Health and Society,
23 may it rest in peace.
24 The first point concerns variants of
25 unknown significance. Perhaps my antennae are

1 poorly calibrated, perhaps I am hanging around with
2 the wrong crowd but I hear a lot of talk about
3 direct to consumer genetic testing and how the tests
4 offered by this renegade band of evil start ups
5 lacks clinical validity. That is to say some or
6 most of these company's tests are not strongly
7 predictive of the presence or absence of disease.
8 We can argue about the significance of this but it
9 is undeniably true. That said, it makes one wonder
10 is this issue peculiar to DTC genetic testing for
11 complex traits or does it also affect testing for
12 Mendelian disorders?
13 In the course of preparing the long QT
14 study I interviewed a prominent cardiologist off the
15 record. When I asked him about his use of
16 commercial long QT testing this is what he said:
17 "Here is the dirty little secret. I tend not to
18 order genetic tests for long QT because it opens up
19 a can of worms. More than half of people with
20 mutations never have a cardiac event. Ten percent
21 of probands have two mutations. Genetic testing in
22 these cases doesn't tell you a lot about phenotype.
23 When you take people with nonspecific symptoms and
24 do genetic testing what you end up with is a person
25 who has a variant of uncertain significance."

1 Without question, long QT testing has
2 benefitted thousands of patients but my point is
3 this: The clinical genetics community must be clear
4 about the limitations of every test it offers,
5 whether marketed directly to consumers or not. It
6 should go out of its way not to give the impression
7 that testing for Mendelian disorders is simple,
8 definitive and always yields unequivocal answers.
9 When we surveyed long QT patients and
10 family members on line several expressed shock
11 and/or dismay that the suite of presumptive gold
12 standard genetic tests for their condition had added
13 little or nothing to their risk profile for sudden
14 cardiac death. Of course, this phenomenon is not
15 unique to long QT. The BRCA genes that confer
16 susceptibility to hereditary breast cancer are
17 littered with variants of unknown significance.
18 More than 1,400 have been reported through 2007 and
19 one in 14 women who receive BRCA testing are found
20 to carry such a variant.
21 I, therefore, believe that every test
22 listed in the GTR should include information about
23 yield, about clinical validity and about what sorts
24 of probabilistic expectations patients and
25 clinicians should have for getting meaningful

1 results.

2 The second point is a broad call for

3 transparency and a plea for test providers to view

4 the GTR not as a threat, not as a burden but as an

5 opportunity. Again I take you back to 2008 when the

6 Duke Center for Public Genomics was gathering

7 information from and exchanging views with long QT

8 test providers at the behest of SACGHS. At the time

9 PGX Health, a subsidiary of Clinical Data, basically

10 had a monopoly on long QT related intellectual

11 property. The company had exclusively licensed

12 patents on the major long QT susceptibility genes

13 from the University of Utah. PGX Health had not

14 shared its long QT mutation data openly, had

15 published few peer reviewed papers on the subject,

16 and had declined to disclose any specifics regarding

17 its patent state. We let it be known that we

18 thought that this was unfortunate. It seemed to us

19 that it was neither good business practice nor in

20 the interest of long QT patients and their at risk

21 family members. So what happened?

22 In 2008, PGX Health announced it would

23 make its mutation data public. In 2009-2010 PGX

24 Health and Mayo Clinic scientists published three

25 peer review cardiac channelopathy (ph) mutation

1 compendium papers based on large numbers of
2 patients. More than in the previous five years
3 since the test was launched. And a few months ago
4 in its 2010 10K form clinical data included an
5 extensive three page list of its IP holdings. When
6 I saw this, my jaw hit the floor. This is not to
7 flatter ourselves and to say that Duke played a
8 significant role in bringing about these remarkable
9 gestures of openness by clinical data. I imagine
10 competition had something to do with it but for the
11 purposes of this discussion that doesn't matter.
12 The point is that the company took these brave steps
13 and the sky didn't fall. Not only that, the entire
14 long QT community can now benefit from having
15 unfettered access to this information. I would
16 argue that if clinical data can do it then so can
17 every other genetic test provider. If done right,
18 the GTR offers the perfect avenue to make these
19 sorts of disclosures regarding mutation data and
20 intellectual property holdings the norm rather than
21 happy anomalies.
22 Thank you.
23 (Applause.)
24 DR. FOMOUS: Thank you, Dr. Angrist.
25 And now our next speaker is Dr. Sherri

1 Bale from Gene DX.

2 **SHERRI BALE, Ph.D.**

3 **GeneDX**

4 DR. BALE: Good morning.

5 My name is Sherri Bale and I am a board

6 certified medical geneticist.

7 Since March of 2000 I have been the

8 President and Clinical Director of GeneDx, a

9 clinical diagnostic laboratory specializing in the

10 development and performance of molecular diagnostic

11 testing in rare hereditary disorders. GeneDX serves

12 the community of patients with rare disorders

13 through their genetic counselors, their geneticists

14 and other physicians.

15 My comments will address points 2 and 4 on

16 the question list.

17 As a lab providing genetic testing, GeneDX

18 is a potential submitter of data to the GTR, and it

19 is of significant concern to us that the curation of

20 submissions that is currently being performed by

21 board certified clinical geneticists and genetic

22 counselors associated with GeneTests be maintained

23 as GeneTests is inactivated and its data

24 transitioned into the GTR.

25 The GTR will be most useful to all

1 stakeholders if the high quality of information
2 currently available through GeneTests, and inclusion
3 of only tests that are valid for the purpose of
4 diagnosis of hereditary disease in the medical
5 setting, is maintained. Thus it is my opinion that
6 information about the clinical validity of a
7 submitted test is best obtained, evaluated, and
8 determined by an appropriate professional review
9 panel consisting of board certified genetics
10 professionals, rather than test developers and/or
11 test providers. It is critical that only those
12 tests that achieve the highest level of utility for
13 the diagnosis of patients with genetic disease are
14 represented in the GTR. As this information is
15 expected to be used for the clinical management of
16 patients and that impact the some of the most
17 important decisions a family will ever make, only
18 the highest quality medically-relevant genetic tests
19 should be represented in the Registry.
20 Thus, those tests that are based solely on
21 associations, as defined in the
22 epidemiology/statistical sense, and identified
23 through retrospective population case/control or
24 cohort studies, should not be listed in the GTR,
25 unless there is prospective data available that

1 support the hypotheses generated by the association
2 studies that can be evaluated by appropriately
3 trained and board certified genetics professionals.
4
5 These reviewers should be responsible for
6 evaluating the utility of the test in the diagnosis,
7 management, and genetic counseling of patients with
8 genetic disorders. The exclusion of tests from the
9 GTR that fail to meet the criteria of high clinical
10 utility and validity is essential. While this level
11 of stringency may lead to the exclusion of many
12 direct to consumer tests that are currently on the
13 market and are based solely on population risk
14 analysis, animal studies or *in vitro* functional
15 assays, their inclusion could lead to the incorrect
16 assumption by the non-cognoscente that these tests
17 have specific medical implications for a specific
18 tested individual when that is a false conclusion.
19 I propose that three levels of genetic
20 tests exist for the purpose of this discussion:
21 1) Medically-relevant genetic tests with
22 high clinical validity and utility, as determined by
23 qualified board-certified genetics professionals.
24 Such tests should be included in the GTR.
25 2) Tests that are being offered by a non-

1 CLIA certified laboratory in support of ongoing
2 research about the relationship of a disease to a
3 gene. Such tests should be clearly labeled in the
4 GTR, as they are currently identified in GeneTests,
5 as research level testing.
6 3) Tests based solely on population risk,
7 animal or *in vitro* functional studies should not be
8 included in the GTR.
9 *Caveat emptor* is not appropriate when
10 dealing with the genetic health of patients and
11 families.
12 Thank you.
13 (Applause.)
14 DR. FOMOUS: Thank you, Dr. Bale.
15 Our next speaker is Ms .Barbara Harrison,
16 who will provide comments on behalf of the National
17 Society of Genetic Counselors.
18 **BARBARA HARRISON, M.S.**
19 **HOWARD UNIVERSITY**
20 MS. HARRISON: Good morning.
21 Good morning.
22 (Chorus of good morning.)
23 Wake up.
24 My name is Barbara Harrison and I'm here
25 representing the National Society of Genetic

1 Counselors or NSGC.

2 NSGC appreciates the work of the NIH to
3 make information about genetic tests available to
4 the public. We strongly recommend that the NIH
5 include an official representative from the NSGC in
6 ongoing discussions about the development of a genet
7 test registry. I am sure you agree that genetic
8 counselors are a critical stakeholder in the GTR and
9 we appreciate that the NIH has genetic counselors
10 already working on this project. However, an
11 official NSGC representative would represent the
12 collective interests of genetic counselors without
13 influence from other perspectives such as employers,
14 colleagues in specific practice areas, and
15 allegiance to other institutions.

16 Before addressing No. 4 I want to briefly
17 comment on Question No. 5. In the NSGC's initial
18 response to the RFI, we recommended a focus on one
19 audience rather than trying to serve multiple
20 audiences. The needs of consumers, researchers,
21 providers, payers and policy makers have some areas
22 of overlap but there definitely are some critical
23 differences.

24 For example, clinicians may value and
25 correctly interpret accuracy and analytical

1 sensitivity and specificity, but consumers may
2 misinterpret some of these data elements as clinical
3 validity. Non-genetics professionals may also
4 incorrectly infer validity.
5 Simply providing a definition of these
6 data elements, as suggested by your Question No. 5,
7 is insufficient and will be difficult to develo9p
8 for an audience with widely varying levels of
9 genetics expertise and knowledge. If the NIH is
10 committed to serving multiple audiences, the NSGC
11 strongly recommends development of different
12 interfaces for different users.
13 In direct response to Question No. 4
14 regarding safeguard to prevent misunderstanding,
15 misinterpreting and misusing information, the NSGC
16 does not believe that adequate safeguards exist to
17 prevent misinterpretation or misuse of information
18 if the GTR is intended to be used by multiple
19 audiences. However, assuming the project moves
20 forward, we would recommend a prominently displayed
21 disclaimer throughout the site stating that
22 inclusion of attest does not imply any type of
23 regulatory review. Inclusion of a data element
24 about the applicability and status of regulatory
25 oversight would be appropriate for each test.

