



Presidential Commission
for the Study of Bioethical Issues

TRANSCRIPT

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DR. GUTMANN: Welcome everybody. I'm Amy Gutmann. I'm President of the University of Pennsylvania. And I'm Director and Chair of the Presidential Commission for the Study of Bioethical Issues. And on behalf of myself and our Vice Chair, Jim Wagner, and all of our Commission members, I'd like to welcome you to this, our nineteenth meeting. I will begin by noting the presence of our designated federal official, Bioethics Commission Executive Director Lisa M. Lee. Lisa, please stand up. Thank you. And then I would like to go around, I will begin with Nita and have each Commission member introduce herself or himself.

DR. FARAHANY: Nita Farahany from Duke Law School, and Duke Science and Society.

DR. KUCHERLAPATI: Raju Kucherlapati. Harvard Medical School.

DR. ALLEN: Anita Allen, Vice Provost for Faculty at the University of Pennsylvania and Professor of Law and Philosophy.

DR. HAUSER: Stephen Hauser, Chair of Neurology, university of California, San Francisco.

DR. WAGNER: Jim Wagner, Emory University.

DR. GRADY: Christine Grady, from the Department of Bioethics at the National Institute of Health Clinical Center.

DR. SULMASY: Dan Sulmasy, from the Department of Medicine and Divinity School at the University of Chicago.

DR. ATKINSON: Barbara Atkinson, Planning Dean, University of Nevada, Las Vegas.

DR. ARRAS: John Arras, philosophy, bioethics, University of Virginia.

DR. GUTMANN: So I just wanted to make one comment on the Commission members, who I've become very admiring and fond of. But that wasn't the comment that I wanted to make. That's just a preface to say there's an incredible and very productive diversity of background that this Commission represents, and I think it has served us well in the past, judging from the reception to our deliberations and reports. But most importantly, for what we are going to deliberate about today and tomorrow, I think it will serve us in very good stead. During this meeting, we will continue our work in response to President Obama's charge to review the ethical issues associated with neuroscience research and the application of neuroscience research findings. We will hear from two speakers this morning and then we are going to devote the rest of the day to discussions so we can move forward our report on neuroscience.

And tomorrow we will turn to another project which, broadly framed, is deliberation and education in public bioethics. But we are going to focus tomorrow on the Ebola case study for us, as a case study in public deliberation and education as a basis for making our own recommendations and analysis for future public health emergencies. So before we get started, I'd like to take a moment to explain how we take public comments. I'd also like to ask our Vice-Chair, Jim Wagner, if he would like to make a few prefatory comments. At the registration table there are comment cards. Bioethics Commission staff members here in the room have comment cards, as well. And they are all wearing name badges that say "Staff." Just hold up your hands there. So anybody, just pull a card, write down a question, one of the staff members will bring it up to us, and we will try to address it. That's all I have to say by way of prefatory remarks. I'm going to turn it over to Jim for a few comments.

DR. WAGNER: Amy, thank you very much. Thanks to the Commission staff for all the work you do in making these meetings come together. Welcome and thanks to guests who are

with us, especially those who are going to be offering remarks and helping to guide us.

Welcome, Commissioners. It's good to be with you, as Amy said.

If you are like me, you have been anticipating the sessions for today and tomorrow with some excitement about how the Commission can contribute to what has turned out to be a rather broad range of subjects here in the next day and a half. And if you are like me, you also have been tempted to let your mind stray a bit about thoughts and opinions maybe even beyond the scope of what our Commission is called to do. And if you have not had your mind do that, good for you.

But if you have, as I have, it's probably worth a reminder that we have been assembled as we have to consider, to alert, inform, opine on what it is that matters of ethics; how it is that matters of ethics should shape the actions of researchers, policymakers, producers, service providers, health providers, and politicians. We are not ultimately policy makers, research funders, or regulators or politicians, for that matter, thankfully. In fact, I like to imagine the work we do is more foundational and more long-lasting. So with thanks for that moment of reminder, let's get on with the agenda.

Our first session is about ethical responsibilities to direct-to-consumer neuroscience companies. At our last meeting we had good discussion, fruitful discussion about direct-to-consumer neurotechnology. And this morning we are going to continue that with a focus on the ethical responsibilities of DTC neuroscience companies. And as with all of our meetings, each panelist will present for about ten minutes. And then once we have heard from both of you, I will open the session for questions and discussions.

Serena Viswanathan - she helped me on that is Assistant Director in the Federal Trade Commission's Division of Advertising Practices, where she supervises enforcement actions on deceptive and unfair advertising practices. Since joining the FTC in 2000, she has investigated and litigated deceptive advertising claims for a broad range of products, with focus on health claims for dietary supplements, devices, and foods, including things we have all heard about; the Q-Ray ionized pain reliever bracelet, POM Wonderful pomegranate products, and brainstorm cognitive dietary supplements, and the list goes on. We are delighted to have you here this morning. Please, the floor is yours.

VISWANATHAN: Good morning. I'm pleased to be here today to discuss how the Federal Trade Commission approaches deceptive advertising, and we would evaluate claims for neuroscience products. First, I have to give a disclaimer. These remarks today are my own views and not the views of the full Federal Trade Commission or any particular commissioner.

