Public Comments

DR. TEUTSCH: With that, let's turn to the real major work of the day and to complete the work on the Oversight Committee. I think we made good progress yesterday, and we will continue to do that. As we did yesterday, though, we will do that informed by the public input, and I believe we still have several individuals whom I would like to call up to do that.

The first one is Pam Dixon. Pam, are you here, from the World Privacy Forum?

I'm going to ask each of you, as I did yesterday, to please hold your comments to five minutes, since we have a very large agenda.

Is Kimberly Layton here? If you don't mind just coming up so that we can have a quick transition from one of you to the other.

DR. BILLINGS: Steve, I wanted to make one comment about the public comments from yesterday. There was some discussion after the 23 and Me presentation about their laboratory oversight and their views about laboratory oversight.

I just wanted to make it clear that from my knowledge the tests that are run by 23 and Me are significantly run from a CLIA-certified laboratory, in fact from a laboratory that is regularly FDA inspected. So for whatever their position is on oversight, they are using a reviewed lab.

DR. TEUTSCH: I think we will welcome them here when we get a chance to, hopefully for the July meeting.

While we get the slides up for Pam, Kimberly Layton, are you here? Not here yet? Robert DiTullio, are you here? Great. Kathy, are you here? Everybody has slides. Let's just wait a second until we know which slides we have up.

Kathy provided us some comments as a taskforce member yesterday and has some additional comments, I think, that she wanted to talk about from the perspective of the Policy Institute. So Kathy, thank you.

DR. HUDSON: Good morning. My name is still Kathy Hudson and I'm still from the Genetics and Public Policy Center. The public believes and expects that genetic tests that they take to make important health-related decisions are analytically and clinically valid. As the taskforce report has clearly documented, they cannot have that confidence today.

Your recommendations need to make sure that there is adequate evidence and that that evidence is transparent to the public. As Marc Williams suggested, we need to lift that curtain.

Yesterday's discussion, as you may have surmised by the murmuring in the audience, was troubling in several respects. There was a constant refrain that increased oversight will stifle innovation. In the absence of evidence that such stifling has or will occur, today manufacturers of IVD kits are subject to FDA regulation and if they were being stifled we would have expected to hear about it in the public comments.

To the contrary, the comments of AdvaMed, a trade association for device manufacturers, and Roche argue that more and not less oversight is needed.

There was no discussion about the deleterious impact yesterday of the status quo on innovation. IVD manufacturers face significant disincentives to produce validated test kits. The problem, of course, is that for any test kit a manufacturer can present evidence to FDA and go to market and the very next day Joe's Genetic Tests R Us can offer the very same test or make identical claims without having the oversight from FDA.

The absence of discussion of this yesterday may reflect that while there are significant numbers of LDT providers on the Committee there are no IVD manufacturers on the Committee.

The Committee will not fulfill its mandate unless it makes recommendations that substantially level the playing field for businesses that can and are innovating in this space at a time doing the work necessary to get FDA approval.

Yesterday Steve made recommendations of what FDA does do and can do, and there were suggestions that perhaps we should wait and push a pause button on FDA oversight until various committees have met and registries are formed and we have achieved world peace. I would really make a very strong suggestion that you not handcuff FDA.

There was also considerable discussion yesterday about direct-to-consumer genetic testing. I want to make five points about direct-to-consumer testing. First, the map that was provided by Lewin was a map describing current oversight. I pointed out yesterday that the Lewin Group inaccurately showed that there is a non-CLIA regulatory pathway for genetic tests.

With the exception of those tests where it is unclear whether or not those tests provide a health assessment, and that is a distinct minority, selling an LDT without CLIA certification is against the law. I would argue we do not want to include a pathway on our regulatory map that includes breaking the law.

Second, on a related point, the vast majority of DTC tests are subject to CLIA and they make explicit or implicit claims of health assessments. We have recently done a review of the direct-to-consumer tests, and that has been passed around. The majority of those claim that they are providing those tests from CLIA-certified labs. Of course that is difficult to verify because there is no publicly available list of CLIA-certified labs. We called Judy Yost to verify those claims.

Our review in this slide is already outdated, and it is about a week old. It shows that there are 30 companies offering health or health-related tests direct to consumer. So I would suggest that we don't want to make DTC companies the scapegoat here. There is a much bigger problem with all laboratory-developed tests, and it would be misleading and inaccurate to point the finger solely at DTC providers. The failures in oversight apply across the board.