1 Lastly, peer review by genetics experts
2 would also allow for an avenue of mediation of the
3 most significant risks.
4 Thank you for this opportunity to provide
5 additional input today and we would like to provide
6 additional comments through another forum.
7 Thank you.
8 (Applause.)
9 DR. FOMOUS: Thank you, Ms. Harrison.
10 Our next speaker is Dr. Jan Nowak, who
11 will provide comments on behalf of the College of
12 American Pathologists.
13 **JAN NOWAK, M.D., Ph.D.**
14 **COLLEGE OF AMERICAN PATHOLOGISTS**
15 DR. NOWAK: It's clear to CAP members who
16 frequently serve as medical directors of clinical
17 laboratories and who are charged with the immediate
18 oversight and usage of all clinical tests that the
19 registry's definition of genetic testing goes well
20 beyond what most of us think as genetic and the
21 breadth of this registry under that definition has
22 not been fully comprehended. Therefore, we believe
23 that a very structured and deliberate approach be
24 pursued to make this registry truly useful.
25 CAP has a long record of working to ensure

1 the quality of diagnostic tests. As the major
2 hospital laboratory accrediting organization in the
3 United States, we have confidence that all tests,
4 including genetics tests performed in CAP accredited
5 laboratories, achieve the highest standards required
6 of a clinical test. Our program of laboratory
7 inspection, proficiency testing, and standards
8 development is designed to accommodate novel
9 technical and biological innovations as needed to
10 advance clinical care.
11 There are some tests, however, that fall
12 outside the purview of the CAP laboratory
13 accreditation program. We increasingly encounter
14 tests performed by sole source laboratories that do
15 not avail themselves of the extensive professional
16 peer review and inspection processes available
17 through the college's accreditation program. Many
18 of these tests are genetic in the broad definition
19 provided, often utilizing novel emerging
20 technologies and not infrequently claim to portend
21 the future of personalized medicine. If they remain
22 outside the traditional clinical testing processes,
23 such tests will remain problematic. Consequently,
24 we suggest that this test registry focus initially
25 on tests that fall outside the traditional clinical

1 laboratory oversight systems.
2 We believe these are the tests that are in
3 greatest need of demonstrated quality assurance, of
4 demonstrated clinical utility and, indeed, if they
5 are as forward reaching as some claim, would be the
6 test of greatest research interest. We would
7 consider in this category those tests performed by
8 one or a few laboratories in such a manner that
9 eludes the level of safeguards--
10 (Microphone squeal.)
11 Okay. I made my point.
12 (Laughter.)
13 So we would consider in this category
14 those tests performed by one or a few laboratories
15 in such a manner that eludes the level of safeguards
16 established by the CAP accreditation program. We
17 include in this category tests whose interpretation
18 is dependent on proprietary information that is not
19 available to professional peer review and critique.
20 We include in this category tests which are
21 performed without the kind of medical oversight of
22 usage and interpretation that is required of the
23 laboratory medical director by CAP standards.
24 Development of a registry that can
25 accommodate these tests would immediately address

1 many of the concerns that have been raised about
2 genetic tests but which we do not believe are in
3 question for the vast majority of tests already in
4 clinical use. We would suggest that after this
5 initial phase due consideration can be given to the
6 gradual and logical introduction of other test
7 categories into the registry in a manner that will
8 be useful and not duplicate previous or processes
9 already in place.
10 The development, understanding and vetting
11 of clinical utility evidence is a multidisciplinary
12 process that encompasses laboratory professionals,
13 researchers and the clinicians who order these tests
14 for their patients. Their experiences and
15 observations, whether structured or anecdotal, are
16 captured in the medical scientific literature where
17 they are presented for insight, comment, critique
18 and the ever present challenge of validation and
19 refinement or rejection.
20 Further, clinical validity and clinical
21 utility are linked to the various clinical contexts
22 in which a test may have relevance so any model
23 whereby each individual lab is required to submit
24 clinical utility evidence would be problematic. It
25 is difficult to capture this dynamic process in any

1 single index or entry and, indeed, it's critical
2 that this process not be diminished by
3 oversimplification. Misunderstanding of information
4 in the GTR is of great concern to the College of
5 American Pathologists. The medical directors of
6 clinical laboratories have responsibilities that
7 extend from appropriate test selection for a patient
8 specific clinical context to correct interpretation
9 and reporting to the ordering physician. Test
10 directories and registries can be an important tool
11 in that process but unless these are constructed in
12 such a manner and with sufficient safeguards there
13 is potential that misunderstanding and misuse could
14 compromise patient safety or, indeed, create harm.
15 That possibility gives us pause.
16 There is an opportunity here and we
17 strongly recommend that NIH establish appropriate
18 monitors to document that such misunderstandings,
19 misinterpretations, misuses or other harms are not
20 occurring through the use of this registry.
21 I thank you for your attention.
22 (Applause.)
23 DR. FOMOUS: Thank you, Dr. Nowak,
24 especially for putting up with the technical
25 difficulties.

1 Our next speaker is Mr. Jason DuBois, who
2 will make comments on behalf of the American
3 Clinical Laboratory Association.
4 **JASON DUBOIS**
5 **AMERICAN CLINICAL LABORATORY ASSOCIATION**
6 MR. Dubois: Good morning.
7 The American Clinical Laboratory
8 Association is pleased to have the opportunity to
9 present this statement to the NIH on its plan to
10 develop a Genetic Test Registry. ACLA is an
11 association representing clinical laboratories
12 throughout the country, including local, regional
13 and national laboratories. Many of ACLA's members
14 offer extensive menus of genetic tests. As a
15 result, we have a direct interest in the development
16 of the registry.
17 As stated in our comments in response to
18 the Request for Information, we believe that a
19 registry will provide easy access to information
20 about genetic tests and could increase the
21 understanding of users, including patients and
22 providers, about the valuable information that these
23 tests offer.
24 Our comments today focus largely on the
25 issue of what mechanisms can be used to provide

1 materials that explain the Genetic Test Registry's
2 data elements to audiences with varying technical
3 expertise.
4 One of the tools ACLA recently developed
5 that would be useful as a mechanism for deploying
6 the GTR is a framework for its Laboratory Test
7 Compendium to provide the ability electronically to
8 exchange a Directory of Services. This effort aims
9 to simplify the exchange of data related to test
10 Directories of Service and associated orders, while
11 increasing their functionality and value within
12 compatible electronic medical record systems. Using
13 the Compendium Framework benefits NIH by
14 standardizing the process by which laboratories
15 would make data submissions to the Genetic Test
16 Registry.
17 Development of a standard Laboratory Test
18 Compendium Framework addresses and defines how
19 information that differs from laboratory to
20 laboratory, such as the following, easily can be
21 exchanged among all provider laboratories used by a
22 client and the client's EMR system: The codes used
23 to order laboratory tests and the description of the
24 laboratory test; the nature of the test, profile,
25 single observation, et cetera; the potential reflex

1 observations; the specimen requirements; the
2 processing priorities, meaning the ability to order
3 as stat, routine or other priorities; a list of
4 analytes, including the Lab Order Code; and the
5 additional clinical and useful information required
6 at the time of ordering.
7 In July of 2010, formal ownership of this
8 framework called eDOS was relinquished to Health
9 Level Seven International, an ANSI accredited
10 standards developer. In September, eDOS was
11 successfully balloted at HL7, with plans to move
12 towards certification in the near future.
13 Finally, ACLA recognizes that the
14 Compendium Framework may have to be modified to meet
15 the needs of NIH to facilitate data submissions. As
16 such, ACLA stands ready to work with NIH on
17 modifications to help facilitate use.
18 Thank you.
19 (Applause.)
20 DR. FOMOUS: Thank you, Mr. DuBois.
21 Our next speaker is Dr. David Letterman--
22 Ledbetter--I'm sorry about that--who recently joined
23 Geisinger Health System.
24 **DAVID LEDBETTER, Ph.D.**
25 **GEISINGER HEALTH SYSTEM**

1 DR. LEDBETTER: I get that a lot.
2 Thank you.
3 To maximize the utility of the GTR I would
4 suggest the proposal go beyond the current
5 repository of information about genetic tests to
6 also include or be closely linked to a repository of
7 genetic test results.
8 There are several good pilot models that
9 represent examples of this sort of model. You've
10 heard from Andy Faucett this morning about the CETT
11 program. I'd like to briefly describe a large
12 voluntary genetic testing collaboration and data
13 sharing project that may be a useful model for some
14 elements of the Genetic Test Registry. The ISCA or
15 International Standards for Cytogenetic Arrays
16 started in 2007 and now includes over 145 clinical
17 cytogenetics testing labs performing whole genome
18 cytogenetic microarray analysis or CNV, copy number
19 variation analysis. Three international workshops
20 have been held bringing together experts and
21 stakeholders in clinical genetics genetic
22 counseling, clinical genetic testing labs, genomics,
23 bioinformatics and patient advocacy groups to
24 develop the goals of the consortium.
25 The first work product from the consortium

1 was a consensus statement in the May issue of the
2 *American Journal of Human Genetics* recommending that
3 chromosomal microarrays should be the first tier
4 test in the genetic evaluation of any child with
5 unexplained developmental disabilities replacing the
6 previous gold standard of G-Banded Karyotype
7 analysis in the postnatal setting. The same
8 recommendation has now been put forward by the
9 American College of Medical Genetics in an updated
10 practice guideline posted in September.
11 The goals of the consortium are:
12 To develop standards for genotypic and
13 phenotypic data associated with cytogenetic arrays.
14 Develop standards for the appropriate
15 clinical indications for testing and for
16 interpretation of CMV results, to contribute CMV and
17 phenotype data to a central freely available
18 database housed at NCBI utilizing dbGaP and dbVar.
19 The database currently contains data from about
20 20,000 clinical array test results with a goal of
21 200,000within two years.
22 To develop data analysis and curation
23 methods to create new knowledge regarding the
24 functional and clinical significance of CMVs in the
25 human genome, thus creating a learning CMV database

1 and registry, much like learning electronic health
2 record models that will continue to improve patient
3 care by improving our diagnostic, prognostic and
4 therapeutic approaches to patients with specific
5 CMVs.
6 About 20 percent of children with
7 unexplained developmental disabilities are found to
8 have a single pathogenic CMV responsible for their
9 condition. In a significant subset of these
10 children a deletion is found to include other genes
11 with known disease associations such as deletion of
12 a tumor suppressor gene yielding very high cancer
13 risk. Examples include p53 retinoblastoma, Von
14 Hippel Lindau and others that prompts lifesaving or
15 clinically significant medical management decisions
16 and referrals. This leads to the somewhat ironic
17 situation that children with developmental
18 disabilities often disadvantaged in terms of access
19 to critical medical resources and care are now among
20 the first beneficiaries of truly personalized
21 predictive medicine as a consequence of their whole
22 genome genetic test results.
23 The next challenge will be to integrate
24 this whole genome data into electronic health
25 records in a seamless and useful way. This also