Our website, FTC.gov, has a very detailed description of our agency, so I will just give a very brief overview of the FTC's legal authority. The Bureau of Consumer Protection, where I work, has about 500 employees and we address unfair and deceptive business practices. My division, Advertising Practices, of course we addresses false and deceptive advertising; however, we also have divisions working on general consumer fraud, financial practices, and privacy, among other things.

The five members of the Federal Trade Commission ultimately approve major actions such as filing complaints. Our statute, the Federal Trade Commission Act, prohibits unfair and deceptive acts and practices in commerce. The FTC Act also prohibits false advertising for foods, drugs, devices, services or cosmetics. So we have a

very broad mandate. The FTC investigates and brings lawsuits in federal court or through an administrative law process. In certain instances, we can enact specific regulations, but the majority of our work that's relevant to the discussion today would be these civil lawsuits.

Our remedies are injunctions or cease and desist orders. That can be against companies or it can also be against individuals. We can also seek monetary remedies such as consumer redress, disgorgement of ill-gotten gains, and in certain instances we can also seek civil penalties or fines. So how does the FTC review direct-to-consumer neuroscience products? I just want to put in a quick pitch for our dietary supplement guidelines.

We prepared a guidance document for dietary supplement advertising. It has a very good summary of how we evaluate health advertising claims. And it actually applies to products other than dietary supplements. So I'm giving a ten-minute summary today, but it has a lot more detail.

The basic principles of FTC advertising law are that advertising must be truthful and not misleading, and that advertisers of products or services must have a reasonable basis for their advertisement claims. When those claims are scientific or medical, the reasonable basis has been defined as competent and reliable scientific evidence to back up those claims. And there's more detail about that in this document. Often, with health claims, competent and reliable scientific evidence is going to mean human testing, including clinical trials.

For ads where a product has claimed to be clinically proven or which claims that "studies show," for example, we would look to other experts in the field, would consider the substantiation provided to be sufficient to support that claim. And again, if we are talking about

effects on human health, "the studies show" or "tests prove" type of claim, which we call an establishment claim, often requires rigorous evidence such as clinical trials. I should point out that the FTC is mostly made up of lawyers and economists, so when scientific issues arise we often consult with outside experts for guidance.

So neuroscience is a complicated area, but the basic evaluation you would do is similar to any health claims case. First we look at the advertising and determine what claims we believe are communicated to reasonable consumers. Then we evaluate, with the help of experts in the field, whether the scientific substantiation that's been presented to us is competent and reliable scientific evidence for those claims.

Even if marketers use implied claims or code words instead of express claims, we will go look at what reasonable consumers would take away from the net impression of an advertisement, so that could include images or other aspects of the ad. For example, we have brought cases where a company just used the word "immunity" or "strengthens the immune system," but the actual net impression of the ad was that the product would prevent colds and flu, and the colds and flu claim was unsubstantiated.

So similarly with hypothetical cognitive products, even if an ad only says "supports a healthy brain," depending on the images or other aspects of the ad, if consumers could still take away a claim that it improves memory or that it staves off HOA cognitive decline, then those claims would have to be substantiated.

The substantiation depends very much on the claim. With FDA, much of the regulatory discussion centers around whether this is a structure function claim or a disease claim. The FTC requires competent and reliable scientific evidence for any objective product claim, whether that would be used that a product supports a healthy brain or it improves memory.

Of course, the type of evidence would differ. The stronger the claim, the more likely it is that rigorous evidence would be needed.

When we evaluate science, we'll look at various factors. One thing we look at is the amount and type of evidence, whether these are in vitro, or animal studies, versus clinical trials on humans. We will look at the quality of the evidence, whether the study is well controlled, whether it was – whether there are statistically significant and clinical significant results. We look to the totality of the evidence. Is all the science consistently in the same direction, or do you have one positive study in a sea of negative studies? And we also look to whether the study has relevance to the specific advertising claims. So whether the dosage, the formulation, the population and the outcomes are relevant to the actual claims that are being advertised for the product.

I know the Commission was very interested in our relationship with FDA. We do work very closely with FDA, given that our statutory authority also covers foods, drugs, devices and cosmetics. Under a long-standing Memorandum of Understanding with FDA, FDA has primary authority over product labeling while FTC has primary authority over product advertising.

Unlike FDA, we don't pre-approve products. But we do expect companies to have substantiation for their claims before they are made. And we try to harmonize our evaluation of substantiation with the FDA. So typically, if the FDA has weighed in on a particular issue, we would defer to the FDA's determination of whether there's sufficient support for a health claim. The FTC is more active in areas such as dietary supplements where FDA's legal authority is limited. We are also very active in cases where the ad claims may not rise to the level of disease claims. But we have brought actions against companies where the company also received FDA warning letters. So a company might be making a disease treatment claim in their labeling or their website, and the FDA would send them a warning letter.

But the FTC would also be able to challenge their advertising claims are unsubstantiated and we could seek an injunction or an award of monetary relief. briefly to conclude, I would like to go over a few cases the FTC has brought in the neuroscience area over the years, and all of these have been resolved by settlement. In 2001 we brought an action against sellers of dietary supplements called Pedi-Active ADD. They purported to improve the attention span and school performance of children with ADHD. The company claimed that many of the problems of hyperactive or ADHD children were caused by nutritional deficiencies and therefore this nutritional supplement would address those problems.