Third, there were a number of inaccuracies in statements about the regulatory status of direct-to-consumer tests. The definition of clinical lab is one that examines samples derived from the human body to provide information about the diagnosis and treatment of disease or for the assessment of health of human beings. This definition and all the CLIA regs cover labs whether they are being sold direct to consumers or through a provider.

Concerns were also raised about skirting oversight by claiming that genotype provides research information. Paul, you referred to 23 and Me's comments. There is an exemption in CLIA for research but only if those research results are not provided back to the research subject. So even if someone was saying that they were conducting research, they would have to perform those tests

in a CLIA-certified lab if they are providing the results back, as 23 and Me is, and they are operating in a CLIA-certified lab.

Finally, yesterday the FTC representative said that interagency collaboration on DTC is working. I'm not sure what that means. Since the issuance of a consumer alert 18 months ago, which was prompted, I think, largely by a GAO investigation and a Senate hearing, we haven't heard anything more about FTC's efforts on direct-to-consumer testing. What progress have we actually made.

Matt told the Committee that there have been no enforcement actions, this despite numerous consumer complaints to the agency, a class action lawsuit, and numerous clearly faults or misleading statements on DTC websites. Perhaps the Secretary could ask for or recommend that the Secretary check in on the progress of this collaboration and FTC's evaluation of these faults and misleading claims.

In closing, I ask that at the end of your deliberation you read carefully over your recommendations, and Reed asked that the Committee do this yesterday, to make the recommendations as specific as possible. In a year if we read these recommendations, will we be able to tell if there has been measurable progress or are they so mushy that we can't really discern whether or not there has been progress. Thank you.

DR. TEUTSCH: Thank you, Kathy. Appreciate that. Any comments for Kathy?

DR. BILLINGS: I have one. Kathy, on this list, does that mean that each of these entities is making health-related claims around all these SNPs that have been associated with disease?

DR. HUDSON: Along the top are what they are offering tests for. So there is obesity. I would argue that is a health assessment. There are some that get a little on the borderline, but most of those are explicit health-related, disease-related claims. We haven't included ancestry or sort of recreational, "who were you related to" kinds of stuff.

DR. BILLINGS: Thank you.

DR. HUDSON: Muin?

DR. KHOURY: Kathy, do you have an answer to what the person from 23 and Me said yesterday when I asked her about the difference between health-related claims and otherwise? Because they have a service to try to inform and educate the public and they view this as not giving advice on health-related issues. I don't want to single them out, but I think most of these on the list would probably do the same.

DR. HUDSON: So 23 and Me offers several services and one of those is clearly health-related, giving you information about your risk relative to the general population based on genome-wide association studies for a set of clearly health-related conditions: diabetes, et cetera. There are other parts of their service that I would argue are not health assessments but are providing genetic information.

We are in the process now of doing a careful evaluation, in fact using some of the work that you have led, Muin, from EGAPP. We are comparing what evidence EGAPP has found for various tests to the claims that are being made by the DTC providers and finding significant variance.

DR. TEUTSCH: Great. Thank you. Appreciate those thoughts, Kathy. Let's move on, then, to Robert DiTullio from AdvaMed. It looks like we are good to go with some slides.

MR. DiTULLIO: Good morning, ladies and gentlemen. My name is Robert DiTullio, and I'm with Sequinom, a molecular diagnostics and research company in San Diego, California. I'm also co-chair of the AdvaMed's Diagnostics Taskforce. As such, I'm here to present AdvaMed's least burdensome proposal for the regulation of all diagnostic tests.

AdvaMed is the world's largest association representing manufacturers of medical devices, diagnostic products, and medical information systems. AdvaMed member companies produce the medical devices, diagnostic products, and health information systems that are transforming health care through earlier disease detection, less invasive procedures, and more effective treatments.

As some background, in 1997 FDAMA had a requirement for the least burdensome approach to regulation. More recently, MDUFMA had qualitative goals for the consideration of exempting some of the lower-risk tests. Very recently, the SACGHS Committee drafted a report and in that report they highlighted the need for improvement in the current regulatory scheme.