1 overlaps with the goals of the eMerge Network funded
2 through the National Human Genome Research Institute
3 to integrate genomics data and the HER data for high
4 throughput genomics research.
5 In the near future significantly more
6 genomic data will be generated during the course of
7 routine patient care than through large scale
8 genomics research projects. I expect this to be
9 accelerated and facilitated if the lawsuit against
10 Myriad challenging the validity of human gene
11 patenting continues to proceed and overthrows human
12 gene patents.
13 The lessons learned from routine clinical
14 testing by whole genome cytogenetic arrays may be a
15 useful model for other whole genome technologies
16 such as exome sequencing or whole genome sequencing
17 and developing methods for data submission from
18 routine clinical lab testing and development of a
19 learning database registry that creates new
20 knowledge regarding the functional and clinical
21 significance of sequence variation in the context of
22 phenotypic information on very large datasets from
23 patient and normal populations.
24 In summary, our experience in setting up a
25 voluntary database and registry for whole genome

1 cytogenetic array testing in the clinic lab
2 indicates clinical labs and clinicians are happy to
3 submit patient data to a central freely available
4 learning database registry with some guidance
5 provide regarding IRB protocols and if data
6 submission does not interfere with busy clinical
7 work flows.
8 Industry partners are eager to support the
9 educational activities and to develop software tools
10 that allow clinicians and clinical laboratories to
11 collect and submit phenotypic and genotypic data to
12 a central database in a seamless single click
13 fashion. Data analysis and curation remains
14 challenging but is an opportunity for significant
15 new knowledge generation that will rapidly
16 contribute to improved patient care through a
17 learning database registry process.
18 The Genetic Testing Registry can play a
19 major role in promoting data sharing and
20 collaboration among the large network of clinical
21 genetic testing labs to accelerate our understanding
22 of the functional and clinical significance of
23 sequence and structural genetic variation in the
24 human genome and rapidly translate that knowledge to
25 improve patient care.

1 Thank you.
2 (Applause.)
3 DR. FOMOUS: Thank you, Dr. Ledbetter.
4 Our next speaker is Dr. Lisa Baumbach-
5 Reardon from the Miller School of Medicine at the
6 University of Miami.
7 **LISA BAUMBACH-REARDON, Ph.D.**
8 **MILLER SCHOOL OF MEDICINE**
9 **UNIVERSITY OF MIAMI**
10 DR. BAUMBACH-REARDON: I would like to
11 thank the organizers very much for the opportunity
12 for public comment.
13 I'm an associate professor at University
14 of Miami. I'm speaking for myself from
15 approximately 20 years of life in the trenches in
16 terms of molecular genetic testing from running a
17 diagnostic lab to having to arrange genetic testing
18 for a variety of inherited neurological disorder, as
19 well as running an active translational research lab
20 in gene discovery, as well a member of ASHG and the
21 College.
22 I want to begin by stating that GeneTest
23 and Gene Review has been an invaluable resource for
24 the genetics community. There's hardly a time in
25 the clinic that we don't access GeneTest or we don't

1 refer a patient to Gene Reviews, and I am very glad
2 to see that Gene Reviews will be included in the new
3 plans for the GTR.
4 It also has been very helpful in the
5 GeneTest to be able to see labs as a research
6 setting, as well as labs that are throughout the
7 world for rare diseases.
8 As we go on to develop a Genetic Testing
9 Registry, I certainly applaud NIH in this very
10 important effort and you hear many of the challenges
11 and complexities that have been brought up to date.
12 I want to bring up two additional
13 concerns.
14 One is that we should have increased usage
15 of laboratories throughout the world. They are
16 sometimes the only source or one of the few sources
17 for rare disease testing, as well as research
18 laboratories. Now this, of course, brings up a
19 problem if we're going to have CLIA testing and CAP
20 certification for all the things to be included in
21 GTR and this is one thing that has to be considered.
22 In many cases--I'll take limb girdle
23 muscular dystrophies, for example, there are only a
24 few labs in the country and other places in the
25 world that are offering the kind of testing that is

1 needed and we have to have a resource for that.
2 My second concern is that many academic
3 laboratories have grown up being providers of rare
4 diseases. Homes for these kinds of tests, although
5 they often provide also common disorders, they are
6 often either the sole source or the expert in these
7 areas. And when we test for rare diseases as you've
8 heard these concerns brought up before today, they--
9 we don't often have the data about prevalence,
10 incidence and the other--some of the other datasets
11 that are being called for, and so we need to
12 consider this.
13 In regards to specific questions that
14 we're to answer today, I think if we are to take a
15 phased-in approach it should be taken with the rare-
16 -with the common diseases first. Those are also
17 commonly tested by many laboratories.
18 I fully agree with Dr. Korf's comments
19 that were at the beginning of the session in regards
20 to testing for rare disease and rare variants.
21 Again, more importantly, due to our niche,
22 to consider what to do with new state of the art
23 approaches. Things like NextGen sequencing, exome
24 sequencing, CMVs, and how to use this kind of
25 information when the clinical utility is still not

1 know and there is no FDA validation for this and yet
2 many laboratories are moving to these technologies.
3 And in reference to Question No. 3 I think
4 that cost should not be included. They are often
5 subjective. They are dependent on contract
6 arrangements, Medicare/Medicaid, and they are going
7 to be changing constantly.
8 In closing, I would hope that the GTR as
9 this goes forward carefully considers the very
10 careful comments that have been prepared by the
11 ASHG, the ACMG, the NSGC, Genetic Alliance, and AMP
12 in reference to this and encourage them to use
13 members of these communities to move forward in this
14 process.
15 Thank you.
16 (Applause.)
17 DR. FOMOUS: Thank you, Dr. Baumbach-
18 Reardon.
19 Our next speaker is Mr. Robert DiTullio,
20 who will make comments on behalf of the Advanced
21 Medical Technology Association.
22 **ROBERT DiTULLIO**
23 **AdvaMED**
24 MR. DiTULLIO: Good morning.
25 My name is Robert DiTullio and I'm here

1 representing AdvaMed DX.
2 AdvaMed DX member companies produce
3 advanced IVD tests that facilitate evidence-based
4 medicine, improve quality of patient care, enable
5 early detection of disease and reduce overall
6 healthcare costs. Functioning as an organization
7 within AdvaMed, AdvaMed DX is the only multi-faceted
8 organization that deals exclusively with issues
9 facing IVD companies both in the U.S. and abroad.
10 We appreciate NIH's effort to conduct this
11 public meeting to seek stakeholder input on specific
12 questions in the implementation of GTR. We believe
13 a database of genetic tests as called by SACGHS
14 would be a useful tool to provide information to the
15 public regarding genetic tests available today.
16 Assuring the accuracy and usefulness of
17 such information will be critical for its public
18 utility. We urge NIH to coordinate with FDA to draw
19 on information from its current manufacturer
20 registration and listing databases which will help
21 encourage participation in the GTR.
22 We recognize both the immensity and the
23 potential value of this undertaking and appreciate
24 the importance of the questions NIH raises for the
25 design of this database.

1 To Question 1: AdvaMed supports the
2 inclusion of tests that involve human chromosomes,
3 DNA and genes. Such a scope would be appropriate
4 and would enable NIH to establish the database and
5 ensure that the information provided is accurate,
6 reliable and relevant to end-users. Once the
7 database is established as an accurate and reliable
8 source of information, expansion to a larger scope
9 may be considered.
10 With respect to the information that will
11 be made available by NIH, we believe appropriate
12 safeguards must be applied to verify the accuracy
13 and reliability of the information entered before
14 any information is made accessible for use. Until
15 appropriate systems and safeguards are in place to
16 ensure verification of the information submitted to
17 GTR, we recommend that NIH focus its collection only
18 on the following information: Test name,
19 manufacturer or institution name and contact
20 information, premarket review regulatory status
21 (that is indicating whether the test has been
22 cleared or approved by the FDA), and an option to
23 link to test data that has already been
24 appropriately reviewed, such as FDA product
25 summaries or clinical test results available via

1 clintrials.gov on which NIH has been collaborating
2 with the FDA.
3 Additional data fields that could be add
4 later might include indications for use, warnings
5 and limitations, and specimen requirements. Such an
6 expansion, however, should not be attempted until
7 processes have been put into place to verify the
8 accuracy of the voluntarily entered information,
9 these processes are needed to assure that
10 information provided to the public, most
11 significantly patients and their physicians, is
12 trustworthy and is likely to be relied upon by these
13 parties in shaping healthcare decisions.
14 Accordingly, we urge a judiciously phased approach
15 in implementing the database.
16 To Question 2: AdvaMed supports the
17 principles of evidence-based medicine. Patients,
18 providers, manufacturers and other stakeholders
19 share an interest in assuring that adequate and
20 accurate empirical information is available to guide
21 public health care decision making.
22 AdvaMed supports the posting of published
23 peer reviewed studies that contain information about
24 clinical utility. Studies or data that are not
25 published and subject to peer review should not be

1 included in the database. If the information is
2 limited to published peer review studies then any
3 party should be able to post such information in the
4 database. To the extent that such studies are
5 considered questionable by a party, NIH should
6 provide a mechanism to allow for denoting such a
7 concern so that members of the public who use this
8 information understand the issues that have been
9 raised in relation to such studies.
10 To Question 3: AdvaMed does not support
11 the inclusion of cost as an element in the database.
12 The core purpose of NIH's initiative should be to
13 provide accurate, timely and robust clinical
14 information that will inform patients and their
15 physicians in making clinical decisions. Cost
16 information is outside the scope of this purpose.
17 If NIH includes cost as a data element
18 then the question is what information would be
19 provided in the database and to what end? Whose
20 costs would be recorded in the database and who is
21 the audience for this information? Costs can be
22 defined in many different ways and any cost variable
23 is likely to reflect substantial variation. Would
24 NIH collect data on costs incurred by payers,
25 laboratories or patients? Depending on the answer

1 the data would be completely different.
2 Further, any of this cost information
3 mentioned above is likely to vary significantly and
4 change rapidly as economic variables change leading
5 to a significant burden of keeping the information
6 up-to-date.
7 I'm last. I should be able to go longer.
8 (Laughter.)
9 Well, okay, sorry I ran over.
10 We appreciate the opportunity to share our
11 comments as efforts are underway to develop the
12 framework of this new initiative.
13 Thank you.
14 (Applause.)
15 DR. FOMOUS: Thank you, Mr. DiTullio.
16 And our last speaker is Dr. Edward McCabe.
17 **EDWARD McCABE, M.D., Ph.D.**
18 **AMERICAN SOCIETY OF HUMAN GENETICS, PAST-PRESIDENT**
19 DR. McCABE: Thank you for permitting me
20 to speak to you today.
21 I'm speaking as past president of the
22 American Society of Human Genetics, the largest
23 genetics professional organization with nearly 8,000
24 members.
25 We feel that the quality and accuracy of

1 the information in the GTR are paramount. Let me
2 cite as an example an analogy with the *Physician's*
3 *Desk Reference* or *PDR for Pharmaceuticals*. The HHS
4 Secretary's Advisory Committee on Genetic Testing
5 discussed a PDR for genetic tests. We know that the
6 PDR has oversight to ensure a higher level of
7 quality and accuracy of information than one sees
8 and hears in direct-to-consumer media claims. We
9 urge the GTR to learn from the experience of the PDR
10 and its interaction with the FDA.
11 In addition, the discussion of the GTR
12 appears to be focused on DNA tests. I would urge
13 you to consider phenotypic tests such as biochemical
14 genetic analyses so that these tests are not
15 forgotten and their quality and accuracy are not
16 compromised.
17 Thank you.
18 (Applause.)
19 DR. FOMOUS: We thank all the commenters
20 for their insights and for taking time form their
21 busy schedules to share their thoughts with us
22 today.
23 We'll now move on to the panel discussion
24 and Dr. Kathy Hudson, the NIH Director for Science
25 Outreach and Policy, will moderate this discussion

1 and she will introduce the panelists.