In 2004 we brought an action against sellers of a dietary supplement called Focus Factor. They made claims that the product improved memory, that it improved school performance and focus, and that it would work as quickly as one to ten days. Most recently, as Dr. Wagner mentioned, we brought an action against sellers of the dietary supplement Brain Strong, which contained Dha and was advertised to improve memory and prevent age-related cognitive decline. In this case, the company had done a randomized profile, but the results of the study did not support the actual claims they were making. We continue to monitor advertising in the neuroscience and cognitive area, and another area that we have been involved in, which maybe is not directly related, but it's concussion prevention. So we have investigated manufacturers of football helmets. We have investigated products and sent warning letters to companies making concussion prevention claims for their devices. I thank the members of the Commission for this opportunity to present on the FTC's work in this area, and I'm happy to answer any questions.

DR. WAGNER: Thank you very much. And we will hold questions for you until we have heard from our next guest, who is Margaret Eaton. Dr. Eaton is a former research scholar at Stanford University Center for Biomedical Ethics. She's researched ethical issues, especially

with commercialization of pharmaceutical biotechnology and medical device products. She taught courses in biotechnology and pharmaceutical business ethics, medical law, and biomedical ethics at Stanford University School of Business and School of Medicine. Dr. Eaton served as Chair of the Stanford University Hospital Ethics Committee and worked as a medical and hospital attorney in the Stanford University Office of the General Counsel. In addition to her academic publications, she has authored or co-authored three books, which include *Ethics and the Business of Bioscience*, and also *Innovation in Medical Technology, Ethical Issues and Challenges*. Welcome.

DR. EATON: Thank you very much for inviting me. And I'd like to start by thanking Misty Anderson and Esther Yoo for their very capable assistance in arranging my appearance. My remarks today are, in part, based on a paper that I co-authored with a very talented colleague from the University of British Columbia, Dr. Judy Illes. And I also want to thank her and acknowledge her for her assistance.

I'm glad that you paired me with Serena today because I think many of my remarks are going to reinforce just what she said. So I'd like to begin by saying that the subject of business ethics is fraught with debate. The subject of neuroscience, as you know, is fraught with debate. And the subject of marketing medical products to consumers is, guess what, fraught with debate. But that being said, I'm going to do my best to lay out what I think are the ethical responsibilities of companies that market neuroscience products directly to consumers.

My remarks on this topic are primarily focused on the products that affect brain function in ways that have medical significance. And I posit that most of them do just that. So the first question is whether the traditional mode of business operation, that of maximizing shareholder value, should prevail in marketing these products to consumers, or whether companies should

adopt operating principles of corporate social responsibility which balances the prerogatives of the business interests with corporate social responsibility which broadly seeks to benefit society.

A related question when operating in a field that has human medical significance: Should companies incorporate aspects of the ethical principles of medicine, such as the ones that I've listed on the slide.

So theories and adherence of corporate social responsibility have existed for decades. And medicine has always been governed by ethical principles which place the interests of the patients first. In many respects I think the FDA operates in ways that require regulated companies to adhere to the precepts of both. However, when there's no protective physician or regulatory agency operating between the company and the patient or in this case the consumer, there may be even more of an obligation for companies to prioritize the welfare interest of their consumers and also the social utility of the product over traditional business operational priorities.

With that in mind, what are the primary ethical responsibilities of these companies? The first is to ensure initial validity of the product to meet the consumer's legal and acclaimed rights to safety and advocacy. Basically, are product claims substantiated with credible data. Second is to be mindful of how rapidly neuroscience understanding is evolving and to adapt product claims or maybe even abandon them when relevant understanding changes. So informing consumers that prior claims are no longer valid is a good place to start to satisfy this obligation. A second ethical responsibility concerns privacy of any data that's produced when these products are used. So the relevancy of this issue is captured in a quote by Don Kennedy, who is the former President of Stanford University and former FDA commissioner. And he said, "I already don't want my employer or my insurance company to know my genome. As for my brainome, I don't want anybody to know it for any purpose whatsoever. It is my most intimate identity."

So I have listed on the slide some of the obligations commensurate with the corporate responsibility to safeguard stored brain information data. Companies face a so-called therapeutic gap issue when their product detects a brain deficit with no reliable options to reverse the deficit or halt its progression. In such situations, consumers are at risk for anxiety and social problems akin to those experienced by people who learn about genetic predispositions for disease. So companies marketing a product with this feature should do all they can to prevent this kind of harm.

Next, there are self-interest issues that we should discuss. They can exist when companies have two related products or business interests. In one example, a company could offer a brain evaluation tool and with it a product or service that can be purchased which corrects any detected deficits or improves brain function over that which was measured. An inherent financial incentive exists in this situation to develop the evaluation tool in ways that heightens the perceived need for that second product.

Or a second situation with a similar risk can exist when the value of a predictive test is dependent on the size of the database used to produce those predictions. An example could be where a brain fitness tool measures brain performance against a database of results collected from prior users, whether they are normal or not. The larger the database, the more reliable the testing results can be. So there's an incentive to excessively recruit users just in order to gain a competitive advantage based on the size and therefore the predictive reliability of that database. So curbing a tendency to fall into these traps can consumer.