We at AdvaMed, through our taskforce and our membership, have been working on this proposal for more than a year. Our number one, main underpinning of all of this first and foremost has been that patient safety is the key.

To address safety and effectiveness, we know that there are more than 1,000 genetic disorders where tests are developed in labs and these are not subject to FDA or CMS/CLIA evaluations of safety and effectiveness prior to use on patients. We advocate timely access to all safe and effective diagnostics regardless of where they are manufactured or used using a risk-based approach. We promote the application, as FDAMA required, of the least burdensome approach in doing so.

As the SACGHS report indicated, we need to modernize the regulatory scheme, and this proposal advocates doing so with the least burdensome approach, doing so by realigning the intensity of regulatory oversight with patient risk benefit ratio in mind, and allowing FDA to focus their limited resources on only the highest risks. We promote the FDA oversight of safety and effectiveness of all diagnostic tests regardless of site.

We are presenting this proposal and the underpinnings are seven key principles. The first principle is that all clinical labs should be subject to CLIA requirements and quality standards. We believe FDA should oversee safety and effectiveness of all diagnostic tests no matter where they are made because they have the same risk benefit profile for patients.

We promote FDA oversight of tests, and that oversight should focus primarily on the risk of harm associated with how the test result is used to treat patients, not only on new technology or the novelty of the analyte.

To further the third principle, we believe that low-risk tests and well standardized tests should be exempt from FDA pre-market review or only subject to labeling review of the performance claims. This would allow the FDA's resources to be used toward the higher risk tests, and these should be cleared or approved using a risk-based approach that aligns data submission requirements and the intensity of the review with the risks.

We also promote the fact that patient access to specialized test categories should not be disadvantaged.

FDA and CMS should harmonize regulatory requirements for diagnostic tests and leverage each other's standards and resources for oversight of lab-developed tests. The new oversight system should be implemented through notice and comment rulemaking and guidance as appropriate.

Our seventh principle is that CMS must recognize that all new diagnostics must receive timely and adequate reimbursement.

DR. TEUTSCH: That is helpful. Do we have any comments or questions?

MR. DiTULLIO: There is still some more.

DR. TEUTSCH: I know. We are at five minutes, so if you can finish up in just a few seconds.

MR. DiTULLIO: Yes. Actually, I was not finished, but --

DR. TEUTSCH: Do you have another point or two you would like to make?

MR. DiTULLIO: Actually, what I would like to do is to propose some questions for consideration for the final report of SACGHS. One such question is, will formal, risk-based, independent review of critical elements, such as intended use, analytical and clinical data, limitations, et cetera, take place before the test is commercialized and available to patients? Will it be assured that claims are commensurate with data provided?

Another compelling question we believe, are more limited post-market reporting requirements such as NDRs and recalls alone adequate to assure patient safety? I thank you for the opportunity to comment.

DR. TEUTSCH: Thank you.

DR. BILLINGS: Under your model of FDA oversight of all tests, what role does CLIA play?

MR. DiTULLIO: CLIA plays a role of making sure that all the laboratories follow the existing CLIA regulations with regard to their quality standards and also, as I said in one of the principles, there should be some meeting of the minds between the FDA about a future version of how pre-market regulation might be had.

DR. TEUTSCH: Muin, did you have a comment?

DR. KHOURY: The concept of safety and effectiveness according to AdvaMed, can you go over that? Because I'm struggling with two ideas here: clinical validity of a diagnostic test, meaning sensitivity, specificity, et cetera, and then clinical utility. Are you suggesting the FDA regulate clinical utility as well or just to go after clinical validity? Some of the discussion here yesterday was focused on clinical validity.

MR. DiTULLIO: The FDA process should remain as it has been all along. That is what AdvaMed is proposing. What we are proposing is that they focus only on the higher risk products and do so in a risk-based approach. We are not advocating a change to how FDA currently does their review.

DR. TEUTSCH: Jim and then Reed.

DR. EVANS: Can you just give me a quick example of a low-risk test and an example of a high-risk test?

MR. DiTULLIO: BUN or urea is a low-risk test, and there is no reason for there to be any review of that. A high-risk test could be a viral load HIV.

DR. EVANS: And the criteria for determining low risk and high risk is?