2 **PANEL DISCUSSION**

3 **MODERATOR: KATHY HUDSON, Ph.D.**

4 **DEPUTY DIRECTOR OF SCIENCE,**

5 **OUTREACH, AND POLICY, NIH**

6 DR. HUDSON; Thank you, Cathy.

7 Why don't I go ahead and invite the

8 panelists to come up and take a seat up here?

9 I'm going to offer very brief

10 introductions and then we have asked each panelist

11 to summarize what we've heard about each of the

12 questions and then offer their own thoughts and

13 reflections. I think as we go through each question

14 after each assigned panelists has offered their

15 reflections and summarized the public comments on

16 that question, I think we might engage in a little

17 bit of panel discussion on each question as we go

18 through. And then if we have time at the end, and

19 we are running early, we can open up for questions

20 from you all as well.

21 So I'm going to introduce the panelists in

22 the order in which they will be speaking. First is

23 Dr. Robert Nussbaum, who is the Chief of the

24 Division of Medical Genetics at the University of

25 California, San Francisco. He has been involved in

1 research on various genetic syndromes, including
2 Lowe Syndrome and genetic risk for Parkinson's
3 disease. Before going to UCSF he was a part of the
4 intramural program at the National Human Genome
5 Research Institute.
6 Second is Vicki Pratt, who is the Chief
7 Director of Molecular Genetics at Quest Diagnostics
8 Nichols Institute. She also holds faculty
9 appointments at Duke University and the University
10 of North Carolina in Greensboro.
11 Third is Misha Angrist, who is an
12 Assistant Professor of the Practice, which is the
13 most unusual name for an assistant professor that
14 I've encountered so we'll look forward to hearing
15 what that means exactly, at Duke University
16 Institute of Genome Sciences and Policy. His
17 research includes issues at the intersection of
18 genomics and society.
19 And then fourth is David Mongillo, who is
20 vice-president of the American Clinical Laboratories
21 Association where he oversees their activities.
22 Before going to ACLA he headed the Professional
23 Regulatory Affairs Division of the College of
24 American Pathologists.
25 And then fifth is Myrl Weinberg, who is

1 the president of the National Health Council where
2 she focuses on health, medical research, long term
3 care, and issues that affect people with chronic
4 diseases and disabilities, and their caregivers.
5 And then last is Dr. Joanna Mountain, who
6 is the Senior Director of Research at 23 and Me.
7 Her areas of research include research about genetic
8 interactions with environment, culture and ethical
9 issues in genetics and biology, and concepts of race
10 and ethnicity.
11 So those are our panelists and, as I've
12 mentioned, we have assigned each panelist a question
13 so the questions--it would be nice if they could
14 come back up on the screen. This is telling me that
15 I have to enter a password which, of course, I don't
16 know.
17 Oh. Okay.
18 So maybe, Bob, as you begin, you can
19 remind the folks here what the first question is and
20 then share with us your summary and thoughts.
21

1 ***QUESTION 1: BASED ON AN ANALYSIS OF RFI COMMENTS***
2 ***AND OTHER OPERATIONAL ISSUES, NIH IS CONSIDERING A***
3 ***PHASED APPROACH TO DEVELOPING THE GTR IN WHICH SOME***
4 ***TYPES OF TESTS WOULD BE ELIGIBLE FOR EARLY ENTRY IN***
5 ***THE GTR AND OTHER TYPES OF TESTS WOULD BE ADDED***
6 ***LATER. IF NIH ADOPTS THIS APPROACH, WHAT CRITERIA***
7 ***SHOULD BE USED TO DETERMINE WHICH GENETIC TEST***
8 ***SHOULD BE INCLUDED IN THE FIRST PHASE OF THE GTR,***
9 ***AND WHAT TYPES OF TESTS WOULD MEET THESE CRITERIA?***
10 **ROBERT NUSSBAUM, M.D.**
11 **CHIEF, DIVISION OF MEDICAL GENETICS**
12 **UNIVERSITY OF CALIFORNIA, SAN FRANCISCO**
13 DR. NUSSBAUM: Good morning.
14 Just a quick disclaimer: I am not a
15 stockholder, owner or participant in any testing
16 company of any kind.
17 The first question has to do with what
18 should be the types of tests that would be eligible
19 for early entry into the testing registry and what
20 types of tests would be added later.
21 I was really struck by the fact that we
22 have two completely opposite ends of a spectrum of
23 opinions this morning. And where do we start? I
24 think maybe Dr. Bale and Ms. Terry were pretty
25 strong in recommending that we start with single

1 gene disorders of very high penetrance with known
2 clinical validity and utility. On the other hand, I
3 thought I heard Dr. Korf and Dr. Nowak both say
4 that--for example, Dr. Korf saying, "We should start
5 with common complex results" and Dr. Nowak saying,
6 "Those that fall outside current lab accreditation."
7 So the idea being do we start with those tests
8 where we know the most or do we start with those
9 tests where we think there's the most need of trying
10 to explain and perhaps figure out something about
11 their quality?
12 I also thought it was interesting this
13 morning--that was a good point that Dr. McCabe
14 brought up about the fact that we've been thinking
15 about human chromosomes, DNA and variance all this
16 time and that perhaps some thought should be given
17 to biochemical testing.
18 The second issue I thought that was
19 brought up that was, I think, important to think
20 about that was also reflected in the different
21 comments had to do with whether the registry should
22 really truncate its elements only to those tests
23 with proven clinical validity and utility, which
24 would require some sort of professional curation, or
25 whether we should actually include things that

1 perhaps don't have currently proven clinical
2 validity and utility and perhaps give them a rating,
3 something similar to what AHRQ does. An A through F
4 rating where the A would be documented best gold
5 standard sort of evidence-based support versus all
6 the way down F, which is the evidence actually
7 argues against the validity or the utility of a
8 particular test. And with many tests, probably the
9 vast majority, falling somewhere in the C and D area
10 where perhaps there's some expert opinion one way or
11 the other.
12 And then the other issue, which was not
13 brought up this morning really but I think needs to
14 be addressed--it was kind of implied or referred to-
15 -which is are only genetic tests that are considered
16 medical to be considered to be included in the GTR?
17 What if a provider provides genetic tests but
18 disclaims any utility of the test for either
19 diagnosis or management? Would that be considered
20 a genetic test that should go into an NIH registry?
21 We certainly have plenty of such direct-to-consumer
22 testing where that disclaimer is written all over
23 the homepage of the provider. Should that be there
24 or not?
25 My own personal feeling is that I would

1 really come down on the side of starting with those
2 tests where we have the most information for
3 clinical validity and utility. I share the concern
4 that having an NIH hosted registry that doesn't have
5 tests in it are the ones that we feel most confident
6 about would actually be a mistake. I'm very
7 concerned about starting out with tests where
8 there's a tremendous amount of controversy and
9 almost no information as to whether they are useful
10 or not.
11 I do think, however, that as we add more
12 tests--this is--so what I first said is what I
13 thought would be best to begin with. As we do add
14 more tests, which certainly needs to be done, I
15 would recommend that we use some sort of rating
16 scale similar to what AHRQ uses or other sorts of
17 Cochran evidence-based so that in very large bold
18 letters in a very simple way we can at the current
19 level of knowledge based on what I think should be
20 professional curation, we can give some rating to
21 the value of the test.
22 Finally, the last question I'd like to
23 bring up--the last issue, one that I'd like to hear
24 some comments about--is I'm not sure that we can
25 actually include clinical utility at all in a

1 Genetic Test Registry. Utility is something which
2 is really in the eye of the beholder. Patients,
3 their relatives, their physicians, the third party
4 providers, all different people have different
5 definitions of what it means for a test to have
6 clinical utility. I think it's a highly clinical
7 medical decision about whether something has utility
8 or not.
9 Validity is another story. I think
10 validity does need to be addressed and should be
11 addressed but I would like to split utility and
12 validity.
13 DR. HUDSON: So would other people on the
14 panel like to comment on Bob's comments?
15 And, specifically, maybe I'll start with
16 asking Bob a question.
17 When talking about having some sort of an
18 assessment of a test that's entered into the
19 registry, whether it be a letter grade or whatever,
20 that's going to be based on some sort of an evidence
21 review or some sort of expert opinion. It seems to
22 me that the process of those kinds of reviews have
23 been time intensive and resource intensive, and is
24 that sort of what you have in mind or could we have
25 an expedited sort of a review process for entry if

1 that's the direction we went?
2 DR. NUSSBAUM: Yes. I would be open to
3 some sort of expedited approach but I think leaving
4 out a professional evaluation by people who really
5 know what these tests are about I think is a
6 mistake. This registry has the potential for having
7 a very large impact on medical care and I just don't
8 think we can--I hate to say this but I just don't
9 think we can do it on the cheap. If we're going to
10 do it, we should do it right.
11 DR. HUDSON: Myrl?
12 MS. WEINBERG: Yes. Just so you have a
13 little bit of context. So our organizations, the
14 members of my group, National Health Council, there
15 are over 100 but 50 are core constituency and are
16 advocacy organizations like Cancer, Heart, Diabetes
17 and Alzheimer's. We do a lot of focus group
18 research around the country.
19 I just wanted to make the point that when
20 we've gone out with people and really asked them
21 about these kind of situations we know there's a lot
22 of misunderstanding and not good understanding of
23 the terminology and how some of these tests should
24 be used but I wanted to really accentuate the point
25 that was just made about it's an individual

1 circumstance. And what we hear all the time is that
2 individuals want their circumstances, their personal
3 life circumstances, and their preferences for their
4 treatment taken into account and they want the
5 ability to interact and ask questions. So I think
6 that's an important point to make when we think
7 about clinical validity, in whose mind.
8 DR. ANGRIST: I think that raises the
9 question of who gets to decide who does the
10 evaluating. So there seems to be consensus--well,
11 maybe consensus is too strong a word. There seems
12 to be a notion that they should be board certified
13 medical geneticists but is there a case to be made
14 for a more IRB-like process where you have someone
15 from the community present, someone perhaps--or some
16 ones outside of the clinical genetics community?
17 DR. HUDSON: So I'm going to go back to
18 you again, Bob. If you were going to have an
19 assessment of data coming in and you were going to
20 leave out clinical utility information, then would
21 the assessment of information going in only be
22 genotype/phenotype correlation evidence?
23 DR. NUSSBAUM: Yes. I mean, you know, the
24 validity itself is going to be challenging. I mean,
25 just in the last five days there were two articles.