My last topic concerns direct-to-consumer advertising of medical products, which has been controversial from the start and they're replete, as you know, with cases of abuse of practice. And there's every reason to think that the same controversies and criticisms will exist

in the newer unregulated, relatively unregulated, arena of direct-to-consumer neuroscience products, especially when the FDA is not involved to regulate the fair balance between benefits and risks, the accuracy of the ad, or the prohibitions against misleading statements. Given this situation, it's imperative that companies self-regulate to avoid the offenses seen in the past. So I also want to give you some examples of ads that have been problematic and create controversy. So I will start with two examples from ads about neuropsychotropic drugs.

It's common for a company to create a perceived need for a drug by having the consumer take a self-diagnosis test. And I took one such test in an ad for an anti-depressive drug. Being brave. The questions on the test included: I feel downhearted, blue, or sad; I have trouble sleeping through the night. I'm more irritable than usual. So there were twenty questions in this ad. And the response options were: Not often, sometimes, often, or all the time. So I answered the questions, all of them, "sometimes," because most people sometimes have symptoms like this. In other words, I think it's normal. However, my test answers resulted in recommendation to see my doctor to evaluate me for depression.

In another ad to treat ADHD in children, the names of scholarship winners were listed along with the fact that these kids were taking the advertised drug. Success stories like this have been criticized for overselling the benefits of the drug by making it seem as if this kind of drug and due success is common.

So we will also look at dietary supplements. We all know that neuroscience is still debating the underlying biologic mechanisms of the disease and its treatment options, and yet ads for dietary supplements often claim benefits based on such scientifically legitimate-sounding terms as "enhancing neurotransmitter precursors" with no evidence that these claims have been

substantiated. An ad that I read online just last week stated that the supplement was, and I quote, "Designed to enhance the health of your brain for improved brain function, increased focus, and better memory. With each serving you will be able to reduce stress and increase the blood flow to your brain for more clarity."

And here is an ad that I also found last week online for an EEG headband. And it is a brain fitness tool which claimed to improved focus, attention, and composure; however, with no controlled research to substantiate these claims. They have lots of theories, possibly well-grounded theories, but no real evidence. So given these situations associated with commercializing neuroscience products directly to consumers, I have several general recommendations. First, that companies seek the assistance of ethics groups to help negotiate the sensitive terrain.

Second, that industry groups adopt voluntary guidelines to address the ethical and social issues associated with the activity of the industry. And if product use has medical implications, and as I said most of them we think do, companies should consider adopting a more consumer-centric business operations model using, as guides, the ethical norms of medicine and guidelines of consumer protection agencies. Thank you very much.

DR. WAGNER: Thank you. Thanks to both of you, as a matter of fact. We will open the floor for questions. Maybe -- I've got one. Both of you have presented considerations to ensure that the public is protected from fraudulent -- maybe "fraud" isn't the right word, but from -- in cases where there has not been competent and reliable scientific evidence presented concerning the safety and efficacy of a product.

What about the other side of that coin ?Is it within the FTC's purview to address issues of fairness if and when some of these products actually are useful and efficacious? How is it that we -- how do we go about insuring that there's access to all who could use it?

MS. VISWANATHAN: Well, of course we are focused on the ones that we think aren't substantiated. You know, certainly we have -- you know, there are times where we may open an investigation and then decide not to take action. But yet, I don't know that we have a formal way to kind of bless products. And I don't think --

DR. WAGNER: It may be beyond the scope of what the FTC is supposed to do.

MS. VISWANATHAN: Yes. That's right, exactly. I mean, our statute is about defective and unfair practices, so -- I mean, we either take action or we don't. And when we don't take action, it doesn't become public or doesn't make news.

DR. WAGNER: And unfair and deceptive practices is what triggers the action.

MS. VISWANATHAN: Yes. Exactly.

DR. WAGNER: Okay. Margaret, any thoughts on fairness?

DR. EATON: Yes, I do. I think you're raising an issue of distributive justice and it comes into play especially when these products are actually meaningfully effective. And one of the things that perpetuates maybe unequal distribution of access, is that companies tend to market their products to the target audience that not only wants them but can afford them. So a lot of these novel neuroscience products tend to be on the expensive side. And the good advertisement practices would indicate that you'd want to advertise to those wealthier consumers who can afford them. So I think once they do become uniquely and significantly effective, you are going to see that problem exist, perpetuated by some of the advertising practices of the company.

That being said, I don't really know how to address your concern in total, but just to recognize that this is going to be an access issue.

DR. WAGNER: Thank you. Obviously we do see an FDA approved pharmaceutical and things like that. I've got Christine and then Dan and then John.

DR. GRADY: Thank you both very much. I'd like to hear your views on what kind -- so I understand that we would like companies to adopt corporate social responsibility and for advertisers not to exaggerate their claims. I guess I'm wondering what kinds of incentives are there for companies to do that, to do those kinds of things, to consult with ethicists who care about how balanced their advertisements are. Other than maybe, you know, later on getting dinged by the FTC for not doing it well, what's the incentive at the front end? I'd love to hear both of your views. And then I'd love to hear the description of -- you said something that just struck me as so interesting: Disgorgement of ill-gotten gains. What in heaven's name is that?