MR. DiTULLIO: In one of the slides that I wasn't able to show was that, through the qualitative goals that were given by MDUFMA, we agreed that we were going to make a presentation of an exemption proposal for the low-risk devices and present that to the agency by the middle of this year. We are going to do so with a tier-triage approach where we took into account risk and the novelty of the analyte, the novelty of the technology in a matrix fashion. We are also planning on presenting a flow chart that will help the FDA implement this.

DR. EVANS: I don't mean to belabor this, but risk for? I just haven't --

MR. DiTULLIO: Risk for how the tests are used on patients.

DR. EVANS: So for example, a test that is wrong and the impact that might have on the patient.

MR. DiTULLIO: That's right.

DR. TEUTSCH: Reed.

DR. TUCKSON: Jim got mine. Thanks.

DR. TEUTSCH: Thank you so much.

MR. DiTULLIO: Thank you very much.

DR. TEUTSCH: We also very much appreciate the extensive comments you provided as part of the earlier process. Thank you very much. Appreciate it.

MR. DiTULLIO: Thank you. So, welcome to Pam Dixon from the World Privacy Forum.

MS. DIXON: Good morning. Thank you for waiting. I'm Pam Dixon, executive director of the World Privacy Forum. We are based in San Diego. We are a nonprofit public interest research group. We focus on in-depth analysis of privacy issues and also more longitudinal research of these same kinds of issues. One of our focus areas is on healthcare privacy issues.

Our take is a little bit different than pretty much everything else that I have heard so far in this meeting. We are really interested in the aspects of privacy that we felt were slightly underrepresented in the otherwise very, very thoughtful and deliberative report.

Our concern is will marketing interests and misused science crowd out legitimate genetic testing and privacy. What we are looking at is really occurring outside the clinical sphere. We believe that you guys are doing an excellent job of looking at the issues within the clinical sphere, but we

think that there are other issues and mischief potentials outside that sphere. That is just what I want to walk you through a little bit today.

One of the things that we really looked at in this area is something that is already occurring in the healthcare sector, which is privacy activities related to consumer-consented healthcare data.

For example, right now if you go to something called DirectMeg.com, which is a big direct marketing magazine for marketing companies, and you go to something called the List Finder, you just search the List Finder's 60,000 marketing lists. I typed in "diabetes." The reason I typed this in is because this is a mature market. As you can see, there are 406 lists containing "diabetes."

Now, when you look at these lists, some of them are for magazines and what not, but most of them are generated from actual consumer healthcare data.

This is something called a data card. A data card basically tells you what is being sold about the consumer. In this particular case, you have 2,186,700 consumers who are known and identifiable to this list, and there are 400 data points about the consumer.

You can e-mail them, you can find out all sorts of things about them. It is 53 percent female, 47 percent male. The source of the data was often e-mail. But anyhow, you can select whether they are type I or type II diabetes. You can look at the average household income, which is $48,000 per year.

Then, if you look over here, these are selects. Selects are something that you can choose to purchase along with the base list. You can purchase the age of the person, the age of their children, their education level, their ethnicity, their gender, and again you already saw the income, the prescriptions and what over-the-counter medications they take, and all sorts of other marketing activities and purchasing activities that the consumer has engaged in.

So that is just one of the diabetes lists. I typed in "genetic," and we are early on this, very, very early, but I found a list. If it weren't sad, it would be humorous. These are 54,000 primarily men who expressed interest in Ferrari Hair Centers.

[Laughter.]

MS. DIXON: I apologize if I'm offending anyone in here. Anyhow, I don't know about you, but this sentence is very interesting to me. "The Ferrari concept of genetic hair restoration," blah, blah, blah. You get the idea. Anyhow, these people who opted into this list in some way can be sold, trussed up, and delivered to the marketing company.

The problem here is, this is goofy, but in the future we expect this to look much more like the diabetes list, where you have a person's name, home address, number of their kids, maybe even names of their kids, education level, income, and everything else you might want to know.

This is actually just a random list I pulled. This actually is of mental and behavioral disorders of, again, individually identifiable consumers. At the very top you will see, "Ventee, an Experian company, has the industry's largest and most comprehensive consumer database of self-reported online data compiled from three reliable sources, including online surveys, direct response e-mail marketing, and consumers visiting Ventee websites."