1 One in *JAMA* and the other in *The New England*
2 *Journal of Medicine*, neither one of which are
3 particularly piker journals. I mean, these are
4 pretty serious journals. One of which is saying
5 that Clopidogrel genotype is useless for figuring
6 out whether it's going to--whether Plavix is going
7 to be useful or not; the other that the CYP2C19
8 genotype is useful and it gives a hazard ratio of 50
9 percent if you're not a good metabolizer. I mean,
10 that's what you would think would be a simple
11 validity question. Is the phenotype of response to
12 this drug predictable from a single locus genotype?
13 Utility--I mean, the arguments that flow
14 around ApoE testing, you ask ten people and you'll
15 get 15 different opinions as to whether ApoE testing
16 is useful or not. And people say, "Useful for
17 what?" Useful for prediction, useful for deciding
18 about what I'm going to do with my life, useful for
19 deciding whether I'm going to sell my house and buy
20 a condo in the city? I mean, what do you mean by
21 useful?
22 And so I really think utility is a very
23 personal thing and should be decided--in essence,
24 utility should be decided between a patient, the
25 patient's family and the patient's physicians or

1 counselors.

2 As far as the other issue about who should

3 be the expert, I sort of like that set model with

4 having a group of people involved. The community

5 involvement in trying to decide whether something is

6 valid or not--I'm not sure whether there is that

7 much input that would come from there but having

8 researchers and lab people and clinicians--not

9 necessarily just medical geneticists. I mean, in a

10 lot of areas, for example for Rett testing for MEN2,

11 the best guidelines have been published from the

12 American Thyroid Association. It's a very clear,

13 very strong set of guidelines for giving this

14 mutation in this particular site, what's the risk

15 for X, Y or Z. So I wouldn't restrict it to board

16 certified clinical geneticists but I certainly think

17 that people who have knowledge of genetic disease

18 need to be involved in a test-by-test basis.

19 DR. HUDSON: So if you were to leave out

20 clinical utility data per se, would you want to see

21 as a medical geneticist--would you want to see a

22 link to the citations of published papers that are

23 related to utility and linked to professional

24 guidelines and other sorts of resources in a sort of

25 non-value ladened way?

1 DR. NUSSBAUM: Yes, I think that's a great
2 idea. Yes, I think that would be--the more links
3 and the more information I think the better so
4 that's fine. Yes.
5 DR. HUDSON: Comments from other folks?
6 MR. MONGILLO: Just briefly. I want to
7 thank Dr. Nussbaum for what I think is one of the
8 more articulate statements to be made on clinical
9 utility. I think you said it in a way that's clear.
10 Coming from someone who is doing this work and the
11 fact that it has been so elusive for so long in
12 terms of defining what it is and how you can
13 possibly validate utility, I just appreciate that
14 and thank you for that.
15 DR. HUDSON: Before we leave this
16 question, I also was struck by the wide range of
17 perspectives about what kinds of tests should be
18 entered into the Genetic Testing Registry at the
19 get-go versus later on. Joanna, I'd be interested
20 in your thoughts on sort of the well-validated/well-
21 known tests versus less known/less well validated
22 tests in terms of their utility for inclusion in the
23 registry.
24 DR. MOUNTAIN: Sure.
25 Thanks, Kathy.

1 I tend to agree that, you know, we have to
2 prioritize and getting the information in on the
3 tests that everyone, in general, agrees on the
4 validity at least is of top priority. The reason to
5 go beyond that as soon as possible is because people
6 are interested in the tests they hear about via news
7 magazines or whatever or wherever their sources are.
8 If the GTR can be a place to go for people to find
9 out that there are limitations, why not? I mean,
10 that to me is a very valuable contribution that the
11 GTR could make.
12 So, you know, as representing 23 and Me
13 hopefully my perspective is more broad than that but
14 one of the values of providing highly multiplexed
15 genetic test where we provide information on over
16 100 disorders is we don't profess that many of these
17 are highly--that they have high utility. They are
18 interesting. We don't have the pressure to say you
19 absolutely need this information. This is there for
20 you if you are interested in that particular
21 disorder or disease.
22 And I think the same thing can go--the
23 more people understand that there are genetic
24 components to disease that aren't highly penetrant
25 the better. I think, you know, to give people a

1 broader scope of genetic tests is a key component to
2 the educational effort that this registry can make.
3 So if we say only do the Mendelian or
4 highly penetrant variants that is basically
5 perpetuating a biased view of what genetics is and I
6 think we can go beyond that.
7 DR. HUDSON: Thank you.
8 There was also a diversity of points of
9 view about how to handle tests that are still sort
10 of in the research arena and I'm not sure that we
11 have a particularly robust definition of when
12 something is in the research arena and when it's
13 not. I think in gene tests, you know, there's a
14 CLIA/non-CLIA distinction but that doesn't really
15 help because many tests that are being used in
16 research are performed in a CLIA certified
17 laboratory. So I would be interested in people's
18 perspectives about the utility of including tests
19 that are the subject of ongoing research and what
20 the value would be and what the potential risks of
21 that inclusion would be and how you would identify
22 what would be the demarcation so that you could
23 alert GTR users if they were research versus
24 clinical tests.
25 Thoughts?

1 DR. PRATT: I guess one of my thoughts is
2 in a research situation you never report the results
3 back to the patient so if you are participating in
4 research, whether under Dr. Ledbetter's
5 recommendation of sort of the array CGH model that
6 that data is gathered so to say but that data never
7 goes back to the patient in a research model. In a
8 clinical model you're actually giving data back to
9 the patient.
10 DR. HUDSON: Bob?
11 DR. NUSSBAUM: Well, you know, it all
12 depends on what you mean by research. I mean, there
13 are certainly research that's done on the results of
14 clinical lab testing. The example that was provided
15 earlier about publishing papers based on the results
16 of the PGX health testing for long QT. That was
17 clinical laboratory testing and those were results
18 that were given back to the patients and yet
19 somebody scanned those and published what one would
20 consider to be a research paper based on that.
21 So I would say that you have to define
22 what you mean by research. So, first of all, is the
23 person giving consent for clinical testing or is the
24 person consenting for a research protocol. That's
25 the major fork in the road for me.

1 We do have patients who are in research
2 protocols who have had CLIA approved testing and get
3 the results back so that I don't think is as
4 distinguishing as it needs to be. I would say it
5 really has to do with as to whether you--what is the
6 patient consenting? Is the patient consenting for
7 research or consenting for a clinical test? And
8 that--you know, that I think could be put right up
9 front.
10 And having the availability of research
11 testing I think is extremely important. I'm sure
12 that Sharon Terry--Ms. Terry would agree that having
13 in the Genetic Test Registry the availability of
14 patients being able to look and see, oh, someone is
15 actually working on my disorder and is interested in
16 doing some testing or research on it would be really
17 valuable.
18 DR. ANGRIST: I would echo that. I think
19 to some extent it should be a function of demand.
20 So when I was a graduate student in the 1990s
21 studying Hirschsprung's disease and we learned that
22 RETT was a major susceptibility gene, we got CLIA
23 certification so that we could return results to
24 patients because we had meaningful information and
25 we were hamstrung without it, and families

1 appreciated it.

2 DR. MOUNTAIN: Kathy, I wanted to just

3 emphasize I don't see a distinct--a clear dividing

4 line between clinical and research tests. I think

5 all of them could be considered to be potential

6 components of research. You know, across the board

7 there's always more to be done, Phase 4 trials and

8 so on. So it's really a matter of whether--of the

9 clinical validity, I think, that puts you into that

10 particular bend where there is let's say greater

11 confidence in clinical validity.

12 DR. HUDSON: So on the topic of clinical

13 utility information and its value and being included

14 in the registry, the second question turns on that.

15 Vicki, do you want to share with us your

16 thoughts and a summary of what you heard?

17

1 ***QUESTION 2: SEVERAL RFI RESPONDERS, WHO ARE***
2 ***POTENTIAL DATA SUBMITTERS, NOTED THAT IT MAKES***
3 ***MORE SENSE FOR CLINICIANS AND GENETICS PROFESSIONALS***
4 ***TO BE THE SOURCE OF CLINICAL UTILITY EVIDENCE RATHER***
5 ***THAN TEST DEVELOPERS AND/OR TEST PROVIDERS. GIVEN***
6 ***THAT DATA SUBMITTERS ARE UNLIKELY TO HAVE CLINICAL***
7 ***UTILITY INFORMATION, HOW IS THIS DATA ELEMENT BEST***
8 ***ADDRESSED IN THE GTR?***
9 **VICTORIA PRATT, Ph.D.**
10 **CHIEF DIRECTOR, MOLECULAR GENETICS**
11 **QUEST DIAGNOSTICS NICHOLS INSTITUTE**
12 DR. PRATT: From the summary of what I
13 heard today it seemed like most of the commenters
14 who did discuss this really wanted a centralized
15 database or a centralized repository of the clinical
16 validity data. And it also was clear to me that,
17 whether they stated it or not, they are really
18 looking for some sort of objectivity. So whether it
19 be a board of--a panel of experts under the CETT
20 model or some sort of model that experts are
21 reviewing the data to be able to say a test is
22 clinically valid or not.
23 I do think that raises the concern,
24 though, if a test is so new there may not be enough
25 information and the clinical experts may not be able

1 to have enough information at that point. We see
2 that with the eGAP reviews all the time that maybe
3 there's not enough information. I think in those
4 instances you may just have to have a literature
5 review, some sort of document provided by the
6 laboratories because under CLIA they have to
7 document the usefulness of a test and supporting
8 literature.
9 I also believe that it seemed like there
10 was a lot of--that there's a lot of support, and I'm
11 glad to hear that Gene Reviews is going to continue,
12 and I think that Gene Reviews really is an
13 instructive summary of the clinical validity and the
14 clinical utility of many of the tests that are in
15 GeneTests already.
16 DR. HUDSON: Vicky, as a test provider,
17 can you comment on the interesting proposal that
18 Elaine Lyons made about utility information not
19 necessarily being best provided by an individual lab
20 or an individual test provider but perhaps sort of
21 centrally or as sort of aggregate information that
22 if you're offering testing for X, Y, Z that
23 everybody sort of uses the same standardized
24 language about utility? I think that's sort of what
25 she was--