DR. EATON: I'll start. I think there are -- other than the punitive consequences of overstepping claims made about DTC neuroscience products, I think the positive reinforcements can come from two sources. One is that companies that are seen to overstep the bounds can lose their -- the trust in the product. And so there are internal incentives in companies not to go way over the bounds, not to get punished, not to be in The New York Times for having been sanctioned by government agencies. So there are some internal controls. I think it can be reinforced with some --you know, if there's access to ethics advisors or those who are interested in social responsibility operational practices of businesses.

But also I think that there now, especially since there's an industry group associated with these products, that that industry group can have a significant impact on asking companies to conform voluntarily to practices to prevent those kinds of backlash harms.

DR. WAGNER: I neglected to notice our chair, who wanted to jump in. Go ahead.

DR. GUTMANN: So we are going to talk in the next session about cognitive enhancement. So I want to, Margaret, address this to you. And then, Serena, if you have anything, I'd be really interested in hearing what you have to say, too.

I'm a high school student and I'm stressed out before a test. And I'm giving this as a very typical -- this is a very typical example. You can fill in "college student" for it, but a high school -- let's just -- because it happens in high school. I'm a high school student, very stressed out before a test, and I have access to a pill that's known or thought to focus you on a test -- focus me more on the test. I don't feel I'm as prepared as I should be. I'm under a lot of pressure to perform. Test success is very important among a certain strata in our society. So what I want you to reflect on -- I mean, these are off-label uses of drugs. They are widely known among certain people. And am I right -- I'm just going to spell out, because as a Commission we need to spell this out, some things that I think and I want you to reflect on. First, I think the term "cognitive enhancement" is unfortunately misleading. These are thought to be cognitive enhancement drugs. I think it is unfortunately misleading because if you just take the term "cognitive enhancement," what's wrong with enhancing your cognition? So what I think they are referring to - and here is where I'm asking you, and correct me if I'm wrong, elaborate - is the difference between a very temporary effect, so you perform better on the test, versus long-lasting cognitive effects, A. Two, unknown or -- health risks or considerable health risks to just popping such drugs versus safe things you can do, like get a good night's sleep, like study more, you know? Those -- right? We laugh but I'm using this because this is very common. And it feeds into a narrative of short-term versus long-term. Do well on tests versus -- So the third thing is -- I've

done two: Temporary versus long-lasting; unknown, risky versus safe. And the third is bypassing broad and deeply applicable cognitive capacity versus developing broad and deeply applicable cognitive capacity.

So the concern from an ethics perspective is having the use of drugs for really not enhancing cognition in the way that's broadly applicable, safe, and long-lasting. And that's very different from policies of -- I don't know how you have a policy that prevents kids who have access to this, or adults who have access to it, to using it. But ought we, as an ethics commission, to be saying something about the problems of marketing and not having out there the destructive aspects of popping pills for this purpose?

DR. EATON: I think you raise a very important issue. And I have been concerned a lot about off-label use of prescription drugs for uses that the company may or may not have anticipated when they first marketed the drug.

Companies are very well adapted to knowing the product stream of their drug, the distribution stream of their drug. They know how many prescriptions are written. They know if a certain percentage of their distribution channel ends up in off-label markets or in black market uses. They know this. And so I think possibly one of the things the Commission could say is to urge companies to monitor that sort of activity and voluntarily attempt controls to enforce the prohibition against it. OxyContin drug misuse is a prime example, and the company went to great extremes to prevent those kinds of detrimental uses. In the second arena which you mentioned, which is in academic areas, one of my past responsibilities at Stanford was as the lawyer for the student health center. I have to say that this kind of drug use on campus is

widespread. And you know that probably from your experience at Penn. It is unfortunate. And it is widespread. And we used to see --

DR. GUTMANN: Can I just -- it doesn't start at college. It is widespread in high school. Correct?

DR. EATON: Yes. I believe that's the case, too, but I don't have any direct experience about that. So we used to see a lot of students show up with all sorts of anxiety disorders and blood pressure problems and that sort of thing as a direct result of taking some of these drugs that you take to cram for exams, for instance. So I think one of the other arenas -- if you want to incorporate the ethical principles of neuroscience product development in ethically responsive ways for society as a whole and you know that there's a problem use in academic arenas, then that might be a target population for consideration. Training for the nurses and the physicians who treat students in this arena about these hazards and what to do about them might be a worthwhile endeavor. You mentioned temporary versus long-term effect. I think there is a certain population of student that only uses the drugs temporarily, but unfortunately that's not the case all the time. And we know that drugs that have an amphetamine-like stimulatory effect on the brain can have long-term detrimental effects. And I'm not even talking sometimes about drugs. But the amount of caffeine in some of these hyper-caffeinated drinks causes a similar problem. So yeah, there has to be a consciousness about that.

DR. WAGNER: Serena?

MS. VISWANATHAN: Yes, I agree. I mean, one of the concerns we have -- obviously we're talking with the FTC it would be non-prescription dietary supplements or devices and the like. You know, there's, of course, an economic harm that consumers are wasting money on something if it is ineffective.

But also, our concern is, especially with some of the products we are seeing about, you know, preventing cognitive decline, I mean, that consumers may not take actions that we know are useful. I mean, you know, following a healthy diet, exercise, learning new things, all of which, you know, people might be less likely to do if they think there's a pill out there that solves the problem. And, Dr. Grady, since you asked about disgorgement of ill-gotten gains --

DR. WAGNER: I apologize. I cut you off.