So that is just the point. This is not clinical data that is leaking. This is consumer-reported data. Our concern is that as this area of direct-to-consumer advertising and genetic testing and also consumer-initiated genetic testing matures and also the price drops, I think we are looking at a situation where this kind of thing can really get worse and start to impact consumers.

I think the outcome that we all want to avoid is a wild west data rodeo where consumers have initiated genetic testing through some kind of Web portal or online site and the genetic test can be a fake genetic test, or it can be a real one, but the point is that the data is collected and then used for marketing purposes.

Now, in the genomic world, you have a consumer whose information impacts them, their employability, insurability, and other potential harm, but also,their family, their progeny. So this is a persistent privacy issue.

We submitted comments last December. I will leave those to you. You can look them up online. We made three recommendations in those comments. First, we asked that privacy be expressly included in the draft report as an issue to be looked at, including privacy outside the clinical setting.

The second recommendation was to task a group. We worked with this and we were thinking who could it be. We thought maybe NCBHS. But anyhow, to figure out how that might look to address the specific privacy issues that come up in this context because they are complex, and not to be flip here in showing you genetic Ferrari whatever, but it is a difficult task. When you mix the complexity of genomic work and then also privacy work, it gets quite difficult.

But a recommendation we wanted to add is, the Federal Trade Commission right now is working on and asking for input on what to do about advertising to consumers online and whether or not medical information or healthcare information should be included in that tracking kinds of advertising or not.

We are asking the Committee to think about working with the FTC to urge them to say that no, genetic data and requests for genetic tests on websites and this sort of thing should be off the table in terms of advertising, being able to use this data for marketing purposes, or any purposes other than a person's health care. Thank you very much.

DR. TEUTSCH: Thank you very much, Pam. These are obviously important issues. Marc.

DR. WILLIAMS: I also wanted to say thank you for that. I must admit, as I have reviewed the comments I thought that they were eye-opening. I think you will find that we incorporated some of the suggestions that you had made in our recommendations.

The specific question I wanted to ask you is, it doesn't appear from your presentation that you have actually identified any of the direct-to-consumer genetic testing companies that are actively asking for permission to collect this information, but I'm just curious. Looking at this list that Kathy Hudson presented, how thoroughly have you looked at the landscape, and are you aware of anywhere they are asking consumers basically to check and say would you be willing for us to share your information.

MS. DIXON: We are aware of some companies that are already doing that. We are debating on how we want to approach that issue, whether we want to do a substantive longitudinal research study or if there is some other mechanism.

So our first step in addressing this issue is to address it broadly without going after any particular company and see what this Committee came up. We are hoping for a deliberative process that is thoughtful and hoping for the best.

That being said, we are very concerned about some of the information our research in this area has turned up. One of the great issues is that a privacy policy really is a very thin scrap of contractual material to separate a consumer from harm. The privacy policies, some of them are quite dense. I think it would be difficult for a consumer to read and have a really clear understanding of what is happening.

So that is one concern. But then, of course, the second concern is right now a lot of the actors in the field are primarily good actors. We are thinking that down the line there will be a proliferation of bad actors who make the current landscape look like Disneyland.

DR. WILLIAMS: I would just follow up on that and say that in our discussion of those recommendations yesterday -- I don't think you were here for that.

MS. DIXON: No. I was trying to get here.

DR. WILLIAMS: I can tell you that when I presented, inadequately, but attempted to present the information that you had provided for us that there was quite a bit of interest from FTC about this because it seemed to be something that they were not specifically aware of. So I think that there would be a receptive ear if you have some data that suggests there really is some untoward activity.

MS. DIXON: Thank you very much.

DR. TEUTSCH: Joseph.

DR. TELFAIR: Thank you, again, for the presentation. I think Marc's last statement almost covered what I was going to ask. As you are considering your study, one of the concerns I know that has come up is the building of the evidence that there is harm, not just potential for harm but actual harm itself. I was wondering in your considerations of your design of your study, are you going to begin to put into the study a means by which you can detect that through either firsthand cases, secondhand cases, or whatever?

MS. DIXON: Absolutely. We will have a peer-reviewed methodology before we ever begin. So if you are volunteering, that would be fabulous. But yes, thank you.

DR. TEUTSCH: Thank you very much, Pam. These are particularly important issues and we appreciate your demonstrating them so vividly and also for your comments earlier.

MS. DIXON: Thank you very much.