1 DR. PRATT: As a member of AMP and largely
2 involved in helping shape those comments, so in
3 discussions that Elaine and the group of us at AMP
4 and even within Quest that providing that data over
5 and over again seems like a duplication of effort so
6 that's where we thought whether that's that expert
7 panel that has that review already similar to
8 Orphanet model that these experts already document
9 the clinical validity and the clinical utility so it
10 doesn't have to be reproduced by every laboratory
11 offering X, Y, Z test.
12 DR. NUSSBAUM: I just to go back and say I
13 really would like people to stop talking about
14 clinical validity and utility. There's clinical
15 validity and there's clinical utility. I mean, if
16 you think about something like long QT, I think we
17 have pretty good information about what specific
18 mutations in which genes cause a certain risk for
19 sudden death. That's what I consider to be clinical
20 validity.
21 Now, given that information, whether
22 you're going to put an ICD in, whether you're going
23 to use beta blocker, what the age of the patient is,
24 what the sex of the patient is, these are medical
25 cardiologist decisions that are made, that's

1 utility. I can't imagine you can have that sort of
2 information in the GTR where you're going to put in,
3 oh, if you have two first degree relatives who had
4 sudden death before age 40 then the utility is to
5 put in an ICD but if not, you won't. I just can't
6 imagine it.
7 The validity is a different issue. I
8 think we should separate these apart and speak about
9 them quite specifically and differently.
10 DR. PRATT: I guess, I sort of look at
11 utility under the CETT model that Andy Faucett
12 talked about that what's the usefulness of a test--
13 and I was on the CETT review board reviewing these
14 submissions--that the laboratory because most of all
15 of these were rare disorders would actually look at
16 and say, "Okay. Here's the diagnostic odyssey a
17 patient goes through. If we do this test here is
18 this algorithm. We believe this test is useful."
19 Whether that changes the utility or any medical
20 management of that patient may or may not change but
21 it's still useful for that patient.
22 DR. HUDSON: Other comments?
23 So let's move to question 3. What are the
24 benefits, risks and challenges of including cost
25 information in the GTR?

1 And I should say there were a lot of
2 excellent comments on this, this morning, and I
3 think that when we use the word "cost" in the RFI we
4 misspoke and what we really were talking about was
5 price. So if we could limit our comments to the
6 value or lack thereof of including price information
7 in the GTR.
8 And we're going to have two comments here,
9 Misha and David.
10 ***QUESTION 3: AMONG RESPONDENTS TO THE RFI QUESTION***
11 ***ABOUT INCLUDING A DATA ELEMENT FOR TEST COST, HALF***
12 ***WERE IN FAVOR OF INCLUDING COST INFORMATION AND HALF***
13 ***WERE OPPOSED. WHAT ARE THE BENEFITS, RISKS, AND***
14 ***CHALLENGES OF INCLUDING COST INFORMATION IN THE GTR?***
15 **MISHA ANGRIST, Ph.D.**
16 **ASSISTANT PROFESSOR**
17 **INSTITUTE FOR GENOME SCIENCE AND POLICY**
18 **DUKE UNIVERSITY**
19 DR. ANGRIST: So I went through the
20 written comments a few days ago and tried to divide
21 them into potentially in favor of people who saw
22 value added to including that information and people
23 who either said no or were very dubious. So I
24 should say that I am among the written commenters
25 that am in favor of including price information so

1 my biases are on the table. That said, I think the
2 question is right. It's about 50/50. And the
3 arguments against including cost are essentially--I
4 think you heard many of them recapitulated this
5 morning.
6 Cost is irrelevant to the goals of the
7 GTR. It is hard to define. It's difficult to
8 identify, particularly when you're talking about
9 third party payer information. That's not going to
10 be available. You heard a commenter say that the
11 information will be out of date before it becomes
12 useful. It's not within the scope of a scientific
13 resource, which the commenter presumed the GTR to
14 be. The information is proprietary. One comment
15 was that if we include this information then it will
16 supersede considerations of sensitivity and
17 specificity, which are more important. And I think
18 that covers it. There were several commenters who
19 focused on just how difficult this would be to pull
20 off for various reasons.
21 Those in favor simply focused on the
22 relevance of cost in all of our decisions as
23 consumers, that there should be transparency
24 throughout the GTR. That the cost, as you heard
25 from Sharon Terry, will inform consumer decisions

1 and it will allow patients and health professionals
2 to make targeted comparisons. And the word
3 "comparison" was used many times in the pro-pricing
4 comments. One commenter said that you can't
5 separate price from considerations of utility. And
6 one clinician said, "Listen, I shop around. I
7 routinely save my patients hundreds of dollars. It
8 would be nice if that process ware easier."
9 And as far as the challengers go, I think
10 this goes back to the notion of how do you get this
11 information, how do you calculate it, how do you
12 standardize it, and there was an AMP survey that
13 said, "Listen, only 23 percent of people we ask were
14 willing to even provide this information." And
15 there were concerns that the public would
16 misinterpret it and that again price is constantly
17 in flux. It's sensitive to market forces and payer
18 policies and the like.
19 So I would simply say a couple of things.
20 One is I think we have to ask ourselves as people
21 involved in genetic testing what sort of industry
22 and community we want to be. Do we want to be like
23 pharmacy benefits managers, whose industry is sort
24 of based on the notion of opacity and if you've ever
25 tried to read SEC documents from a pharmacy benefits

1 manager it's kind of like the movie Brazil or Dr.
2 Strangelove.
3 And the other thing is simply what I said
4 during my public comments about IP and mutation
5 data. And I would say that this is an opportunity.
6 So, yes, it's hard to SUs cost but I think it's
7 possible to include a range of costs. Someone
8 without insurance is going to pay the list price and
9 I don't see how that's proprietary information. And
10 I think it's an opportunity for the test provider to
11 say, "Yes, this is an expensive test. It costs
12 $3,000." But in another field, "Yes, we have
13 insurance coverage available. Yes, we have patient
14 assistance for people who can't afford it, don't
15 have coverage and the like."
16 I think to say that the information is
17 irrelevant is paternalistic and that's not something
18 I would want to look Sharon Terry in the face and
19 say, you know, price is really not relevant to you
20 or your hundreds of disease advocacy groups that
21 you're representing. I think it is relevant and it
22 is a function. It does feed into utility.
23 DR. HUDSON: David?
24

1 **DAVID MONGILLO**

2 **VICE PRESIDENT, POLICY AND MEDICAL AFFAIRS**

3 **AMERICAN CLINICAL LABORATORY ASSOCIATION**

4 MR. MONGILLO: That's an excellent
5 summary, I think, of what we heard today but because
6 it's World Series season I guess I heard that the
7 score was 4-1, maybe 4-2 in terms of not including
8 cost or, more appropriately, price as a data
9 element.
10 Essentially what we heard was that there
11 is a major distinction between cost and price and
12 Kathy has already pointed that out. I think,
13 though, that we can't jump to think that price is a
14 simple concept. It's extremely complex. There's a
15 lot of aspects of price. There's an asking price.
16 There's a bid price. There's a fee schedule price.
17 All of these are somewhat--they're all different
18 and they all vary significantly. Multiple variables
19 all go into pricing. Volume will enter into how
20 pricing is done. Geographic area will enter in to
21 pricing and fee for service managed care, whether it
22 is government pricing or not. So price is not a
23 simple concept.
24 But that aside, we really do recognize--
25 and I heard it over and over the purpose, as Dr.

1 Collins started with and that was reiterated through
2 all the presentations, of the Genetic Test Registry
3 are to share information about availability and
4 utility of the test, although I think we're
5 discussing whether utility should be used, provide
6 information about the location or test providers and
7 facilitate genomic test sharing.
8 I really do think that price is not
9 applicable to those kinds of discussions and it is a
10 difficult element to include in a database of this
11 nature.
12 You know, Dr. Terry always brings up very
13 important aspects of patients and their needs in
14 terms of testing and in terms of this case of having
15 some knowledge about what the cost might be or the
16 price might be for these tests. She also brought it
17 up in the context of the larger context of not only
18 this genetic arena and how we move forward in that
19 but in our whole health care delivery. No one would
20 argue that in the price of our health care delivery
21 system there are issues and we have to be thinking
22 about those issues. I happen to believe that the
23 fact that the NIH is moving forward on the Genetic
24 Test Registry will bring a lot of visibility to the
25 component of genetic testing or personalized

1 medicine, which I think in the long run will have a
2 positive impact on the delivery of health care to be
3 able to keep cost in control. But even with that I
4 don't think a registry of this nature should be
5 looked at as something that would address an issue
6 that goes way beyond what this registry's stated
7 purpose is.
8 In terms of the ability for folks who need
9 to know what the cost or price of a test is, I
10 checked with ACLA members before I came here and
11 asked them how they might address that kind of an
12 issue. They would be more than happy to
13 individualize that on a case-by-case basis to
14 provide that information either to the provider
15 that's providing the test or to the patient that
16 needs the test. I really think it can be
17 personalized given all the aspects you pointed out,
18 insurance, no insurance, whether there's some help
19 and things of that nature. So I think that's the
20 answer to that aspect of it.
21 DR. HUDSON: Bob?
22 DR. NUSSBAUM: I am going to make myself
23 unpopular. Is the reason not to put the price up
24 because it's too complicated and there are so many
25 different prices depending on who you are and how

1 you're insured and whether you're a Medical patient
2 and you need to go to a laboratory in California or
3 not? Or is it because the providers of the tests
4 would rather not have that sort of transparency
5 because it's going to produce too much scrutiny of
6 what their pricing structures are?
7 MR. MONGILLO: Thank you, because you
8 allow me to probably make the most important point
9 that has already been made. I don't think--I mean,
10 I don't think anybody would agree that cost
11 comparisons should be the basis for making decisions
12 about whether you allow a test to be ordered or not
13 be ordered. I think it really shouldn't enter in to
14 a large degree as to whether a patient does or
15 doesn't get a test. I think if you don't have
16 insurance and you don't have any way to pay for it
17 you certainly want to know the price or cost of a
18 test but I don't think a provider--and I think
19 that's the reason why we don't price shopping on a
20 genetic test registry for a test. I think that's
21 really one of the reasons why it shouldn't be
22 included in that.
23 DR. NUSSBAUM: Why not? I do.
24 MR. MONGILLO: Well--
25 DR. NUSSBAUM: When I have a patient who