MS. VISWANATHAN: Oh, that's okay. No, no. It's essentially just a calculation of monetary damages in the sense of if a company has taken in X million dollars selling a product, that we could seek a court order for them to disgorge -- you know, pay that money back to either the consumers or just the money that they got themselves. This way the company hasn't profited from their activities.

DR. SULMASY: It is colorful, I like the language, too. I have one quick technical question for Serena, and then a broader one for Margaret, I guess. The quick one for Serena is, how do cases come to your attention? Is there an active surveillance or do you wait for complaints? How does that happen?

MS. VISWANATHAN: Many sources. We do do surveillance in the sense of we are monitoring ads that are out there on television, wherever. We get complaints from consumers. We have a large consumer complaint database that receives complaints. We get complaints from competitors, even. This actually goes to Dr. Grady's question. You know, I think there are companies that are doing the right thing and they want a fair marketplace. And when they see companies that aren't following the rules, it undermines their ability to sell a product fairly. So we get complaints from companies. All sorts of sources. We watch TV.

DR. SULMASY: And then my question for Margaret is a bit broader. I was fascinated by your pointing out how these self-diagnosis tests can actually be used to increase market share. And it leads to a sort of broader sort of social concern: The way in which that plays itself out and the way in which the medical community may even be complicit in this sort of thing. So we create new categories of illness, which have the advantage of increasing market share for corporations but also physicians are involved in some of this, too. So we move from diabetes, we have changed the definition of it and we have pre-diabetes which becomes a market share. The advertisement, "Is she just shy or is it social dysphoria syndrome," and we create a new category. There's cognitive decline which is a new one, and there's probably going to be pre-cognitive decline. So, you know -- and sometimes there's some evidence for these things, but I'm wondering how this fits into your scheme of sort of thinking through the ethics of some of this. And if physicians are involved in it, to what extent do you think they are being sort of bought, if you will, and to what extent is it just therapeutic enthusiasm on the part of physicians that leads them to sort of easily acquiesce to this kind of gradual expansion of the category of illness?

DR. EATON: Well, I think it might be both. As you know, I think Pharma has promulgated voluntary guidelines for pharmaceutical companies not to over-promote and not to over-incentivize physicians to prescribe the drugs they are advertising. And it used to be a very common practice to do things like, you know, golfing trips and tickets to ball games and that sort of thing. It is no longer allowed in the industry. And by and large I think the industry is trying to tamp down that kind of incentive. But it's very hard to tease out where physicians are being prompted to use a drug for a patient because they believe in the benefits of it and they want to help their patients, versus the economic gain that they can get from prescribing and getting patients into their office and enjoying the fact that the pharmaceutical advertising is driving

patients to go there, to seek help. And I know many of us on the panel are such an age where we start to think about, "Well, what's happening to me," when you can't remember where you put your keys.

Pharmaceutical companies have to recognize that they are marketing to a vulnerable patient population when they are talking about cognitive decline and brain deficits and that sort of thing. And other than the voluntary controls that I have recommended, I think the regulatory agency has a lot of responsibility to see what they can do to prevent that.

DR. SULMASY: And just with respect to the broader question, sort of expanding about the diagnoses. Is that sort of a question outside of the sort of business ethics that you are thinking about? Or how does that -- how do you evaluate that? There's a famous New England Journal of Medicine article, about 15 years ago, about the last well person. We found him. He was in Peoria.

DR. GUTMANN: Like a 2000-year-old man?

DR. EATON: No, I don't think that's outside the scope of ethical concern. In fact, I think it is fundamental to our concern about ethical practices and business. You know, there is a big population of what they call the worried well, and they are very susceptible to hints that they might be suffering from various different conditions. And we do know that many times, until there is a medical product to treat behavior or illnesses -- or conditions, I won't call them illnesses -- treat conditions, there oftentimes isn't an illness to treat. In other words, there was no such thing as Short Stature Syndrome in children until human growth hormone was approved and marketed. First it was an off-label use, but regulators were convinced that Short Stature Syndrome was an illness that could be treated and it is now approved for human growth hormone treatment.

The same thing happens with neuroscience. And I think maybe the temptation to do that now is even higher when you don't have physical symptoms, when you don't have a chemical test to tell you if something is out of balance, and especially since the underlying biologic processes of brain function we are still in relatively primitive understanding mode for those kinds of things. So I think it behooves everybody involved in the situation to be acutely aware of the fact that we are tempting people to believe that they are no longer normal when they have evidence or episodes where then they don't think their brain is functioning as well as it should or as well as it used to.

DR. WAGNER: John and then Steve.

DR. ARRAS: Thank you very much. Very enlightening panel. Maybe you can help me. I'm puzzling over the case of Lumosity. So as you know, we are all TV watchers, right? Very eye-catching ads. Very attractive young people having fun with brain games and it's supposed to really improve your cognition, right? So they are saturating the airwaves. But at the same time, I read occasionally, with some frequency, reports of studies by scientists in various places alleging that products like this really don't deliver the goods promised; you know, that there's no real-world improvement in people's cognition. And yet, the ads just keep coming. Okay?

So I'm wondering, do companies like Lumosity just fall into some sort of dead zone, regulatory dead zone where there's nothing much that can be done about this?

MS. VISWANATHAN: No. No, I don't think so. We are often investigating products and companies that it doesn't become public for a long time. So just because you don't hear anything does not mean that this is an endorsement of any such product. Emerging science is a difficult area and we want to make sure that even if the science is emerging and it's still tentative,

we do have a concern that companies might be overstating that. And I have seen those commercials. That's enough said.

DR. GUTMANN: Before Steve goes, this is just off the cuff, not serious. But for some reason -- you know how you get these pop-up ads on your websites? Lumosity pops up for me all the time as if to say, "You need this." I see other people nodding.

DR. HAUSER: Well, just as an aside, I think Dan's point is such an important one and I'm thinking in the neuro area there are many examples. But one is a very rare -- relatively rare syndrome called pseudo bulbar palsy. And with the approval of the first medication, essentially an old cough medication, for this rare problem there was a push to rename this the Laughing and Crying Syndrome. And this push was pushed by numerous academic leaders.

And I would like to ask Dr. Eaton about how we can get our hands around thinking about some of the non-directly financial relationships, relationships that don't merit disclosure by current rules of conflicts of interest, but that involve companies using people whom they consider thought leaders as surrogates with incentives such as access to rich data sets, leadership in clinical trials, a place at a podium. These are, for many people, more important than the economic relationships.

DR. EATON: When you talk about conflicts of interest that are commonly required to be disclosed, for instance, now when you publish in journal articles, the main concern typically is your financial interest with the subject matter or the sponsor of the research. But I think actually sometimes, especially in academia, the conflict can be stronger when it's a self-reputational benefit that you get, from being the top of your field, from having a certain number of publications, from getting the Lasker prize. For instance, those reputational perks lead to promotion, lead to recognition, lead to grants, that sort of thing. So they are intricately linked.

And I think we do a disservice, when we talk about conflicts of interest, when we exclude the reputational self-interest that most of us have in whatever we do. It happens to be acutely strong in academia because that's the trade, you know, that we are engaged in. And if we don't have influence with our scientific publications, for instance, we don't have influence in our work. So I think we have to consider both. I absolutely agree with you. What to do about it, I'm not sure, because it's been an industry practice from the time that I've been involved in pharmaceuticals early in the '70s, that when companies want to market a product that's exactly where they go. They go to the thought leaders. They go to the people who have the most experience and the biggest research programs because those are the people who influence the members of the profession.

It's a standard practice, and I don't know how you get around it. But a recognition that it exists and it is powerful, the influence there is powerful, that's why it is used. But recognition about that influence is an important thing to comment on.

DR. WAGNER: Thank you. I have one from the audience and then come to you, Anita. The question is from Lisa Lehmann, who is with Brigham and Women's Hospital. Actually, there are two questions here. One is about the concern about justice and equal access. And I think we talked about that earlier, and perhaps having -- it may not be the direct to consumer -- certainly not the direct-to-consumer regulators. It's important to ask that question.

But the second actually follows Amy Gutmann's earlier question about intermittent use of -- whether it's off-label use of drugs or caffeine. The question I think is about do we have data to support that that is necessarily detrimental. Where do we even where do we draw the line between the user's responsibility and the supplier or producer's responsibility. DR. EATON: I don't know the answer to that question. But I will go back to a recommendation that if you are

talking about that kind of drug use, the educational component is huge. In high school, I think health classes should include education to the potential users or the current users about the potential detriment and the risks that they are engaging in.

And I'm not familiar enough to know whether there's credible data to support whether cognition is enhanced temporarily in these situations. My personal feeling from reading the limited amount that I've read is that students feel that it's beneficial. Whether that's because their cognition has actually been enhanced or not, something in the effects of the drugs that they are taking make them feel like they are achieving more than they could without them. It's very problematic I think, and not clear about how you link the pharmaceutical effect of the product to enhanced cognition per se.

DR. GUTMANN: Just to follow up on that. So is the lack of evidence here -- so is the lack of evidence here part of the problem that when something is used off-label, and no respectable doctor that I know will prescribe it for enhancing your test results, that there isn't a gathering of data?

I'd be interested in hearing Lisa say what she -- what the source of her issue is as to whether it's skepticism that it is broadly used and dangerous, or the worry that there isn't evidence of that. Because the number of stories about -- at the high school level and college level of people who deal in distributing these drugs and the number of issues we have at high school and about the overuse of drugs just feeds into a concern that if we don't know enough about ethics, why aren't we learning more.

DR. LEHMANN: Just to clarify -- thank you for taking my question. If I could just clarify. My question wasn't really about whether or not we have enough data to show whether or not they are effective in enhancing cognition. And I don't have skepticism about their use. Even

though we could probably have better data about how widespread they are both in high school and on college campuses, I think that there's enough concern that they are being used fairly widely. My question was really much more skepticism about the harms of using the drug and the assumption or the claim that we shouldn't be enhancing our cognition in this way. If, in fact, intermittent use of off-label drugs is not harmful -- and I think that we are developing safer drugs, also, over time that can enhance cognition. If, in fact, this intermittent use is not harmful, then why shouldn't we be using these drugs? And that may sound a little bit radical, but I think it is something that is worth reflecting on. I think, as I said, my bigger concern with the use of the drugs really has to do with justice if, in fact, there isn't harm associated with it.