1 has a cardiomyopathy and I need to have the genes
2 screened I take a look at a bunch of different
3 companies and decide which one provides me with the
4 best information for the least money. I mean, and
5 best information includes, for example, I like their
6 reports, I think their reports are thorough and
7 complete.
8 MR. MONGILLO: That's exactly right.
9 DR. NUSSBAUM: I mean, lots goes into it
10 than just the cost or just the price but price
11 certainly plays a role.
12 MS. WEINBERG: Kathy, I don't know if
13 Sharon is still here.
14 I believe that patients and people and all
15 of us want as much information as we can possibly
16 get. And certainly what something costs is a major
17 piece of the decision.
18 I also think, however, that if we're going
19 to have price then we need to--as I will say with
20 other data elements--be incredibly clear about how
21 we're defining price, what the limitations are so
22 that people can understand that if, you know, here's
23 a price but this is what it means, you know, and
24 that you may want to--if we're really doing this for
25 patients and the public to access as well as

1 providers and others, you may want to think about
2 this or go into this particular other place to get
3 additional information. I mean there are ways to do
4 it and still provide enough information to give
5 people a sense of--you know, and some transparency
6 around what will it cost them or their insurer or
7 Medicaid or Medicare. I just think we have to get
8 this out in the open.
9 DR. HUDSON: I would be interested--and
10 maybe, Vicki, you can respond to this question and
11 Joanna as well--for tests that you currently
12 provide, is price information--how readily available
13 is price information? And then, secondarily, how
14 quickly does price information change as compared to
15 some of the other elements in the Genetic Testing
16 Registry about validity and indication and so forth?
17 DR. PRATT: If you are asking me
18 personally what the price of any my tests are, I
19 couldn’t tell you.
20 DR. HUDSON: But could you figure it out?
21 DR. PRATT: I think I would have to go to
22 somebody within Quest but--and what the--there may
23 be a list price. There may be--and all the
24 contracted prices. We have negotiations with
25 everybody--because we provide testing to anybody and

1 everybody that we have negotiated prices for
2 everybody. And what we get paid is totally
3 different than what a list price somewhere in a book
4 somewhere that I don't know where it is. So, I
5 mean, that's why I think it's a little bit
6 irrelevant.
7 I sort of look at this as if you have your
8 prescription and you have your prescription and your
9 doctor writes you a script to go get whatever drug
10 you need, whether it's clopidogrel or whatever,
11 that--I mean, you have a contracted price with your
12 insurance and that's what all the laboratories--or
13 many laboratories have a contracted price with the
14 insurance companies and whatever that list price is,
15 is not what you pay, it's whatever your contract
16 with your insurance is. The test is the same as
17 maybe whatever drug a physician has prescribed you.
18 DR. HUDSON: Joanna?
19 DR. MOUNTAIN: Just to be provocative,
20 there should be a mean price that's paid/received
21 and a range. That--I don't know if that's
22 proprietary but that might be of interest.
23 There is the issue that in many cases
24 health care providers aren't sure whether a test
25 will be covered by insurance so that in talking to

1 their patient and saying, well, you know, hopefully
2 it will be covered, we think it might--you know, so
3 there is some incentive to keep the cost down just
4 in case it's not covered for some reason.
5 So 23 and Me, I would say in terms of
6 price changes, it's probably on the same order as
7 some of the other changes we make so it's not as big
8 a deal to be transparent about that. It's easy for
9 us to be transparent. It's always right there on
10 the web but keeping it up to date I think will be
11 some burden but not overly burdensome.
12 DR. HUDSON: Any other comments on this?
13 DR. ANGRIST: Well, just to follow up on
14 Vicki's pharmacy analogy, it's possible that my
15 doctor writes me a script and then I pull up to the
16 window at CVS and I find out that it's $300 or, you
17 know, I don't have coverage and, you know, there's
18 no co-pay or whatever it is. I think to quote Dr.
19 Evil (?), "I'm just saying y throw me a freaking
20 bone here."
21 (Laughter.)
22 I know people said, you know, "Well, this
23 is too complicated and we should just include a link
24 to the test provider's website." That's fine if
25 that information is readily apparent on that website

1 and is not buried. I mean, I've had experiences as
2 a patient where it has been relatively simple. I
3 call an 800 number and I say, "I don't have
4 insurance. What do you charge for this test?" And,
5 you know, maybe they put me on hold for a minute but
6 it's fairly straightforward. So I think at a
7 minimum we can provide a mechanism of direct route
8 without, you know, a lot of detours to getting
9 patients--and I'm concerned primarily about
10 patients--that information without a runaround.
11 DR. HUDSON: Thank you.
12 Moving now to Question 4--I think this is
13 the question that has most concerned me as we've
14 been developing the Genetic Testing Registry--of how
15 do we make sure that the information is not
16 misunderstood and, most importantly, is not used in
17 ways that could be harmful to patients. So I'd be
18 interested, Myrl, in your summary here of what we
19 have heard and both--and also your own views about
20 this very important topic.
21

1 ***QUESTION 4: WHAT SAFEGUARDS CAN BE PUT IN***
2 ***PLACE TO PREVENT GTR USERS FROM***
3 ***MISUNDERSTANDING, MISINTERPRETING, OR MISUSING THE***
4 ***INFORMATION IN THE REGISTRY?***
5 **MYRL WEINBERG, M.A.**
6 **PRESIDENT, NATIONAL HEALTH COUNCIL**
7 MS. WEINBERG: You know, it's interesting,
8 and I wasn't too surprised, we didn't hear a whole
9 lot from the commenters in relation to Question 4.
10 We did hear some.
11 Dr. DiTullio, he used the word that I was
12 going to use in that as you just think about the
13 entire enterprise that it be perceived and believed
14 to be trustworthy. It doesn't make much to
15 undermine trust for someone, for anyone, and then
16 the whole thing is up--you know, kind of up the
17 question.
18 So I had several points that I believe I
19 heard and that we would certainly bring, and that is
20 as we talk about the information, and I've alluded
21 to this, whether it's the data elements that we look
22 at and make sure that they are standardized, the
23 explanation, the definitions, that they are clear in
24 the way that they are presented, and I have to say
25 upfront I think that anything that we would do to

1 make this more understandable and useful for
2 patients would be probably just as much help for the
3 providers as well.
4 What we suggest often, and we do ourselves
5 all the time, is that on certain aspects of the
6 registry where there's going to be sort of a
7 narrative that there be thought given to what would
8 I say if it were a patient that I knew was on the
9 site right now. What would they want to know
10 upfront? If there's going to be additional
11 information that would be added based on that
12 thought process, what would they want to know if
13 they got to this point, whether it was price and
14 where do I go find out or additional information and
15 how is that presented. I would strongly urge the
16 use of a plain language expert. Plain language
17 experts--many people think of health literacy and
18 plain language and dumbing down. It's not that at
19 all. It's a very rich science and robust
20 international community. These are people that can
21 take information and make it abundantly clear
22 without dumbing it down but presented in ways that
23 are very easily understood, and I think in this case
24 because there are a lot of risks with this registry
25 that it would be worth it to at least pull out

1 pieces that are there for the public and have a
2 plain language expert really go over it and make
3 some suggestions.
4 I think it's critically important when we
5 talk about things like validity to state on the site
6 what is being done to assure validity and what the
7 limitations are. If there is not the ability, which
8 I'd hope there would be, to have independent
9 objective reviews of the validity or they can only
10 go so far then I think we just need to be clear this
11 is what we were able to do but we, you know, still
12 need to find out these things and if there were
13 limitations to the types of review and oversight
14 that we were able to bring. It will take one test
15 one time to have something bad happen and, you know,
16 then the whole thing is tainted. So I think being
17 very clear about what's done but if it can't be
18 done, fine.
19 One of the things that kept coming up in
20 some of the comments was about empty data fields.
21 I'm thinking this is so simple. If it's empty tell
22 them why. If it's this reason because they don't
23 have the data or it's this because the company
24 didn't provide it, say we do not have the data, the
25 company didn't provide it. I mean check a box but

1 don’t leave something empty. It’s so simply to take
2 care of those problems because an empty box is going
3 to raise questions, and you can avoid them, you
4 know, right up front. And I’m sure there are other
5 places where that same approach could be taken where
6 you look at it data element by data element from the
7 patient-public point of view.
8 The last thing I would say is the idea--a
9 couple of people did talk about this--of really
10 piloting the database with different groups, and I
11 know some of that is going on but focus groups
12 piloting with end-users, potential end-users, and
13 that would be people in different situations around
14 the country, people that have different cultural
15 backgrounds, people that have rare diseases, people
16 that have diseases that are not so rare, and having
17 them involved every step of the way. I would even
18 say when you’re looking at validity you need to have
19 people there that represent their point of view.
20 People can be trained in the core competencies
21 needed for them to play a meaningful role. They
22 don’t have to be a token. And I would say every
23 decision making body about the registry should
24 involve people who come representing the patient’s
25 perspective. I just think that in the end it will

1 pay off greatly.

2 And so piloting aspects, NIH has done it

3 with other things in the past, and finding out

4 upfront what words work, what don't, what are the

5 questions. Let them answer questions. I mean, I

6 would say health providers--you probably also--I

7 mean, I'm sure you all appreciate it but including

8 people in the pilots in the focus groups and in all

9 the decision making committees and bodies would be,

10 I think, very productive.

11 DR. HUDSON: Thank you.

12 Go ahead, David.

13 MR. MONGILLO: I think it's clearly

14 important that we have all of the information that

15 has been discussed, the points that were made for

16 the users, and it sounds like there's going to be a

17 lot of interest and intent to make sure they have

18 advice and explanations as to how the Genetic Test

19 Registry is useful for them.

20 I'm thinking that as a--before we get the

21 Genetic Test Registry up and running maybe there

22 should be a submitters' manual. Maybe there should

23 be a lot of discussion with the folks who have to

24 submit the data so that they understand what might

25 be expected for them for these elements and some

1 range of what would be acceptable in terms of what's
2 submitted because if you don't do it upfront I think
3 you're going to have problems with the user as it--
4 you'll have a mixed match of what's submitted and
5 how valuable the information is.
6 So, I know you're talking and we
7 appreciate the fact that you're completely talking
8 to the clinical lab industry about these things but
9 maybe we need to formalize it a little bit more and
10 have more opportunity to think about some kind of a
11 submitters' manual or something like that that is
12 guidance that would help ease that process.
13 DR. HUDSON: Thank you.
14 Other comments?
15 Bob?
16 DR. NUSSBAUM: This is for Jim. So I
17 noticed in your movie--I think a prime example of
18 how we can have misunderstanding, misinterpretation
19 and misusing is a big green checkmark FDA next to a
20 test, which simply means that as a device or as a
21 kit it's approved for its analytic validity. I
22 think we have to pay very careful attention to make
23 sure that that doesn't get misinterpreted to mean
24 great test, highly predictive, extremely useful and
25 we should all go out running and get this test right

1 now because the FDA says it's a great test.
2 DR. ANGRIST: Flowing from that I was
3 struck by Jim's prototype that on the one hand you
4 had very genome browser looking images and
5 descriptions of genes and genomic regions but it
6 also included for more information those sorts of
7 things. So I think that's exactly appropriate that
8 they are going to be a wide range of users and, no,
9 you can't be all things to all people. But I think
10 part of the reason why there weren't many comments
11 on this is because--I'd like to think this anyway.
12 I think the utility of something like this, and I'm
13 sorry to use that word, is that it's self-evident.
14 Just as my IRB meets every month and asks the
15 question about every protocol, do the benefits
16 outweigh the risks, and I think this is clear. And,
17 yes, it's appropriate to be cautious but I think one
18 of the--this is--I'm on my soapbox now. This is one
19 of the ongoing problems with public understanding of
20 genetics is we start from this place of fear and
21 Congressman Stupak saying, "Someone is going to jump
22 off a building." But I think we can do a world of
23 good and that's it.
24 DR. HUDSON: So I was intrigued by the
25 comment from the CAP spokesperson about having a

1 system in place to monitoring misunderstandings or
2 bad things happening. I'm wondering--I was
3 intrigued by the idea but also scratching my head of
4 how would you actually do that and I'd be interested
5 in people's thoughts, if you have any, about how
6 would you monitor sort of adverse events from the
7 GTR out there in the world when it's publicly
8 accessible.
9 Any thoughts? Stumped silent.
10 (Laughter.)
11 DR. ANGRIST: Well, I mean, how do we
12 monitor adverse events from WebMD and things that
13 are publicly--
14 DR. HUDSON: I don't know the answer to
15 that.
16 DR. ANGRIST: --available? I mean, there
17 are all sorts of crazy stuff out there.
18 DR. HUDSON: You're not saying that the GTR
19 is crazy?
20 DR. ANGRIST: No. I'm saying it's at the
21 far end of non-crazy.
22 DR. HUDSON: Okay. So, moving on to our
23 last question: What mechanisms can be used to
24 provide materials that explain the GTR's data
25 elements to audiences with varying technical

1 expertise? And, again, I'm sort of as a preface to
2 this harkening back to comments that Francis made
3 this morning that the primary audience at least
4 initially is for health care providers but certainly
5 with any web-based resource sophisticated users and
6 even unsophisticated users of all stripes are going
7 to be able to access the information so how can we
8 do best to provide good information for them?
9 ***QUESTION 4: WHAT MECHANISMS CAN BE USED TO PROVIDE***
10 ***MATERIALS THAT EXPLAIN THE GTR'S DATA ELEMENTS TO***
11 ***AUDIENCES WITH VARYING TECHNICAL EXPERTISE?***
12 **JOANNA MOUNTAIN, Ph.D.**
13 **SENIOR DIRECTOR OF RESEARCH**
14 **23 AND ME**
15 DR. MOUNTAIN: Well, this follows up
16 really closely on Question 4, I think. I think
17 that's the motivation--primary motivation probably.
18 I mean, I think both in the written and the spoken
19 comments there's an underlying clear call for
20 providing materials to help educate the users
21 because this is a key step towards mitigating the
22 risk of misunderstanding, misinterpreting or
23 misusing the information.
24 And that would be on the part not just of
25 patients or individuals but also health care

1 providers. You know, I really think there's a
2 spectrum, and we can put the lay consumer on one end
3 and the clinical geneticist on the other but I think
4 you have many primary care physicians who are
5 somewhere in the middle or actually cover that whole
6 spectrum in terms of their understanding of
7 genetics. So even if we simply focus on that
8 particular audience I think we're going to have--we
9 have a very broad range of expertise and, therefore,
10 that becomes essential.
11 I think I am concerned that there's some
12 risk of this educational effort being given a lower
13 priority than other components because they've got
14 to get the registry up and going but because of the
15 concerns listed in number four I think warrants
16 upfront attention.
17 And coming to the comments today, we did
18 hear a range. We heard everything from let's focus
19 on a single audience because it's too much to go
20 beyond a single audience all the way to we live in a
21 world of misunderstanding of genetics right now so
22 anything we can do will be an improvement on that
23 and let's go for it. It's an exciting challenge and
24 a real opportunity.
25 We did hear also from a couple of the

1 speakers today encouragement for developing
2 different interfaces to help multiple audiences. I
3 think that's obviously a great way to go. I'm a
4 little concerned about having sort of the expert and
5 the lay person interfaces because many people will
6 be in between and are there ways to be more
7 integrative in the approach so that any person can
8 go to the level of technical detail that they need
9 quickly but without necessarily having to put
10 themselves in one bin or the other.
11 So I have to admit that with Dr. Ostell's
12 prototype my immediate reaction putting on my naïve
13 hat was to be overwhelmed. Of course, I have been
14 looking at NCBI since forever but I've also learned-
15 -trained myself to step back and put that naïve hat
16 of my mother on or even my primary care--my primary
17 care physician who is not a geneticist and go,
18 "Okay. I really don't want to look at that."
19 I--let's imagine a case where someone says
20 something about seeing Marfan Syndrome and they have
21 some--their child or someone they know has some
22 symptom that makes them think, well, I wonder--I
23 want to learn more about Marfan Syndrome and the
24 genetic testing for that. And so they come to the
25 Genetic Testing Registry and they look up Marfan and

1 they see all this kind of stuff and they quickly go
2 somewhere else, and maybe that's okay and maybe they
3 go to an association focused on Marfan's but you
4 would love for them to see the GTR as a place to get
5 the basics. What I think you want there is like
6 with Gene Reviews, and it's something--what is
7 Marfan's--and of course it can all be done with
8 links but making those very obvious is critical.
9 But also how do we help people understand
10 what the genetic landscape is? And by genetic
11 landscape I mean are there multiple genes involved?
12 Are there--for any given gene, how many mutations
13 are involved? Are we in the world of BRCA with
14 thousands of variants or are we in something more
15 Mendelian? And how common are these variants, which
16 actually is non-trivial. It's really tough to
17 figure out those frequencies.
18 And very, very importantly, what are the
19 other risk factors that are involved? I am very
20 hesitant to use the word "penetrance" around anybody
21 who hasn't studied genetics but there are ways to
22 convey ideas of incomplete penetrance to people that
23 this is one of many factors and it actually plays a
24 relatively minor role but is one piece possibly of a
25 diagnostic toolkit. So, you know, ways to explain

1 these kind of basic concepts, I think, could be very
2 valuable.
3 Now, if someone has--any test provider has
4 to put all this in every time that would be overly
5 burdensome but I think that many of these key
6 concepts could be shared but we may be able to bin
7 tests or otherwise group tests so that the tests
8 with shared features could be grouped. And I think
9 there are ways--you know, taking advantage of the
10 internet and the ability to layer information, to
11 use links and to--I do have to say that just
12 defining terms doesn't work. Putting links to
13 definitions, it doesn't really help people. They
14 trip up and they hardly want to read anyway. Most
15 people--I mean, whether it's a busy physician or a
16 consumer who is up for hours late at night, they
17 tend to--you know, sometimes they read but
18 haphazardly in many cases so putting in links to
19 definitions is nice but it's not the only answer.
20 I think we have to--I love the idea of
21 having ranking systems and using images and so on.
22 I think we really can take advantage of the internet
23 and help people really focus on where they trip up.
24 In an industry environment instead of labeling--
25 calling people plain language experts, having pilot

1 testing and recall them product development experts.
2 Those are people who know how to design things that
3 people use appropriately. I mean, we could call it
4 usability testing. So it's really the same thing
5 and there are lots of experts in this area who know
6 how to make sure or to analyze how well people
7 understand information.
8 And the great thing, too, is that there
9 will be opportunities for iteration. We're not
10 writing a book that's going to be static and I
11 think, you know, start small and include the key
12 concepts and then move on from there.
13 Did I miss anything from today? Oh,
14 Misha's point was pointing out be clear about the
15 limitations. And that--I mean that goes without
16 saying but--and how do you get test providers to
17 talk about limitations? I think that's perfectly
18 reasonable and, you know, I don't see test providers
19 being unwilling to do that. I think it's part of
20 what they do regularly. So I think that again
21 that's a key step.
22 DR. HUDSON: Myrl?
23 MS. WEINBERG: I have two follow up
24 comments.
25 One, I certainly wasn't recommending that

1 we have sections in the registry for this audience,
2 that and the other. It's really away to think about
3 all of the information that's there and I think what
4 we're agreeing on is that it would be helpful to
5 everyone but we need to really think about how well
6 and how clear things are explained.
7 I wanted to really reinforce the notion of
8 having a more formal education campaign and program,
9 and I think there are ways to do it where it doesn't
10 cost, you know, millions of dollars. We did some
11 research--it has been a number of years now--about
12 what people perceive, think, think they know about
13 the whole field of genetics, and they knew more than
14 probably they thought they did but they didn't have
15 the language. They didn't have the words.
16 So we talked a lot about the need to have
17 some education around the concepts, the words and
18 what they mean in order for them to form a metal
19 (sic) framework. In the past you would have
20 probably said a metal file cabinet and now it's a
21 metal database of their own but they just didn't
22 have the framework so that when they got information
23 they didn't know where to store it basically.
24 So if we can around the registry use this
25 as an opportunity to create across the board a

1 really solid educational campaign about this whole
2 field I think it would be very beneficial, and one
3 way to do it that isn't as expensive is use the
4 umbrella groups. The National Health Council is
5 one. We represent, you know, hundreds of millions
6 of people through our member organizations and
7 through companies and others, certainly the Genetic
8 Alliance and their other organizations, and then
9 there are of course the professional societies that
10 represent all of the health care providers who
11 absolutely may not have much more or any information
12 than a lot of the patients. So I think there are
13 ways we could work it out if we could--if it made
14 sense to form some group to sit down and really talk
15 about separately how do we do an educational
16 campaign around the registry to really help move the
17 country forward in the whole area of genetics.
18 **CONCLUDING REMARKS**
19 DR. HUDSON: Thank you.
20 Other comments?
21 If not, I think we can move towards
22 wrapping up today's public meeting.
23 Speaking for myself and for the GTR team
24 at NIH, this has been really useful to us as yet
25 another step in our collection of input and

1 continuing to collaborate with all of you in the
2 building of this Genetic Testing Registry, so our
3 efforts will continue.
4 We will accept public comments in response
5 to today's questions until November 12th and comments
6 are accepted any time on the GTR website and the web
7 address is listed there at the bottom.
8 I want to thank you for your interest in
9 GTR and for your thoughtful input today.
10 And I particularly want to thank the
11 panel, ASHA for helping us have this meeting and you
12 for your participation so thank you very much.
13 (Whereupon, at 11:44 a.m., the proceedings
14 were concluded.)
15