DR. GUTMANN: So let Margaret answer, and then I do want to say something to that because it's an important set of questions.

DR. EATON: Okay. Thanks. I think that it is very difficult when you start uncoupling efficacy with adverse drug reactions. When there's no efficacy of the drug, that means that the only potential effect of the drug is going to be a harmful one, an adverse one. And in a college population they tend to be not single drug or substance-using people. They tend to mix cocktails of things based on what their friends are doing, what they see online. So, for instance, even if there's only minimal benefits to taking some of these stimulant drugs to cram for an exam, what about the presence of the hyper-caffeinated drinks, what about the presence of other things that are floating around the campus community that these kids can take? And what about what happens when they are coming down from the high and they need to go back up and they are trying to modulate their reactions to the drugs? So I think you need to have evidence of safety in order to balance that against the potential risk, because there is no drug on the market that I'm aware of that is without the potential for side effect.

DR. GUTMANN: So could I just – because it's important for us to put on the public record. There is -- so there is a difference between temporary and long-lasting cognitive abilities. And to the extent that we want to -- if we are taking these for tests, to the extent that we want to measure more long-lasting versus temporary, there's a problem if the drugs just give you temporary, not long-lasting results.

Secondly, if they are effective, I agree with Lisa, there's a distributive problem of justice, not for regulating them, because that's not the issue, but for how we measure test results. It's the same problem, then, if they are safe. And that's a big "if." If they are safe and they're effective, then they are, like the Princeton Review, which they are accessible only to a subset of students and they are giving those students an advantage that students who don't have access to them don't have. And we have to -- as educators, we need to deal with that. That's an issue. Right? Because we believe in access and opportunity in education regardless of your socioeconomic background. And the difference is that there's a lot of research on the effects of Princeton Review and there's very little, if any, research on the effects of popping these drugs. And I use "popping" neutrally. Taking the drugs sporadically. There's just so – we don't know the risks well and we don't know the benefits very well.

DR. WAGNER: Serena, did you want to comment before we go to the last question?

MS. VISWANATHAN: No. This seems like prescription drug issues beyond the scope of the FTC.

DR. WAGNER: Margaret?

DR. EATON: I do want to mention one thing, too, that we should throw into the mix. All high school and college students are internet savvy and you can go online and for any drug you want, you can find a website that says how to convince your doctor to prescribe the drug for

you, how to fake the symptoms. That sort of thing. So I think that's a powerful undermining influence to any kind of educational or safety attempts that we make about this drug.

DR. ALLEN: I'll keep this short. I think that one of the reasons why suddenly, twenty years ago or so, we started seeing a lot of advertising about drugs on television is that there was a sense that people needed to know more about drugs and it was good for the consumer, was an empowering mechanism for the consumer.

From your presentations, we are focusing more on the exploitation of the consumer rather than on the empowerment. And I wondered if you could say anything positive, given your words, about the empowerment of the consumer which might flow from advertisements on TV about antidepressants or weight loss medications or diabetes or other kinds of medications.

And a little brief anecdote: You mentioned Short Stature Syndrome, and I know that you don't think it's a bad thing if a person is very short to take a drug. But I just wanted to say that in my life, there was a young person who at the age of eight was the size of a four-year-old and this person's parents took their child to a major research university that prescribed human growth hormone and this young person is now a student at West Point and an outstanding military officer of normal height. It can be a good thing.

DR. EATON: Thank you for that. I didn't intend, by my comments, to mean that there was no benefit to taking human growth hormone, in certain situations. It's just that the disease entity Short Stature Syndrome didn't exist until there was something pharmaceutical that you could do about it. And I do appreciate your comments about the beneficial effects of direct-to-consumer advertising of medical products, because I think that I have seen some stellar ads in that regard. They are educational, they are accurate, they are recognizing a need and fulfilling a need in society for people to have more information about and therefore enhancing their ability

to consent to seeking and accepting these products. Those, as far as I'm concerned, are -- in my line of inquiry, are wonderful, but not what I tend to focus on because I believe in them and I think they are beneficial. And I didn't also mean to suggest that most ad practices are abusive and deceptive. It's not the case. There is a mix.

DR. ALLEN: Can I put you on the spot? Give us an example of a great ad for a pharmaceutical.

DR. EATON: It's easy to find. Where did I look recently? I can't bring it to mind. It's easy to find if you --

DR. GUTMANN: Not Lumosity?

DR. EATON: It's not Lumosity. No, it tends to be, I think, with companies that have voluntarily adhered to responsible ad practices. And you get away from -- if you go online and look at these, there aren't these attractive people doing very normal things like, oh, they took an anti-arthritis drug and now they're swimming and playing golf and that sort of thing. They tend to eschew those kinds of glowing things of what can happen when you are on the drug. I'm sorry, the names of the products that I've looked at that I think are responsible don't come to mind, but they aren't difficult to find.

DR. WAGNER: Serena, last thought?

MS. VISWANATHAN: Just the fact the FTC -- you know, we're interested in making sure the consumer is fully informed. It's not about taking products off the market. We don't do that. As long as consumers are fully informed, they can make a decision based on the actual, true, and accurate information on the efficacy of what they are buying.

DR. WAGNER: Serena and Margaret, thank you so much for stimulating conversation.

And the Commission will reconvene at 10:30.